Nickel-Catalyzed N-Vinylation of Heteroaromatic amines via C-H bond Activation

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Contents

1. General Information

All catalytic experiments were carried out using standard Schlenk techniques. All solvents were reagent grade or better. Deuterated solvents were used as received. *p*-cymene and toluene were refluxed over sodium/benzophenone ketyl and distilled under argon atmosphere and stored over sodium. Metal salts and other chemicals used in catalysis reactions were used without additional purification. Thin layer chromatography (TLC) was performed using silica gel precoated glass plates, which were visualized with visualized with UV light at 254 nm or under iodine. Column chromatography was performed with SiO_2 (Silicycle Siliaflash F60 (230-400 mesh). ^1H NMR (400 or 500 MHz), $^{13}C\{^1H\}$ NMR (100 MHz) spectra were recorded on the NMR spectrometer. Deuterated chloroform was used as the solvent, and chemical shift values (δ) are reported in parts per million relative to the residual signals of this solvent [δ 7.26 for ^1H (chloroform-d), δ 77.2 for $^{13}C\{^1H\}$ (chloroform-d). Abbreviations used in the NMR follow-up experiments: br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. GC analysis was carried out using a HP-5 column (30 m, 0.25 mm, 0.25μ). Mass spectra were obtained on a GCMS-QP 5000 instruments with ionization voltages of 70 eV. High resolution mass spectra (HRMS) were obtained on a High-resolution mass spectra (HRMS) were obtained by fast atom bombardment (FAB) using a double focusing magnetic sector mass spectrometer and electron impact (EI) ionization technique (magnetic sector-electric sector double focusing mass analyzer). HPLC analysis was performed on Agilent Technologies 1260 Infinity with UV detector.

2. Experimental Section

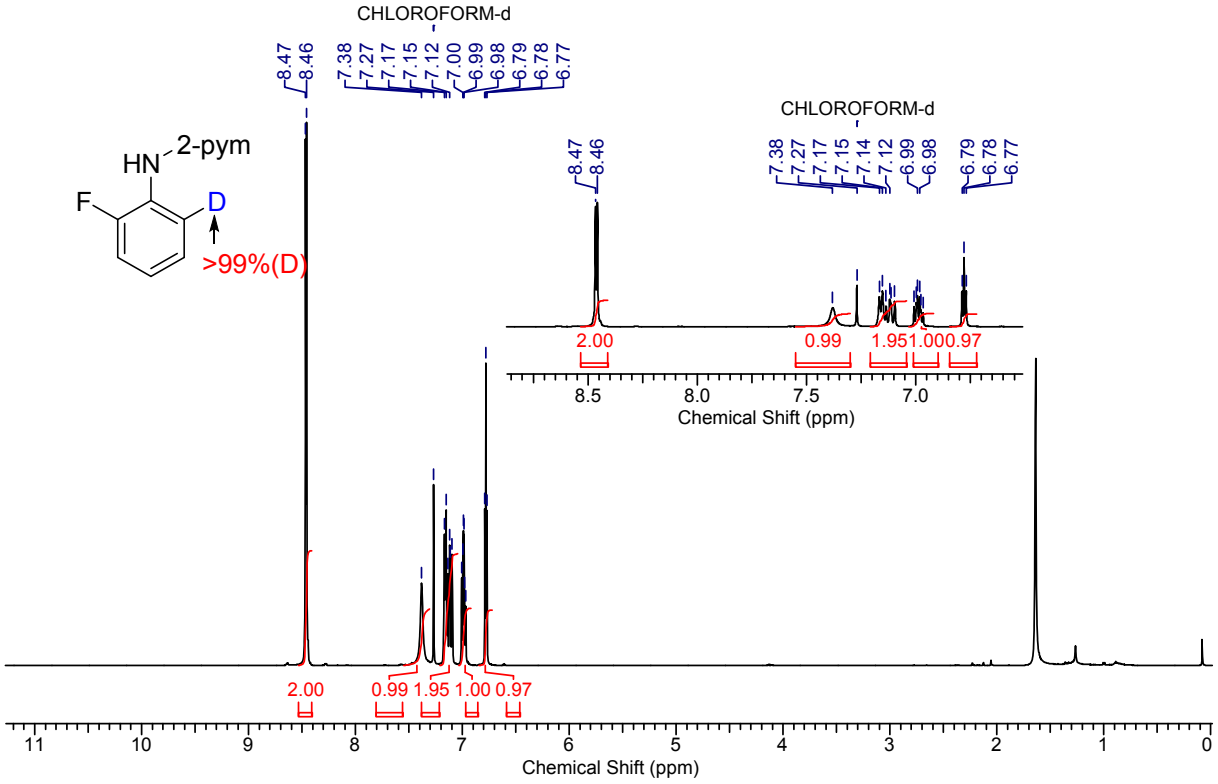
2.1 Synthesis of Starting Materials

All the starting materials (*N*-(pyrimidine-2-yl)anilines[S1-S2] and β-bromostyrenes[S3] were prepared in accordance with the literature method.

2.2 Synthesis of $[D_1]$-1c

Aniline **1c** (300 mg, 1.88 mmol), $[Cp^*RhCl_2]_2$ (5.0 mol %), $Cu(OAc)_2.H_2O$ (1.88 mmol), D_2O (1.1 mL, 10.3 equiv) were placed in a 25 mL Schlenk tube and HFIP (1.5 mL) was added under

nitrogen atmosphere. The mixture was stirred at 130 °C for 24 h. After cooling to ambient temperature, the reaction mixture was extracted with EtOAc (3 x 3 mL). The combined organic layers were dried with Na_2SO_4 and concentrated *in vacuo*. The residue was purified on a silica gel column with petroleum ether as the eluent to afford deuterated product **[D$_1$]-1c** in (240 mg, 80%). ^{1}H NMR analysis showed >99% deuterium incorporation in the *ortho*-position.



^{1}H NMR of [D$_1$]-1c

2.3 General Procedure for the Nickel-Catalyzed *N*-Alkenylation of Anilines

To an oven-dried 10 mL screw-capped vial, aniline **1** (0.5 mmol), vinyl bromide **2** (0.75 mmol), $NiCl_2$ (2 mol%), Li*t*OBu (1.2 equiv) and *p*-cymene (2 mL) were added under a gentle stream of argon. The mixture was heated at 120 °C for 12 h followed by cooling to room temperature. The reaction mixture was filtered through a celite pad with several washings with dichloromethane (3 x 3 mL) and concentrated *in vacuo*. The residue was purified on a silica gel column (eluent: pet ether/EtOAc) to afford the desired alkynylated product **3** or **4**.

3. Synthetic Application

3.3 Procedure for the synthesis of 5

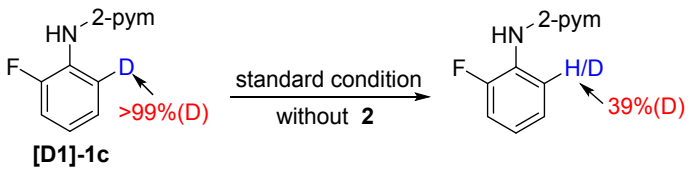
To an oven-dried 10 mL screw-capped vial, K_3PO_4 (0.5 mL, 2 M aqueous) and toluene (1 mL), and the resulting biphasic mixture was sparged with N_2 for 1 h. To the solution were added **3i** (30 mg, 0.113 mmol, 1 equiv), 4-chloro phenylboronic acid (21 mg, 1.2 equiv) and $Pd(PPh_3)_4$ (20 mg, 15 mol%). The resulting mixture was sparged with N_2 for 10 min. The vial was sealed with a Teflon-coated screw-cap and heated at 90 °C for 14 h. The reaction mixture was filtered through a celite pad with several washings with dichloromethane (3 x 3 mL) and concentrated *in vacuo*. The residue was purified on a silica gel column to afford the desired product **5**.

3.4 Procedure for the synthesis of 6

To an oven-dried 10 mL screw-capped vial, aniline **3i** (0.1 mmol), morpholine **2** (0.15 mmol), $Pd_2(dba)_3$ (5 mol%), BINAP (10 mol%), Na*t*OBu (2 equiv) and toluene (1 mL) were added under a gentle stream of argon. The mixture was stirred at reflux for 12 h followed by cooling to room temperature. The reaction mixture was filtered through a celite pad with several washings with dichloromethane (3 x 3 mL) and concentrated *in vacuo*. The residue was purified on a silica gel column to afford the desired product **6**.

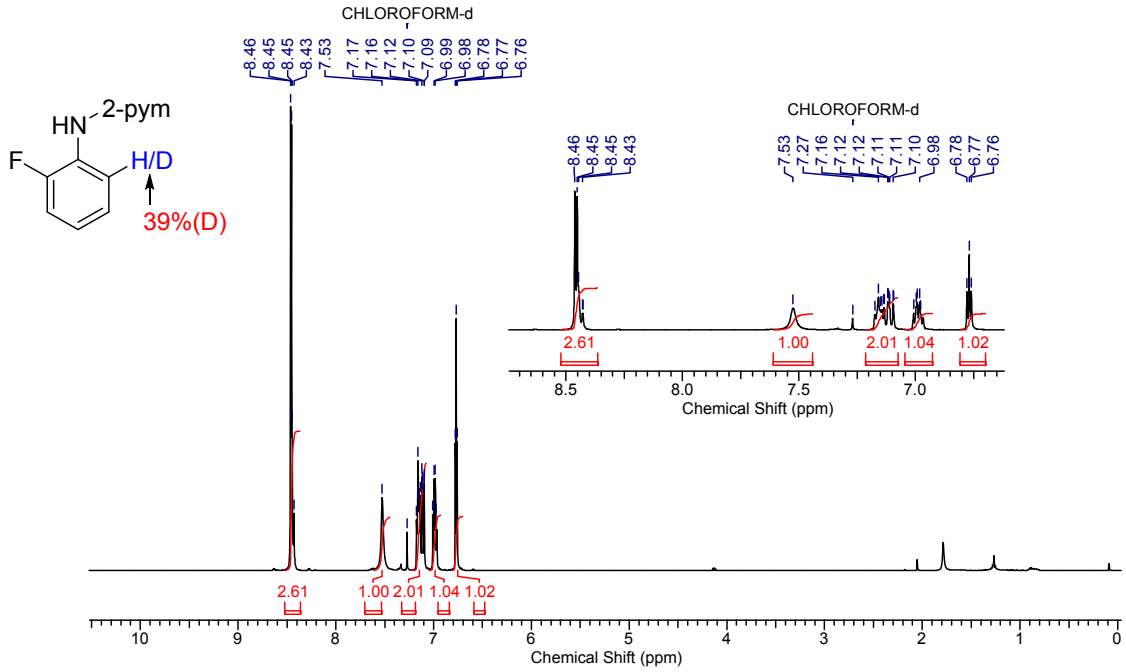
4. Mechanistic Investigation

4.1 Reversibility of *N*-alkenylation *via* C-H bond activation

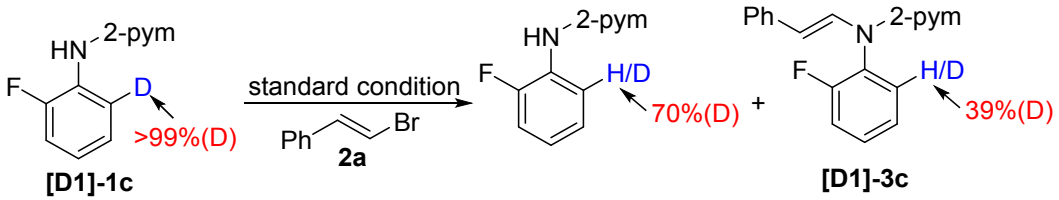


To an oven-dried 10 mL screw-capped vial, aniline **[D_1]-1c** (50 mg, 0.26 mmol), $NiCl_2$ (2 mol%), Li*t*OBu (1.2 equiv) and *p*-cymene or toluene (1 mL) were added under a gentle stream of argon. The reaction mixture was heated at 120 °C for 12 h followed by cooling to room temperature. The mixture was filtered through a celite pad with several washings (3 x 3 mL dichloromethane) and concentrated *in vacuo* and the starting material (**[D_1]-1c**) showed 39% *ortho*-deuteration.

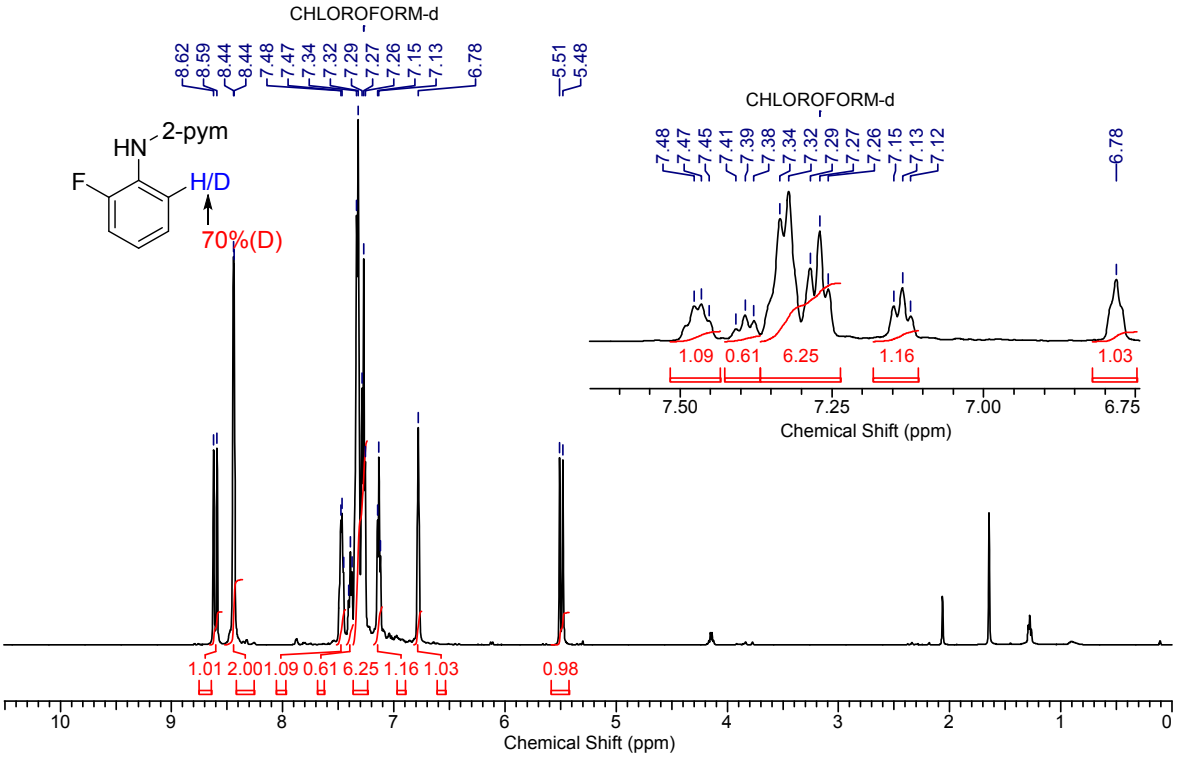
Note: Under the optimal condition, toluene (1 mL) also gave the same yield (~90%) in the *N*-vinylation of aniline (**1a**). Thus, in all the mechanistic experiments (D-studies) toluene was used as a solvent.

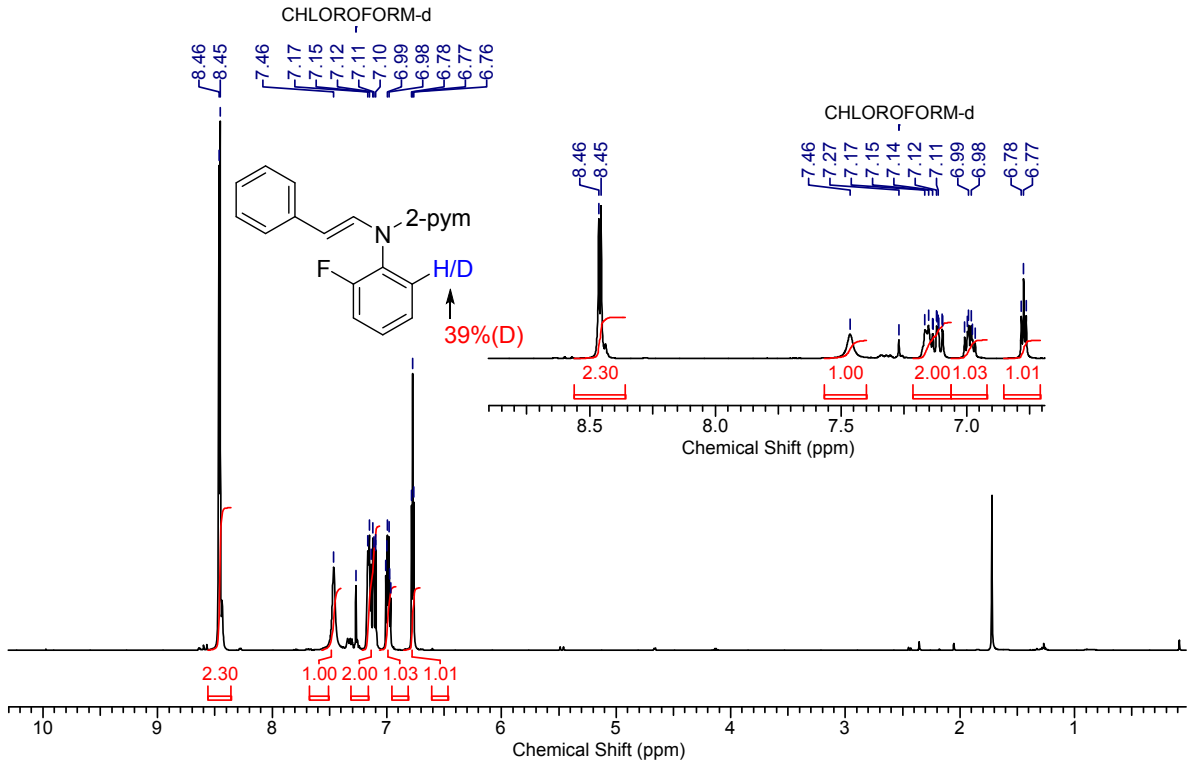


4.2 H/D Scrambling study

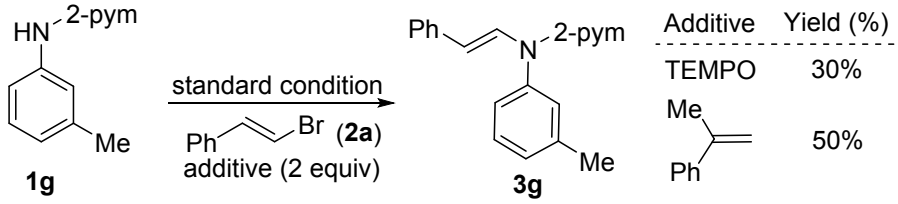


To an oven-dried 10 mL screw-capped vial, aniline **[D_1]-1c** (50 mg, 0.26 mmol), **2a** (0.39 mmol), $NiCl_2$ (2 mol%), Li*t*OBu (1.2 equiv) and *p*-cymene or toluene (1 mL) were added under a gentle stream of argon. The reaction mixture was heated at 120 °C for 4 h followed by cooling to room temperature. The mixture was filtered through a celite pad with several washings (3 x 3 mL dichloromethane) and concentrated *in vacuo*. The residue was purified by column chromatography. The obtained product **[D_1]-3c** (54% yield) showed 39% *ortho*-deuteration and the recovered starting material **[D_1]-1c** 70% *ortho*-deuteration.



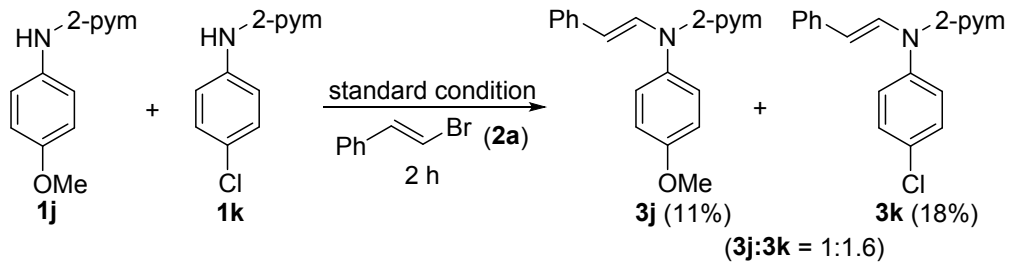


4.3 Radical trapping experiment



To an oven-dried 5 mL screw-capped vial, **1g** (0.3 mmol), **2a** (0.36 mmol), TEMPO or prop-1-en-2-ylbenzene or cyclohexa-1,4-diene (0.9 mmol), $NiCl_2$ (2 mol %), LiO*t*Bu (1.2 equiv.) and *p*-cymene (1 mL) were added under argon atm. The reaction mixture was heated at 120 °C for 12 h and followed by cooling to room temperature. The solution was filtered through a celite pad and washed with 10 mL of dichloromethane. The filtrate was concentrated *in vacuo*. The yield of **3g** was determined by ^{1}H NMR.

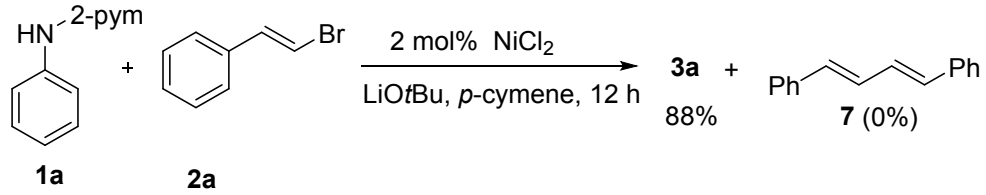
4.4 Intermolecular competition experiment



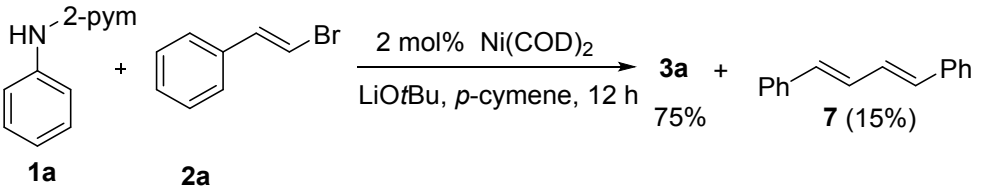
To an oven-dried 5 mL screw-capped vial, benzamides **1j** (0.3 mmol), and **1k** (0.3 mmol), **2** (0.3 mmol), $NiCl_2$ (2 mol %), Li*O*t*Bu (1.2 equiv.), and *p*-cymene (1 mL) were added under argon atm. The mixture was heated at 120 ^oC for 2 h and followed by cooling to room temperature. The solution was filtered through a celite pad and washed with dichloromethane (3 x 5 mL). The filtrate was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (eluent: pet ether/EtOAc) to afford the alkynylated products **3j** and **3k** with the isolated yields of 11% and 18% respectively.

4.5 Product distribution study

(a) To an oven-dried 5 mL screw-capped vial, **1a** (0.3 mmol), **2** (0.36 mmol), $NiCl_2$ (2 mol %), Li*O*t*Bu (1.2 equiv.), and *p*-cymene or toluene (1 mL) were added under argon atm. The reaction mixture was heated at 120 ^oC for 12 h and followed by cooling to room temperature. The solution was filtered through a celite pad and washed with 10 mL of dichloromethane. The filtrate was concentrated *in vacuo*. The filtrate was concentrated. The products were analyzed by GC and GC-MS and no formation of self dimer product (**7**) was observed.



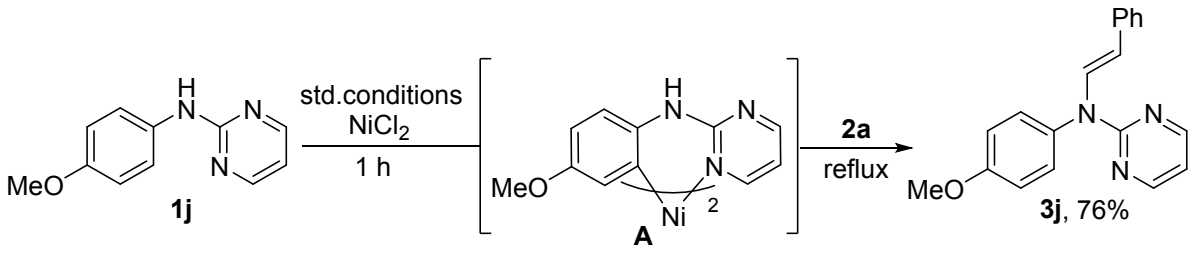
(b) To an oven-dried 5 mL screw-capped vial, **1a** (0.3 mmol), **2** (0.36 mmol), $Ni(COD)_2$ (2 mol %), LiO*t*Bu (1.2 equiv.) and *p*-cymene or toluene (1 mL) were added under argon atm. The reaction mixture was heated at 120 °C for 12 h and followed by cooling to room temperature. The solution was filtered through a celite pad and washed with 10 mL of dichloromethane. The filtrate was concentrated *in vacuo*. The filtrate was concentrated. The products were analyzed by GC and GC-MS. A formation of self dimer product (**7**) in 15% was observed.



4.6 Reaction profile for the Nickel-catalyzed *N*-alkenylation

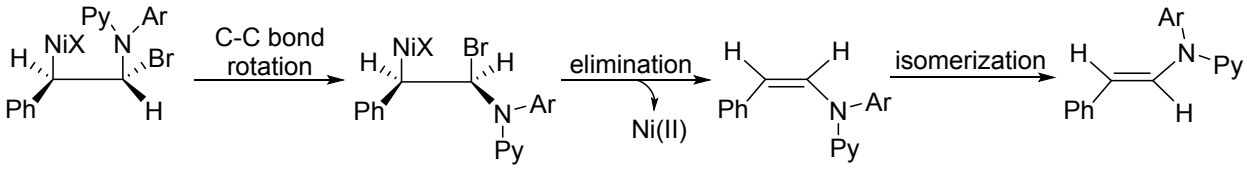
To an oven-dried 10 mL screw-capped vial, aniline **1a** (0.2 mmol), (*E*)-(2-bromovinyl)benzene **2a** (0.3 mmol), $NiCl_2$ (2 mol%), Li*t*OBu (1.2 equiv), n-decane as internal standard and *p*-cymene (1 mL) were added under a gentle stream of argon. The mixture was heated at 120 °C and a periodic aliquot was removed and analyzed by GC.

4.7 Identification of C-H bond activated intermediate



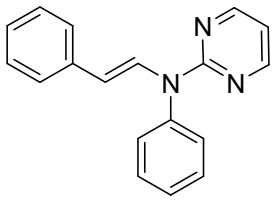
To an oven-dried 10 mL screw-capped vial, aniline **1j** (0.2 mmol), Li*t*OBu (1.2 equiv), $NiCl_2$ (2 mol%), and *p*-cymene (1 mL) were added under a gentle stream of argon. The mixture was heated at 120 °C and after 1 h an aliquot was removed and analyzed by HRMS (EI). The observed *m/z* value is 459.1074 {[M+H] $C_{22}H_{21}O_2N_6Ni$}.

An alternative mechanism would involve the insertion of an alkene into a N-Ni bond, C-C bond rotation, the elimination of Ni(II), and isomerization to the more thermodynamically stable trans-isomer cann't be rolled out. Indeed, we didn't detect the formation of a *cis*-isomer when the reaction was stopped at a shorter reaction time.



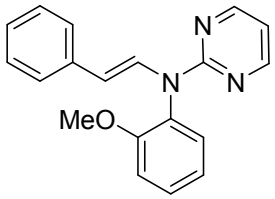
5. Characterization Data

(*E*)-*N*-phenyl-N-styrylpyrimidin-2-amine (3a)



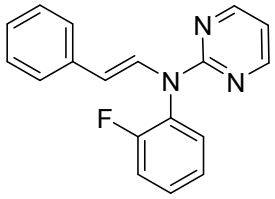
21 mg, 80% isolated yield. R_f = 0.32 (hexane/EtOAc = 5/1). Orange solid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.64 (d, *J* = 14.9 Hz, 1 H), 8.43 (br s, 2 H), 7.59 (br s, 2 H), 7.48 (br s, 1 H), 7.36 - 7.29 (m, 4 H), 7.13 (br s, 1 H), 6.76 (br s, 1 H), 5.43 (d, *J* = 14.5 Hz, 1 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 159.8, 157.8, 140.0, 137.5, 130.5, 129.9, 129.3, 128.5, 127.9, 125.6, 125.2, 113.0, 111.0. HRMS (EI): *m/z* Calcd for [M+H] $C_{18}H_{16}N_3$: 274.1344; Found: 274.1339.

(*E*)-*N*-(2-methoxyphenyl)-N-styrylpyrimidin-2-amine (3b)



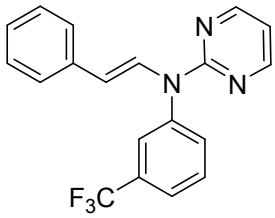
18 mg, 60% isolated yield. R_f = 0.32 (hexane/EtOAc = 10/1). Yellow liquid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.65 (d, *J* = 14.5 Hz, 1 H), 8.44 (d, *J* = 4.6 Hz, 2 H), 7.52 - 7.42 (m, 1 H), 7.37 - 7.22 (m, 6 H), 7.21 - 7.09 (m, 3 H), 6.75 (t, *J* = 4.8 Hz, 1 H), 5.44 (d, *J* = 14.5 Hz, 1 H), 3.78 (s, 3 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 159.6, 157.8, 155.7, 137.7, 130.6, 129.7, 129.5, 128.4, 128.3, 125.4, 125.2, 121.4, 112.9, 112.7, 109.7, 55.8. HRMS (EI): *m/z* Calcd for [M+H] $C_{19}H_{18}ON_3$: 304.1450; Found: 304.1444.

(*E*)-*N*-(2-fluorophenyl)-N-styrylpyrimidin-2-amine (3c)



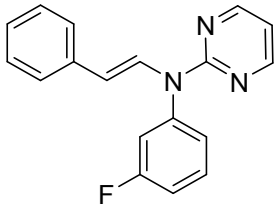
25 mg, 88% isolated yield. R_f = 0.32 (hexane/EtOAc = 10/1). Yellow Liquid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.62 (d, *J* = 14.5 Hz, 1 H), 8.45 (d, *J* = 5.0 Hz, 2 H), 7.52 - 7.45 (m, 1 H), 7.44 - 7.38 (m, 1 H), 7.38 - 7.25 (m, 6 H), 7.18 - 7.12 (m, 1 H), 6.79 (t, *J* = 4.8 Hz, 1 H), 5.51 (d, *J* = 14.5 Hz, 1 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 159.9, 159.3, 158.0, 157.9, 137.3, 131.3, 129.9, 129.9, 129.4, 128.5, 127.5, 127.4, 125.8, 125.4, 125.2, 125.2, 117.2, 117.0, 113.6, 110.6. HRMS (EI): *m/z* Calcd for [M+H] $C_8H_{15}FN_3$: 292.1250; Found: 292.1245.

(*E*)-*N*-styryl-N-(3-(trifluoromethyl)phenyl)pyrimidin-2-amine (3d)



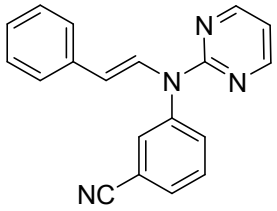
26 mg, 75% isolated yield. R_f = 0.32 (hexane/EtOAc = 5/1). White solid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.61 (d, *J* = 14.9 Hz, 1 H), 8.44 (d, *J* = 4.6 Hz, 2 H), 7.77 - 7.67 (m, 2 H), 7.62 (s, 1 H), 7.54 (d, *J* = 7.6 Hz, 1 H), 7.35 - 7.22 (m, 4 H), 7.22 - 7.10 (m, 1 H), 6.80 (t, *J* = 4.8 Hz, 1 H), 5.42 (d, *J* = 14.5 Hz, 1 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 159.6, 157.9, 140.7, 137.1, 133.1, 132.5, 132.3, 130.5, 130.2, 128.6, 126.7, 126.6, 125.9, 125.3, 124.8, 124.7, 124.7, 122.6, 113.6, 111.4. HRMS (EI): *m/z* Calcd for [M+H] $C_{19}H_{15}F_3N_3$: 342.1218; Found: 342.1213.

(*E*)-*N*-(3-fluorophenyl)-N-styrylpyrimidin-2-amine (3e)



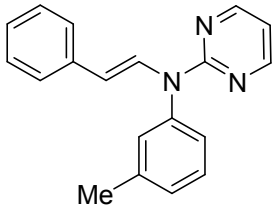
23 mg, 78% isolated yield. R_f = 0.32 (hexane/EtOAc = 5/1). White solid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.59 (d, *J* = 14.9 Hz, 1 H), 8.44 (d, *J* = 5.0 Hz, 2 H), 7.59 - 7.48 (m, 1 H), 7.38 - 7.27 (m, 4 H), 7.24 - 7.12 (m, 3 H), 7.08 (d, *J* = 9.5 Hz, 1 H), 6.78 (t, *J* = 4.8 Hz, 1 H), 5.49 (d, *J* = 14.9 Hz, 1 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 164.4, 162.5, 159.6, 157.9, 141.6, 141.5, 137.2, 131.0, 130.9, 130.1, 128.5, 125.8, 125.3, 125.2, 125.1, 117.0, 116.8, 115.2, 115.0, 113.3, 111.3. HRMS (EI): *m/z* Calcd for [M+H] $C_{18}H_{15}FN_3$: 292.1250; Found: 292.1245.

(*E)*-3-(pyrimidin-2-yl(styryl)amino)benzonitrile (3f)



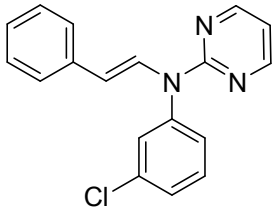
19 mg, 65% isolated yield. R_f = 0.32 (hexane/EtOAc = 5/1). White solid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.56 (d, *J* = 14.9 Hz, 1 H), 8.43 (d, *J* = 5.0 Hz, 2 H), 7.75 (d, *J* = 7.6 Hz, 1 H), 7.72 - 7.62 (m, 2 H), 7.60 (d, *J* = 8.0 Hz, 1 H), 7.34 - 7.26 (m, 5 H), 7.19 - 7.12 (m, 1 H), 6.83 (t, *J* = 4.8 Hz, 1 H), 5.41 (d, *J* = 14.5 Hz, 1 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 159.4, 157.9, 141.1, 136.8, 134.5, 133.4, 131.4, 130.9, 130.0, 128.6, 126.1, 125.3, 118.0, 114.1, 113.8, 111.7. HRMS (EI): *m/z* Calcd for [M+H] $C_{19}H_{15}N_4$: 299.1297; Found: 299.1291.

(*E*)-*N*-styryl-N-*m*-tolylpyrimidin-2-amine (3g)



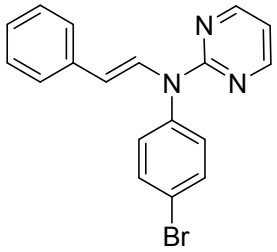
26 mg, 90% isolated yield. R_f = 0.32 (hexane/EtOAc = 5/1). White solid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.63 (d, *J* = 14.5 Hz, 1 H), 8.44 (d, *J* = 4.6 Hz, 2 H), 7.47 (s, 1 H), 7.35 - 7.25 (m, 6 H), 7.18 - 7.04 (m, 3 H), 6.75 (t, *J* = 4.8 Hz, 1 H), 5.44 (d, *J* = 14.5 Hz, 1 H), 2.46 (s, 3 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 159.9, 157.9, 139.9, 139.9, 137.6, 130.5, 129.8, 129.7, 128.8, 128.5, 126.2, 125.5, 125.2, 112.9, 110.9, 21.5. HRMS (EI): *m/z* Calcd for [M+H] $C_{19}H_{18}N_3$: 288.1501; Found: 288.1495.

(*E*)-*N*-(3-chlorophenyl)-*N*-styrylpyrimidin-2-amine (3h)



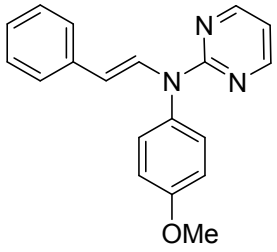
27 mg, 88% isolated yield. R_f = 0.32 (hexane/EtOAc = 5/1). White solid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.60 (d, *J* = 14.5 Hz, 1 H), 8.45 (d, *J* = 4.6 Hz, 2 H), 7.60 - 7.42 (m, 2 H), 7.41 - 7.23 (m, 6 H), 7.21 - 7.12 (m, 1 H), 6.80 (t, *J* = 4.8 Hz, 1 H), 5.49 (d, *J* = 14.9 Hz, 1 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 159.6, 157.9, 141.2, 137.2, 135.2, 130.8, 130.1, 129.8, 128.5, 128.2, 127.7, 125.8, 125.3, 113.4, 111.4, 77.3, 76.7. HRMS (EI): *m/z* Calcd for [M+H] $C_{18}H_{15}N_3Cl$: 308.0955; Found: 308.0949.

(*E*)-*N*-(4-bromophenyl)-*N*-styrylpyrimidin-2-amine (3i)



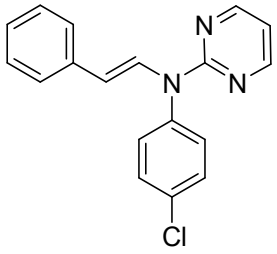
28 mg, 80% isolated yield. R_f = 0.32 (hexane/EtOAc = 5/1). White solid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.60 (d, *J* = 14.5 Hz, 1 H), 8.44 (d, *J* = 5.0 Hz, 2 H), 7.71 (d, *J* = 8.4 Hz, 2 H), 7.40 - 7.25 (m, 5 H), 7.22 (d, *J* = 8.4 Hz, 2 H), 7.20 - 7.11 (m, 1 H), 6.78 (t, *J* = 4.8 Hz, 1 H), 5.47 (d, *J* = 14.5 Hz, 1 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 159.6, 157.8, 139.1, 137.2, 133.2, 131.1, 130.2, 128.5, 125.8, 125.2, 121.7, 113.3, 111.2, 77.3, 76.7. HRMS (EI): *m/z* Calcd for [M+H] $C_{18}H_{15}N_3Br$: 352.0449; Found: 352.0444.

(*E*)-*N*-(4-methoxyphenyl)-*N*-styrylpyrimidin-2-amine (3j)



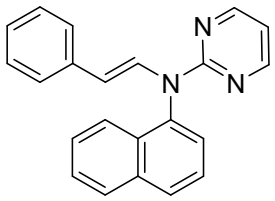
26 mg, 85% isolated yield. R_f = 0.32 (hexane/EtOAc = 4/1). Yellow liqiud. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.69 (d, *J* = 14.5 Hz, 1 H), 8.46 (d, *J* = 5.0 Hz, 2 H), 7.42 - 7.20 (m, 7 H), 7.20 - 7.05 (m, 3 H), 6.76 (s, 1 H), 5.48 (d, *J* = 14.5 Hz, 1 H), 3.92 (s, 3 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 160.0, 158.8, 157.8, 137.6, 132.5, 130.7, 130.2, 128.4, 125.5, 125.2, 115.2, 112.9, 110.7, 55.3. HRMS (EI): *m/z* Calcd for [M+H] $C_{19}H_{18}ON_3$: 304.1450; Found: 304.1444.

(*E*)-*N*-(4-chlorophenyl)-*N*-styrylpyrimidin-2-amine (3k)



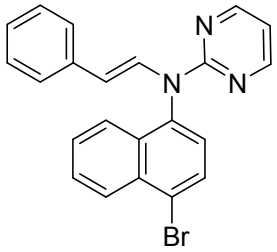
28 mg, 90% isolated yield. R_f = 0.32 (hexane/EtOAc = 5/1). White solid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.61 (d, *J* = 14.9 Hz, 1 H), 8.44 (d, *J* = 4.6 Hz, 2 H), 7.55 (d, *J* = 8.8 Hz, 2 H), 7.38 - 7.22 (m, 7 H), 7.22 - 7.07 (m, 1 H), 6.78 (t, *J* = 4.8 Hz, 1 H), 5.46 (d, *J* = 14.5 Hz, 1 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 159.6, 157.9, 138.6, 137.2, 133.6, 130.8, 130.3, 130.2, 128.5, 125.8, 125.2, 113.3, 111.2. HRMS (EI): *m/z* Calcd for [M+H] $C_{18}H_{15}N_3Cl$: 308.0955; Found: 308.0949.

(*E*)-*N*-(naphthalen-1-yl)-*N*-styrylpyrimidin-2-amine (3l)



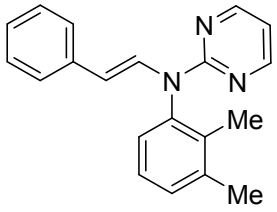
24 mg, 75% isolated yield. R_f = 0.32 (hexane/EtOAc = 5/1). White solid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.93 (d, *J* = 14.5 Hz, 1 H), 8.44 (d, *J* = 4.6 Hz, 2 H), 8.03 (t, *J* = 8.2 Hz, 2 H), 7.79 - 7.63 (m, 2 H), 7.61 - 7.50 (m, 2 H), 7.50 - 7.43 (m, 1 H), 7.33 - 7.22 (m, 4 H), 7.19 - 7.06 (m, 1 H), 6.76 (t, *J* = 4.8 Hz, 1 H), 5.33 (d, *J* = 14.5 Hz, 1 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 160.0, 158.0, 137.5, 136.6, 134.9, 130.5, 130.0, 128.6, 128.6, 128.4, 127.3, 126.9, 126.3, 126.2, 125.5, 125.2, 123.0, 113.1, 110.8. HRMS (EI): *m/z* Calcd for [M+H] $C_{22}H_{18}N_3$: 324.1501; Found: 324.1495.

(*E*)-*N*-(4-bromonaphthalen-1-yl)-*N*-styrylpyrimidin-2-amine (3m)



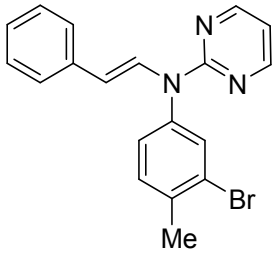
28 mg, 70% isolated yield. R_f = 0.32 (hexane/EtOAc = 5/1). White solid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.84 (d, *J* = 1.9 Hz, 3 H), 8.87 (d, *J* = 1.5 Hz, 3 H), 8.47 - 8.33 (m, 17 H), 8.00 (d, *J* = 7.6 Hz, 6 H), 7.74 - 7.61 (m, 12 H), 7.55 - 7.44 (m, 7 H), 7.38 (d, *J* = 7.6 Hz, 7 H), 7.32 - 7.21 (m, 26 H), 7.19 - 7.01 (m, 7 H), 6.78 (t, *J* = 4.6 Hz, 7 H), 5.29 (d, *J* = 14.5 Hz, 6 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 159.9, 158.0, 137.2, 136.6, 133.4, 131.7, 130.3, 129.9, 128.5, 128.0, 127.8, 127.7, 125.7, 125.2, 123.6, 123.2, 113.3, 111.1. HRMS (EI): *m/z* Calcd for [M+H] $C_{22}H_{17}N_3Br$: 402.0606; Found: 402.0600.

(*E*)-*N*-(2,3-dimethylphenyl)-*N*-styrylpyrimidin-2-amine (3n)



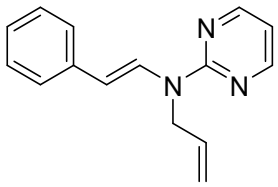
20 mg, 65% isolated yield. R_f = 0.32 (hexane/EtOAc = 5/1). White solid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.67 (d, *J* = 14.5 Hz, 1 H), 8.45 (d, *J* = 4.6 Hz, 2 H), 7.39 - 7.19 (m, 6 H), 7.18 - 7.04 (m, 2 H), 6.75 (t, *J* = 4.8 Hz, 1 H), 5.30 (d, *J* = 14.5 Hz, 1 H), 2.41 (s, 3 H), 2.03 (s, 3 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 159.5, 158.0, 138.5, 138.4, 137.7, 135.3, 129.9, 129.3, 128.5, 126.8, 126.8, 125.5, 125.2, 112.8, 110.120.5, 13.8. HRMS (EI): *m/z* Calcd for [M+H] $C_{20}H_{20}N_3$: 302.1657; Found: 302.1652.

(*E*)-*N*-(3-bromo-4-methylphenyl)-*N*-styrylpyrimidin-2-amine (3o)



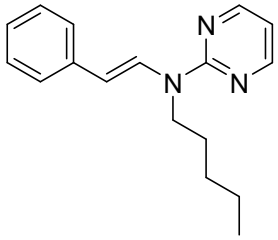
30 mg, 83% isolated yield. R_f = 0.32 (hexane/EtOAc = 5/1). White solid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.61 (d, *J* = 14.5 Hz, 1 H), 8.45 (d, *J* = 4.6 Hz, 2 H), 7.54 (d, *J* = 1.9 Hz, 1 H), 7.46 (d, *J* = 8.0 Hz, 1 H), 7.35 (d, *J* = 7.6 Hz, 2 H), 7.30 (t, *J* = 7.6 Hz, 2 H), 7.21 (dd, *J* = 1.9, 8.0 Hz, 1 H), 7.19 - 7.13 (m, 1 H), 6.79 (t, *J* = 4.8 Hz, 1 H), 5.50 (d, *J* = 14.5 Hz, 1 H), 2.53 (s, 3 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 159.7, 157.9, 138.6, 137.7, 137.3, 133.0, 131.8, 130.2, 128.5, 128.2, 125.7, 125.4, 125.3, 113.3, 111.2, 22.7. HRMS (EI): *m/z* Calcd for [M] $C_{19}H_{16}N_3Br$: 365.0528 Found: 365.0522.

(*E*)-*N*-allyl-*N*-styrylpyrimidin-2-amine (3p)



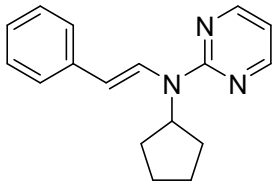
16 mg, 69% isolated yield. R_f = 0.32 (hexane/EtOAc = 5/1). Yellow liquid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.57 - 8.42 (m, 3 H), 7.42 (d, *J* = 7.6 Hz, 2 H), 7.30 (t, *J* = 7.6 Hz, 2 H), 7.19 - 7.10 (m, 1 H), 6.72 (t, *J* = 4.6 Hz, 1 H), 6.03 - 5.91 (m, 2 H), 5.28 - 5.10 (m, 2 H), 4.87 - 4.69 (m, 2 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 158.9, 157.8, 138.0, 132.3, 128.5, 128.1, 125.4, 125.2, 115.9, 112.5, 108.4, 46.2. HRMS (EI): *m/z* Calcd for [M+H] $C_{15}H_{16}N_3$: 238.1344; Found: 238.1339.

(*E*)-*N*-pentyl-*N*-styrylpyrimidin-2-amine (3q)



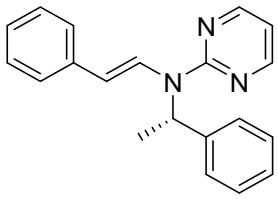
17mg, 63% isolated yield. R_f = 0.32 (hexane/EtOAc = 5/1). Yellow liquid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.59 - 8.38 (m, 3 H), 7.43 (d, *J* = 7.2 Hz, 2 H), 7.31 (t, *J* = 7.6 Hz, 2 H), 7.22 - 7.08 (m, 1 H), 6.69 (t, *J* = 4.6 Hz, 1 H), 5.97 (d, *J* = 14.9 Hz, 1 H), 4.10 - 3.96 (m, 2 H), 1.81 - 1.64 (m, 2 H), 1.53 - 1.35 (m, 4 H), 0.96 (t, *J* = 6.7 Hz, 3 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 159.0, 157.7, 138.3, 128.5, 128.3, 125.3, 125.1, 112.2, 107.3, 43.7, 29.2, 26.0, 22.5, 14.1. HRMS (EI): *m/z* Calcd for [M+H] $C_{17}H_{22}N_3$: 268.1814; Found: 268.1808.

(*E*)-*N*-cyclopentyl-*N*-styrylpyrimidin-2-amine (3r)



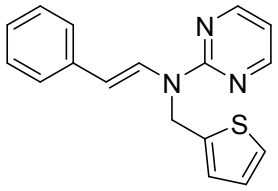
19 mg, 73% isolated yield. R_f = 0.32 (hexane/EtOAc = 5/1). Yellow liquid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ ppm 8.44 (d, *J* = 5.0 Hz, 2 H), 8.15 (s, 1 H), 8.18 (s, 1 H), 7.41 (d, *J* = 7.6 Hz, 2 H), 7.31 (t, *J* = 7.6 Hz, 2 H), 7.06 - 7.18 (m, 1 H), 6.68 (t, *J* = 4.6 Hz, 1 H), 6.18 (s, 1 H), 6.21 (s, 1 H), 5.34 (t, *J* = 9.0 Hz, 1 H), 2.26 (dd, *J* = 11.6, 8.2 Hz, 2 H), 1.86 - 2.05 (m, 4 H), 1.63 - 1.80 (m, 2 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) d = 160.0, 157.4, 138.3, 128.5, 128.2, 125.4, 125.1, 112.1, 110.5, 56.5, 27.3, 25.3. HRMS (EI): *m/z* Calcd for [M+H] $C_{17}H_{20}N_3$: 266.1657; Found: 266.1652

(*S*)(*E*)-*N*-(1-phenylethyl)-*N*-styrylpyrimidin-2-amine (3s)



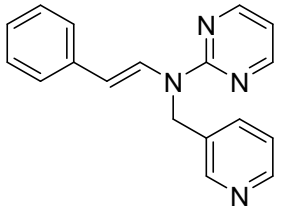
23 mg, 75% isolated yield. R_f = 0.32 (hexane/EtOAc = 5/1). White solid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.49 (d, *J* = 4.6 Hz, 2 H), 8.22 (d, *J* = 15.3 Hz, 1 H), 7.49 - 7.33 (m, 4 H), 7.33 - 7.20 (m, 5 H), 7.16 - 7.07 (m, 1 H), 6.75 (t, *J* = 4.8 Hz, 1 H), 6.64 (d, *J* = 6.9 Hz, 1 H), 5.86 (d, *J* = 15.3 Hz, 1 H), 1.93 (d, *J* = 7.2 Hz, 3 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 160.0, 157.7, 141.5, 138.1, 128.4, 128.4, 126.6, 126.4, 126.1, 125.4, 125.1, 112.5, 112.0, 52.1, 15.8. HRMS (EI): *m/z* Calcd for [M+H] $C_{20}H_{20}N_3$: 302.1657; Found: 302.1652.

(*E*)-*N*-styryl-*N*-(thiophen-2-ylmethyl)pyrimidin-2-amine (3t)



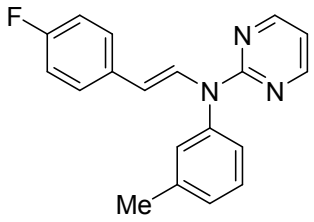
23 mg, 80% isolated yield. R_f = 0.32 (hexane/EtOAc = 3/1). Yellow solid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.54 - 8.40 (m, 3 H), 7.41 (d, *J* = 7.6 Hz, 2 H), 7.30 (t, *J* = 7.6 Hz, 2 H), 7.23 - 7.11 (m, 2 H), 7.09 (d, *J* = 2.7 Hz, 1 H), 6.95 (dd, *J* = 3.8, 5.0 Hz, 1 H), 6.76 (t, *J* = 4.8 Hz, 1 H), 6.13 (s, 1 H), 6.16 (s, 1 H), 5.47 (s, 2 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 158.7, 157.8, 140.1, 137.8, 128.5, 127.8, 126.4, 125.8, 125.5, 125.3, 124.5, 112.9, 108.6, 42.7 HRMS (EI): *m/z* Calcd for [M+H] $C_{17}H_{16}N_3S$: 294.1065; Found: 294.1059.

(*E*)-*N*-(pyridin-3-ylmethyl)-*N*-styrylpyrimidin-2-amine (3u)



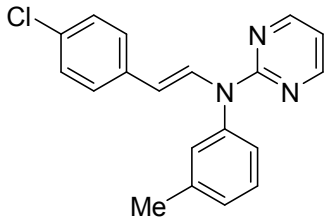
24 mg, 81% isolated yield. R_f = 0.32 (hexane/EtOAc = 3/1). Yellow solid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.65 (s, 1 H), 8.59 (s, 1 H), 8.62 (s, 1 H), 8.52 (d, *J* = 4.2 Hz, 1 H), 8.47 (d, *J* = 4.6 Hz, 2 H), 7.58 (d, *J* = 8.0 Hz, 1 H), 7.36 (d, *J* = 7.6 Hz, 2 H), 7.32 - 7.19 (m, 3 H), 7.19 - 7.10 (m, 1 H), 6.77 (t, *J* = 4.8 Hz, 1 H), 5.91 (d, *J* = 14.5 Hz, 1 H), 5.36 (s, 2 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 159.0, 157.9, 148.6, 148.3, 137.4, 134.2, 133.0, 128.5, 127.9, 125.6, 125.2, 123.3, 113.0, 108.7, 45.1. HRMS (EI): *m/z* Calcd for [M+H] $C_{18}H_{17}N_4$: 289.1453; Found: 289.1449.

(*E*)-*N*-(4-fluorostyryl)-*N*-*m*-tolylpyrimidin-2-amine (4a)



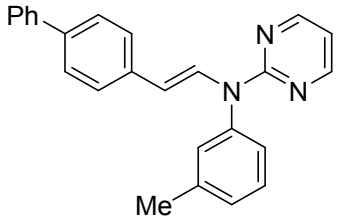
19 mg, 63% isolated yield. R_f = 0.32 (hexane/EtOAc = 5/1). Yellow liquid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.56 (d, *J* = 14.5 Hz, 1 H), 8.45 (s, 1 H), 8.44 (s, 1 H), 7.49 (t, *J* = 7.6 Hz, 1 H), 7.34 - 7.23 (m, 3 H), 7.20 - 7.09 (m, 2 H), 6.98 (t, *J* = 8.8 Hz, 2 H), 6.77 (t, *J* = 4.6 Hz, 1 H), 5.41 (d, *J* = 14.5 Hz, 1 H), 2.47 (s, 3 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 162.1, 160.1, 159.8, 157.9, 139.9, 139.9, 133.7, 133.7, 130.3, 129.8, 129.7, 128.9, 126.5, 126.5, 126.2, 115.4, 115.2, 113.0, 109.8, 21.4. HRMS (EI): *m/z* Calcd for [M+H] $C_{19}H_{17}N_3F$: 306.1407; Found: 306.1401.

(*E*)-*N*-(4-chlorostyryl)-*N*-*m*-tolylpyrimidin-2-amine (4b)



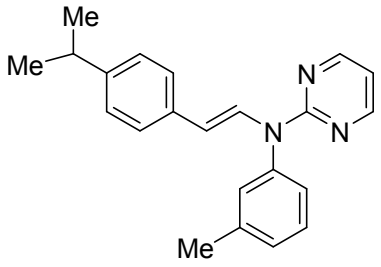
21 mg, 65% isolated yield. R_f = 0.32 (hexane/EtOAc = 5/1). White solid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.60 (d, *J* = 14.5 Hz, 1 H), 8.42 (d, *J* = 4.6 Hz, 2 H), 7.46 (t, *J* = 7.8 Hz, 1 H), 7.28 (s, 1 H), 7.25 - 7.18 (m, 4 H), 7.14 - 7.06 (m, 2 H), 6.75 (t, *J* = 4.8 Hz, 1 H), 5.35 (d, *J* = 14.5 Hz, 1 H), 2.44 (s, 3 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 159.8, 157.9, 140.0, 139.7, 136.2, 131.0, 130.8, 129.7, 128.9, 128.5, 126.3, 126.1, 113.1, 109.5, 21.5. HRMS (EI): *m/z* Calcd for [M+H] $C_{19}H_{17}N_3Cl$: 322.1111; Found: 322.1106.

(*E*)-*N*-(2-(biphenyl-4-yl)vinyl)-*N*-*m*-tolylpyrimidin-2-amine (4c)



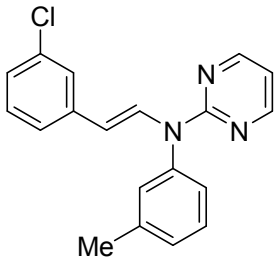
29 mg, 80% isolated yield. R_f = 0.32 (hexane/EtOAc = 5/1). White solid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.71 (d, *J* = 14.5 Hz, 1 H), 8.45 (br. s., 2 H), 7.71 - 7.58 (m, 2 H), 7.58 - 7.37 (m, 7 H), 7.37 - 7.22 (m, 2 H), 7.16 (br. s., 2 H), 6.76 (br. s., 1 H), 5.49 (d, *J* = 14.5 Hz, 1 H), 2.47 (br. s., 3 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 159.8, 157.8, 140.9, 139.9, 138.1, 136.8, 130.6, 129.8, 129.7, 128.8, 128.7, 127.1, 126.9, 126.7, 126.2, 125.6, 113.0, 110.4, 21.4. HRMS (EI): *m/z* Calcd for [M+H] $C_{25}H_{22}N_3$: 364.1814; Found: 364.1808.

(*E*)-*N*-(4-isopropylstyryl)-*N*-*m*-tolylpyrimidin-2-amine (4d)



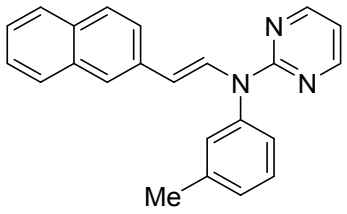
23 mg, 70% isolated yield. R_f = 0.32 (hexane/EtOAc = 5/1). White solid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.60 (d, *J* = 14.5 Hz, 1 H), 8.45 (d, *J* = 5.0 Hz, 2 H), 7.48 (s, 1 H), 7.36 - 7.22 (m, 3 H), 7.22 - 7.09 (m, 4 H), 6.75 (t, *J* = 4.8 Hz, 1 H), 5.46 (d, *J* = 14.5 Hz, 1 H), 2.90 (s, 1 H), 2.47 (s, 3 H), 1.27 (d, *J* = 6.9 Hz, 7 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 159.9, 157.8, 146.3, 140.0, 139.8, 135.1, 129.9, 129.8, 129.6, 128.7, 126.5, 126.2, 125.2, 112.8, 111.0, 33.7, 24.0, 21.4. HRMS (EI): *m/z* Calcd for [M+H] $C_{22}H_{24}N_3$: 330.1970; Found: 330.1965.

(*E*)-*N*-(3-chlorostyryl)-*N*-*m*-tolylpyrimidin-2-amine (4e)



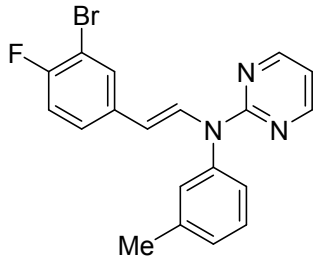
23 mg, 73% isolated yield. R_f = 0.32 (hexane/EtOAc = 5/1). White solid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.66 (d, *J* = 14.5 Hz, 1 H), 8.45 (br s, 2 H), 7.48 (br s, 1 H), 7.37 - 7.26 (m, 3 H), 7.18 (br s, 3 H), 7.12 (br s, 3 H), 6.78 (br s, 1 H), 5.35 (d, *J* = 14.1 Hz, 1 H), 2.46 (br s, 3 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 159.8, 157.9, 140.0, 139.7, 139.6, 134.4, 131.6, 129.8, 129.7, 129.6, 129.0, 126.1, 125.3, 125.0, 123.3, 113.3, 109.3, 21.4. HRMS (EI): *m/z* Calcd for [M+H] $C_{19}H_{17}N_3Cl$: 322.1111; Found: 322.1106.

(*E*)-*N*-(2-(naphthalen-2-yl)vinyl)-*N*-*m*-tolylpyrimidin-2-amine (4f)



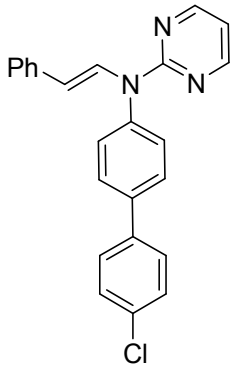
28 mg, 83% isolated yield. R_f = 0.32 (hexane/EtOAc = 5/1). White solid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.62 (d, *J* = 14.1 Hz, 1 H), 8.45 (d, *J* = 4.6 Hz, 2 H), 7.80 (d, *J* = 8.4 Hz, 1 H), 7.83 (d, *J* = 8.0 Hz, 1 H), 7.71 (dd, *J* = 4.8, 7.4 Hz, 2 H), 7.54 (t, *J* = 8.0 Hz, 1 H), 7.51 - 7.39 (m, 3 H), 7.33 (d, *J* = 7.6 Hz, 1 H), 7.26 (br s, 2 H), 6.76 (t, *J* = 4.8 Hz, 1 H), 6.19 (d, *J* = 14.1 Hz, 1 H), 2.50 (s, 3 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 159.9, 157.9, 140.2, 140.0, 134.9, 133.7, 132.5, 131.2, 129.8, 129.8, 128.9, 128.4, 126.3, 126.1, 125.7, 125.5, 125.4, 123.8, 122.3, 113.0, 108.0, 21.5. HRMS (EI): *m/z* Calcd for [M+H] $C_{23}H_{20}N_3$: 338.1657; Found: 338.1652.

(*E*)-*N*-(3-bromo-4-fluorostyryl)-*N*-*m*-tolylpyrimidin-2-amine (4g)



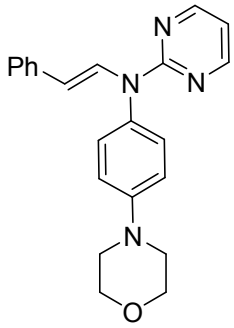
23 mg, 60% isolated yield. R_f = 0.32 (hexane/EtOAc = 5/1). White solid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.55 (d, *J* = 14.5 Hz, 1 H), 8.43 (d, *J* = 4.6 Hz, 2 H), 7.49 - 7.41 (m, 2 H), 7.29 (s, 1 H), 7.23 - 7.14 (m, 1 H), 7.14 - 7.04 (m, 2 H), 6.99 (t, *J* = 8.4 Hz, 1 H), 6.77 (t, *J* = 4.8 Hz, 1 H), 5.30 (d, *J* = 14.9 Hz, 1 H), 2.44 (s, 3 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 159.7, 158.0, 157.9, 156.1, 140.0, 139.6, 135.5, 135.5, 131.3, 129.8, 129.7, 129.7, 129.0, 126.1, 125.3, 125.3, 116.4, 116.2, 113.2, 109.1, 108.9, 108.2, 21.4. HRMS (EI): *m/z* Calcd for [M+H] $C_{19}H_{16}N_3FBr$: 384.0512; Found: 384.0506.

(*E*)-*N*-(4'-chlorobiphenyl-4-yl)-*N*-styrylpyrimidin-2-amine (5)



39 mg, 90% isolated yield. R_f = 0.32 (hexane/EtOAc = 5/1). White solid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.63 (d, *J* = 14.5 Hz, 1 H), 8.45 (d, *J* = 4.6 Hz, 2 H), 7.75 (d, *J* = 8.0 Hz, 2 H), 7.66 - 7.57 (m, *J* = 8.4 Hz, 2 H), 7.51 - 7.43 (m, *J* = 8.4 Hz, 2 H), 7.40 (d, *J* = 8.4 Hz, 2 H), 7.36 - 7.25 (m, 5 H), 7.13 (t, *J* = 7.1 Hz, 1 H), 6.77 (t, *J* = 4.6 Hz, 1 H), 5.52 (d, *J* = 14.5 Hz, 1 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 159.8, 157.9, 139.6, 139.4, 138.9, 137.4, 133.6, 130.5, 129.8, 129.0, 128.5, 128.4, 125.7, 125.3, 113.2, 111.3. HRMS (EI): *m/z* Calcd for [M+H] $C_{24}H_{19}ClN_3$: 384.1268; Found: 384.1262.

(*E*)-*N*-(4-morpholinophenyl)-*N*-styrylpyrimidin-2-amine (6)



27 mg, 80% isolated yield. R_f = 0.32 (hexane/EtOAc = 1/1). Yellow solid. ^{1}H NMR (500 MHz, CHLOROFORM-d) δ = 8.66 (d, *J* = 14.5 Hz, 1 H), 8.44 (d, *J* = 4.6 Hz, 2 H), 7.35 - 7.30 (m, 2 H), 7.30 - 7.25 (m, 2 H), 7.21 (d, *J* = 8.8 Hz, 2 H), 7.15 - 7.06 (m, 3 H), 6.74 (t, *J* = 4.8 Hz, 1 H), 5.48 (d, *J* = 14.5 Hz, 1 H), 3.95 - 3.89 (m, 4 H), 3.33 - 3.25 (m, 4 H). ^{13}C NMR (126 MHz, CHLOROFORM-d) δ = 160.1, 157.8, 150.3, 137.7, 131.6, 130.8, 129.8, 128.4, 125.4, 125.2,

116.4, 112.8, 110.7, 66.9, 48.8. HRMS (EI): *m/z* Calcd for [M+H] $C_{22}H_{23}ON_4$: 359.1872; Found: 359.1866.

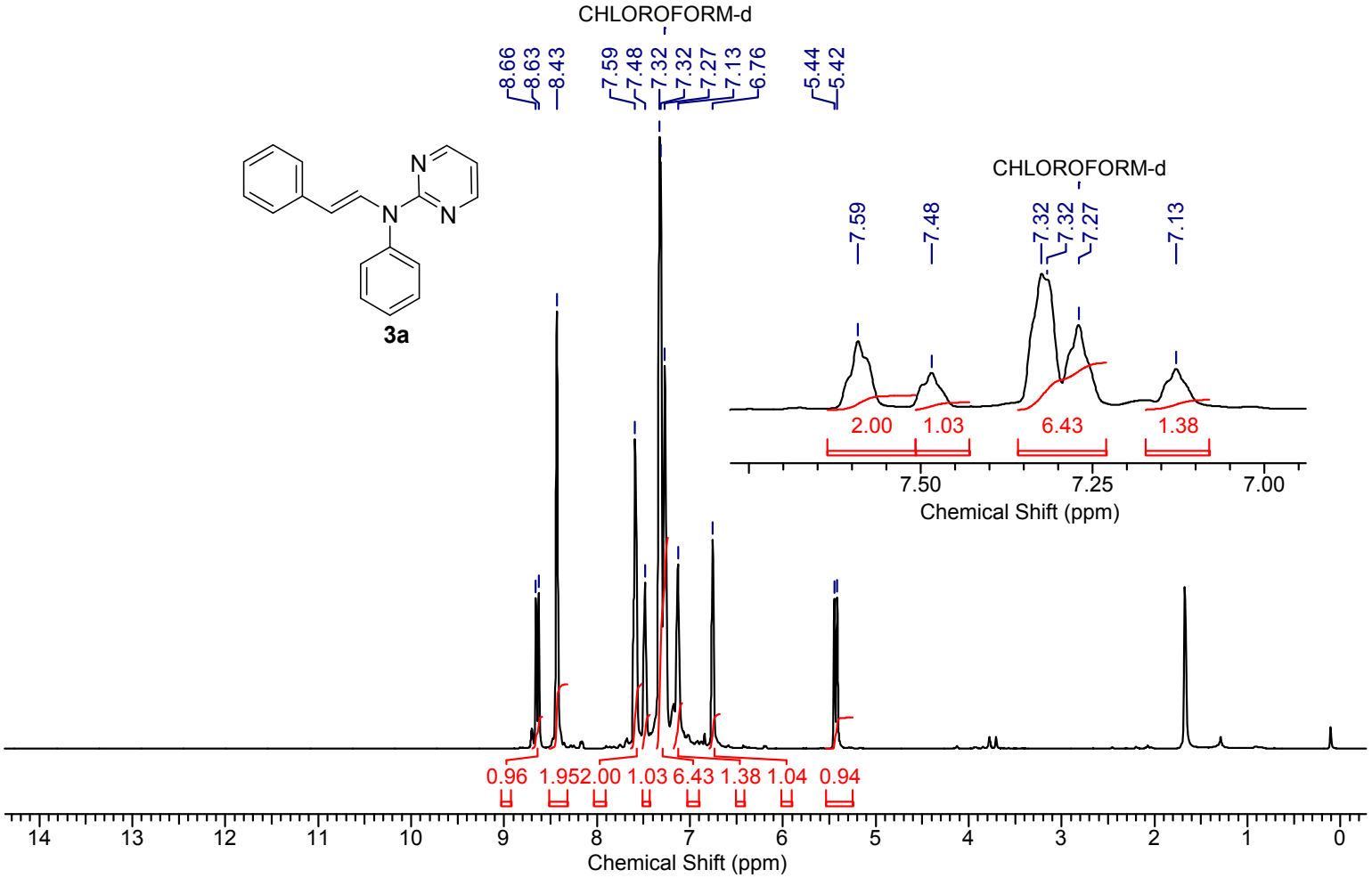
6. References

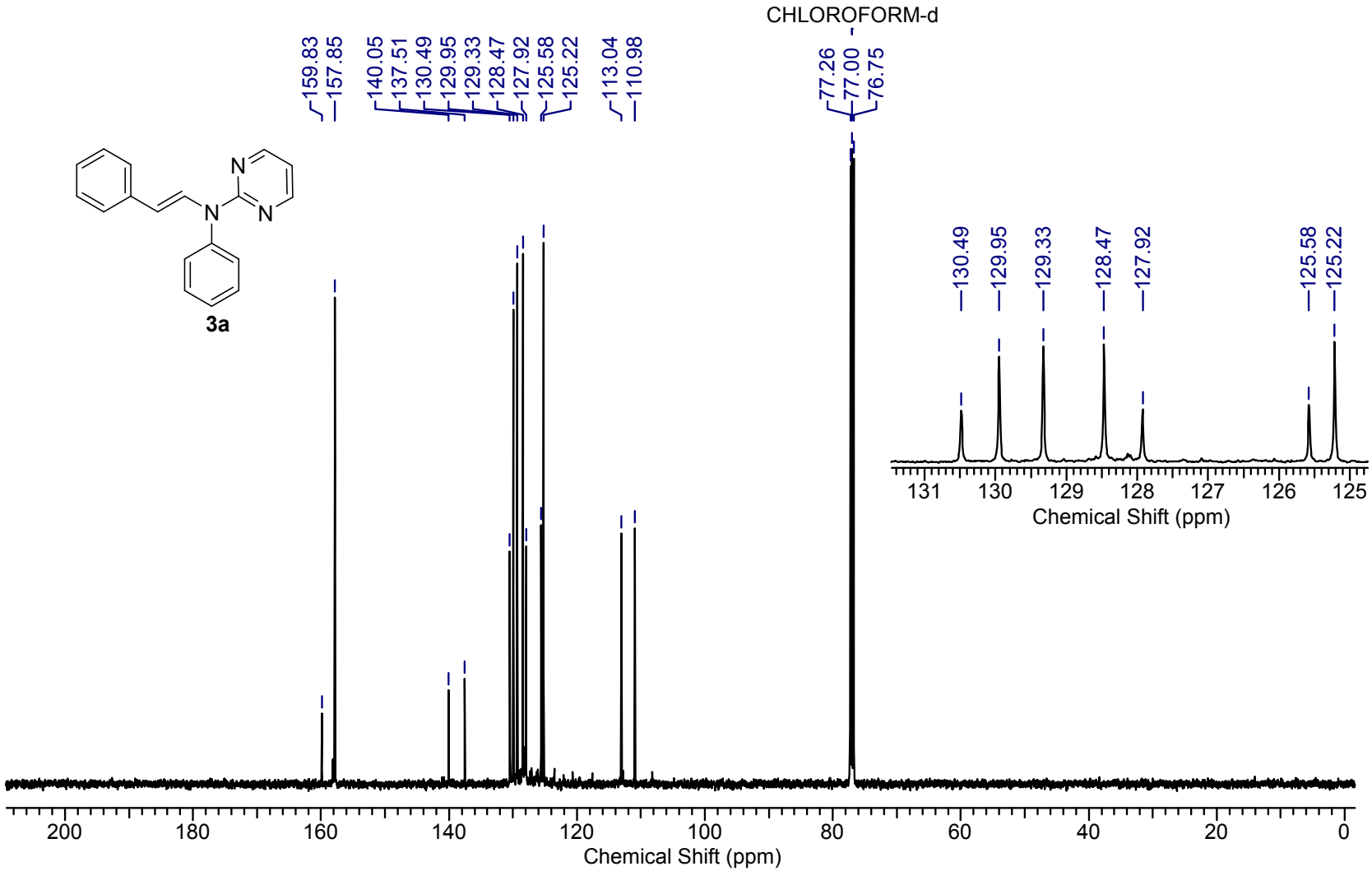
[S1] Ackermann, L.; Lygin, A. V. *Org. Lett.* **2012**, *14*, 764.

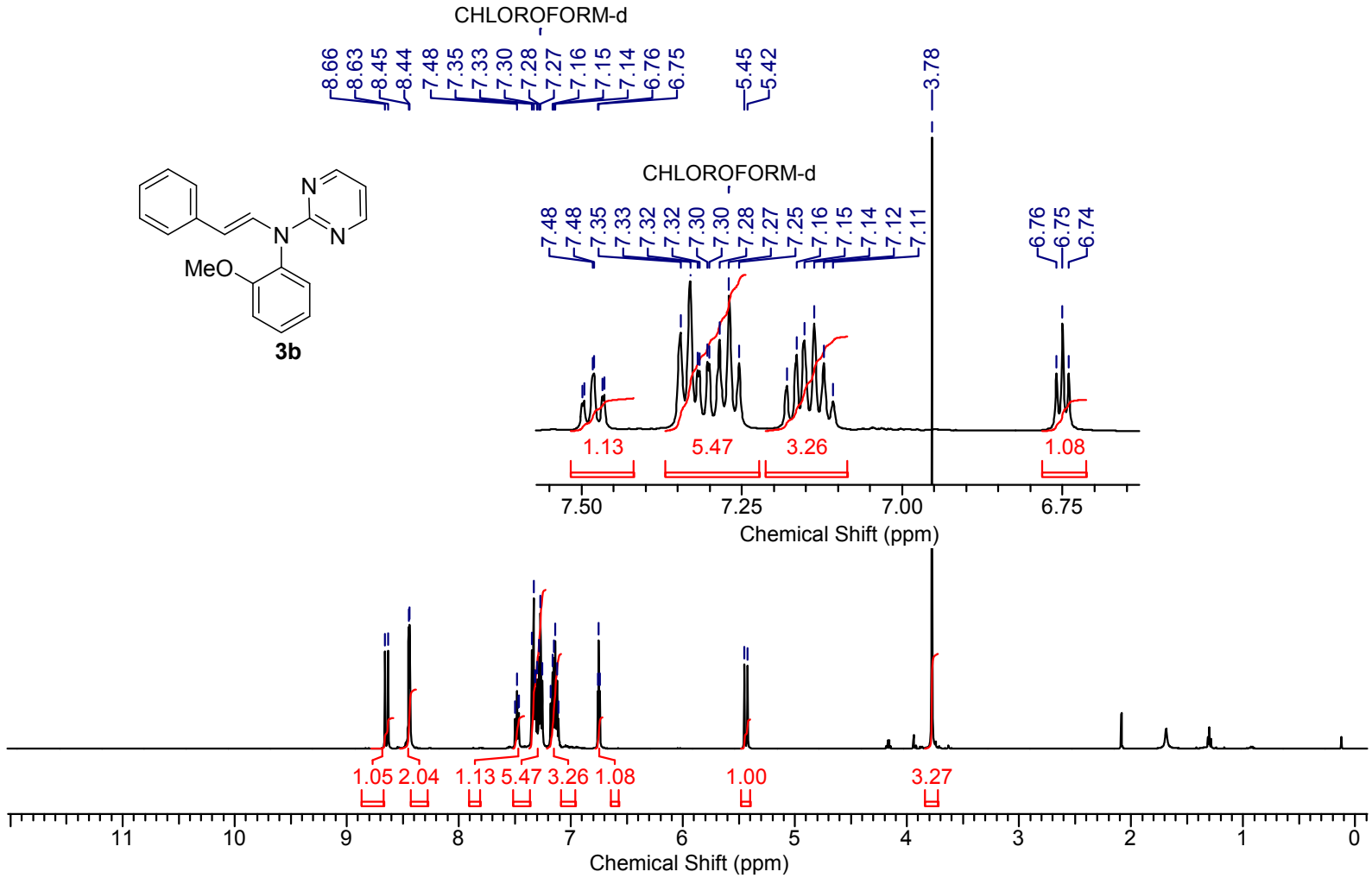
[S2] Huang, X.; Xu, S.; Tan, Q.; Gao, M.; Lia, M.; Xu, B. *Chem. Commun.* **2014**, 50, 1465

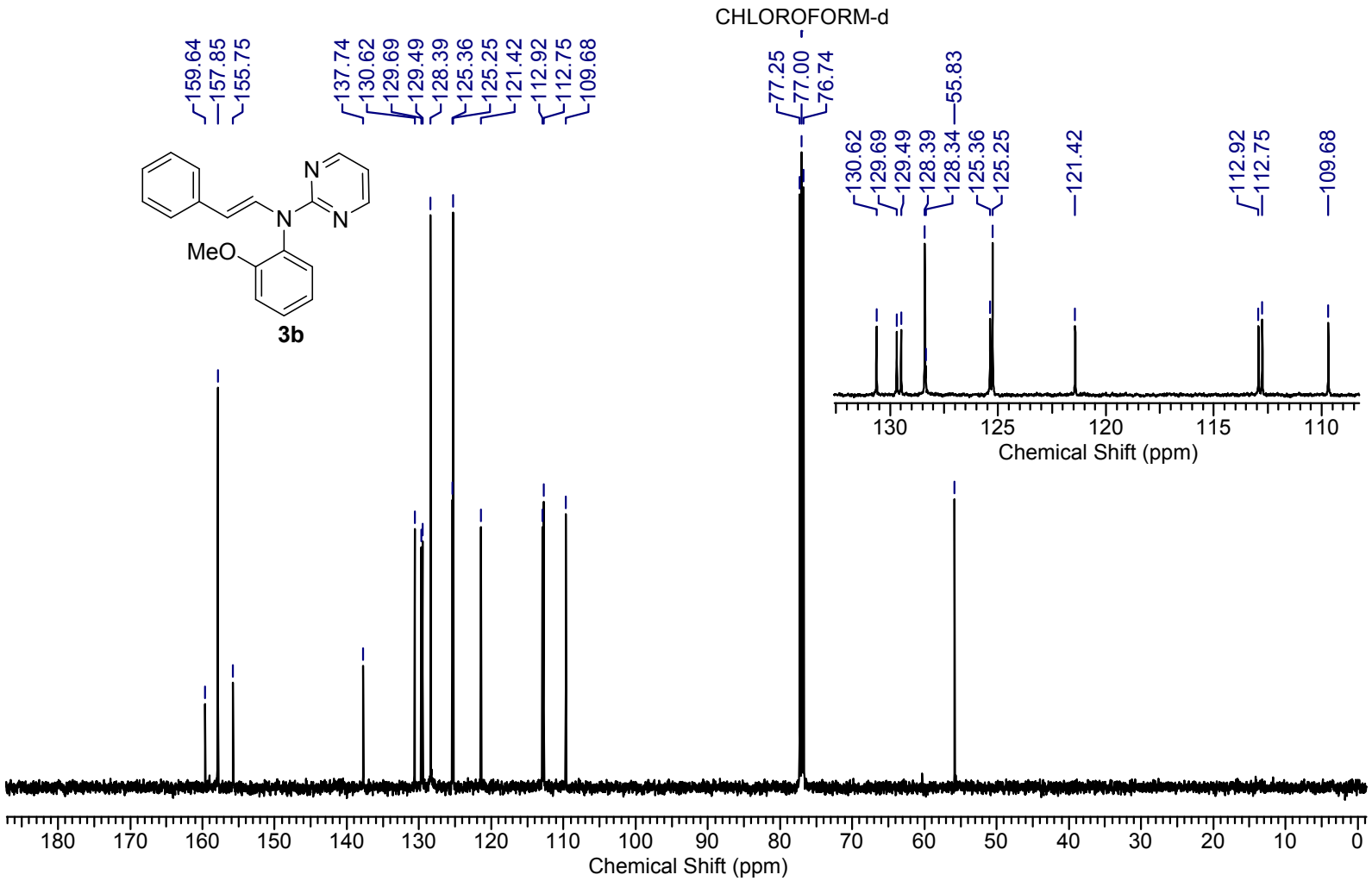
[S3] Tlvekar, V. N.; Arote, N.D.; Herlekar, O. P. *Synlett* **2005**, 16, 2495

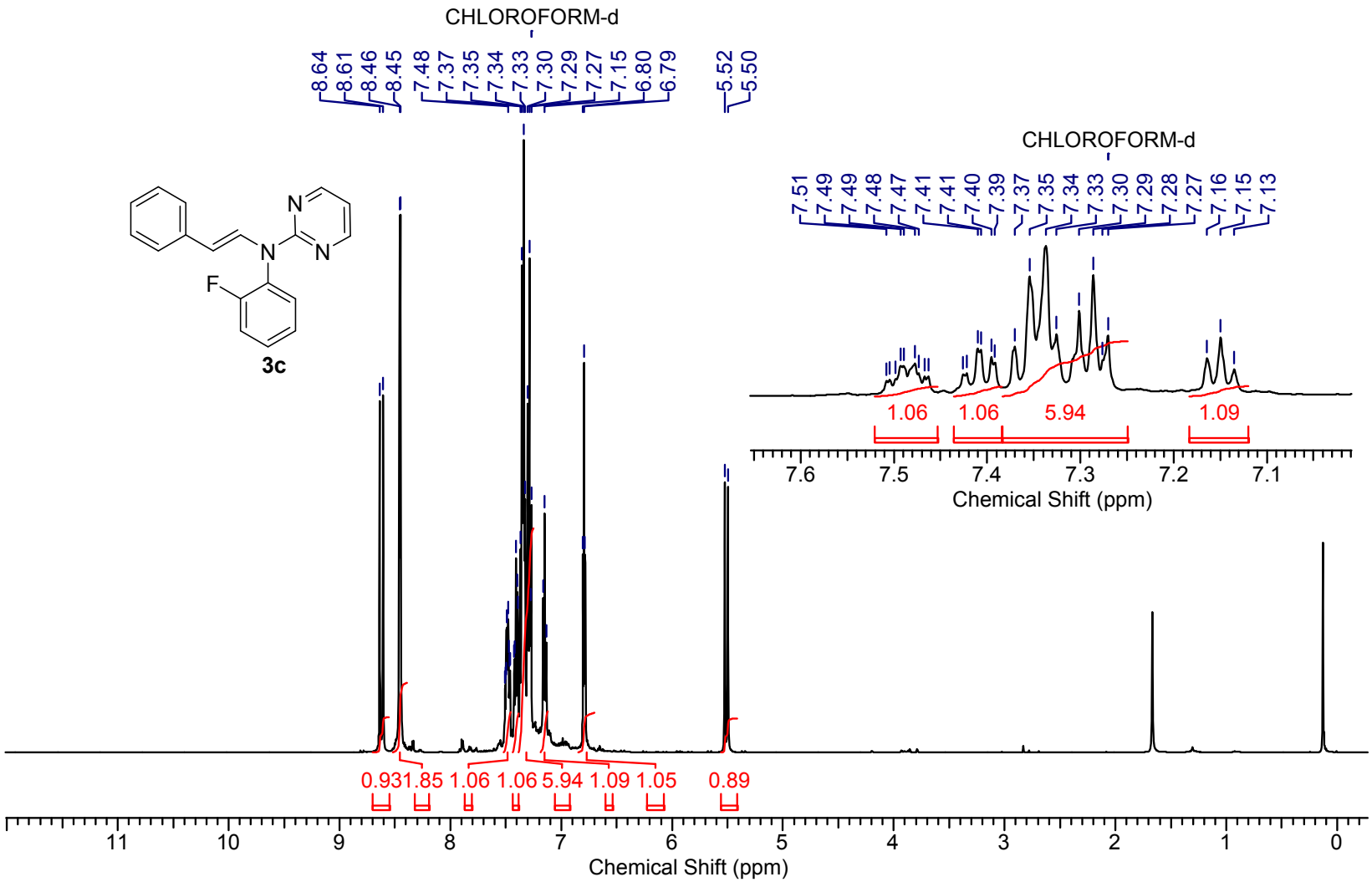
7. Spectra

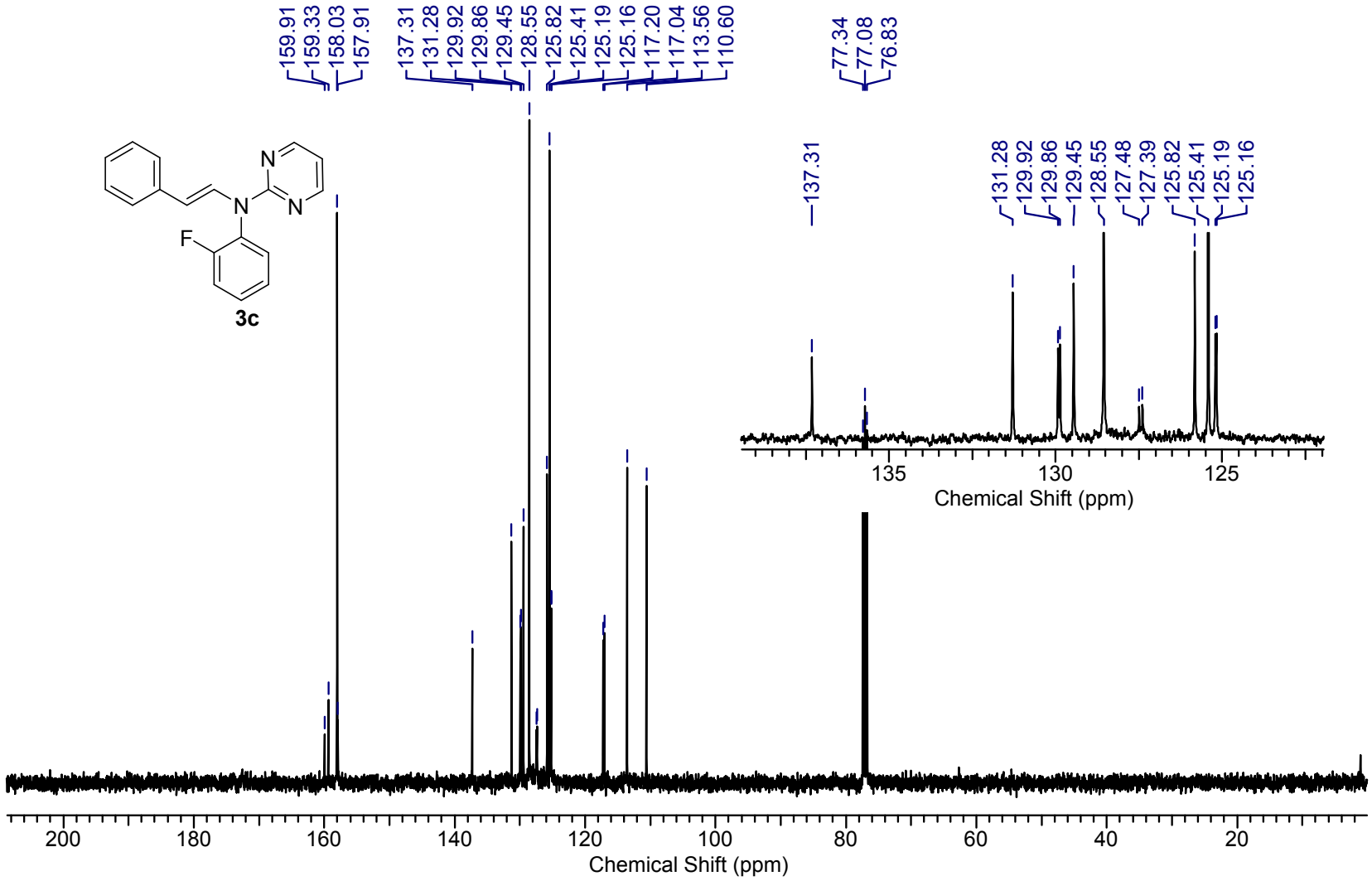

CHLOROFORM-d
8.66
8.63
8.43
7.59
7.48
7.32
7.32
7.27
7.13
6.76
5.44
5.42
N
N
N
3a
CHLOROFORM-d
7.59
7.48
7.32
7.32
7.27
7.13
2.00
1.03
6.43
1.38
7.50
7.25
7.00
Chemical Shift (ppm)
0.96
1.95
2.00
1.03
6.43
1.38
1.04
0.94
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

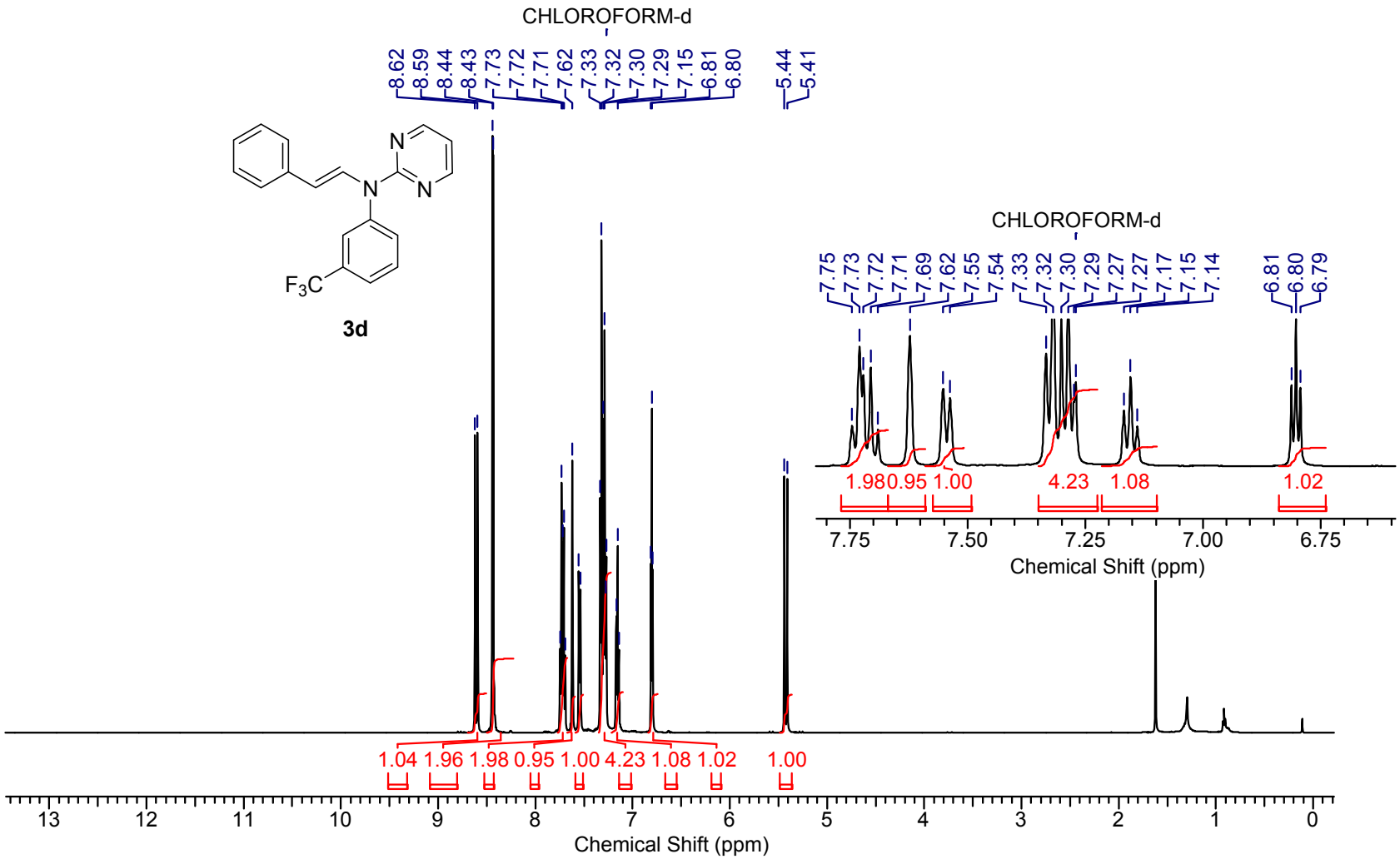

CHLOROFORM-d
159.83
157.85
140.05
137.51
130.49
129.95
129.33
128.47
127.92
125.58
125.22
113.04
110.98
77.26
77.00
76.75
N
N
N
3a
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)
130.49
129.95
129.33
128.47
127.92
125.58
125.22
131
130
129
128
127
126
125
Chemical Shift (ppm)

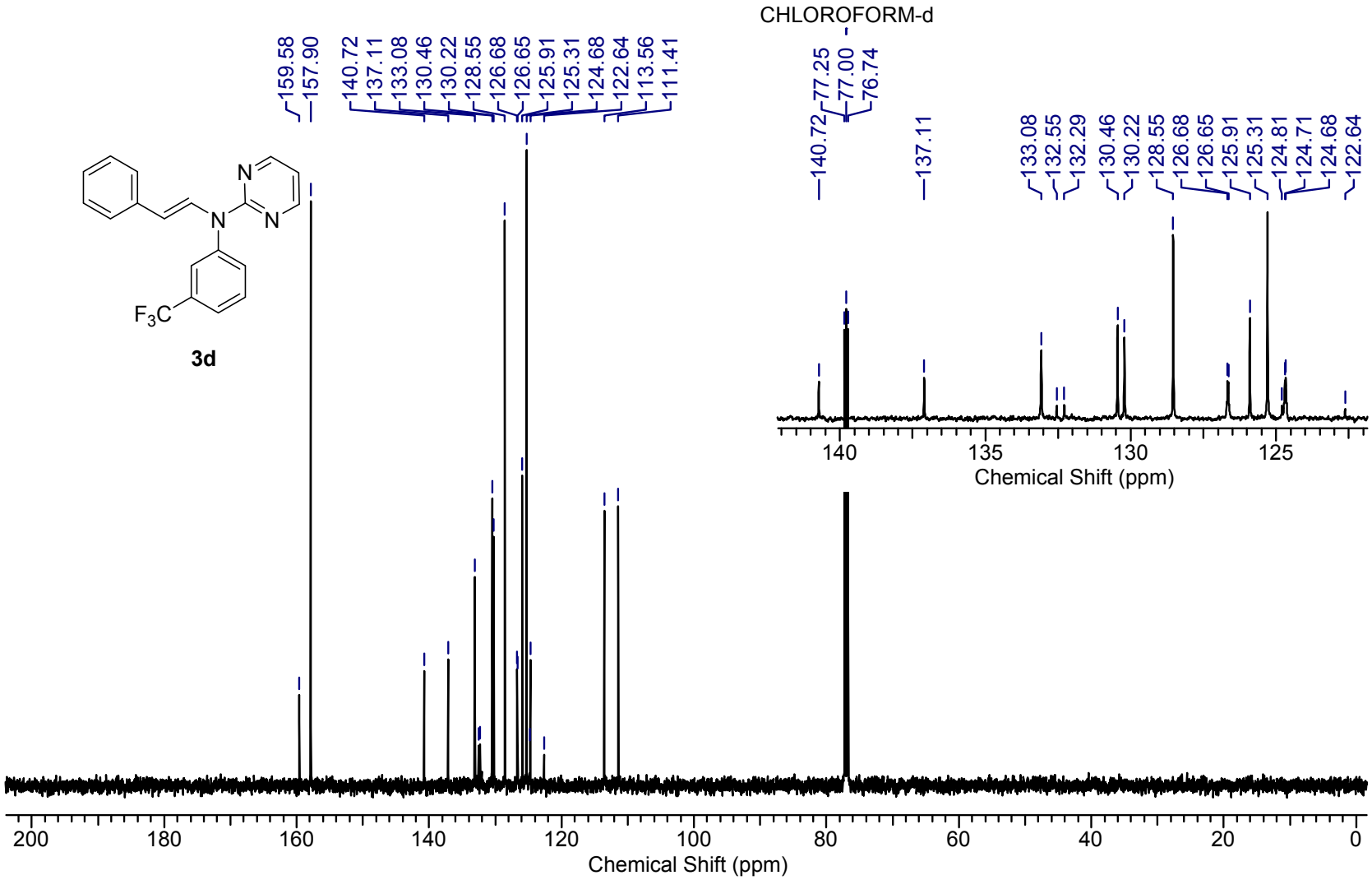

CHLOROFORM-d
8.66
8.63
8.45
8.44
7.48
7.35
7.33
7.30
7.28
7.27
7.16
7.15
7.14
6.76
6.75
5.45
5.42
3.78
N
N
N
MeO
3b
CHLOROFORM-d
7.48
7.48
7.35
7.33
7.32
7.32
7.30
7.30
7.28
7.27
7.25
7.16
7.15
7.14
7.12
7.11
6.76
6.75
6.74
1.13
5.47
3.26
1.08
7.50
7.25
7.00
6.75
Chemical Shift (ppm)
1.05
2.04
1.13
5.47
3.26
1.08
1.00
3.27
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

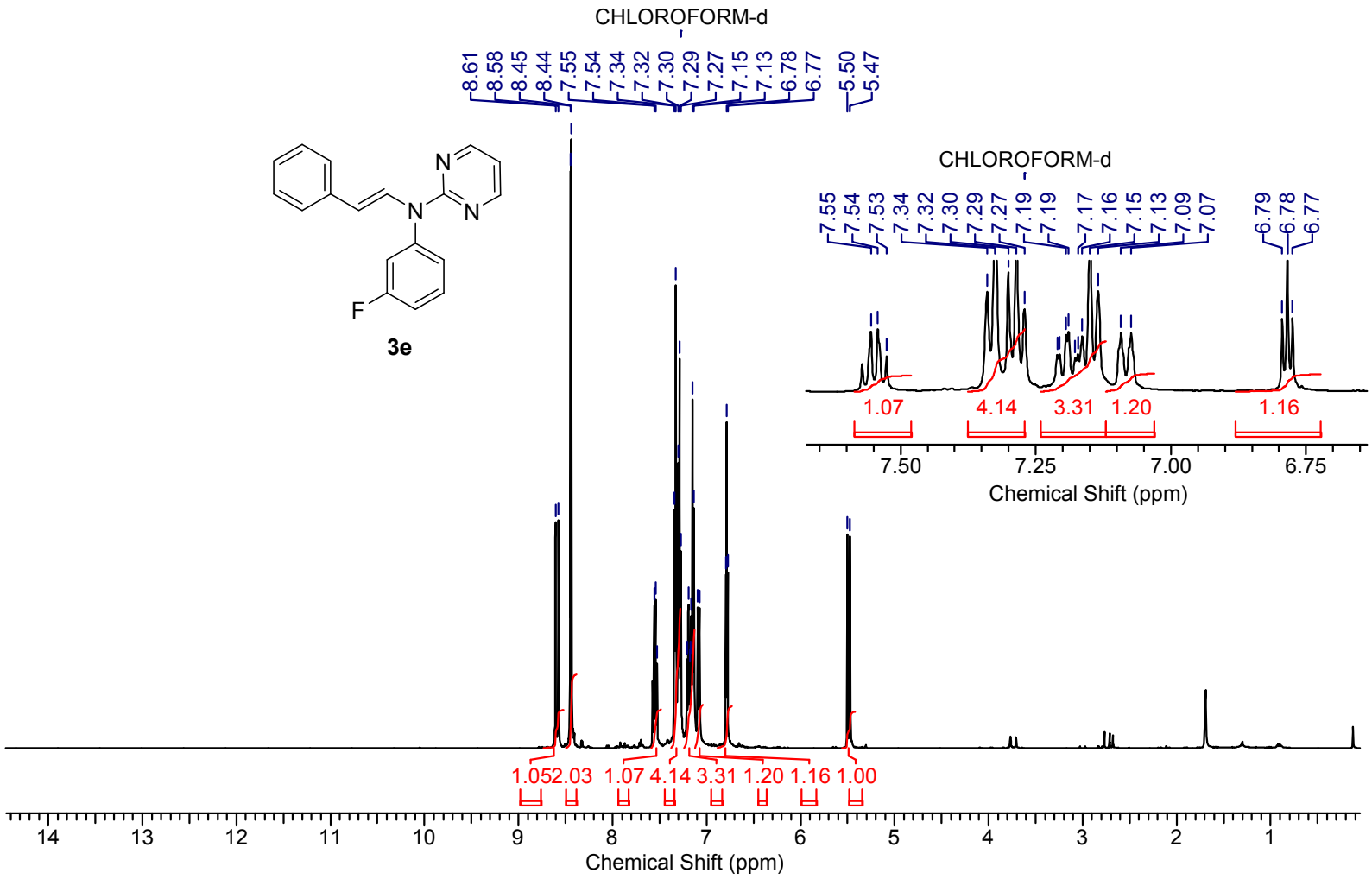

CHLOROFORM-d
159.64
157.85
155.75
137.74
130.62
129.69
129.49
128.39
125.36
125.25
121.42
112.92
112.75
109.68
77.25
77.00
76.74
55.83
MeO
N
N
N
3b
Chemical Shift (ppm)
Chemical Shift (ppm)

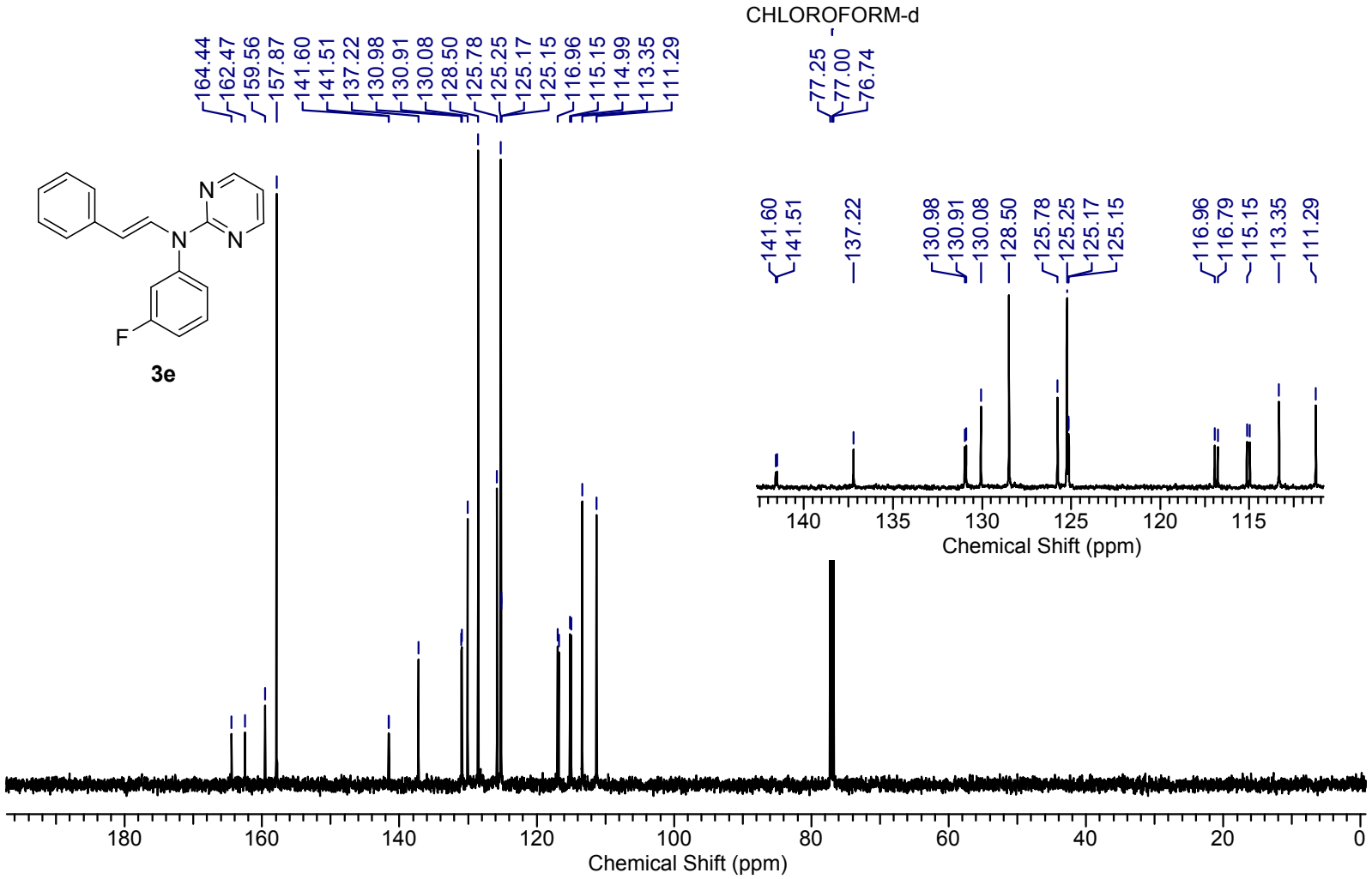

CHLOROFORM-d
8.64
8.61
8.46
8.45
7.48
7.37
7.35
7.34
7.33
7.30
7.29
7.27
7.15
6.80
6.79
5.52
5.50
N
N
N
F
3c
0.93
1.85
1.06
1.06
5.94
1.09
1.05
0.89
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)
CHLOROFORM-d
7.51
7.49
7.49
7.48
7.47
7.41
7.41
7.40
7.39
7.37
7.35
7.34
7.33
7.30
7.29
7.28
7.27
7.16
7.15
7.13
1.06
1.06
5.94
1.09
7.6
7.5
7.4
7.3
7.2
7.1
Chemical Shift (ppm)

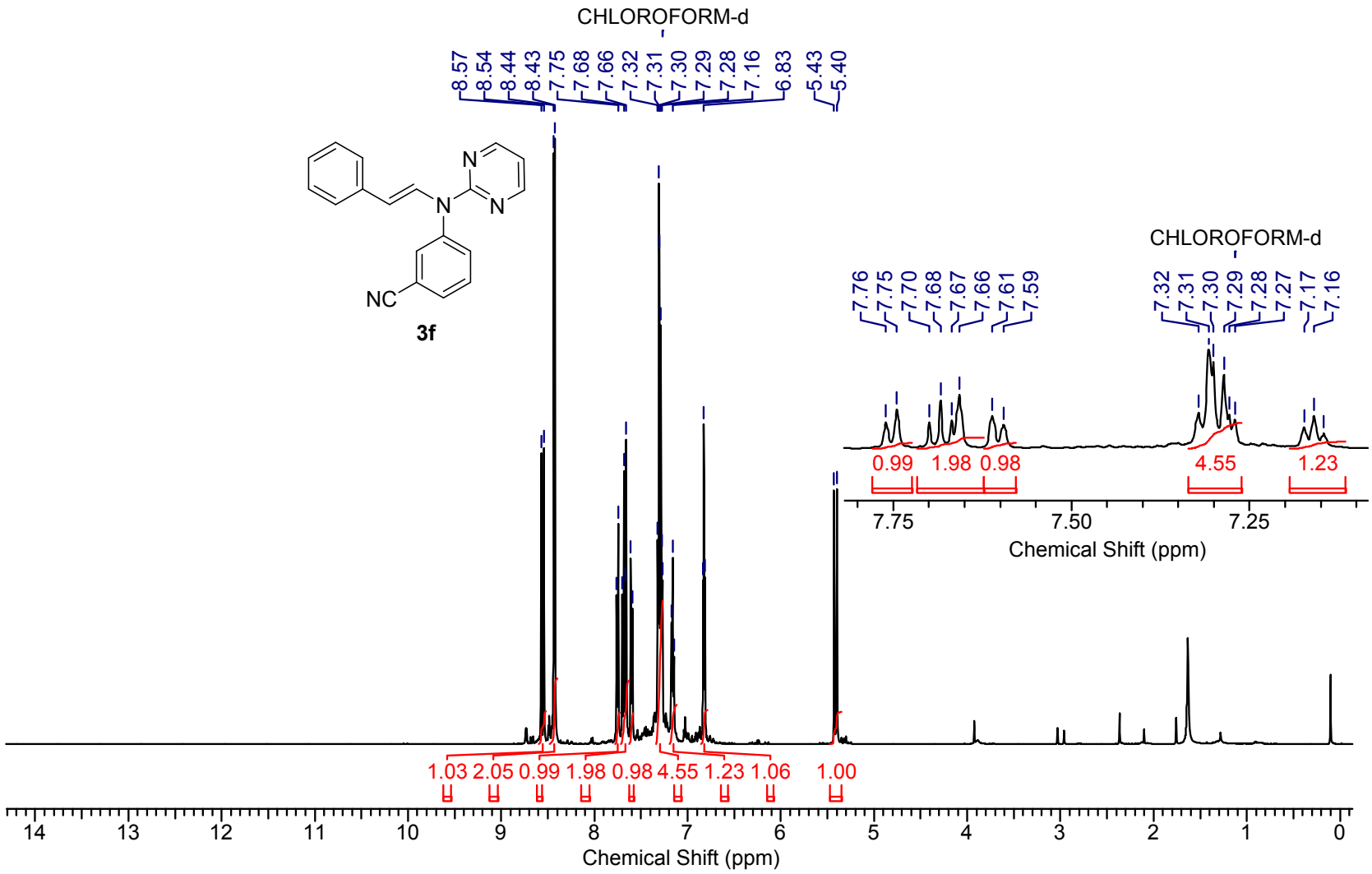

159.91
159.33
158.03
157.91
137.31
131.28
129.92
129.86
129.45
128.55
125.82
125.41
125.19
125.16
117.20
117.04
113.56
110.60
77.34
77.08
76.83
N
N
N
F
3c
137.31
131.28
129.92
129.86
129.45
128.55
127.48
127.39
125.82
125.41
125.19
125.16
135
130
125
Chemical Shift (ppm)
200
180
160
140
120
100
80
60
40
20
Chemical Shift (ppm)

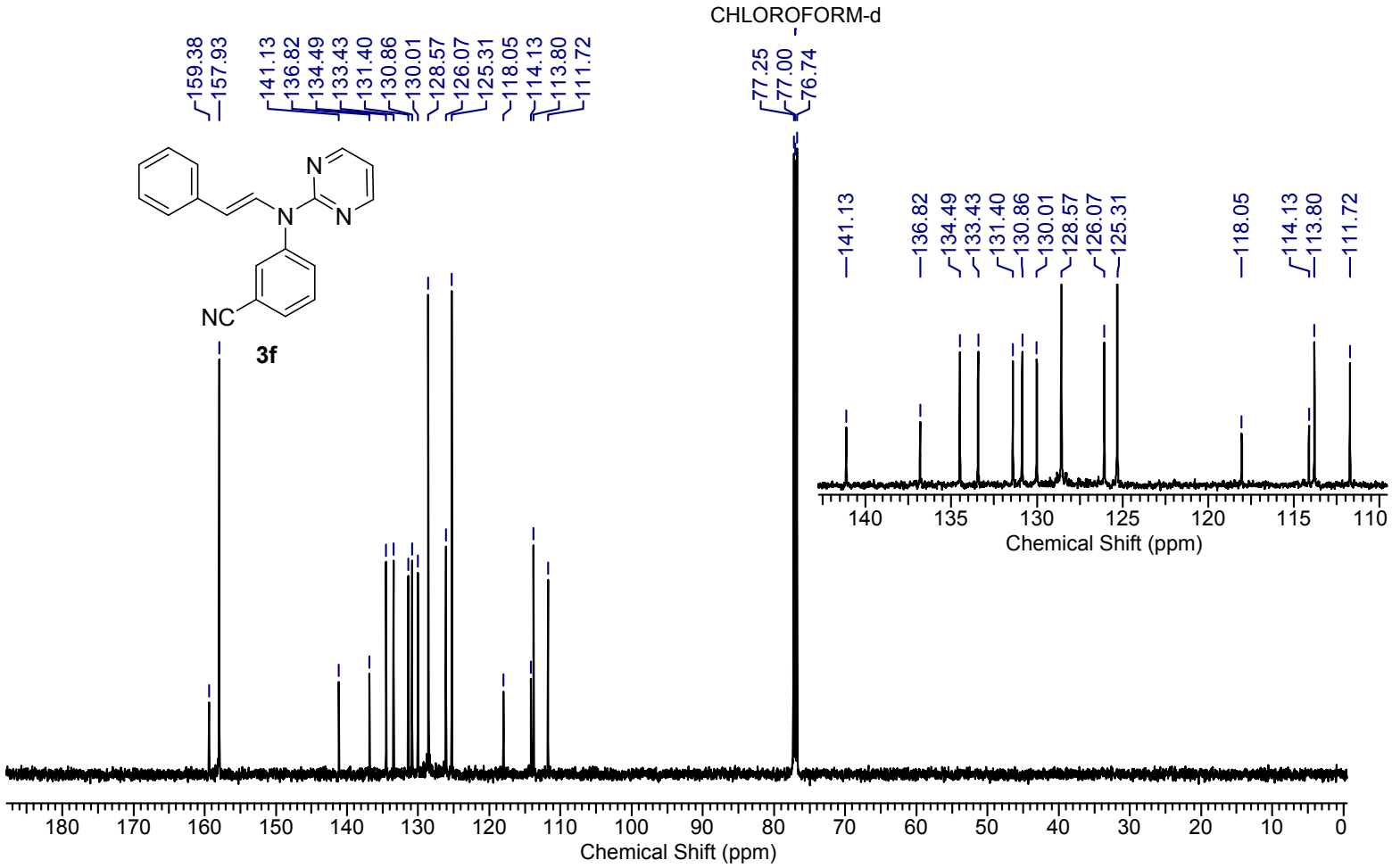

CHLOROFORM-d
8.62
8.59
8.44
8.43
7.73
7.72
7.71
7.62
7.33
7.32
7.30
7.29
7.15
6.81
6.80
5.44
5.41
N
N
N
F3C
3d
1.04 1.96 1.98 0.95 1.00 4.23 1.08 1.02
1.00
13 12 11 10 9 8 7 6 5 4 3 2 1 0
Chemical Shift (ppm)
CHLOROFORM-d
7.75
7.73
7.72
7.71
7.69
7.62
7.55
7.54
7.33
7.32
7.30
7.29
7.27
7.27
7.17
7.15
7.14
6.81
6.80
6.79
1.98 0.95 1.00
4.23
1.08
1.02
7.75 7.50 7.25 7.00 6.75
Chemical Shift (ppm)

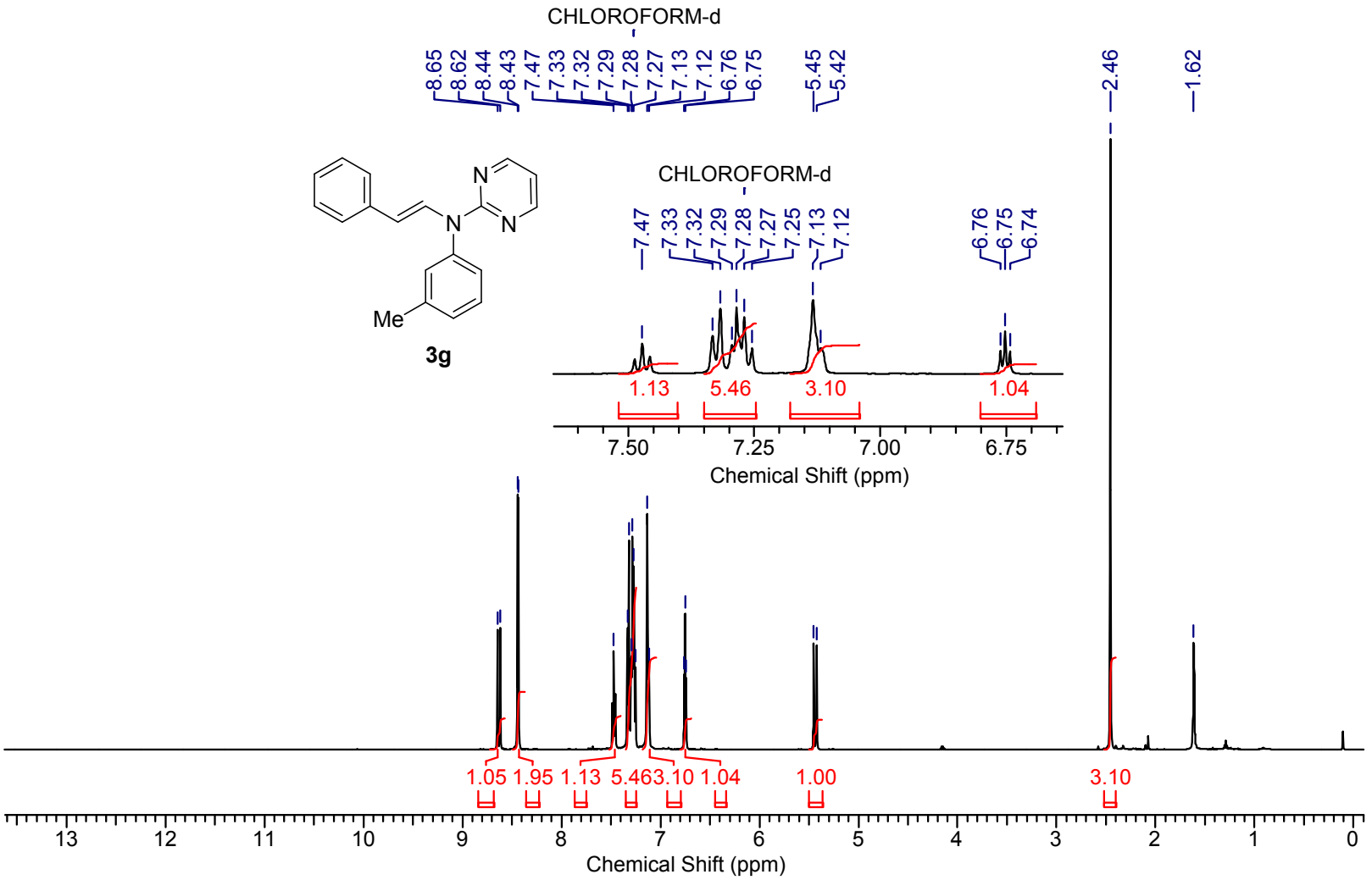

CHLOROFORM-d
159.58
157.90
140.72
137.11
133.08
130.46
130.22
128.55
126.68
126.65
125.91
125.31
124.68
122.64
113.56
111.41
77.25
77.00
76.74
N
N
N
F3C
3d
Chemical Shift (ppm)
Chemical Shift (ppm)

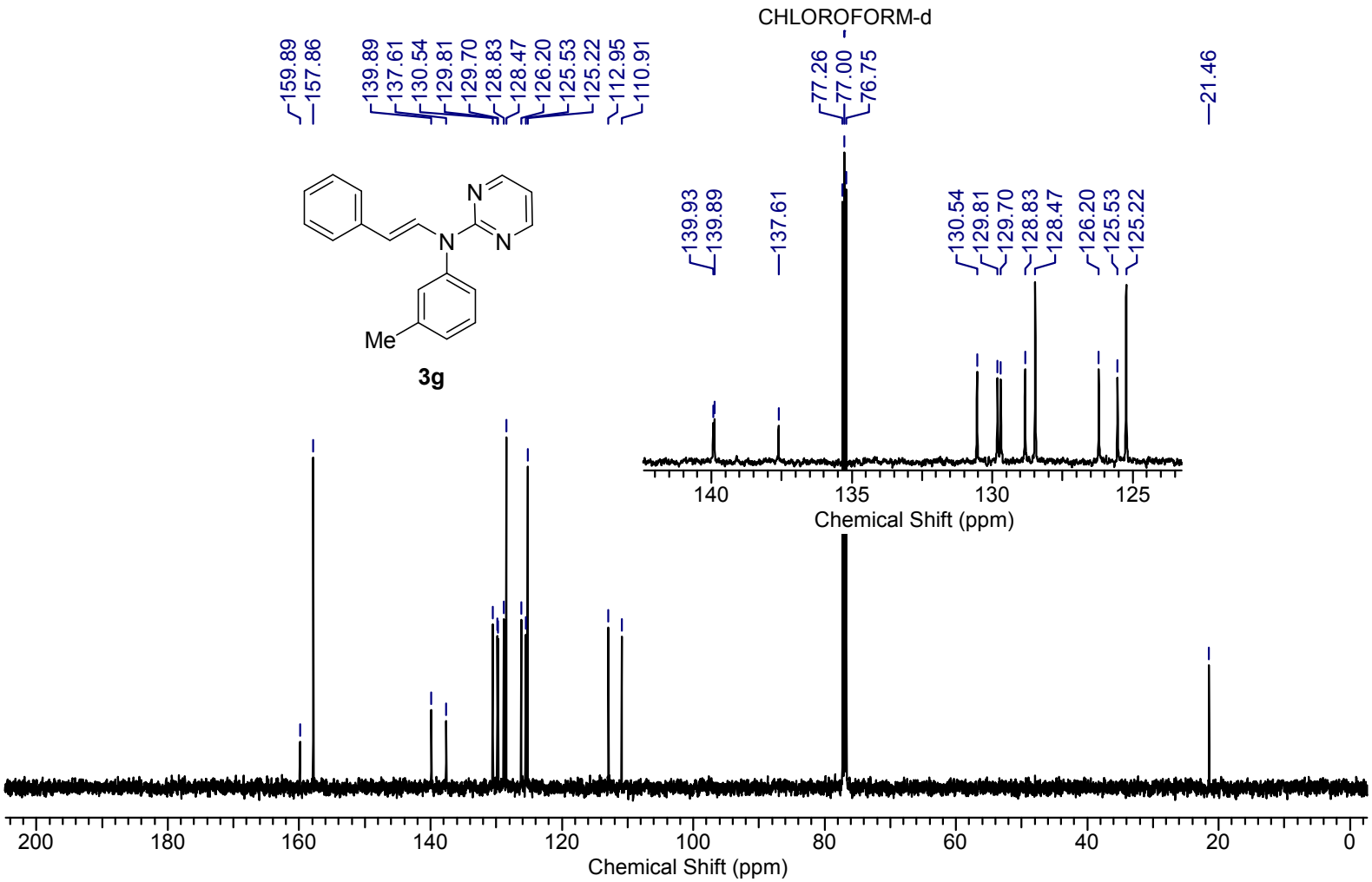

CHLOROFORM-d
8.61
8.58
8.45
8.44
7.55
7.54
7.34
7.32
7.30
7.29
7.27
7.15
7.13
6.78
6.77
5.50
5.47
N
N
N
F
3e
CHLOROFORM-d
7.55
7.54
7.53
7.34
7.32
7.30
7.29
7.27
7.19
7.19
7.17
7.16
7.15
7.13
7.09
7.07
6.79
6.78
6.77
1.07
4.14
3.31
1.20
1.16
7.50
7.25
7.00
6.75
Chemical Shift (ppm)
1.05
2.03
1.07
4.14
3.31
1.20
1.16
1.00
14
13
12
11
10
9
8
7
6
5
4
3
2
1
Chemical Shift (ppm)

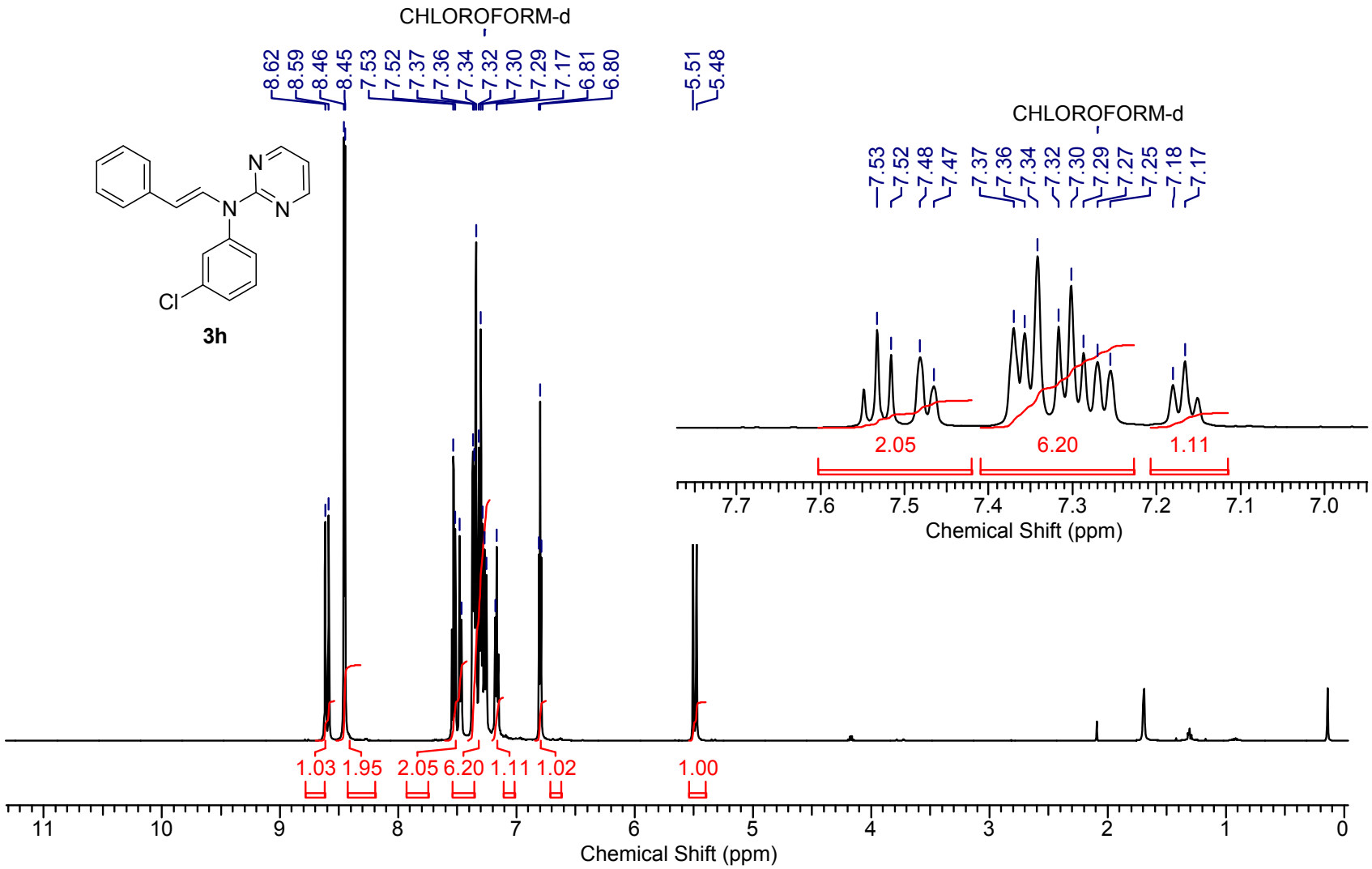

CHLOROFORM-d
164.44
162.47
159.56
157.87
141.60
141.51
137.22
130.98
130.91
130.08
128.50
125.78
125.25
125.17
125.15
116.96
115.15
114.99
113.35
111.29
77.25
77.00
76.74
N
N
N
F
3e
Chemical Shift (ppm)
Chemical Shift (ppm)

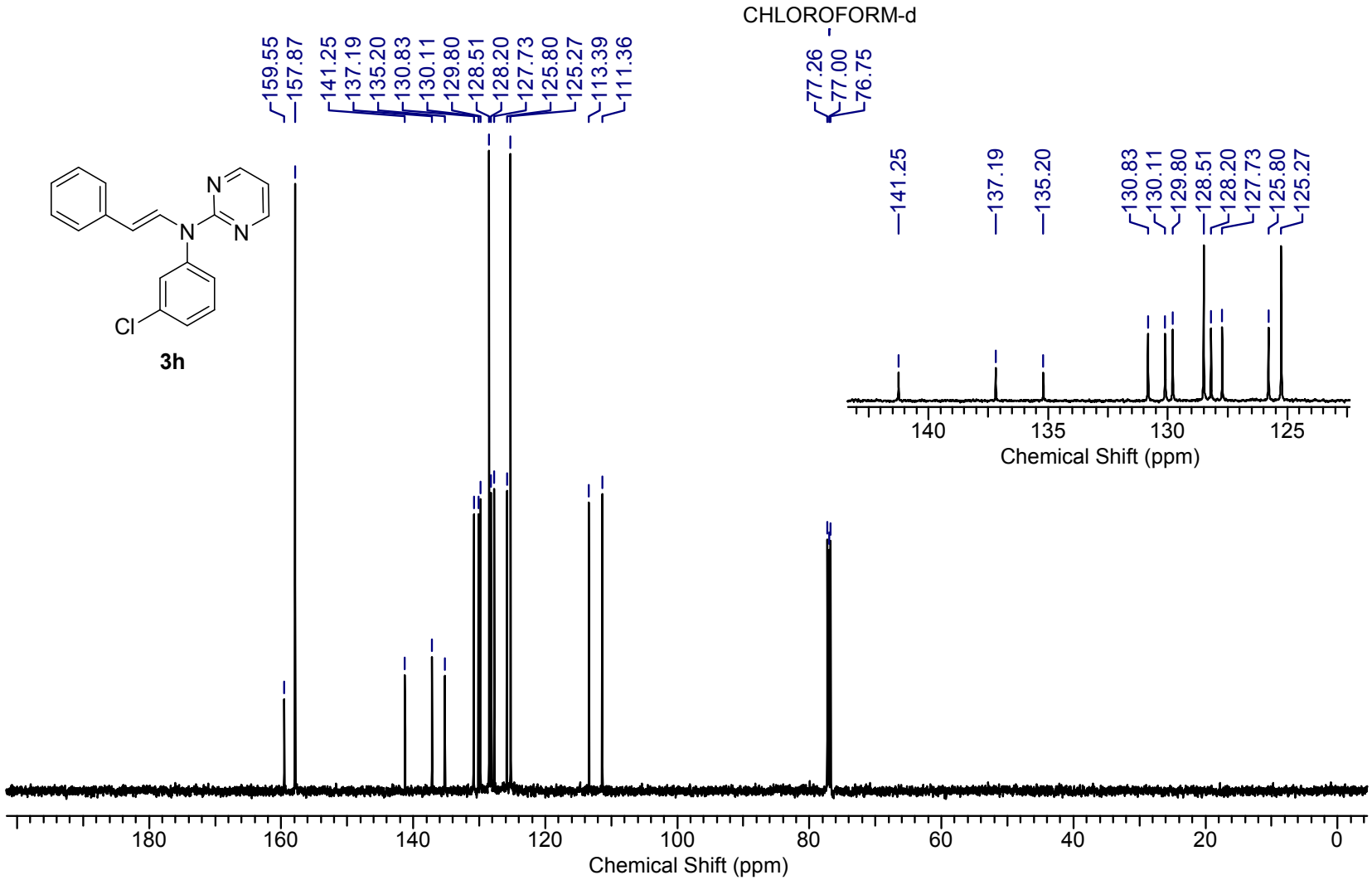

CHLOROFORM-d
8.57
8.54
8.44
8.43
7.75
7.68
7.66
7.32
7.31
7.30
7.29
7.28
7.16
6.83
5.43
5.40
N
N
N
NC
3f
1.03 2.05 0.99 1.98 0.98 4.55 1.23 1.06
1.00
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
Chemical Shift (ppm)
CHLOROFORM-d
7.76
7.75
7.70
7.68
7.67
7.66
7.61
7.59
7.32
7.31
7.30
7.29
7.28
7.27
7.17
7.16
0.99 1.98 0.98
4.55
1.23
7.75
7.50
7.25
Chemical Shift (ppm)

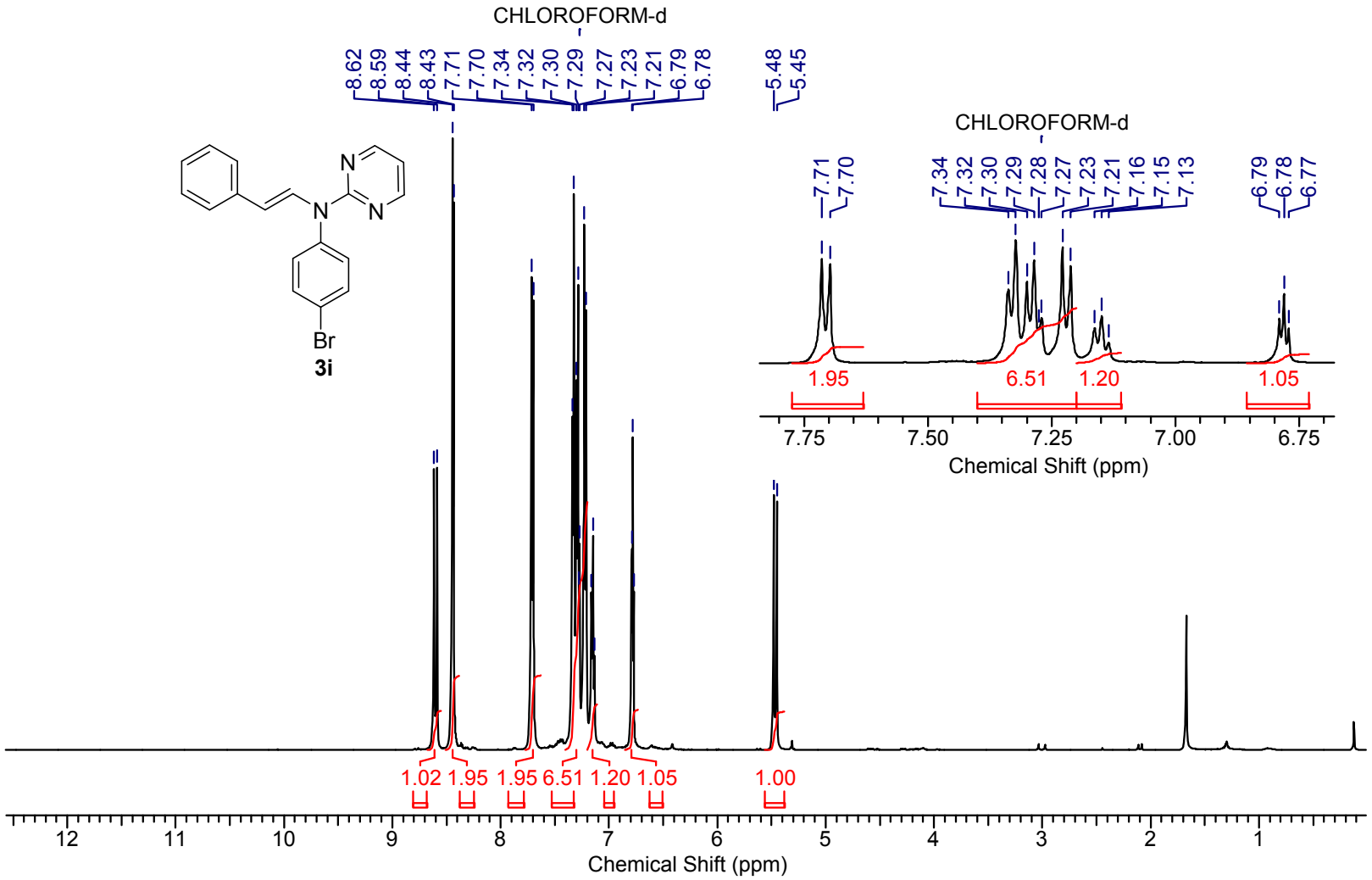

CHLOROFORM-d
159.38
157.93
141.13
136.82
134.49
133.43
131.40
130.86
130.01
128.57
126.07
125.31
118.05
114.13
113.80
111.72
77.25
77.00
76.74
N
N
N
NC
3f
Chemical Shift (ppm)
Chemical Shift (ppm)

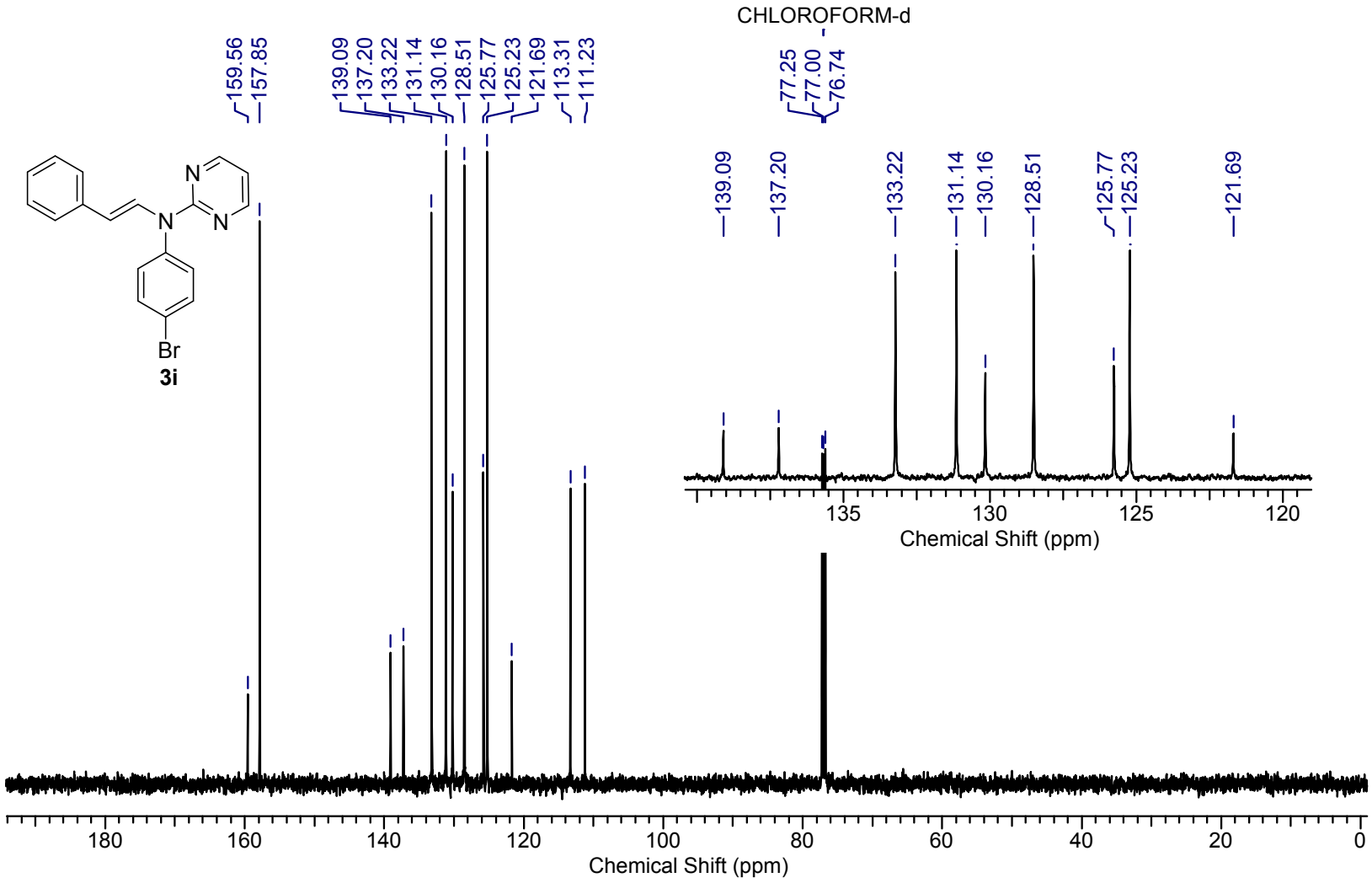

CHLOROFORM-d
8.65
8.62
8.44
8.43
7.47
7.33
7.32
7.29
7.28
7.27
7.13
7.12
6.76
6.75
5.45
5.42
2.46
1.62
N
N
N
Me
3g
CHLOROFORM-d
7.47
7.33
7.32
7.29
7.28
7.27
7.25
7.13
7.12
6.76
6.75
6.74
1.13
5.46
3.10
1.04
7.50
7.25
7.00
6.75
Chemical Shift (ppm)
1.05
1.95
1.13
5.46
3.10
1.04
1.00
3.10
13
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

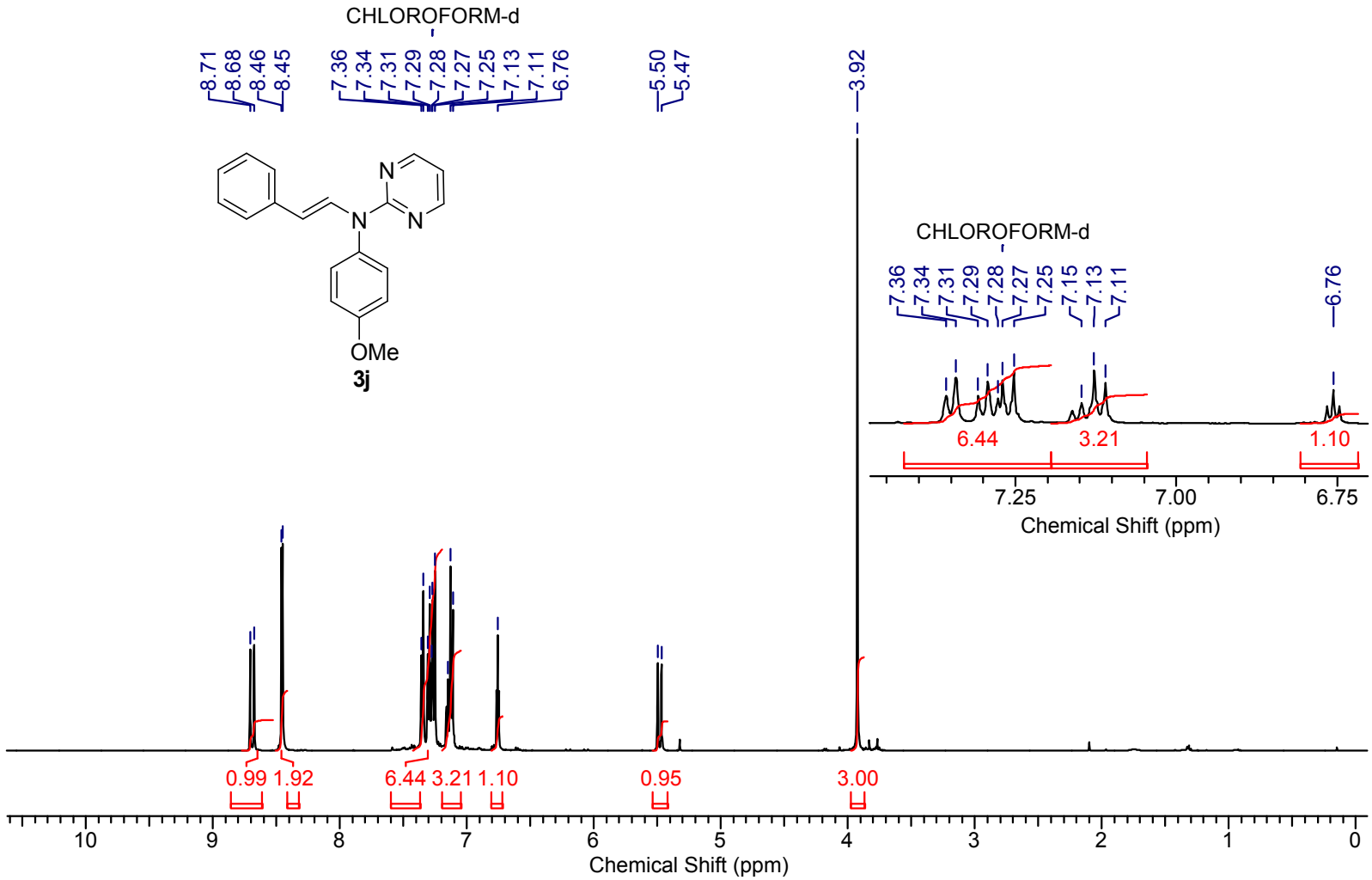

CHLOROFORM-d
159.89
157.86
139.89
137.61
130.54
129.81
129.70
128.83
128.47
126.20
125.53
125.22
112.95
110.91
77.26
77.00
76.75
21.46
N
N
N
Me
3g
139.93
139.89
137.61
130.54
129.81
129.70
128.83
128.47
126.20
125.53
125.22
140
135
130
125
Chemical Shift (ppm)
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

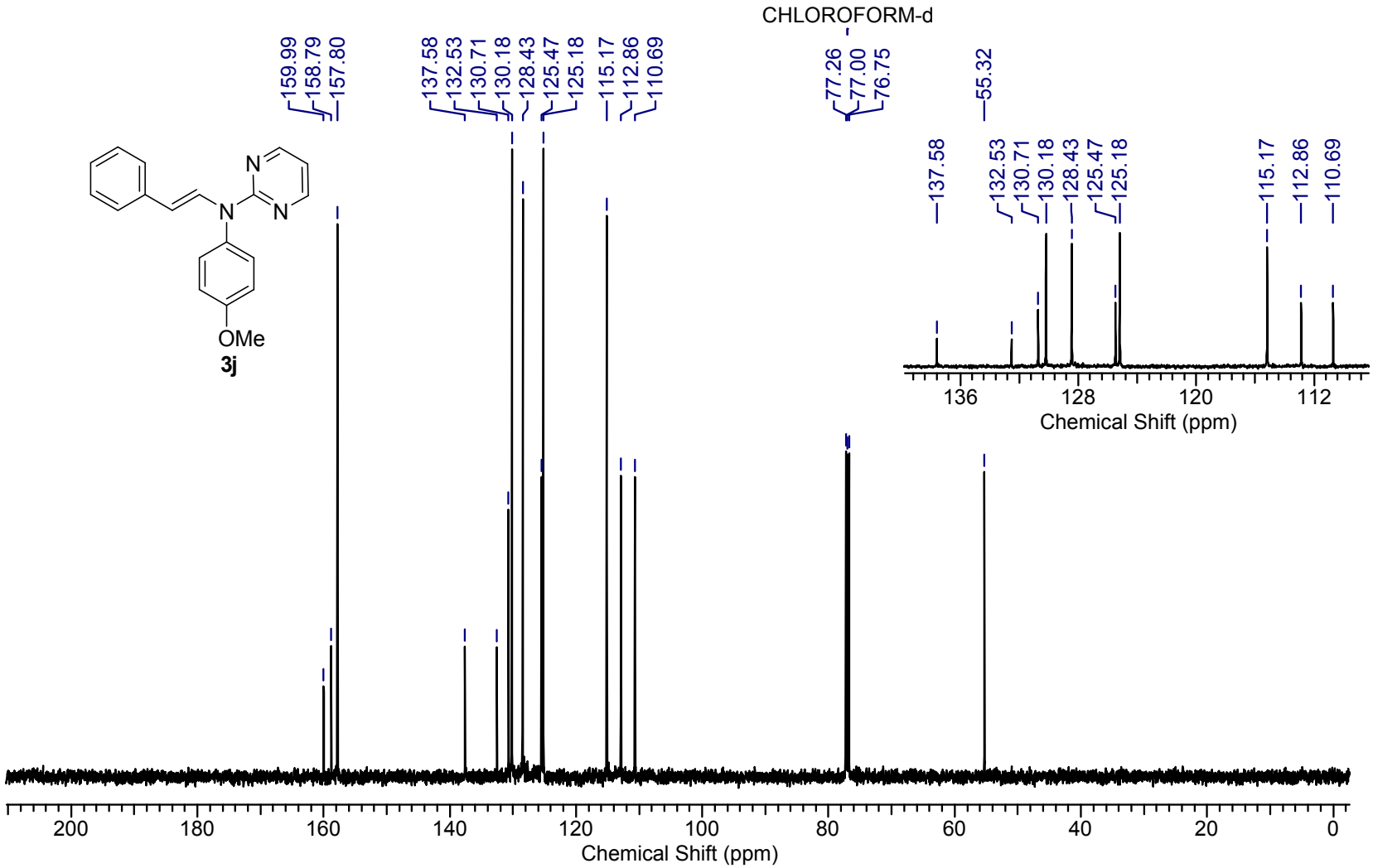

CHLOROFORM-d
8.62
8.59
8.46
8.45
7.53
7.52
7.37
7.36
7.34
7.32
7.30
7.29
7.17
6.81
6.80
5.51
5.48
N
N
N
Cl
3h
1.03
1.95
2.05
6.20
1.11
1.02
1.00
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)
CHLOROFORM-d
7.53
7.52
7.48
7.47
7.37
7.36
7.34
7.32
7.30
7.29
7.27
7.25
7.18
7.17
2.05
6.20
1.11
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
Chemical Shift (ppm)

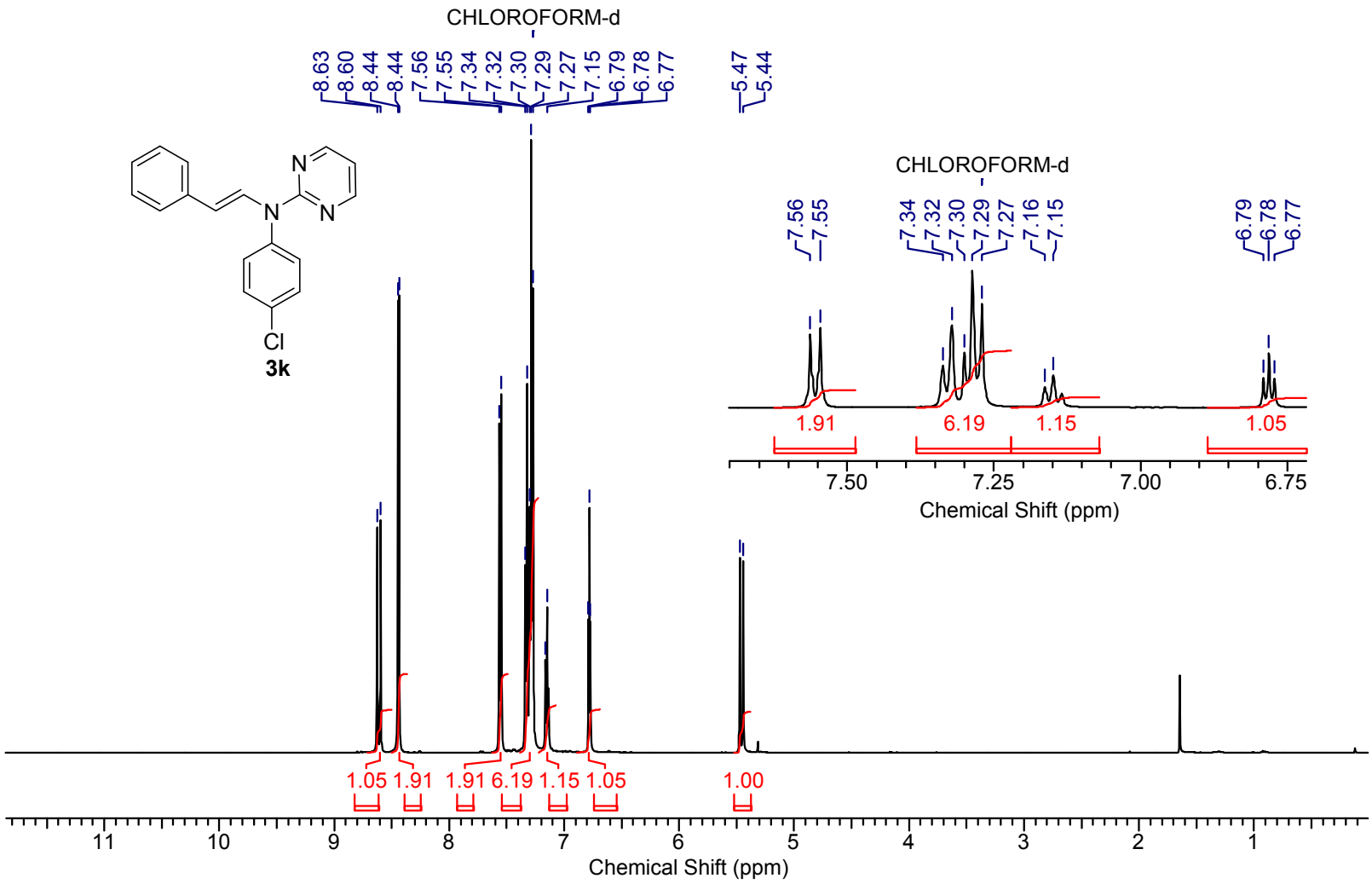

CHLOROFORM-d
159.55
157.87
141.25
137.19
135.20
130.83
130.11
129.80
128.51
128.20
127.73
125.80
125.27
113.39
111.36
77.26
77.00
76.75
N
N
N
Cl
3h
Chemical Shift (ppm)
Chemical Shift (ppm)

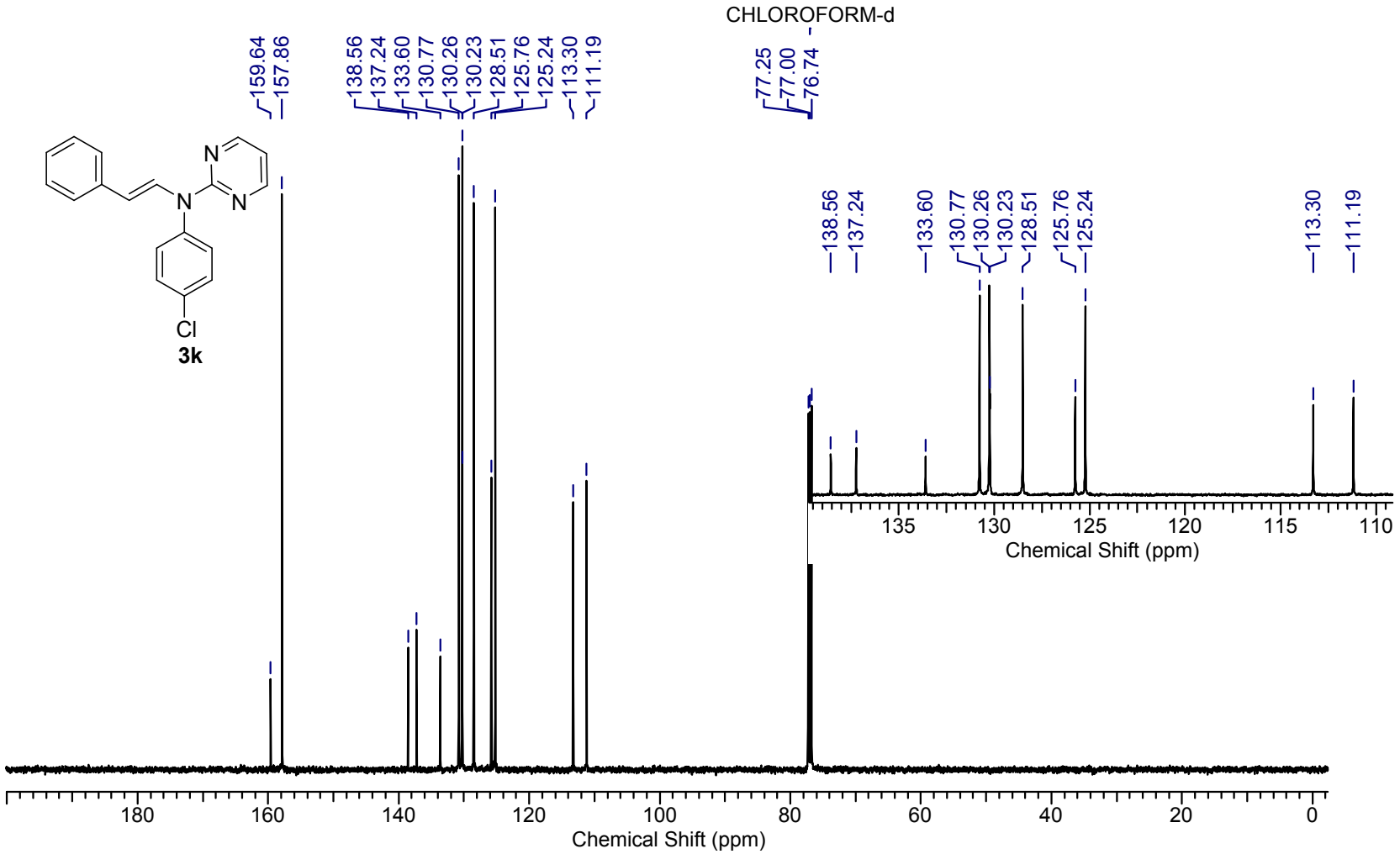

CHLOROFORM-d
8.62
8.59
8.44
8.43
7.71
7.70
7.34
7.32
7.30
7.29
7.27
7.23
7.21
6.79
6.78
5.48
5.45
N
N
N
Br
3i
1.02
1.95
1.95
6.51
1.20
1.05
1.00
12
11
10
9
8
7
6
5
4
3
2
1
Chemical Shift (ppm)
CHLOROFORM-d
7.71
7.70
7.34
7.32
7.30
7.29
7.28
7.27
7.23
7.21
7.16
7.15
7.13
6.79
6.78
6.77
1.95
6.51
1.20
1.05
7.75
7.50
7.25
7.00
6.75
Chemical Shift (ppm)

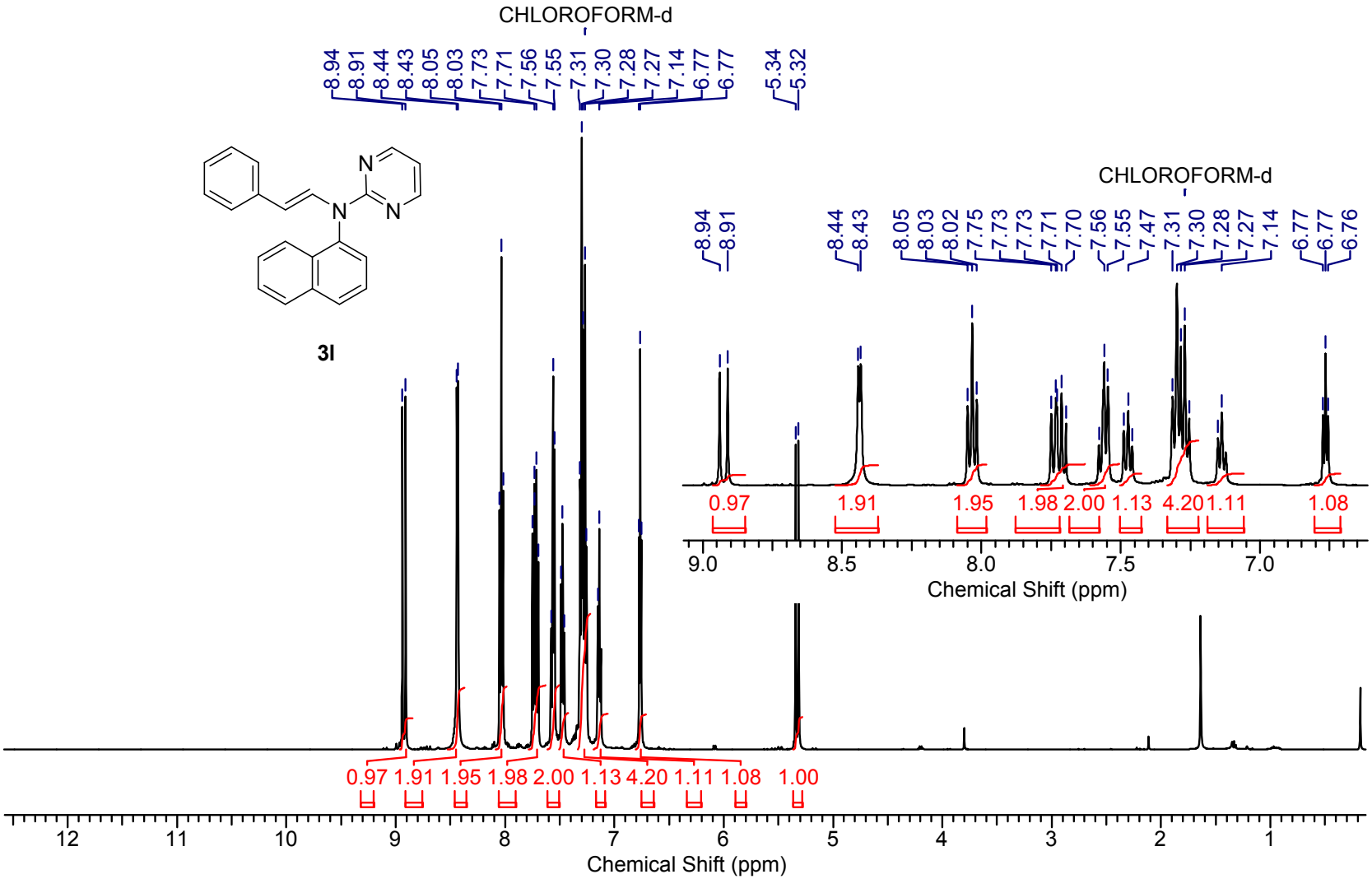

CHLOROFORM-d
159.56
157.85
139.09
137.20
133.22
131.14
130.16
128.51
125.77
125.23
121.69
113.31
111.23
77.25
77.00
76.74
N
N
N
Br
3i
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)
135
130
125
120
Chemical Shift (ppm)

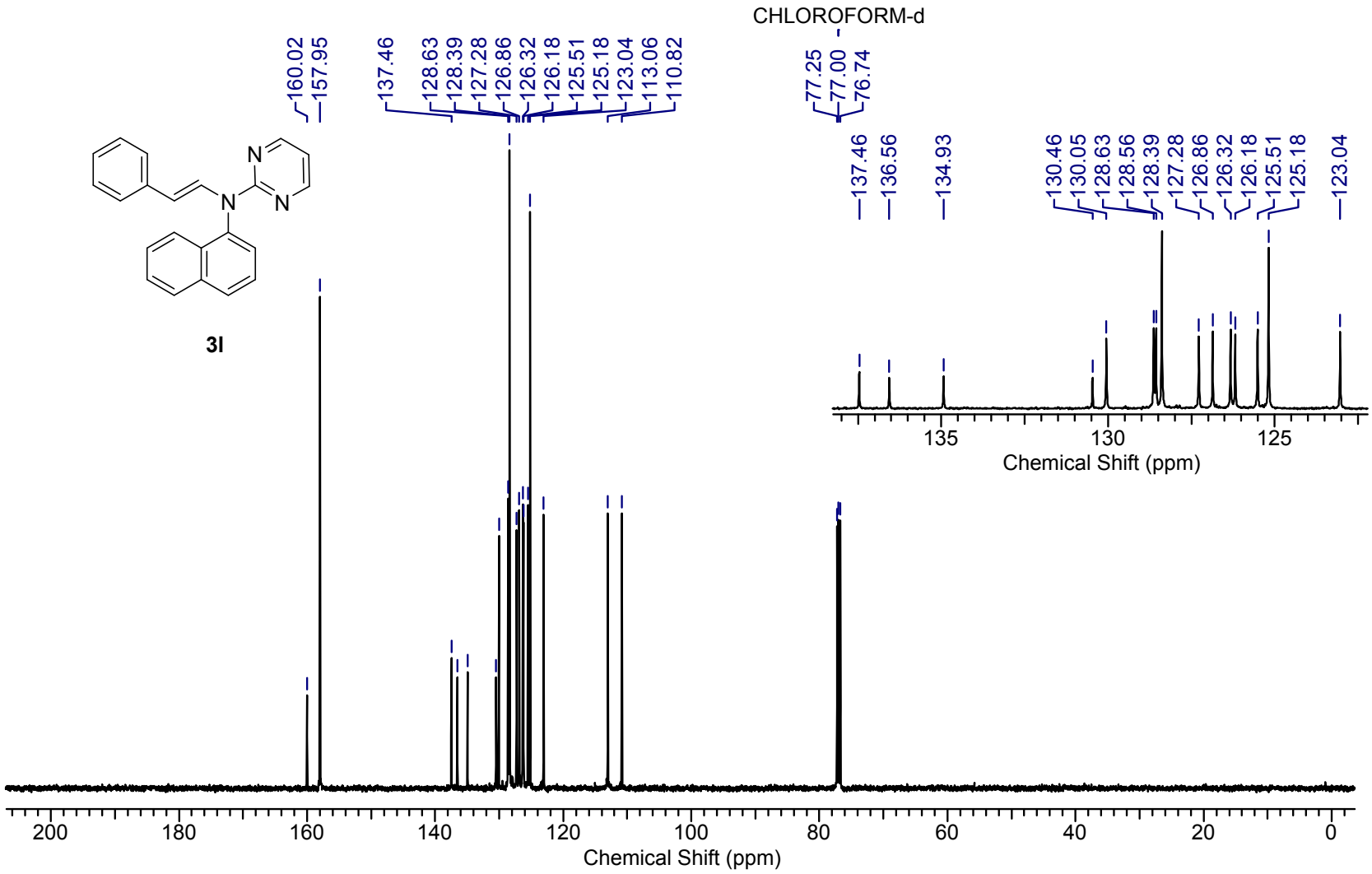

CHLOROFORM-d
8.71
8.68
8.46
8.45
7.36
7.34
7.31
7.29
7.28
7.27
7.25
7.13
7.11
6.76
5.50
5.47
3.92
N
N
N
OMe
3j
CHLOROFORM-d
7.36
7.34
7.31
7.29
7.28
7.27
7.25
7.15
7.13
7.11
6.76
6.44
3.21
1.10
7.25
7.00
6.75
Chemical Shift (ppm)
0.99
1.92
6.44
3.21
1.10
0.95
3.00
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

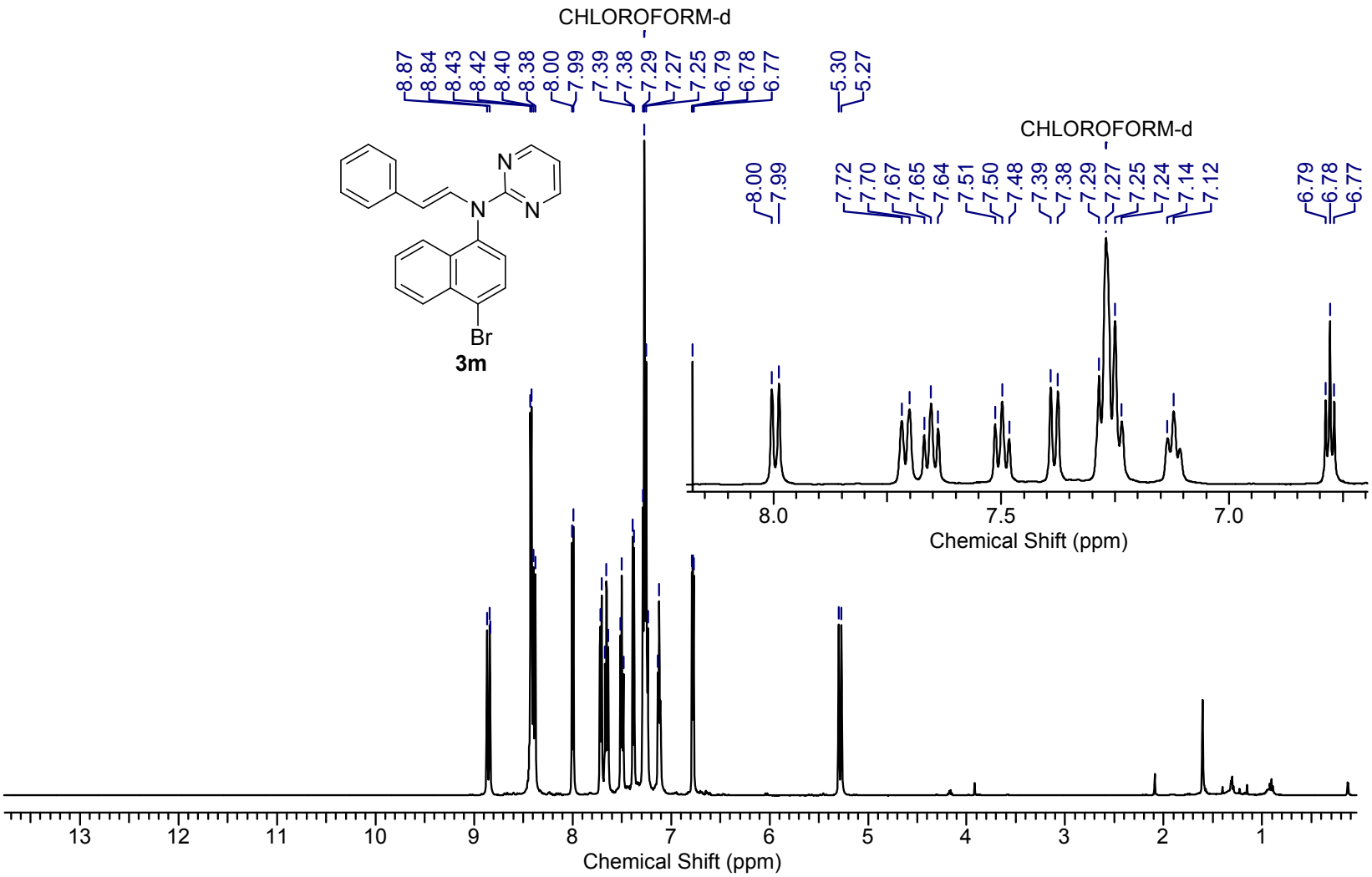

CHLOROFORM-d
159.99
158.79
157.80
137.58
132.53
130.71
130.18
128.43
125.47
125.18
115.17
112.86
110.69
77.26
77.00
76.75
55.32
N
N
N
OMe
3j
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)
136
128
120
112
Chemical Shift (ppm)

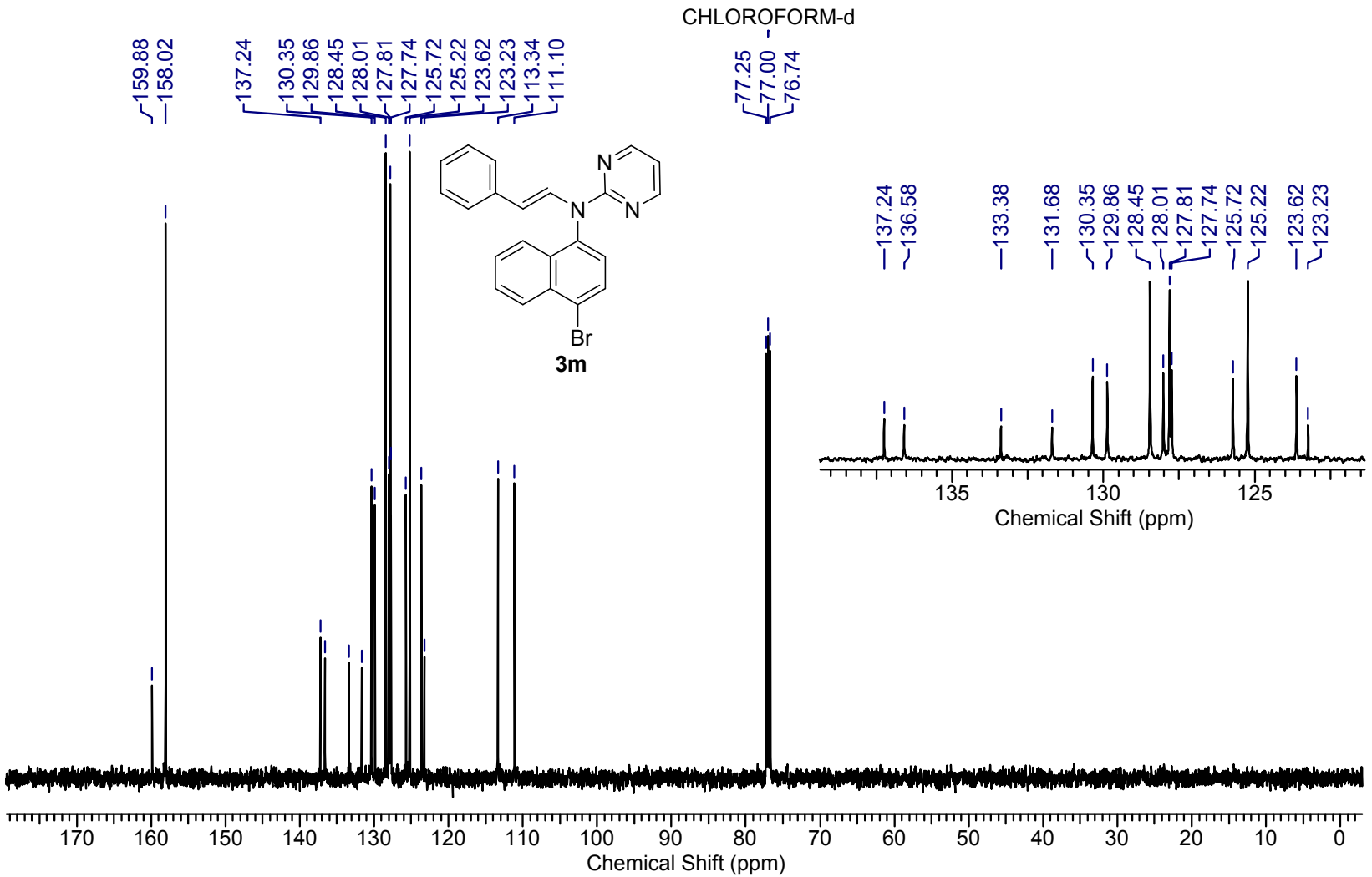

CHLOROFORM-d
8.63
8.60
8.44
8.44
7.56
7.55
7.34
7.32
7.30
7.29
7.27
7.15
6.79
6.78
6.77
5.47
5.44
N
N
N
Cl
3k
CHLOROFORM-d
7.56
7.55
7.34
7.32
7.30
7.29
7.27
7.16
7.15
6.79
6.78
6.77
1.91
6.19
1.15
1.05
7.50
7.25
7.00
6.75
Chemical Shift (ppm)
1.05
1.91
1.91
6.19
1.15
1.05
1.00
11
10
9
8
7
6
5
4
3
2
1
Chemical Shift (ppm)

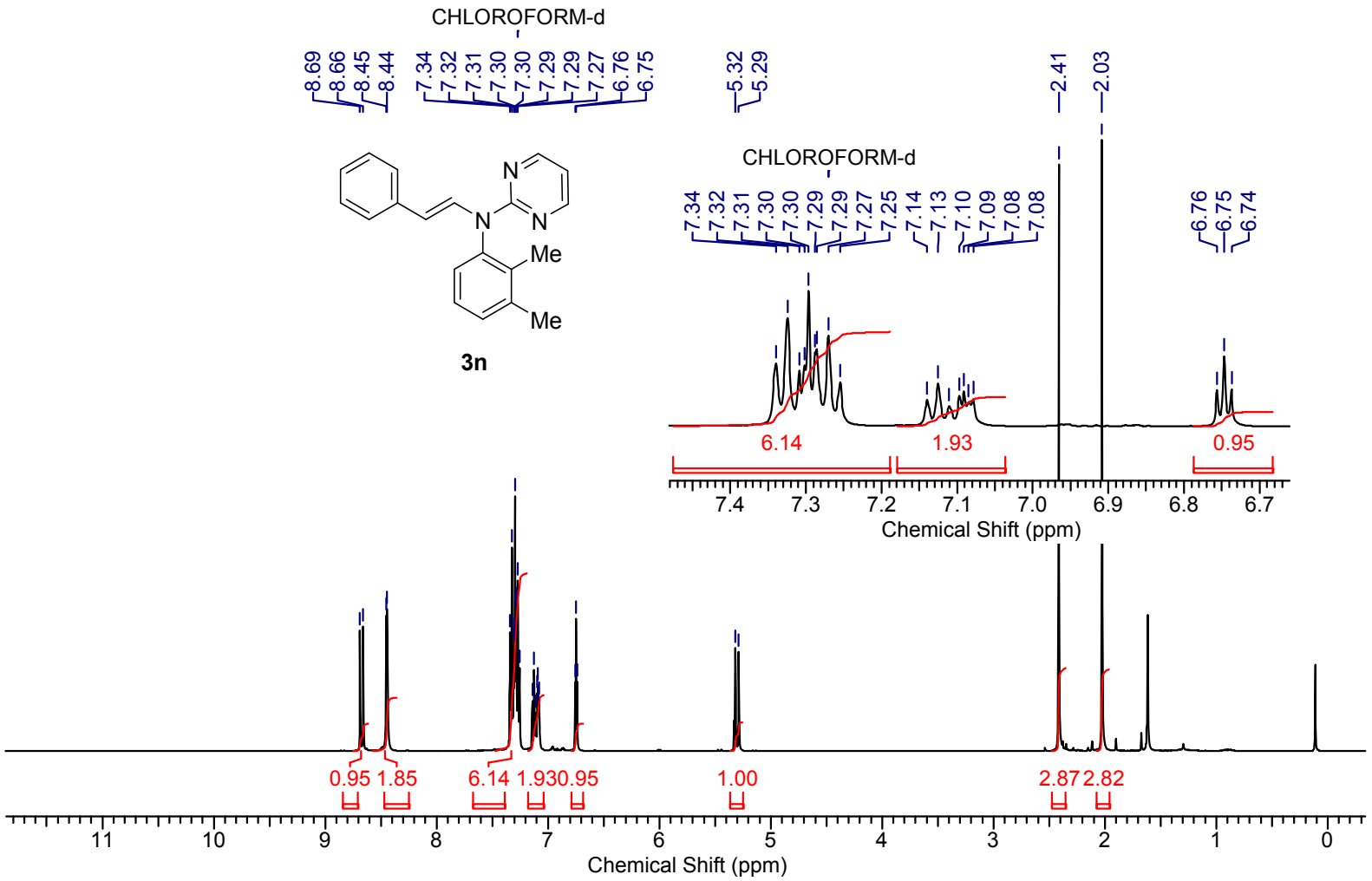

CHLOROFORM-d
159.64
157.86
138.56
137.24
133.60
130.77
130.26
130.23
128.51
125.76
125.24
113.30
111.19
77.25
77.00
76.74
N
N
N
Cl
3k
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)
135
130
125
120
115
110
Chemical Shift (ppm)

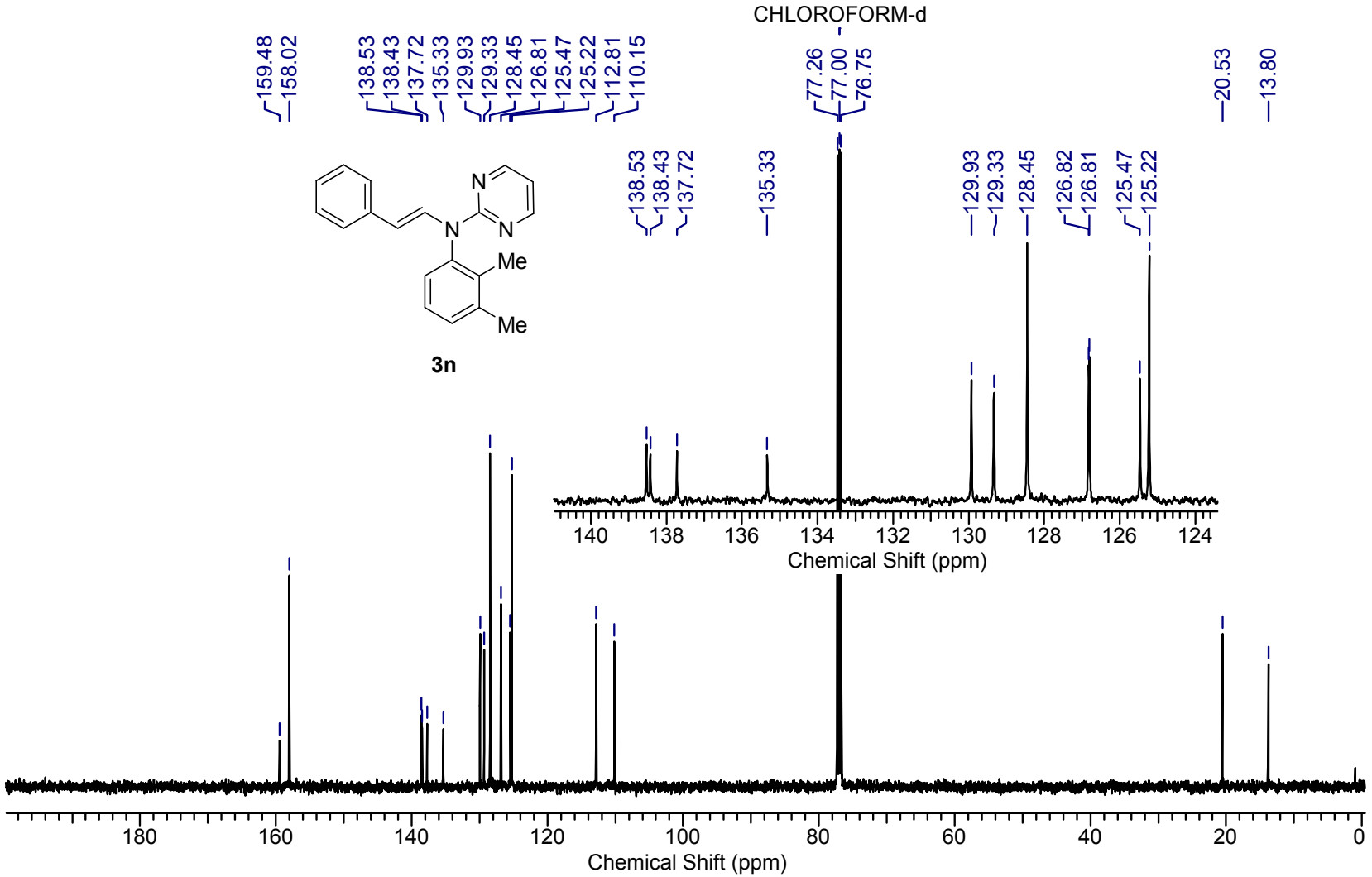

CHLOROFORM-d
8.94
8.91
8.44
8.43
8.05
8.03
7.73
7.71
7.56
7.55
7.31
7.30
7.28
7.27
7.14
6.77
6.77
5.34
5.32
N
N
N
3l
0.97 1.91 1.95 1.98 2.00 1.13 4.20 1.11 1.08 1.00
12 11 10 9 8 7 6 5 4 3 2 1
Chemical Shift (ppm)
CHLOROFORM-d
8.94
8.91
8.44
8.43
8.05
8.03
8.02
7.75
7.73
7.73
7.71
7.70
7.56
7.55
7.47
7.31
7.30
7.28
7.27
7.14
6.77
6.77
6.76
0.97 1.91 1.95 1.98 2.00 1.13 4.20 1.11 1.08
9.0 8.5 8.0 7.5 7.0
Chemical Shift (ppm)

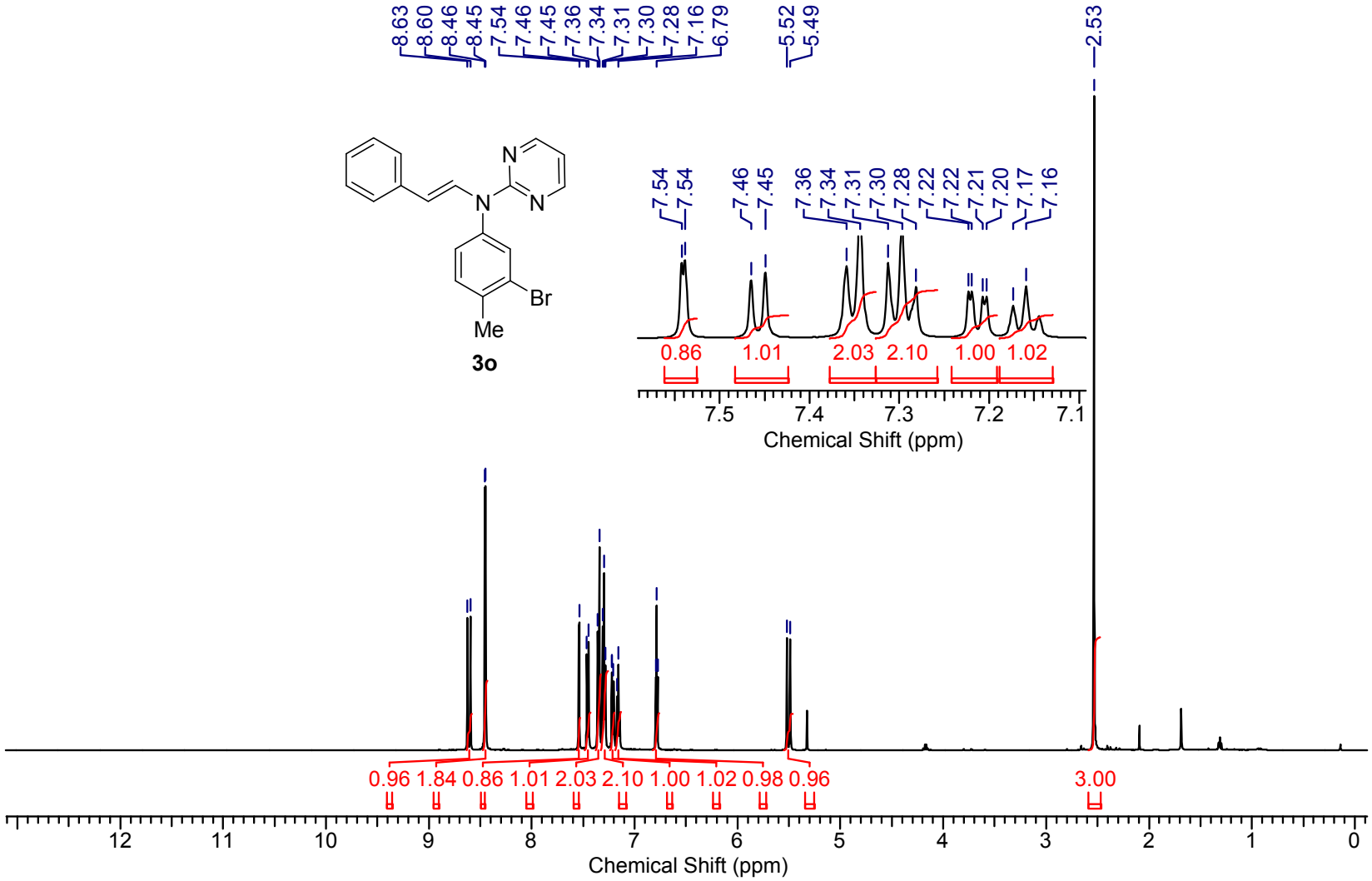

CHLOROFORM-d
160.02
157.95
137.46
128.63
128.39
127.28
126.86
126.32
126.18
125.51
125.18
123.04
113.06
110.82
77.25
77.00
76.74
N
N
N
3l
137.46
136.56
134.93
130.46
130.05
128.63
128.56
128.39
127.28
126.86
126.32
126.18
125.51
125.18
123.04
135
130
125
Chemical Shift (ppm)
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

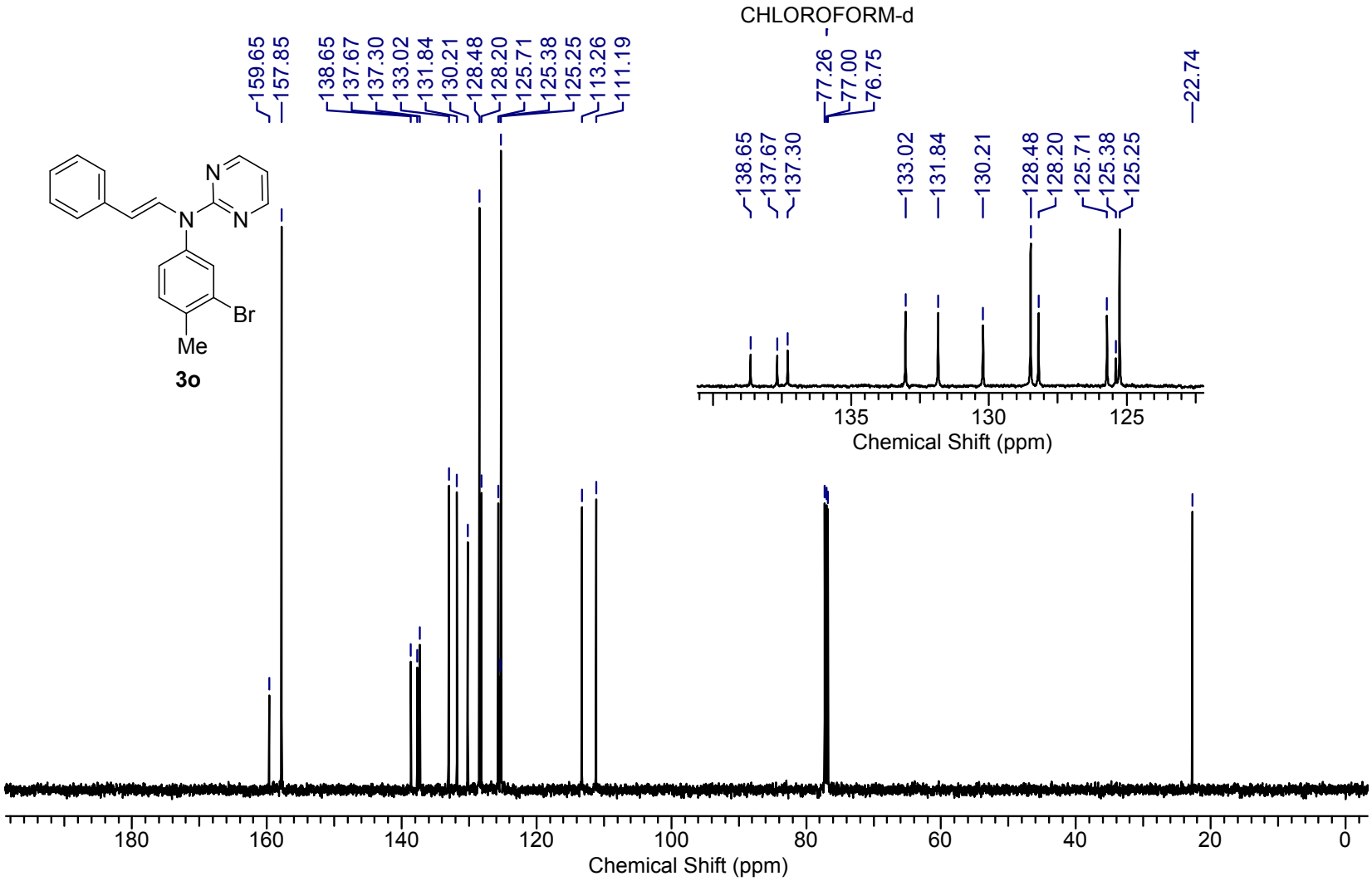

CHLOROFORM-d
8.87
8.84
8.43
8.42
8.40
8.38
8.00
7.99
7.39
7.38
7.29
7.27
7.25
6.79
6.78
6.77
5.30
5.27
N
N
N
Br
3m
CHLOROFORM-d
8.00
7.99
7.72
7.70
7.67
7.65
7.64
7.51
7.50
7.48
7.39
7.38
7.29
7.27
7.25
7.24
7.14
7.12
6.79
6.78
6.77
8.0
7.5
7.0
Chemical Shift (ppm)
13
12
11
10
9
8
7
6
5
4
3
2
1
Chemical Shift (ppm)

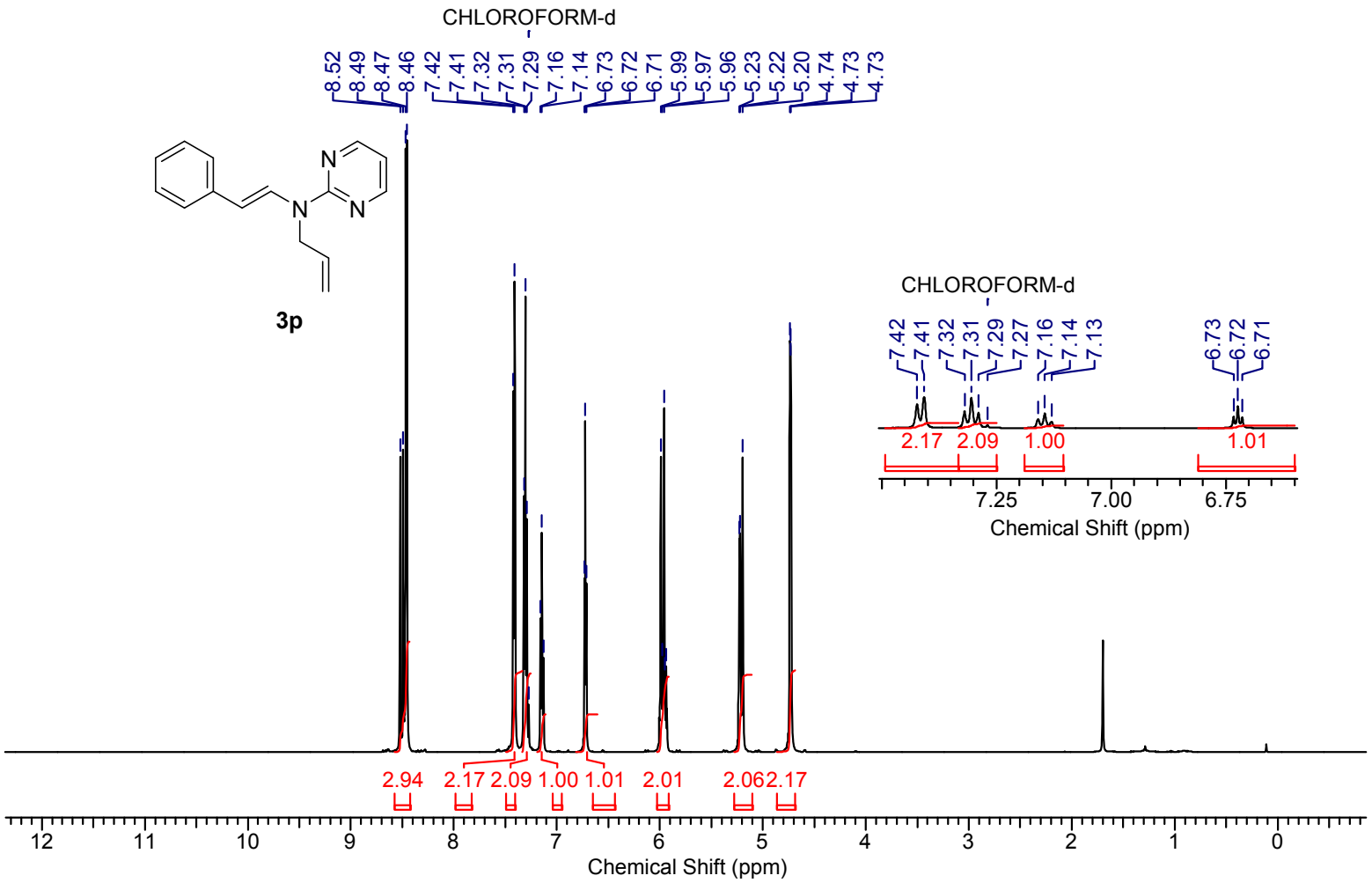

CHLOROFORM-d
159.88
158.02
137.24
130.35
129.86
128.45
128.01
127.81
127.74
125.72
125.22
123.62
123.23
113.34
111.10
77.25
77.00
76.74
N
N
N
Br
3m
137.24
136.58
133.38
131.68
130.35
129.86
128.45
128.01
127.81
127.74
125.72
125.22
123.62
123.23
135
130
125
Chemical Shift (ppm)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)

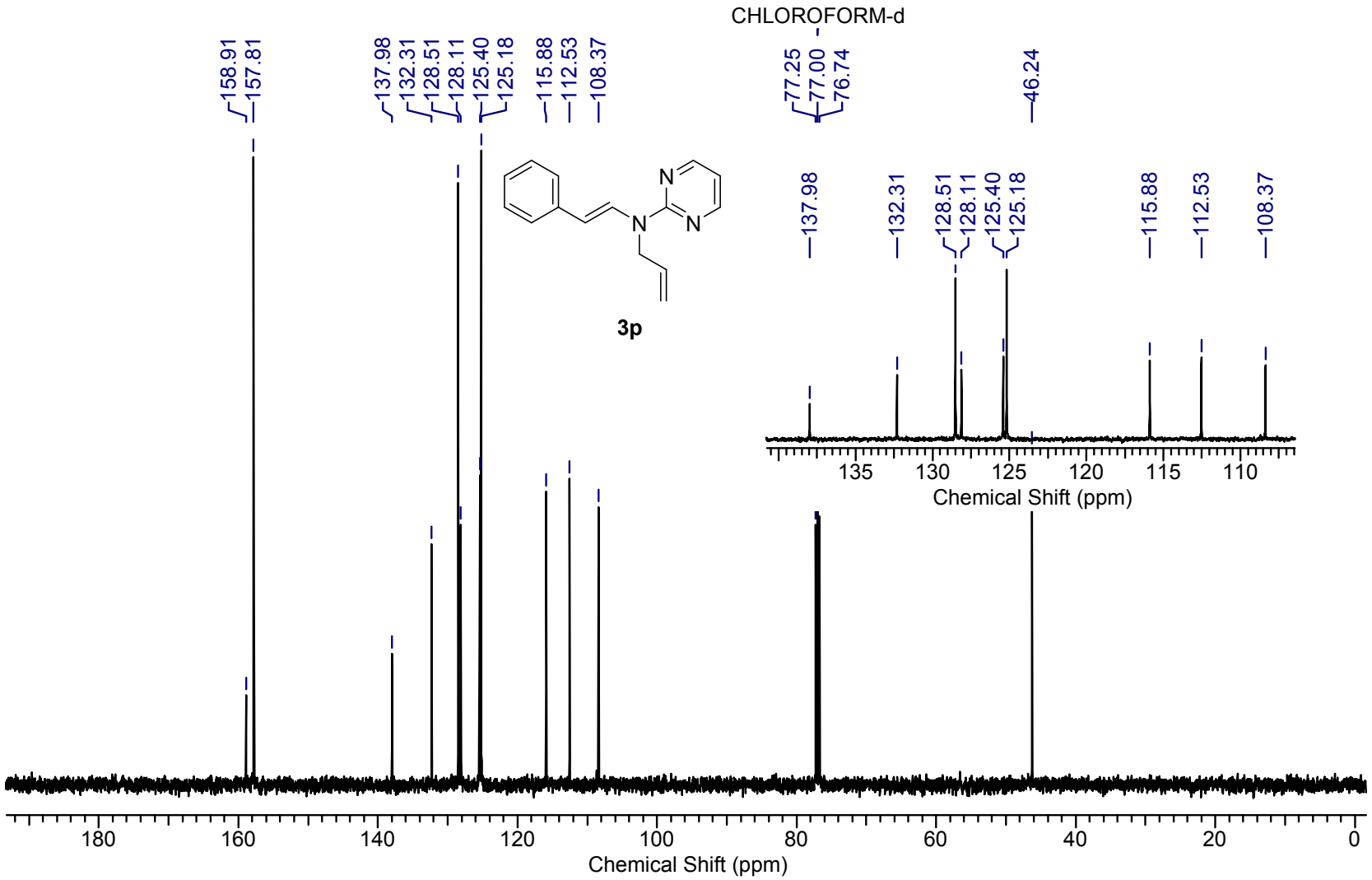

CHLOROFORM-d
8.69
8.66
8.45
8.44
7.34
7.32
7.31
7.30
7.30
7.29
7.29
7.27
6.76
6.75
5.32
5.29
2.41
2.03
N
N
N
Me
Me
3n
CHLOROFORM-d
7.34
7.32
7.31
7.30
7.30
7.29
7.29
7.27
7.25
7.14
7.13
7.10
7.09
7.08
7.08
6.76
6.75
6.74
6.14
1.93
0.95
7.4
7.3
7.2
7.1
7.0
6.9
6.8
6.7
Chemical Shift (ppm)
0.95
1.85
6.14
1.93
0.95
1.00
2.87
2.82
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

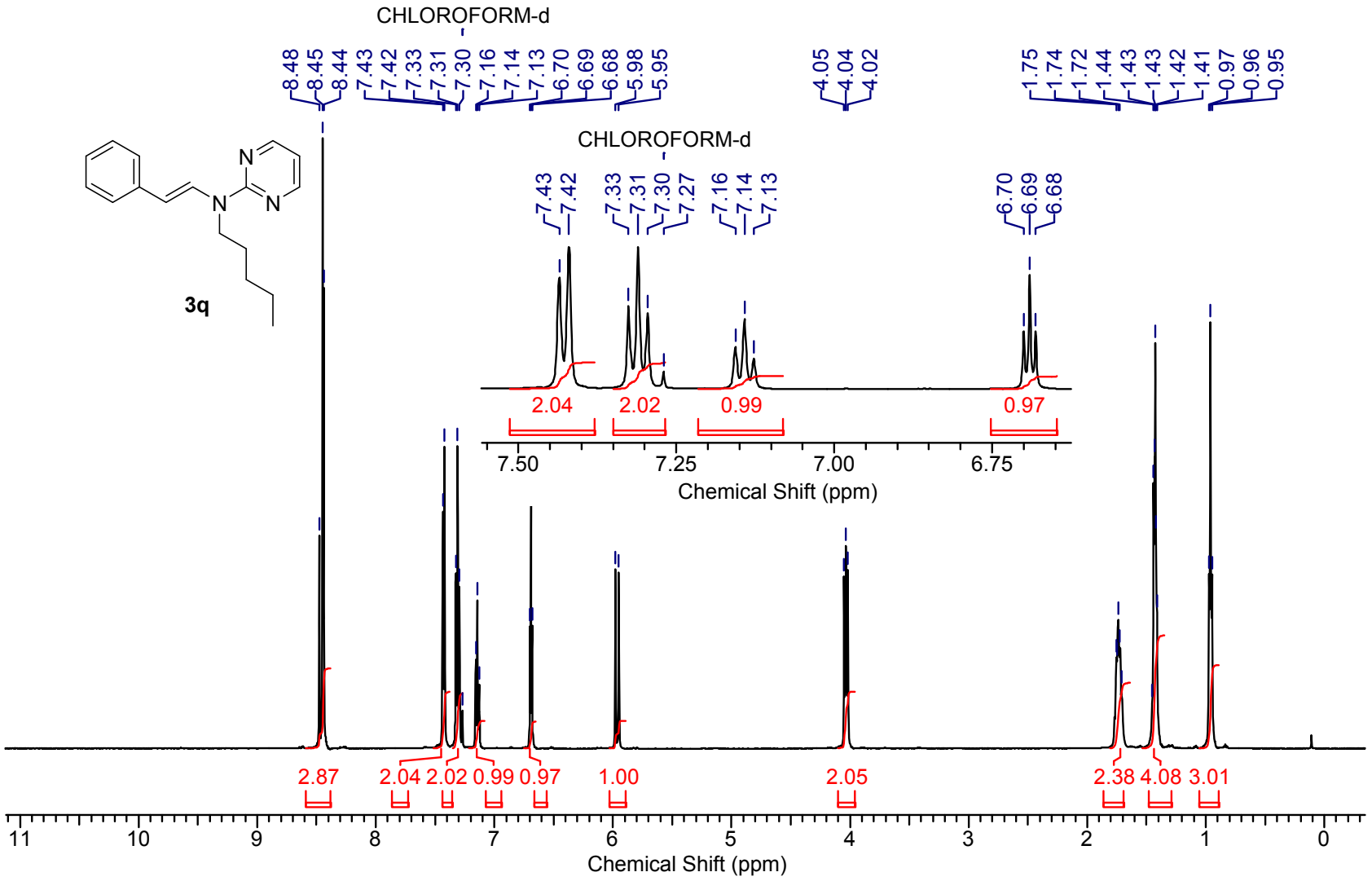

CHLOROFORM-d
159.48
158.02
138.53
138.43
137.72
135.33
129.93
129.33
128.45
126.81
125.47
125.22
112.81
110.15
77.26
77.00
76.75
20.53
13.80
N
N
N
Me
Me
3n
Chemical Shift (ppm)
Chemical Shift (ppm)

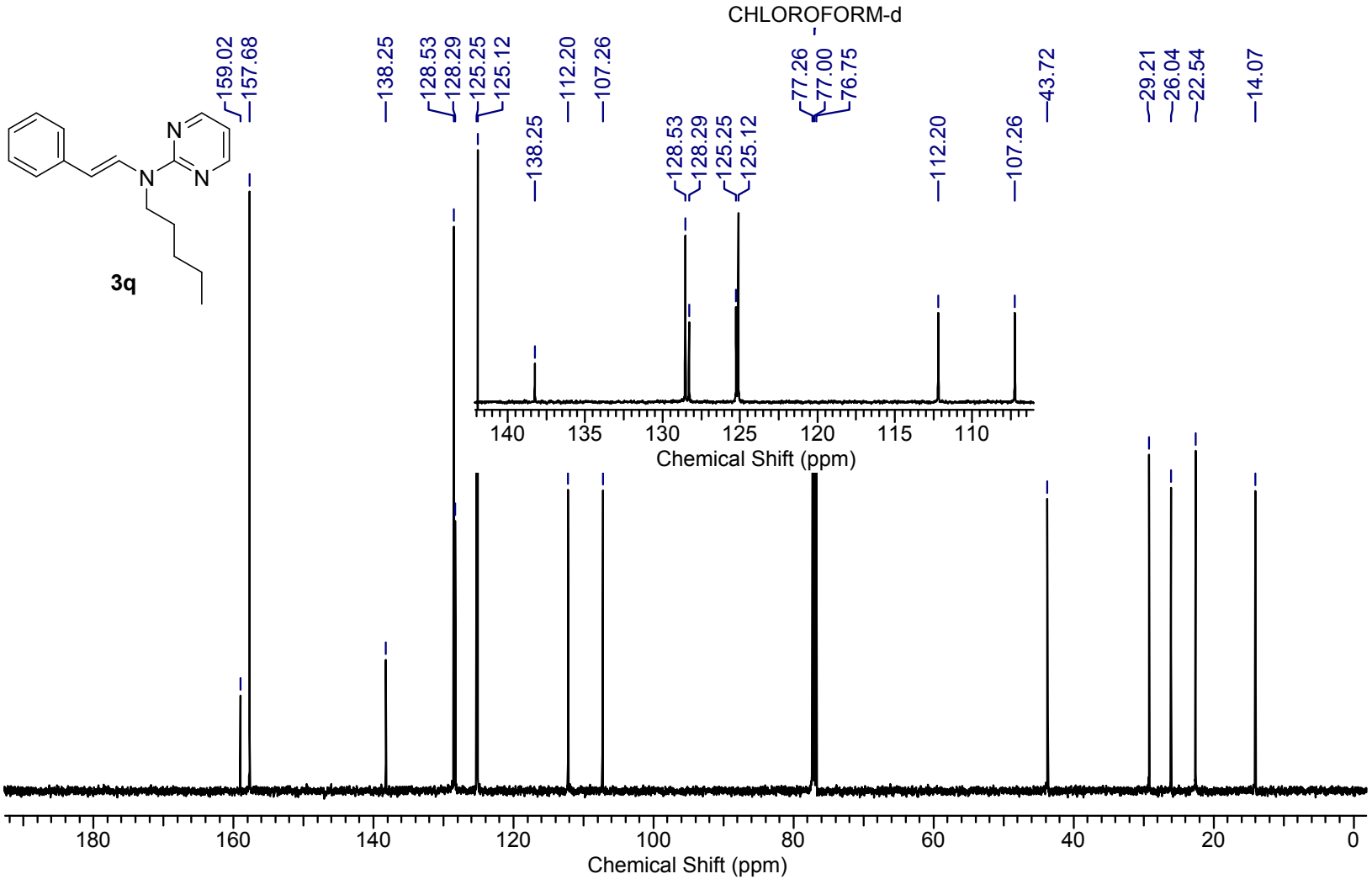

8.63
8.60
8.46
8.45
7.54
7.46
7.45
7.36
7.34
7.31
7.30
7.28
7.16
6.79
5.52
5.49
2.53
N
N
N
Br
Me
3o
7.54
7.54
7.46
7.45
7.36
7.34
7.31
7.30
7.28
7.22
7.22
7.21
7.20
7.17
7.16
0.86
1.01
2.03
2.10
1.00
1.02
7.5
7.4
7.3
7.2
7.1
Chemical Shift (ppm)
0.96 1.84 0.86 1.01 2.03 2.10 1.00 1.02 0.98 0.96
3.00
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

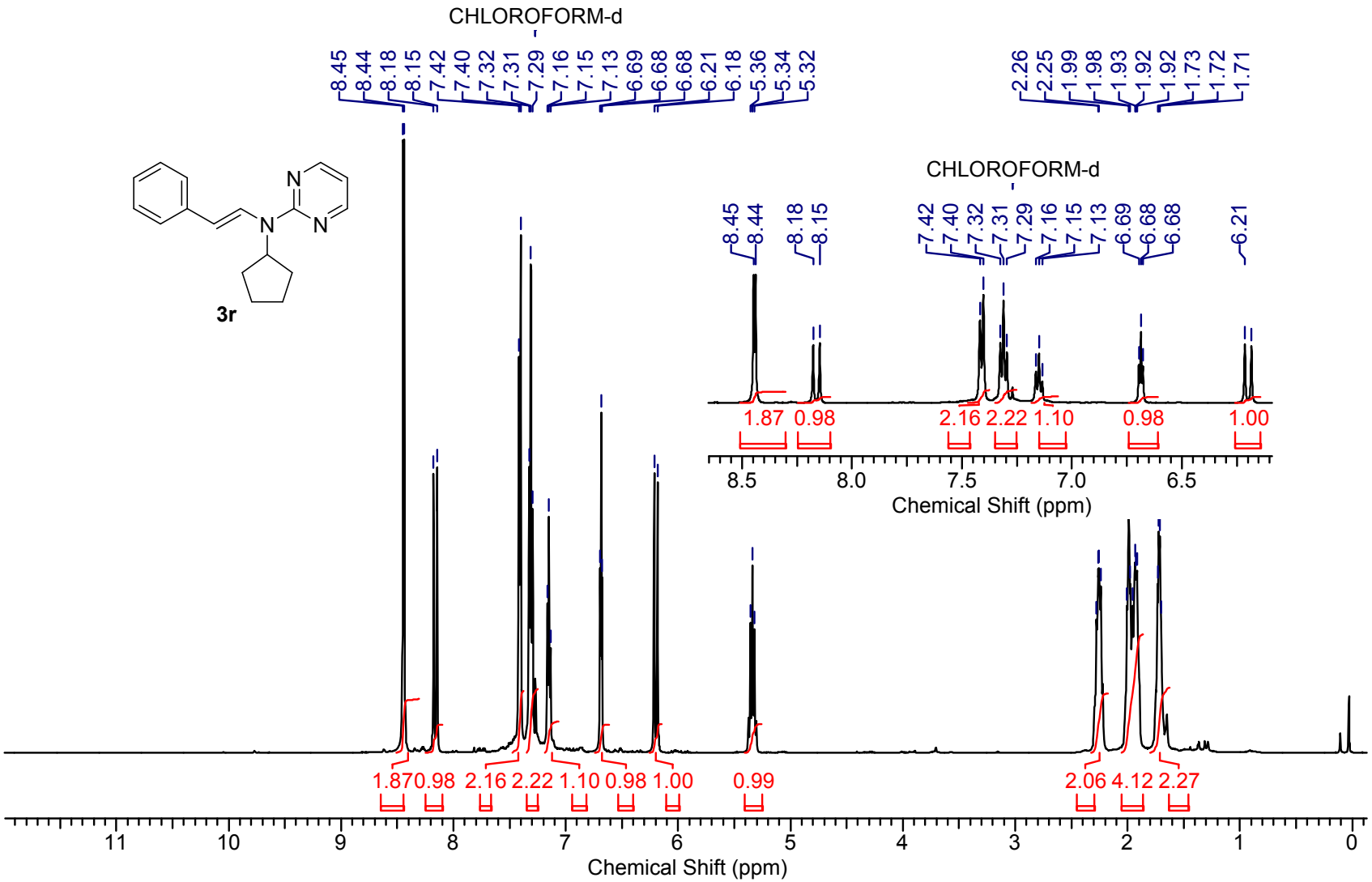

159.65
157.85
138.65
137.67
137.30
133.02
131.84
130.21
128.48
128.20
125.71
125.38
125.25
113.26
111.19
CHLOROFORM-d
77.26
77.00
76.75
22.74
N
N
N
Br
Me
3o
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)
135
130
125
Chemical Shift (ppm)

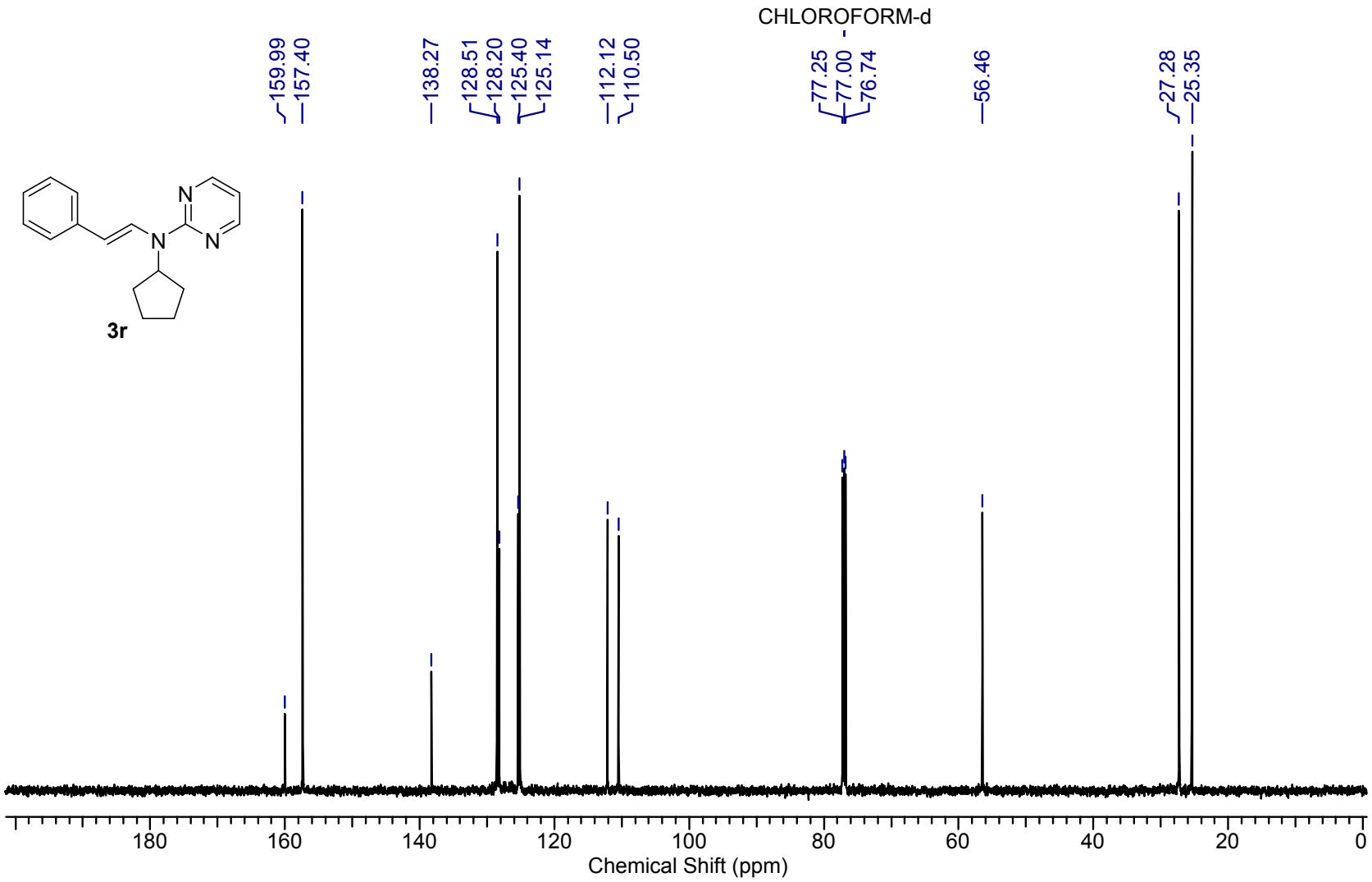

CHLOROFORM-d
8.52
8.49
8.47
8.46
7.42
7.41
7.32
7.31
7.29
7.16
7.14
6.73
6.72
6.71
5.99
5.97
5.96
5.23
5.22
5.20
4.74
4.73
4.73
N
N
N
3p
CHLOROFORM-d
7.42
7.41
7.32
7.31
7.29
7.27
7.16
7.14
7.13
6.73
6.72
6.71
2.17
2.09
1.00
1.01
7.25
7.00
6.75
Chemical Shift (ppm)
2.94
2.17
2.09
1.00
1.01
2.01
2.06
2.17
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

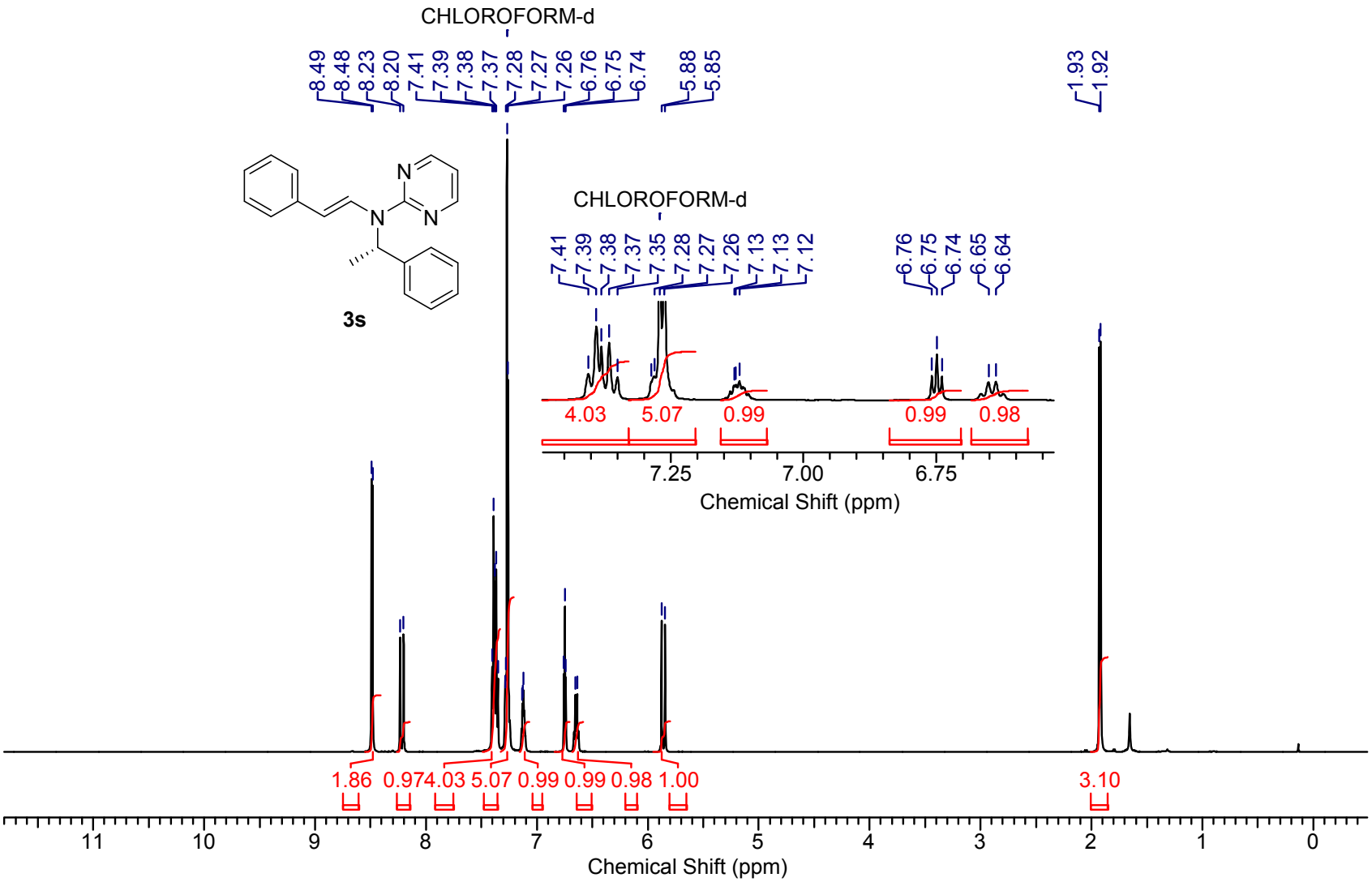

CHLOROFORM-d
158.91
157.81
137.98
132.31
128.51
128.11
125.40
125.18
115.88
112.53
108.37
77.25
77.00
76.74
46.24
N
N
N
3p
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)
135
130
125
120
115
110
Chemical Shift (ppm)

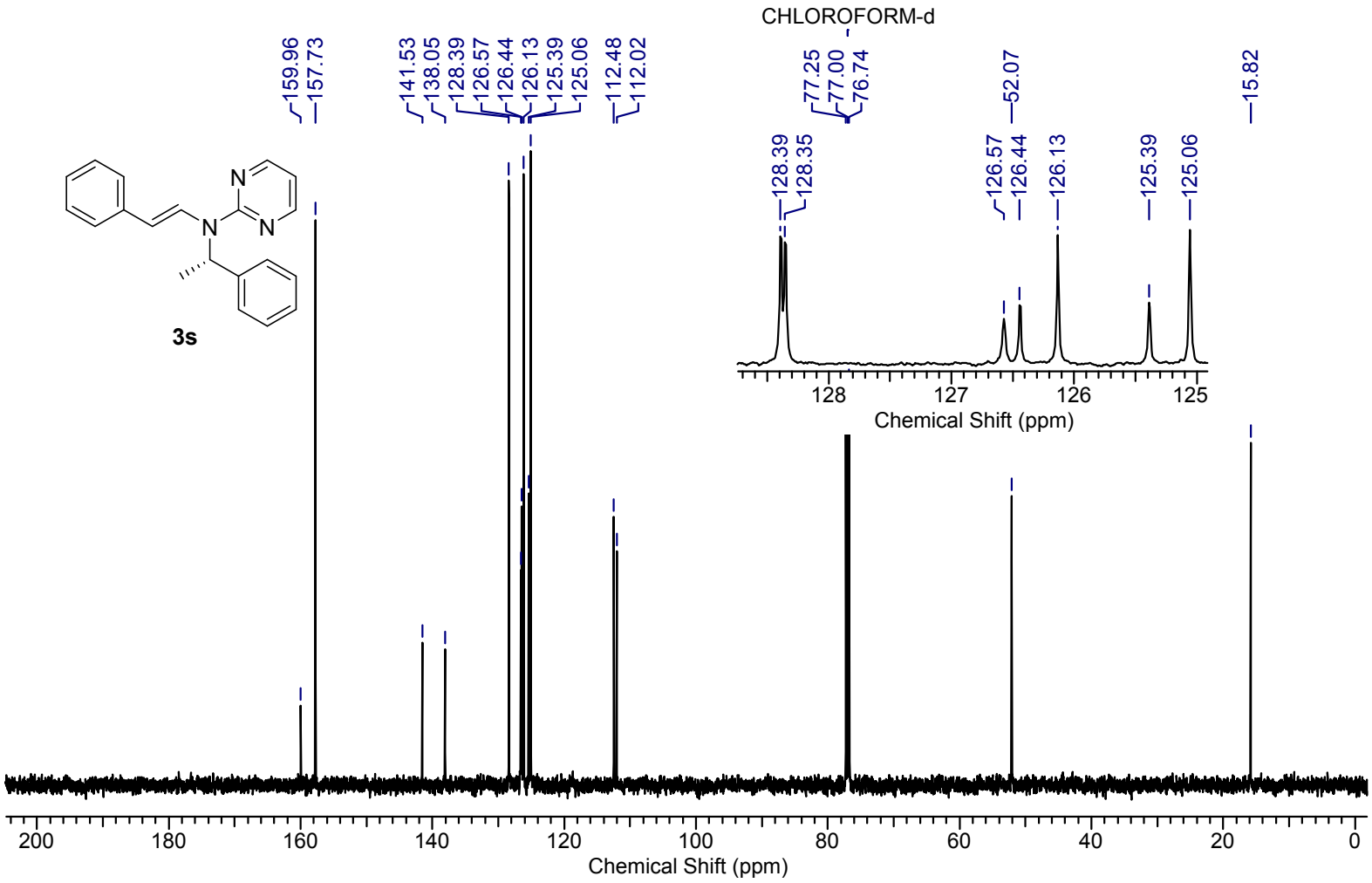

CHLOROFORM-d
8.48
8.45
8.44
7.43
7.42
7.33
7.31
7.30
7.16
7.14
7.13
6.70
6.69
6.68
5.98
5.95
4.05
4.04
4.02
1.75
1.74
1.72
1.44
1.43
1.43
1.42
1.41
0.97
0.96
0.95
3q
CHLOROFORM-d
7.43
7.42
7.33
7.31
7.30
7.27
7.16
7.14
7.13
6.70
6.69
6.68
2.04
2.02
0.99
0.97
7.50
7.25
7.00
6.75
Chemical Shift (ppm)
2.87
2.04
2.02
0.99
0.97
1.00
2.05
2.38
4.08
3.01
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

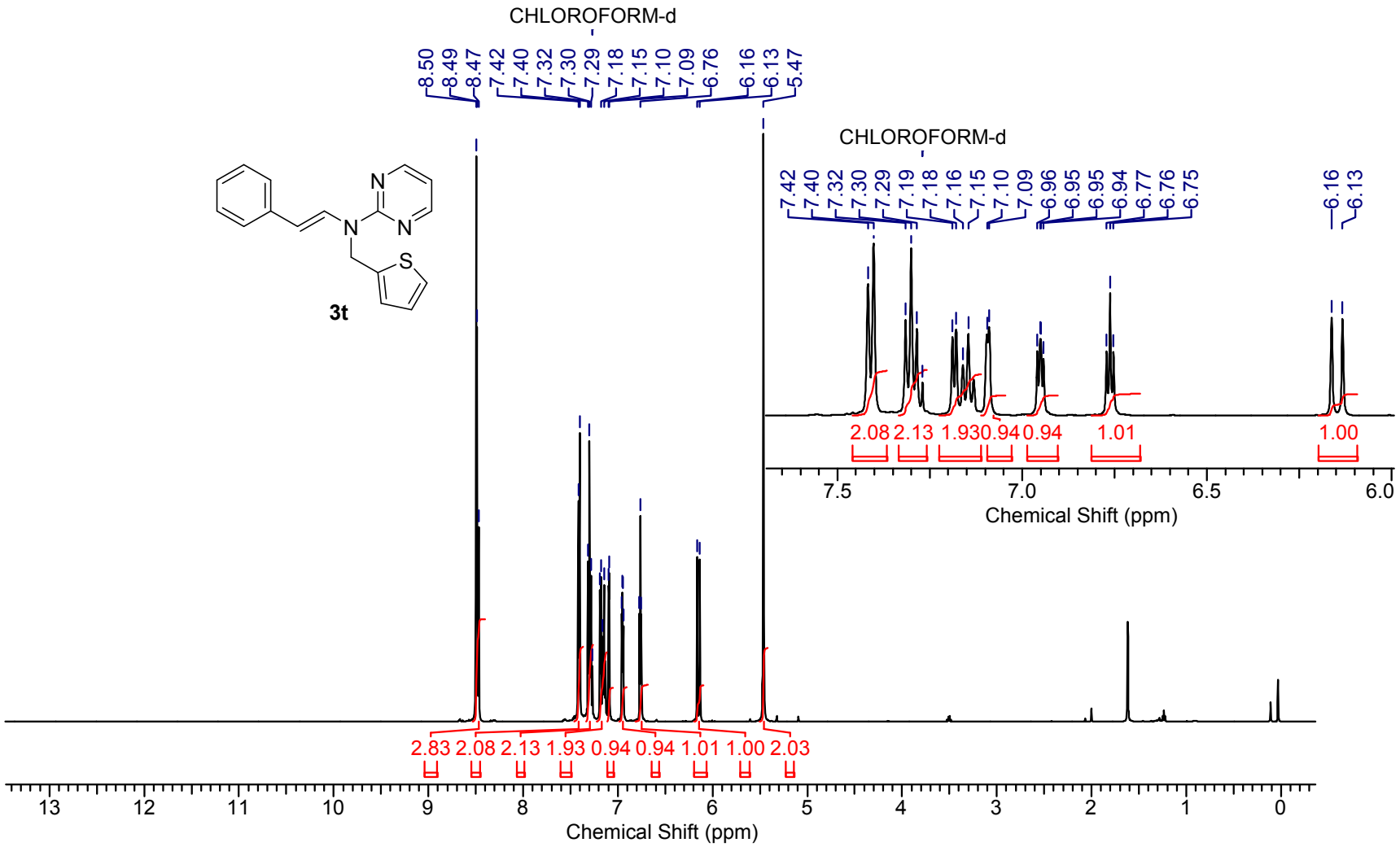

CHLOROFORM-d
159.02
157.68
138.25
128.53
128.29
125.25
125.12
112.20
107.26
77.26
77.00
76.75
43.72
29.21
26.04
22.54
14.07
3q
Chemical Shift (ppm)
Chemical Shift (ppm)

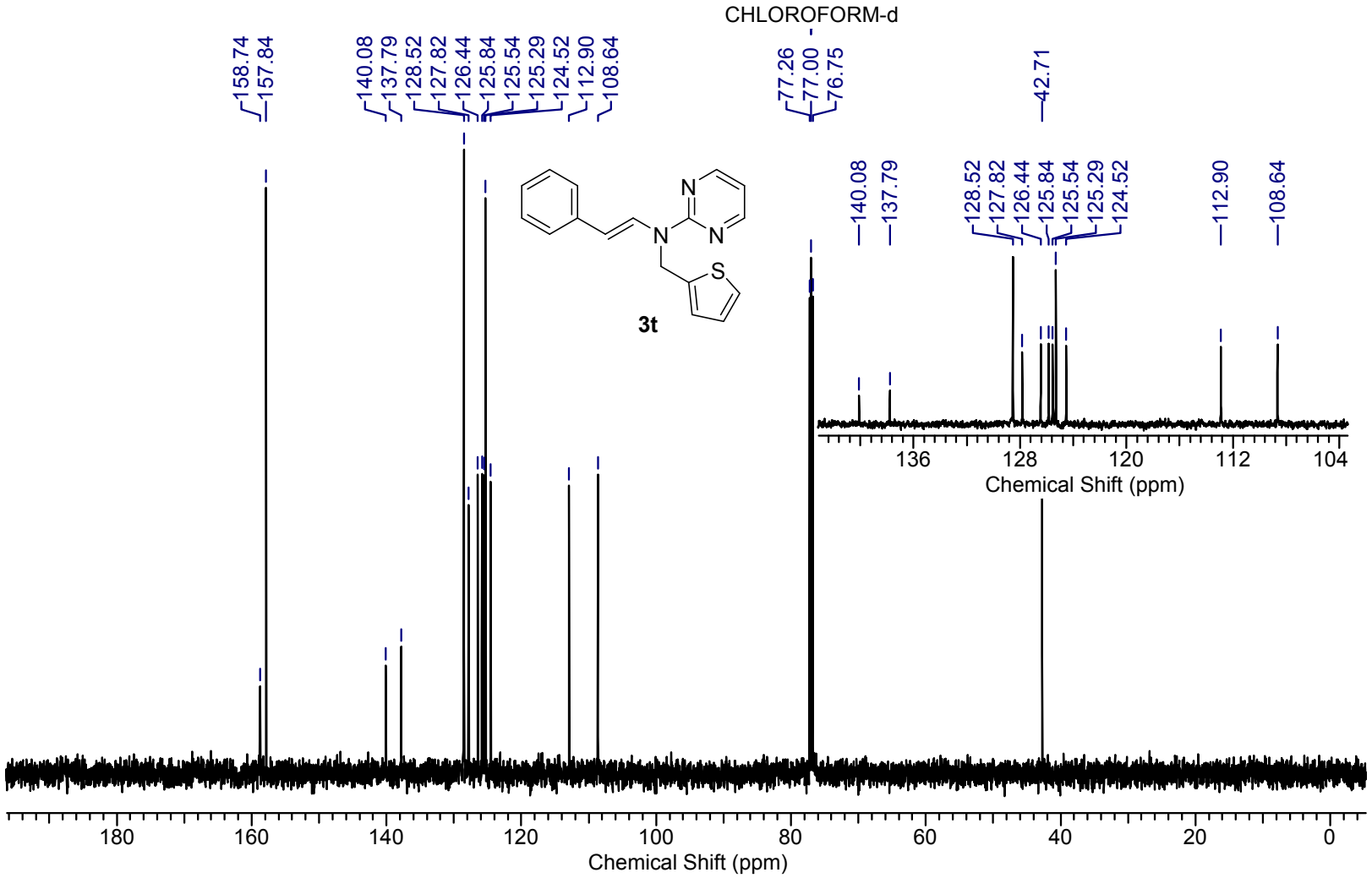

CHLOROFORM-d
8.45
8.44
8.18
8.15
7.42
7.40
7.32
7.31
7.29
7.16
7.15
7.13
6.69
6.68
6.68
6.21
6.18
5.36
5.34
5.32
2.26
2.25
1.99
1.98
1.93
1.92
1.92
1.73
1.72
1.71
3r
CHLOROFORM-d
1.87 0.98 2.16 2.22 1.10 0.98 1.00
Chemical Shift (ppm)
1.87 0.98 2.16 2.22 1.10 0.98 1.00 0.99 2.06 4.12 2.27
Chemical Shift (ppm)

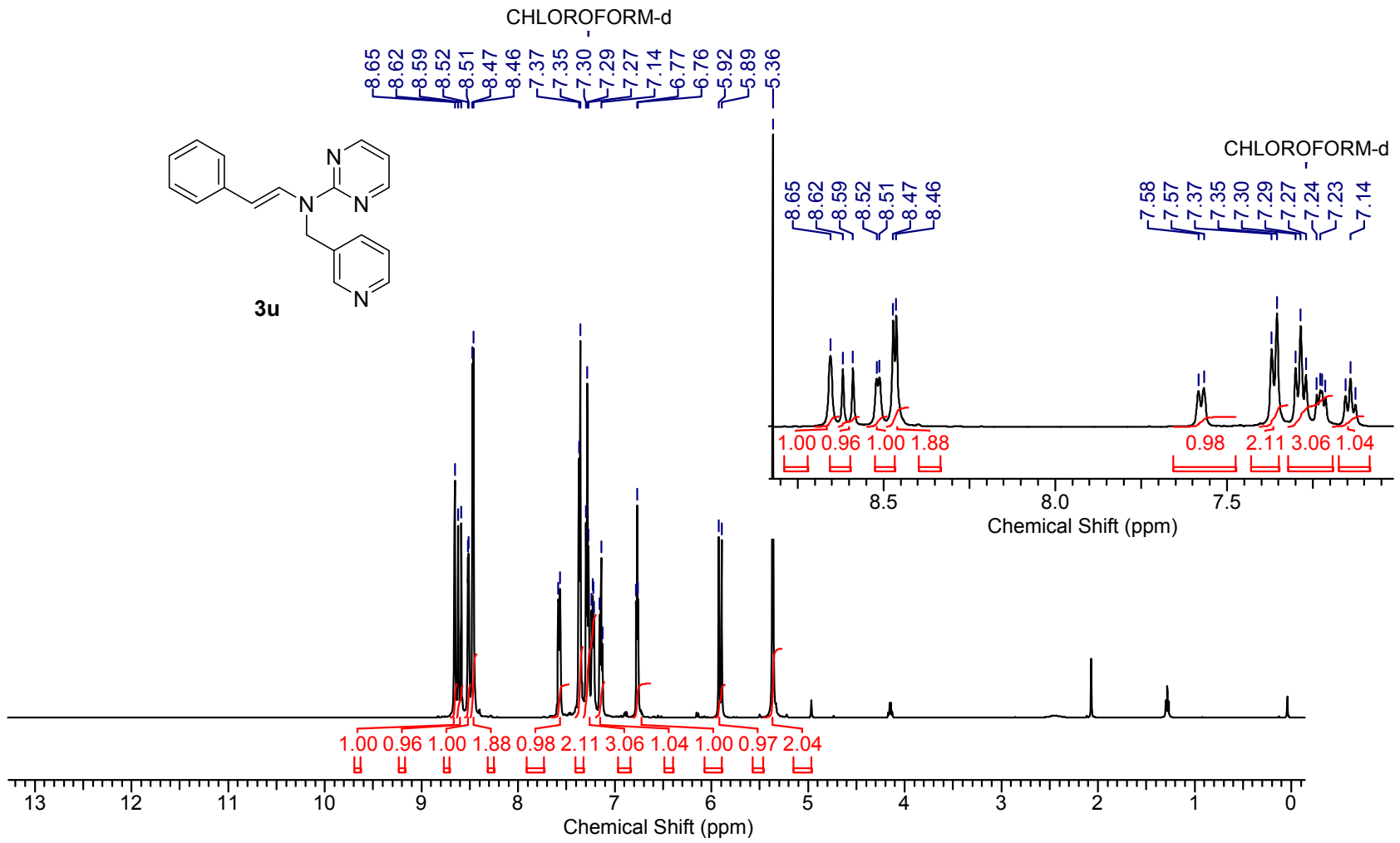

CHLOROFORM-d
159.99
157.40
138.27
128.51
128.20
125.40
125.14
112.12
110.50
77.25
77.00
76.74
56.46
27.28
25.35
N
N
N
3r
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

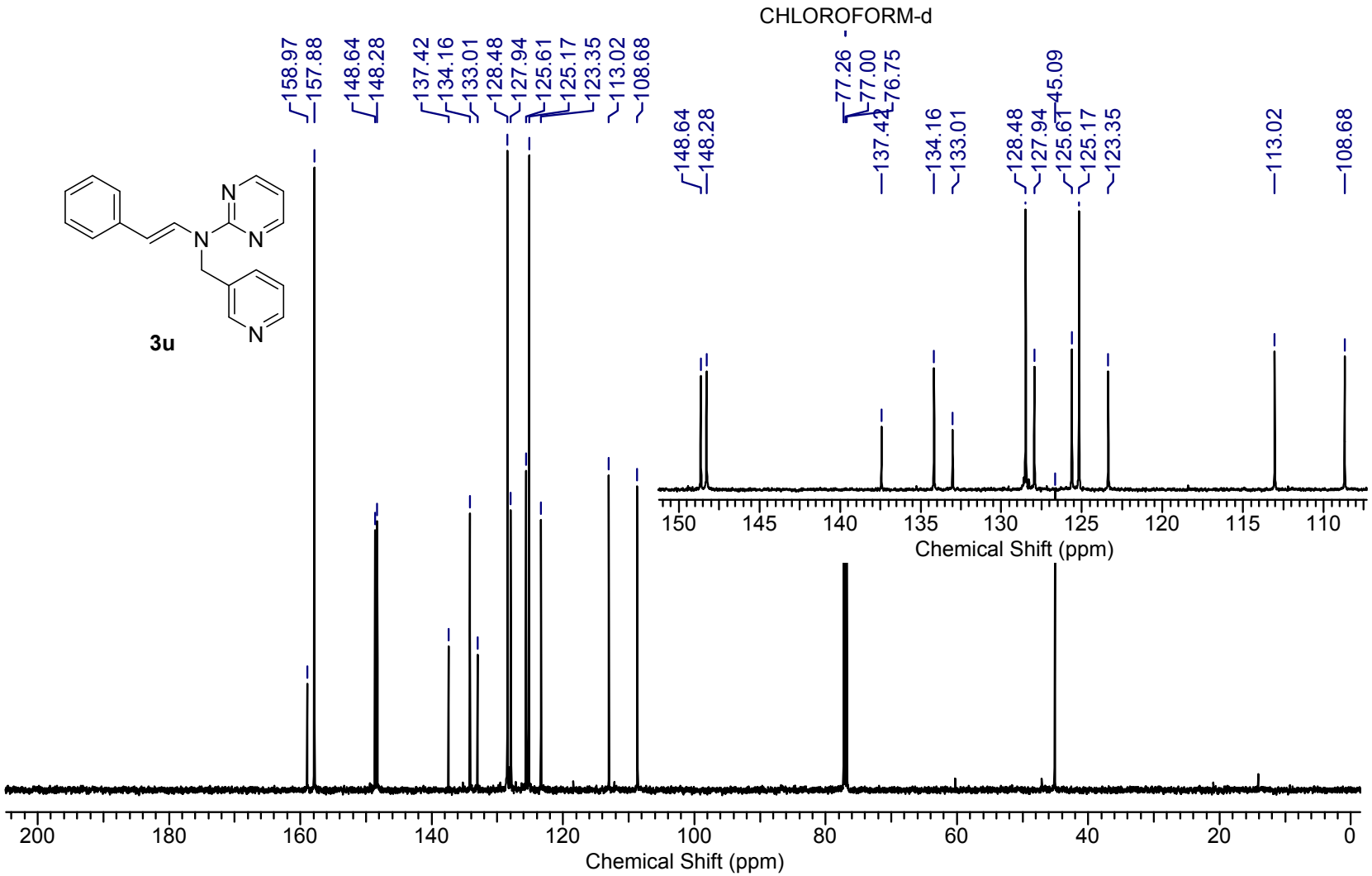

CHLOROFORM-d
8.49
8.48
8.23
8.20
7.41
7.39
7.38
7.37
7.28
7.27
7.26
6.76
6.75
6.74
5.88
5.85
1.93
1.92
N
N
N
3s
CHLOROFORM-d
7.41
7.39
7.38
7.37
7.35
7.28
7.27
7.26
7.13
7.13
7.12
6.76
6.75
6.74
6.65
6.64
4.03
5.07
0.99
0.99
0.98
7.25
7.00
6.75
Chemical Shift (ppm)
1.86
0.97
4.03
5.07
0.99
0.99
0.98
1.00
3.10
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

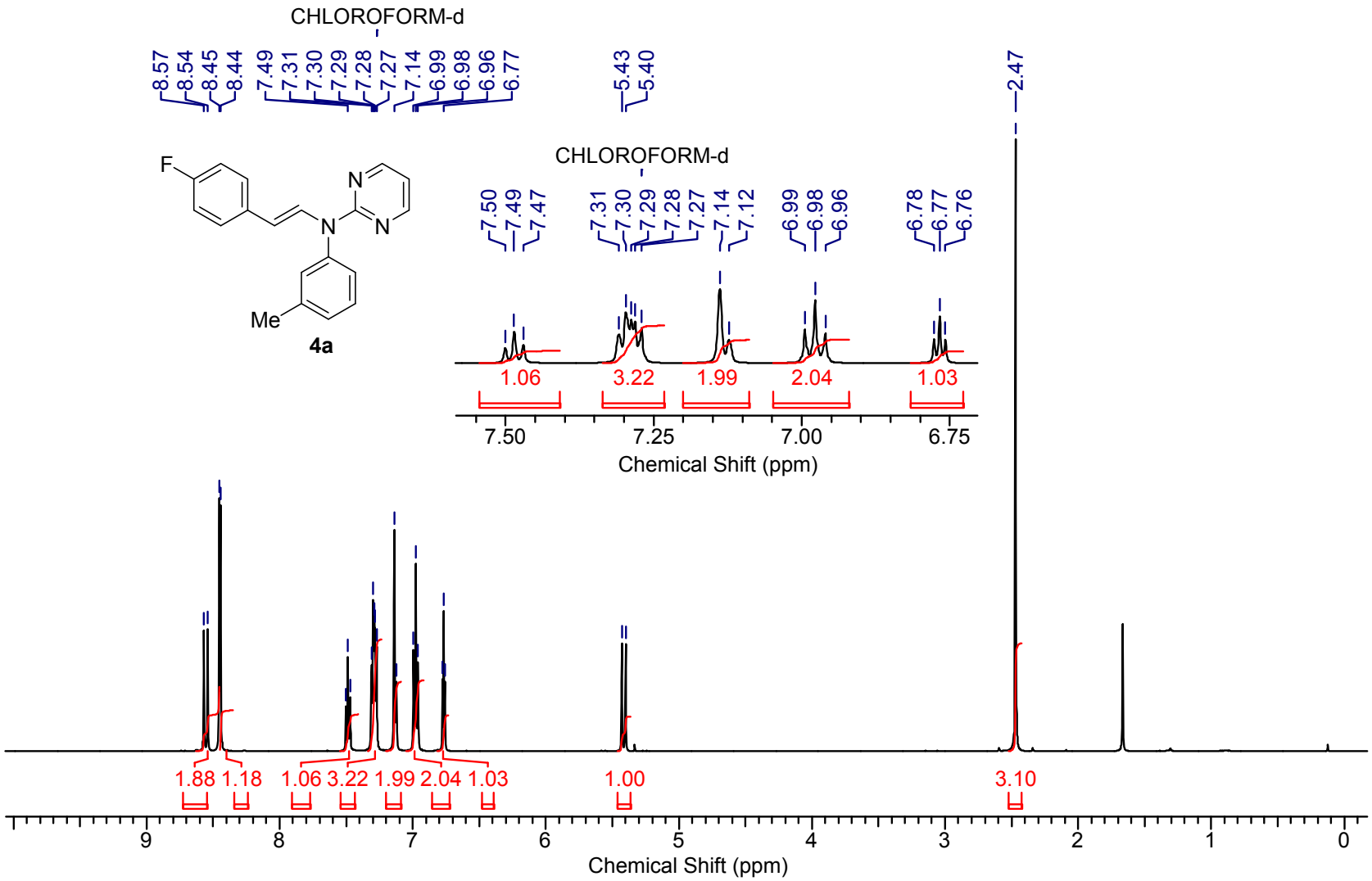

CHLOROFORM-d
159.96
157.73
141.53
138.05
128.39
126.57
126.44
126.13
125.39
125.06
112.48
112.02
77.25
77.00
76.74
52.07
15.82
128.39
128.35
126.57
126.44
126.13
125.39
125.06
N
N
N
3s
128
127
126
125
Chemical Shift (ppm)
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

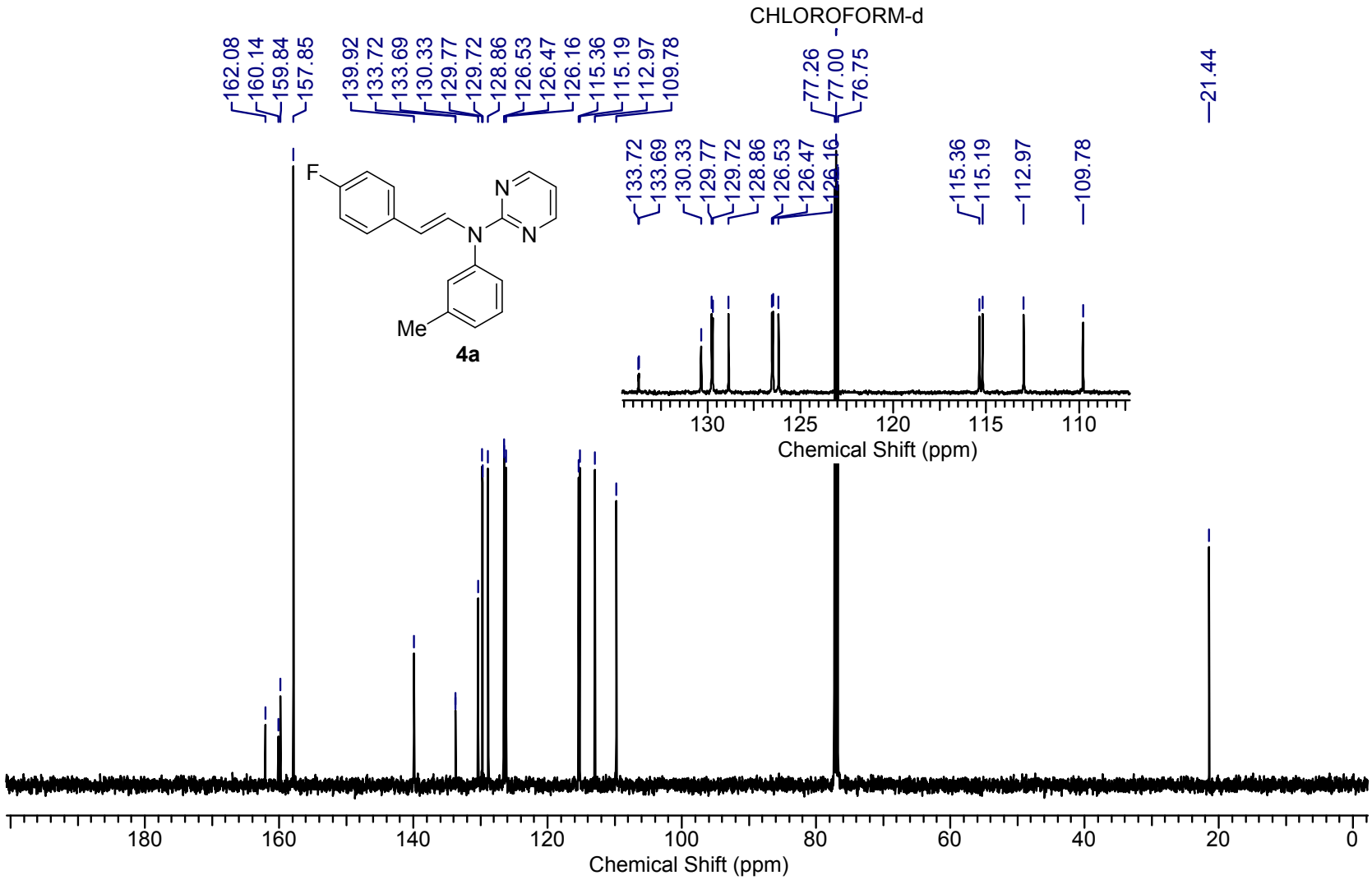

CHLOROFORM-d
8.50
8.49
8.47
7.42
7.40
7.32
7.30
7.29
7.18
7.15
7.10
7.09
6.76
6.16
6.13
5.47
CHLOROFORM-d
7.42
7.40
7.32
7.30
7.29
7.19
7.18
7.16
7.15
7.10
7.09
6.96
6.95
6.95
6.94
6.77
6.76
6.75
6.16
6.13
2.08 2.13 1.93 0.94 0.94 1.01 1.00
7.5
7.0
6.5
6.0
Chemical Shift (ppm)
N
N
N
S
3t
2.83 2.08 2.13 1.93 0.94 0.94 1.01 1.00 2.03
13
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

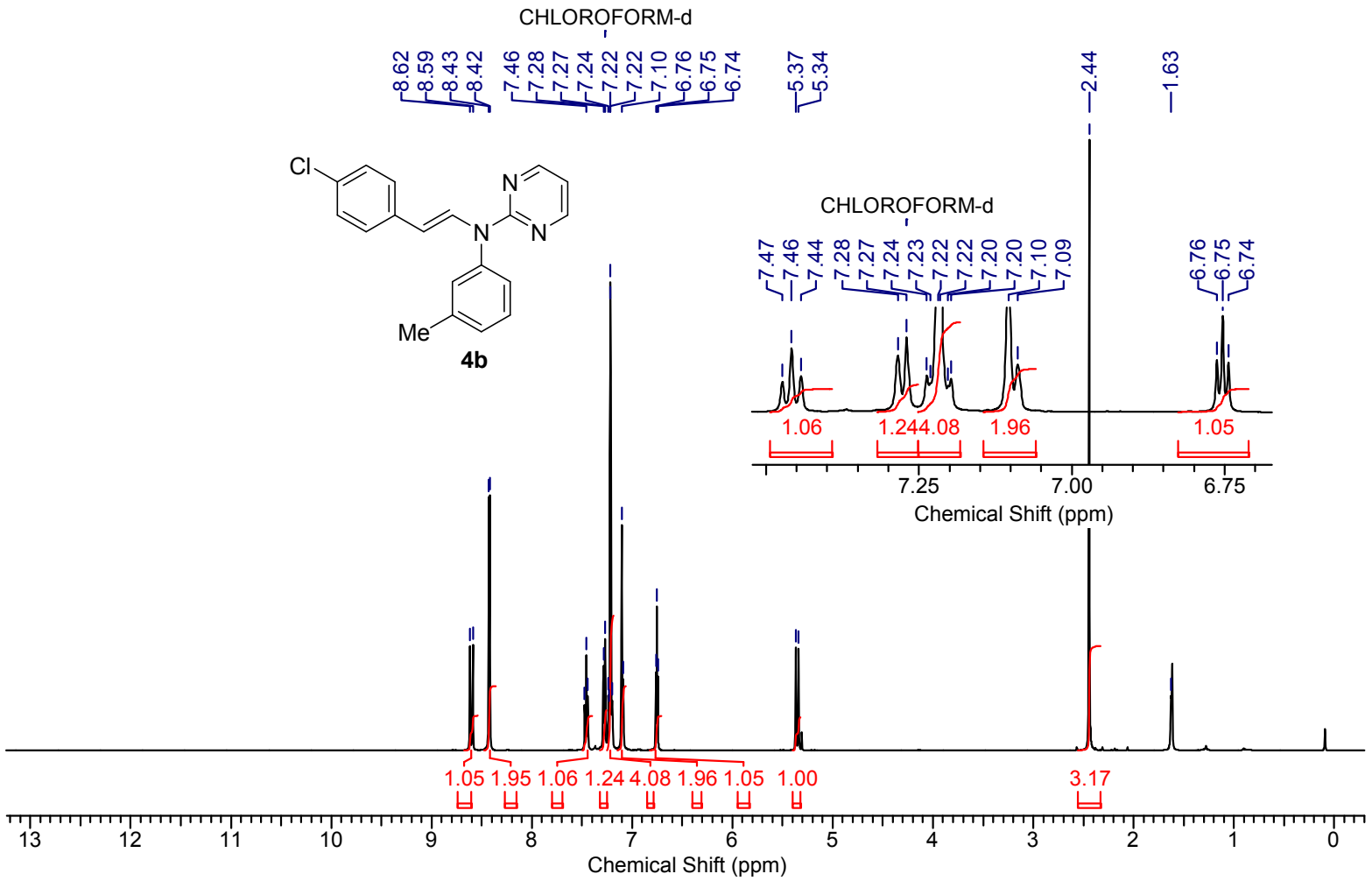

CHLOROFORM-d
158.74
157.84
140.08
137.79
128.52
127.82
126.44
125.84
125.54
125.29
124.52
112.90
108.64
77.26
77.00
76.75
42.71
3t
Chemical Shift (ppm)
Chemical Shift (ppm)

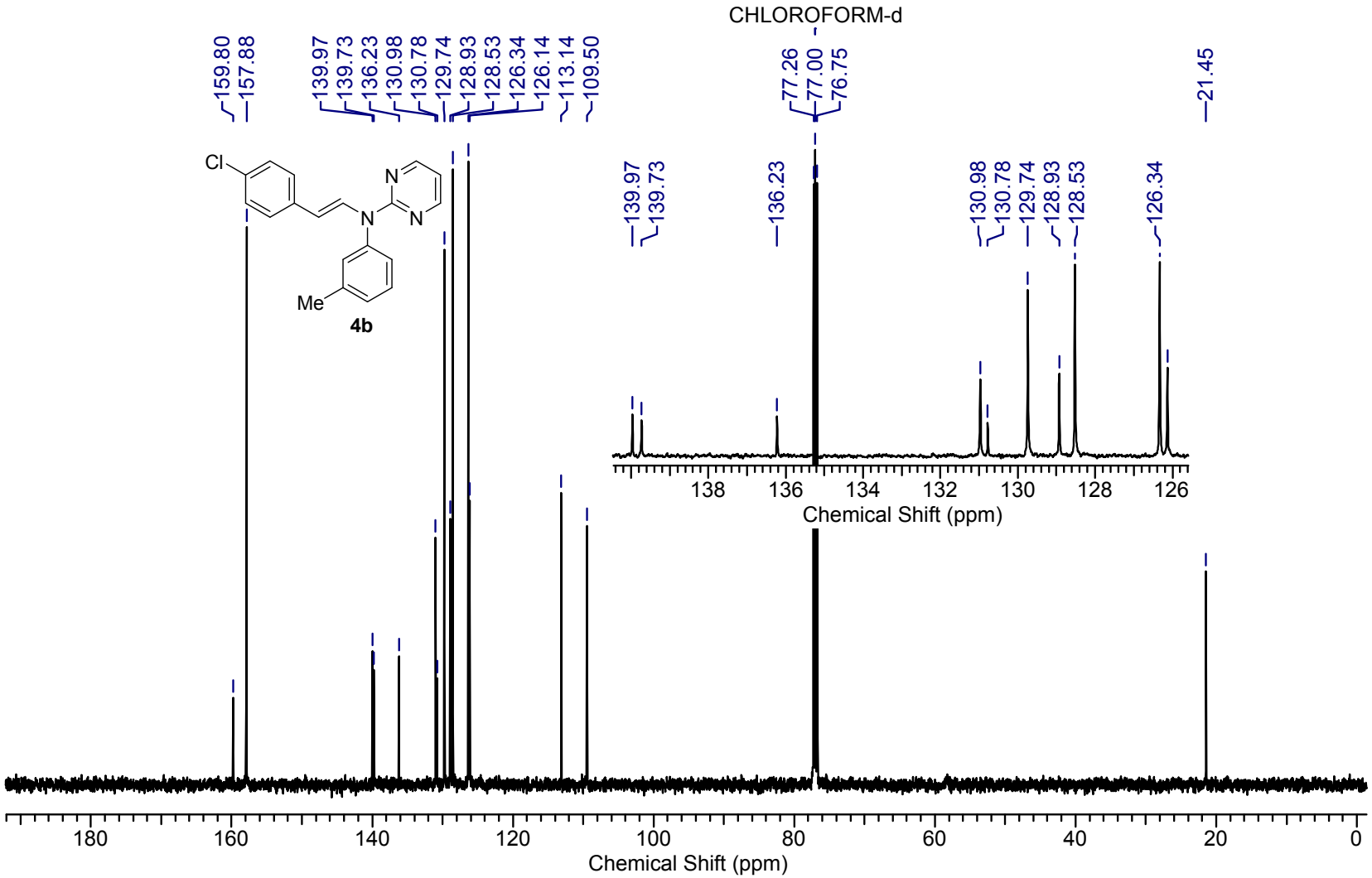

CHLOROFORM-d
8.65 8.62 8.59 8.52 8.51 8.47 8.46 7.37 7.35 7.30 7.29 7.27 7.14 6.77 6.76 5.92 5.89 5.36
3u
1.00 0.96 1.00 1.88 0.98 2.11 3.06 1.04 1.00 0.97 2.04
13 12 11 10 9 8 7 6 5 4 3 2 1 0
Chemical Shift (ppm)
CHLOROFORM-d
8.65 8.62 8.59 8.52 8.51 8.47 8.46 7.58 7.57 7.37 7.35 7.30 7.29 7.27 7.24 7.23 7.14
1.00 0.96 1.00 1.88 0.98 2.11 3.06 1.04
8.5 8.0 7.5
Chemical Shift (ppm)

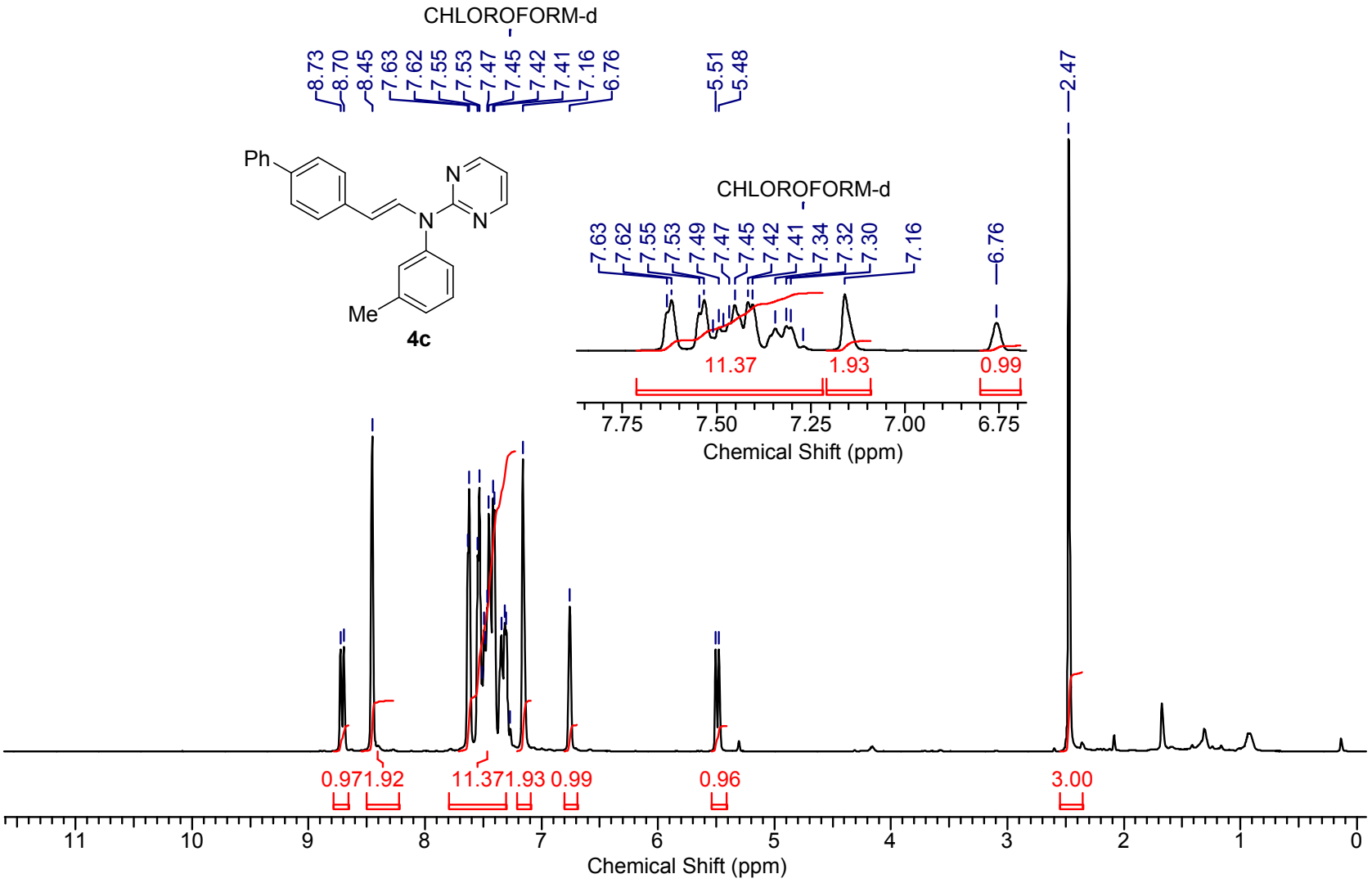

CHLOROFORM-d
158.97
157.88
148.64
148.28
137.42
134.16
133.01
128.48
127.94
125.61
125.17
123.35
113.02
108.68
77.26
77.00
76.75
45.09
3u
Chemical Shift (ppm)
Chemical Shift (ppm)

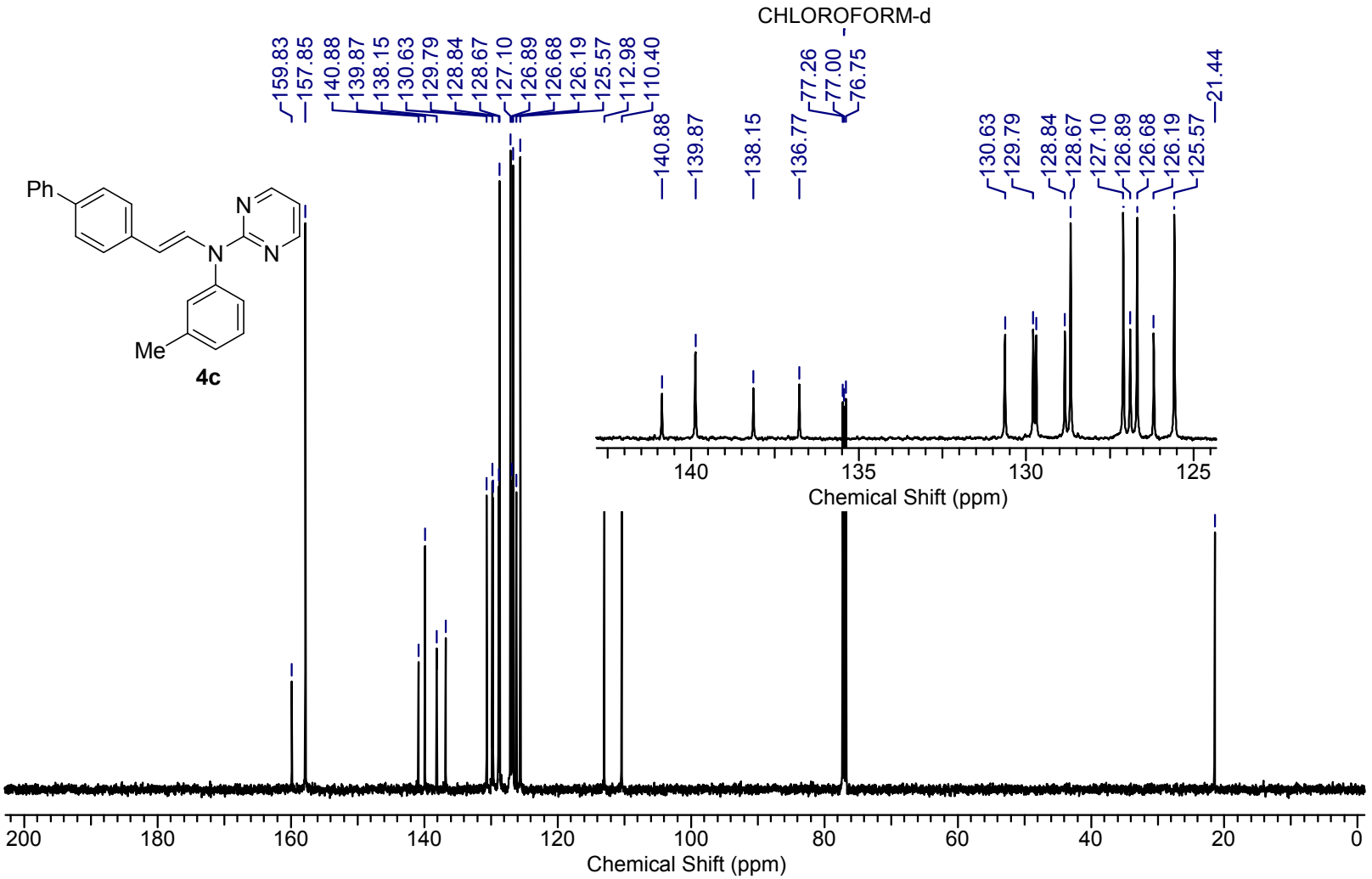

CHLOROFORM-d
8.57
8.54
8.45
8.44
7.49
7.31
7.30
7.29
7.28
7.27
7.14
6.99
6.98
6.96
6.77
5.43
5.40
2.47
F
N
N
N
Me
4a
CHLOROFORM-d
7.50
7.49
7.47
7.31
7.30
7.29
7.28
7.27
7.14
7.12
6.99
6.98
6.96
6.78
6.77
6.76
1.06
3.22
1.99
2.04
1.03
7.50
7.25
7.00
6.75
Chemical Shift (ppm)
1.88 1.18 1.06 3.22 1.99 2.04 1.03
1.00
3.10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

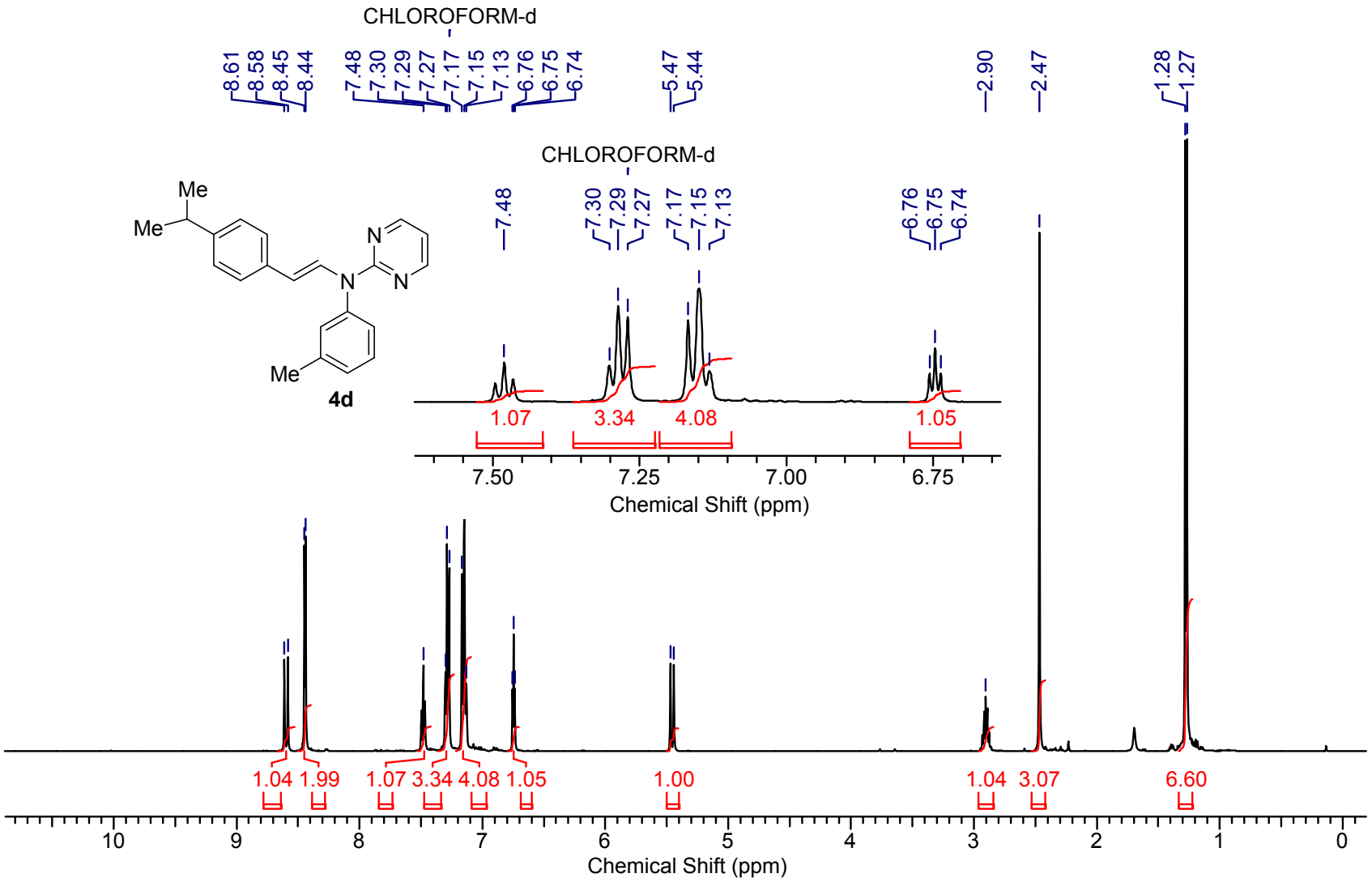

CHLOROFORM-d
162.08
160.14
159.84
157.85
139.92
133.72
133.69
130.33
129.77
129.72
128.86
126.53
126.47
126.16
115.36
115.19
112.97
109.78
77.26
77.00
76.75
21.44
F
N
N
N
Me
4a
Chemical Shift (ppm)
Chemical Shift (ppm)

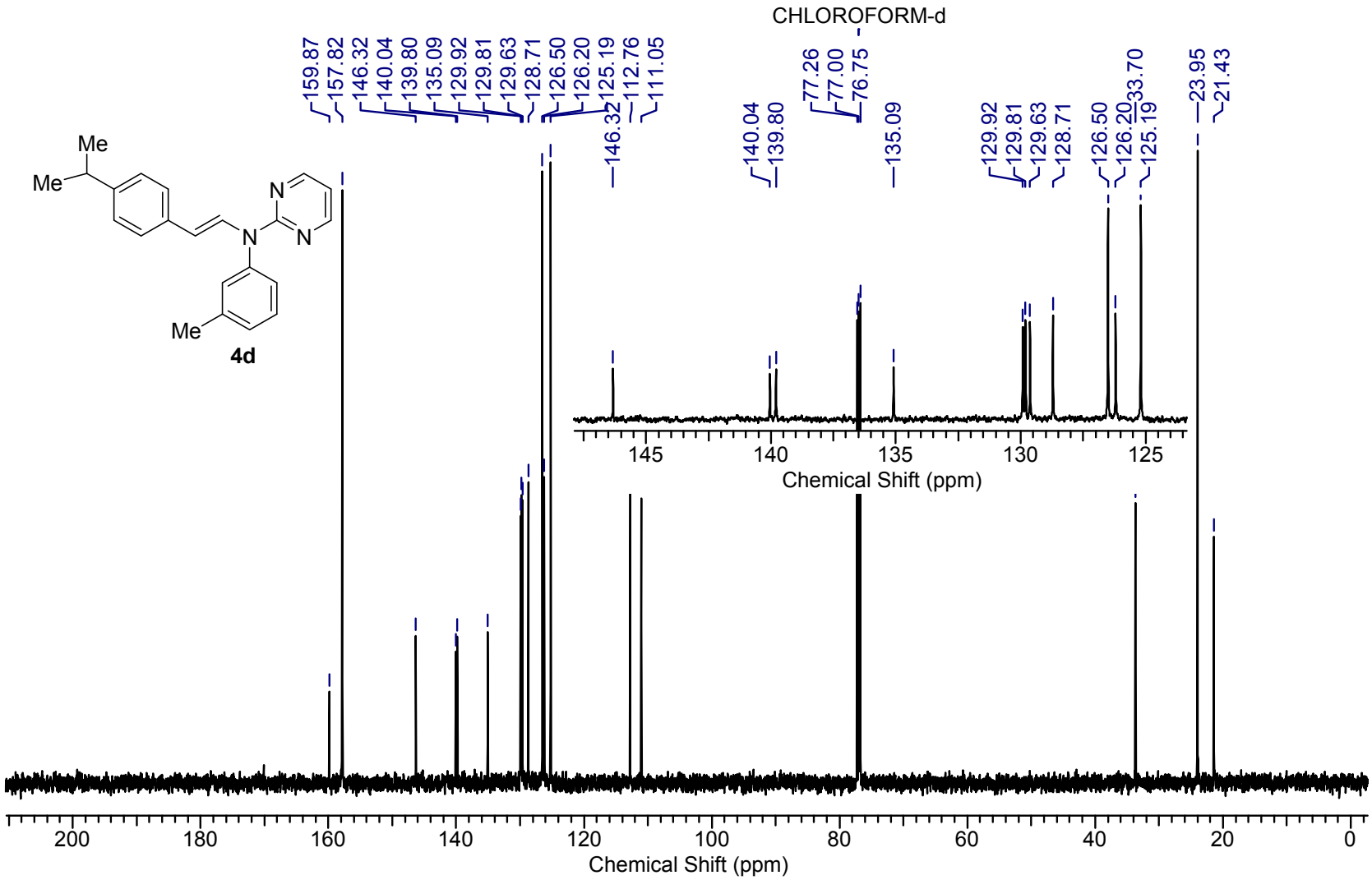

CHLOROFORM-d
8.62
8.59
8.43
8.42
7.46
7.28
7.27
7.24
7.22
7.22
7.10
6.76
6.75
6.74
5.37
5.34
2.44
1.63
Cl
N
N
N
Me
4b
CHLOROFORM-d
7.47
7.46
7.44
7.28
7.27
7.24
7.23
7.22
7.22
7.20
7.20
7.10
7.09
6.76
6.75
6.74
1.06
1.24
4.08
1.96
1.05
7.25
7.00
6.75
Chemical Shift (ppm)
1.05
1.95
1.06
1.24
4.08
1.96
1.05
1.00
3.17
13
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

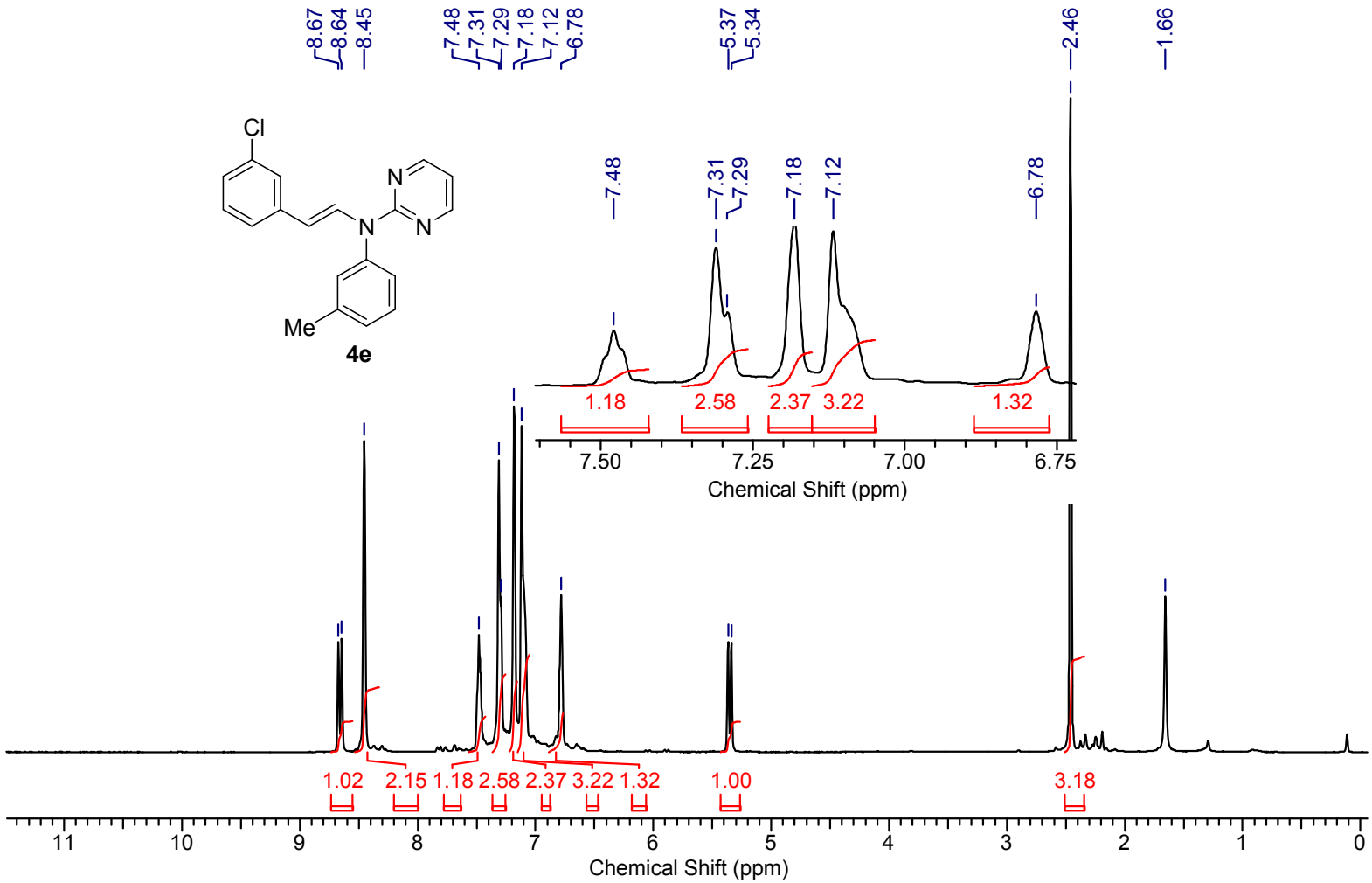

CHLOROFORM-d
159.80
157.88
139.97
139.73
136.23
130.98
130.78
129.74
128.93
128.53
126.34
126.14
113.14
109.50
77.26
77.00
76.75
21.45
Cl
N
N
N
Me
4b
139.97
139.73
136.23
130.98
130.78
129.74
128.93
128.53
126.34
138
136
134
132
130
128
126
Chemical Shift (ppm)
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

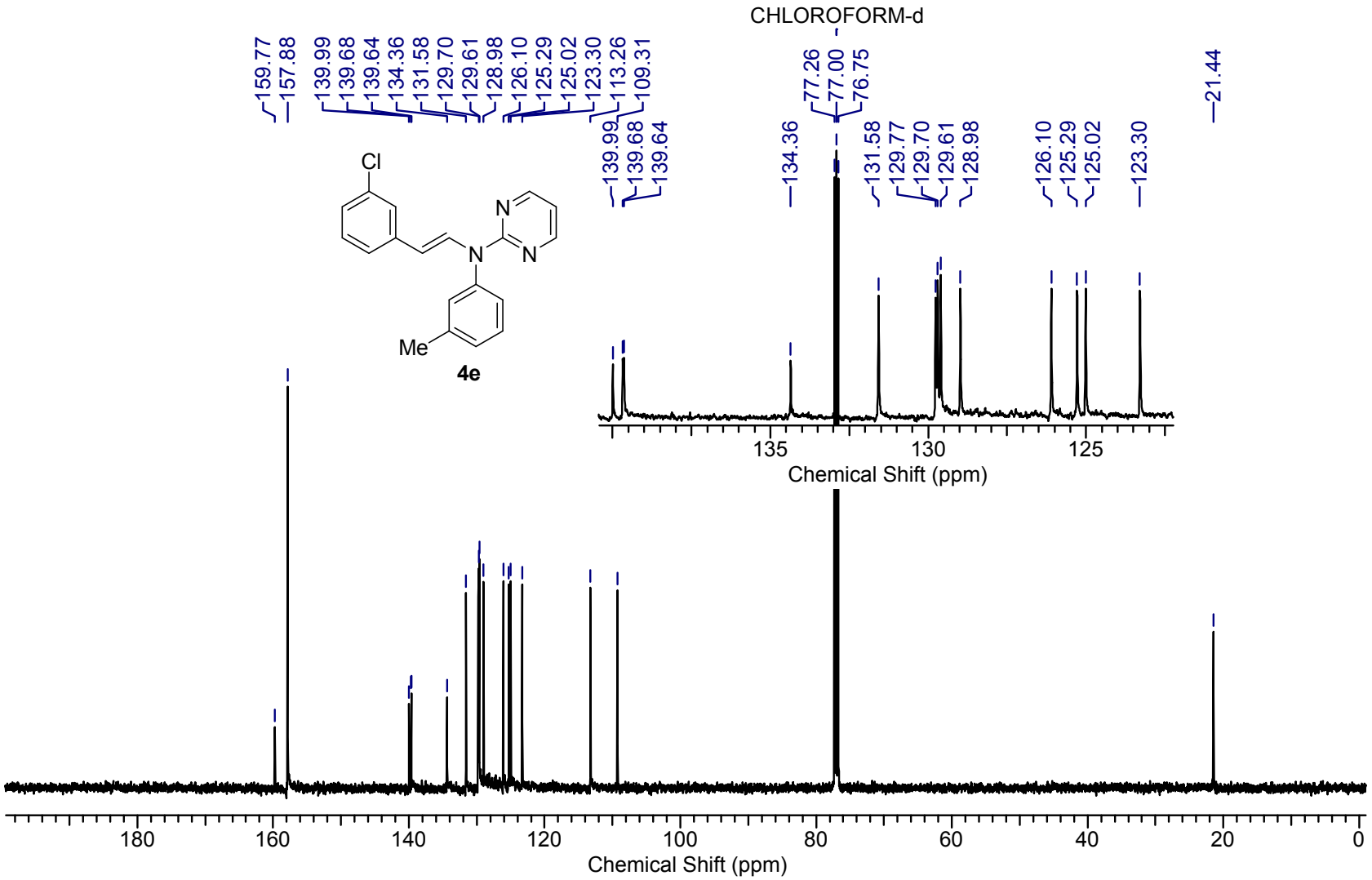

CHLOROFORM-d
8.73
8.70
8.45
7.63
7.62
7.55
7.53
7.47
7.45
7.42
7.41
7.16
6.76
5.51
5.48
2.47
Ph
N
N
N
Me
4c
CHLOROFORM-d
7.63
7.62
7.55
7.53
7.49
7.47
7.45
7.42
7.41
7.34
7.32
7.30
7.16
6.76
11.37
1.93
0.99
7.75
7.50
7.25
7.00
6.75
Chemical Shift (ppm)
0.97
1.92
11.37
1.93
0.99
0.96
3.00
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

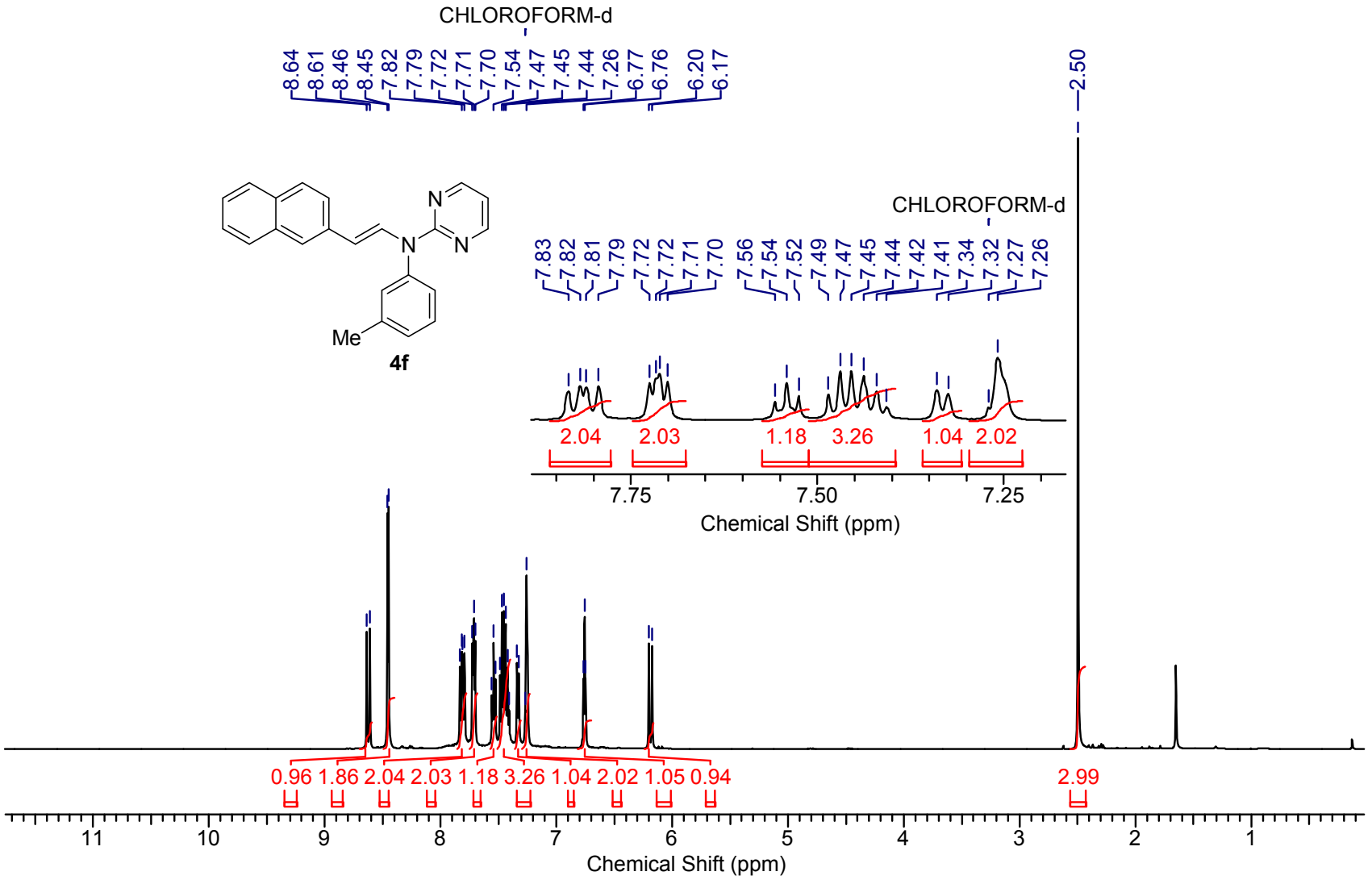

CHLOROFORM-d
159.83
157.85
140.88
139.87
138.15
130.63
129.79
128.84
128.67
127.10
126.89
126.68
126.19
125.57
112.98
110.40
77.26
77.00
76.75
21.44
Ph
N
N
N
Me
4c
Chemical Shift (ppm)
Chemical Shift (ppm)

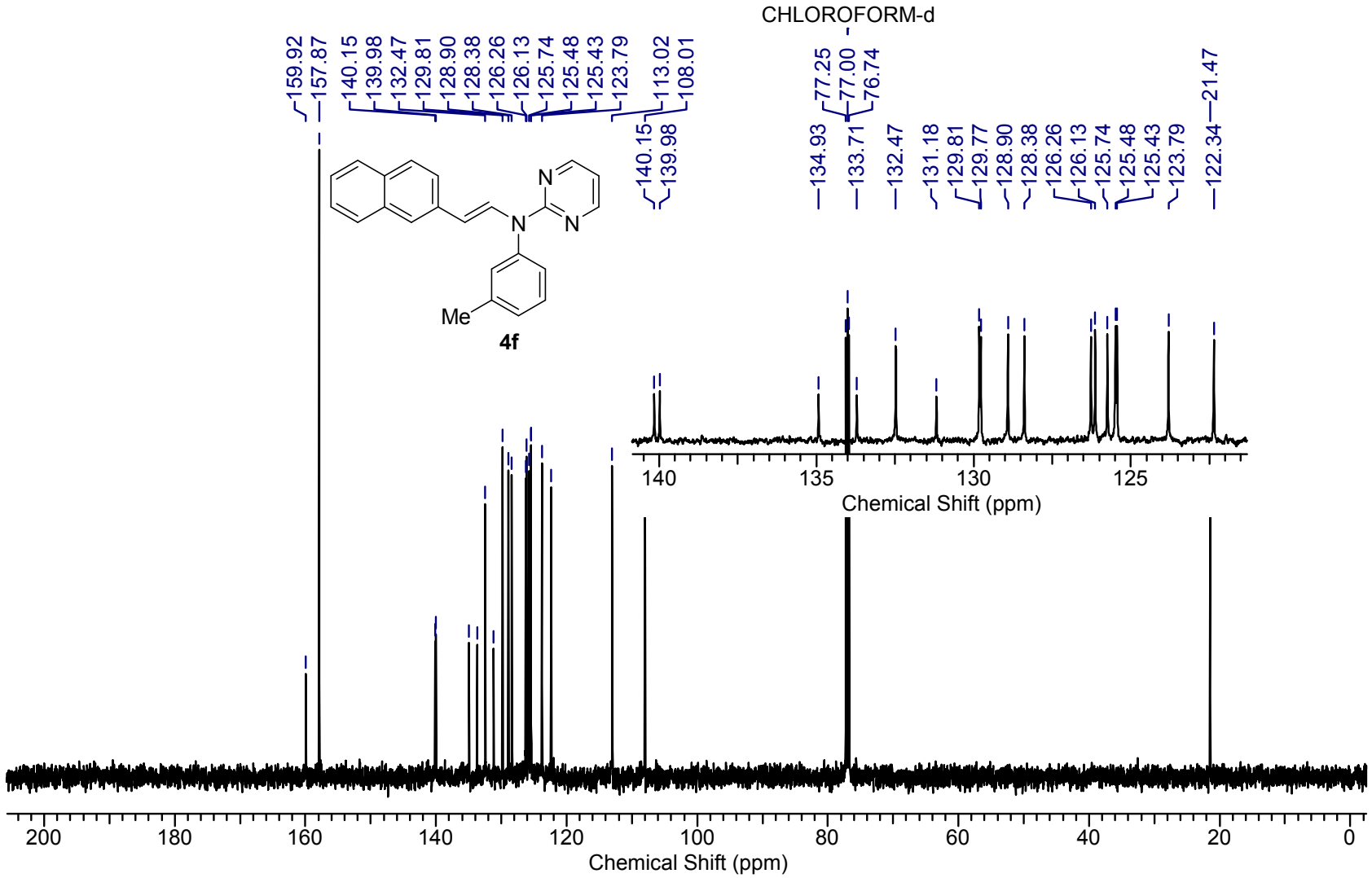

CHLOROFORM-d
8.61
8.58
8.45
8.44
7.48
7.30
7.29
7.27
7.17
7.15
7.13
6.76
6.75
6.74
5.47
5.44
2.90
2.47
1.28
1.27
Me
Me
N
N
N
Me
4d
CHLOROFORM-d
1.07
3.34
4.08
1.05
7.50
7.25
7.00
6.75
Chemical Shift (ppm)
1.04
1.99
1.07
3.34
4.08
1.05
1.00
1.04
3.07
6.60
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

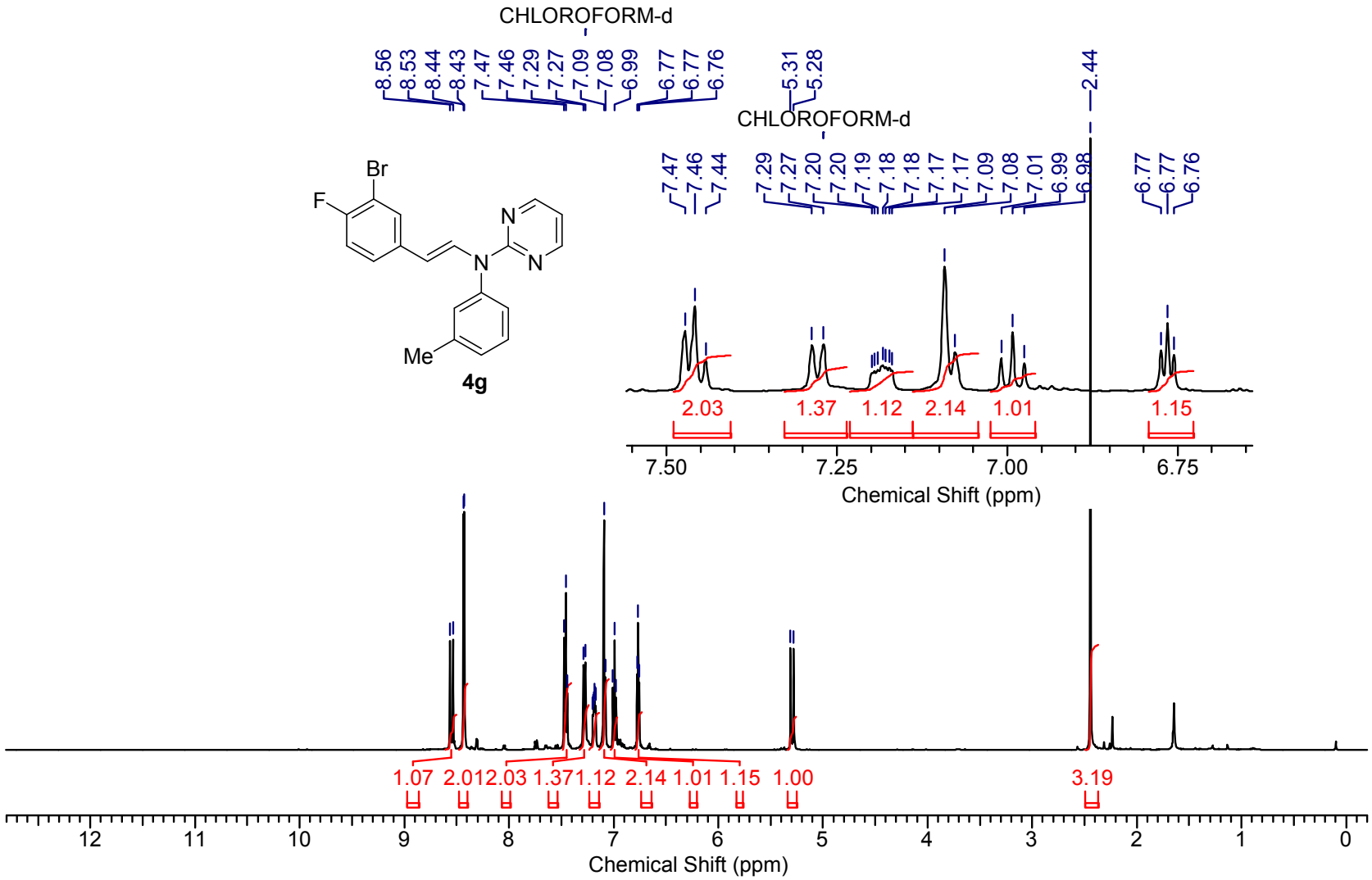

CHLOROFORM-d
159.87
157.82
146.32
140.04
139.80
135.09
129.92
129.81
129.63
128.71
126.50
126.20
125.19
112.76
111.05
77.26
77.00
76.75
33.70
23.95
21.43
Me
Me
N
N
N
Me
4d
Chemical Shift (ppm)
Chemical Shift (ppm)

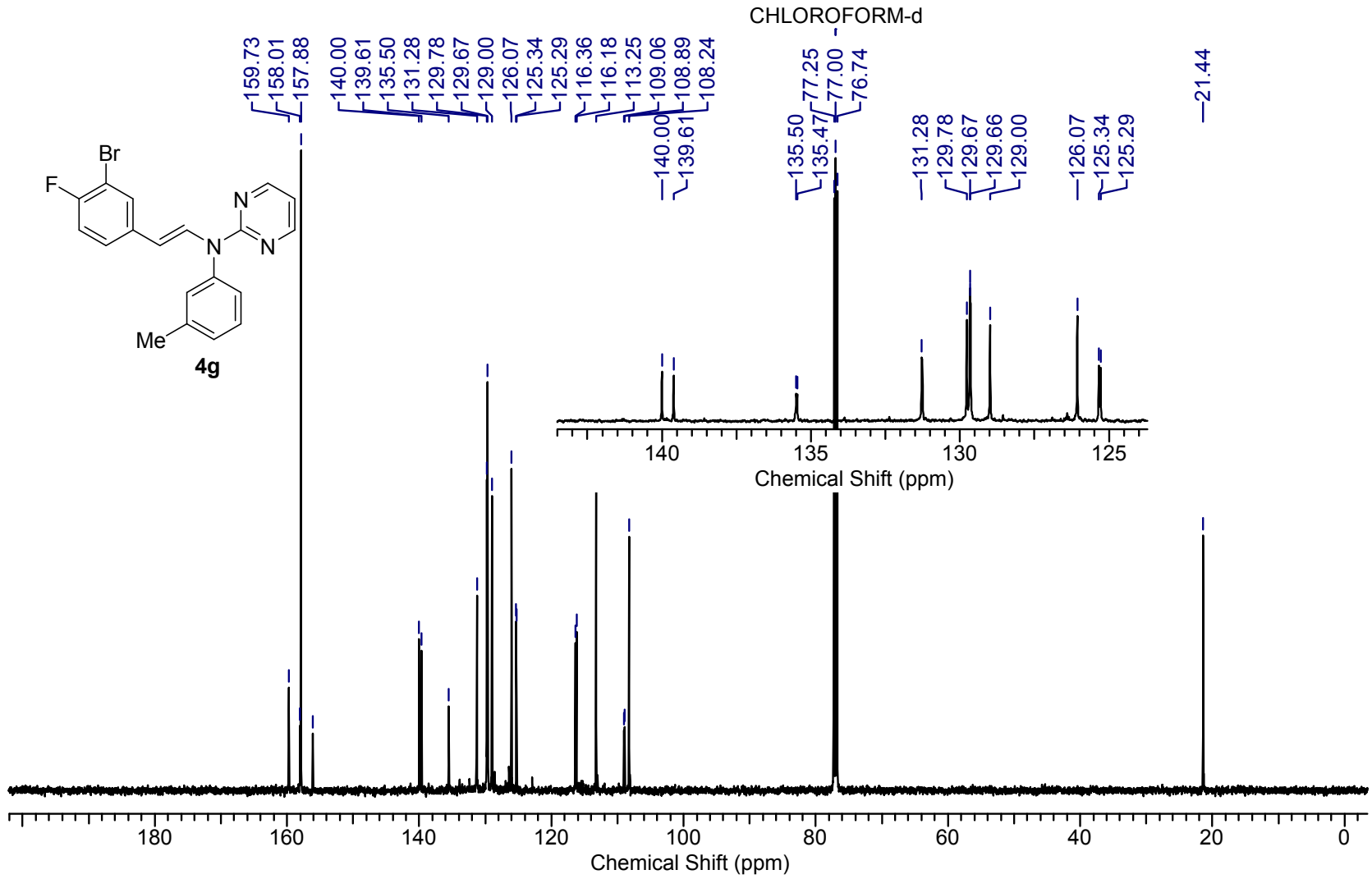

8.67
8.64
8.45
7.48
7.31
7.29
7.18
7.12
6.78
5.37
5.34
2.46
1.66
Cl
N
N
N
Me
4e
1.18
2.58
2.37
3.22
1.32
7.50
7.25
7.00
6.75
Chemical Shift (ppm)
1.02
2.15
1.18
2.58
2.37
3.22
1.32
1.00
3.18
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

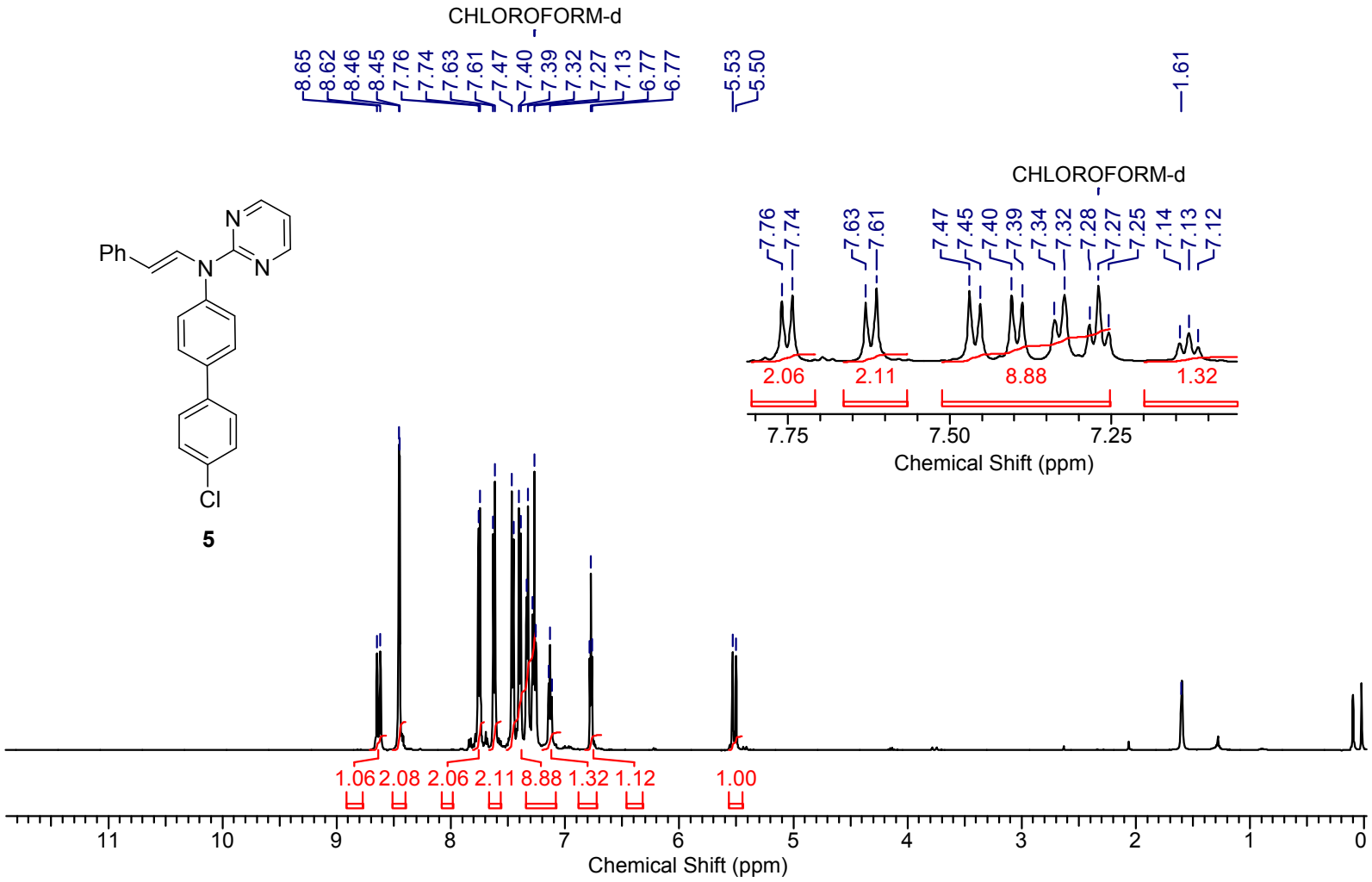

CHLOROFORM-d
159.77
157.88
139.99
139.68
139.64
134.36
131.58
129.70
129.61
128.98
126.10
125.29
125.02
123.30
113.26
109.31
77.26
77.00
76.75
21.44
Cl
N
N
N
Me
4e
135
130
125
Chemical Shift (ppm)
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

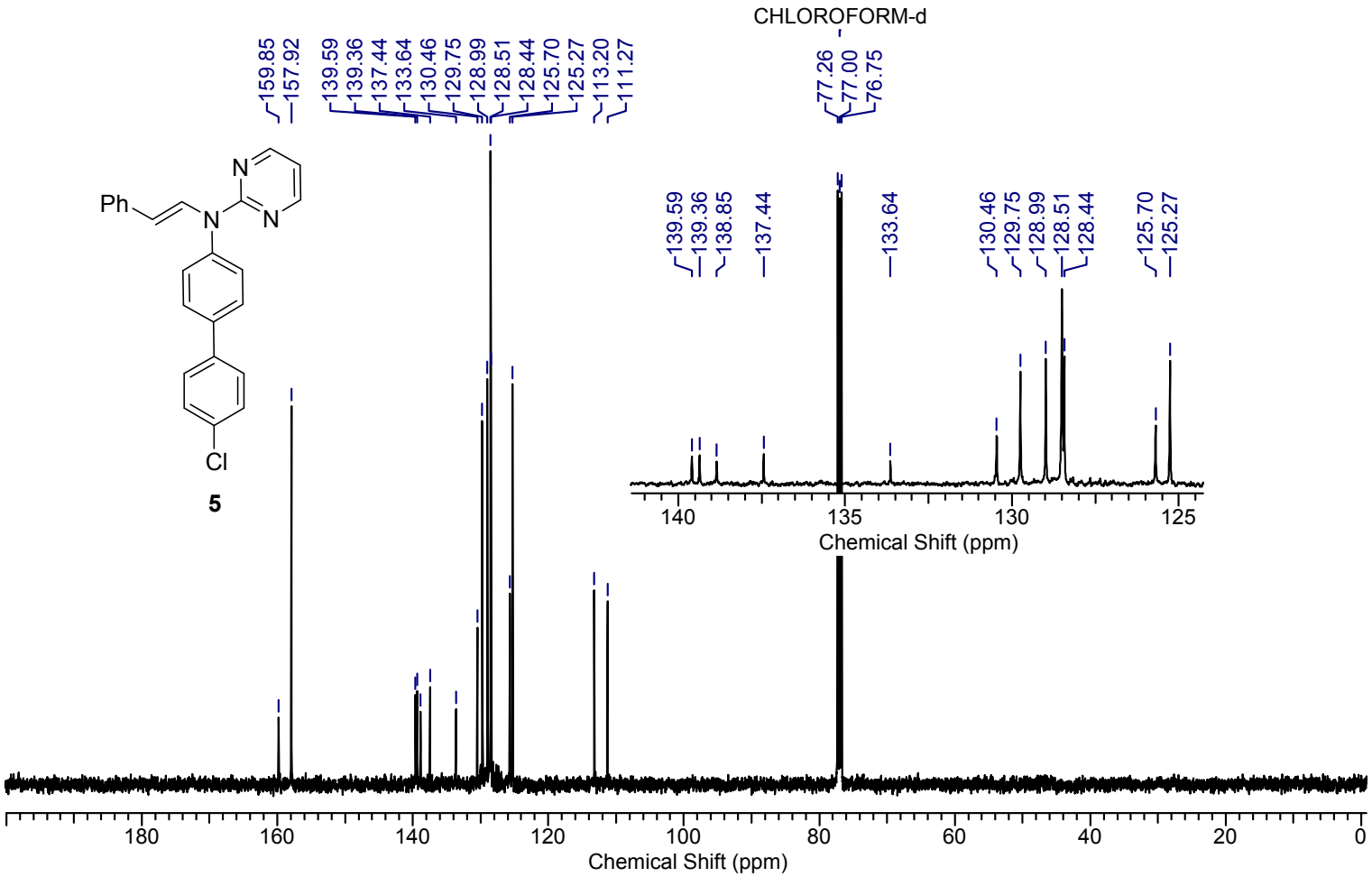

CHLOROFORM-d
8.64
8.61
8.46
8.45
7.82
7.79
7.72
7.71
7.70
7.54
7.47
7.45
7.44
7.26
6.77
6.76
6.20
6.17
2.50
N
N
N
Me
4f
CHLOROFORM-d
7.83
7.82
7.81
7.79
7.72
7.72
7.71
7.70
7.56
7.54
7.52
7.49
7.47
7.45
7.44
7.42
7.41
7.34
7.32
7.27
7.26
2.04
2.03
1.18
3.26
1.04
2.02
7.75
7.50
7.25
Chemical Shift (ppm)
0.96
1.86
2.04
2.03
1.18
3.26
1.04
2.02
1.05
0.94
2.99
11
10
9
8
7
6
5
4
3
2
1
Chemical Shift (ppm)

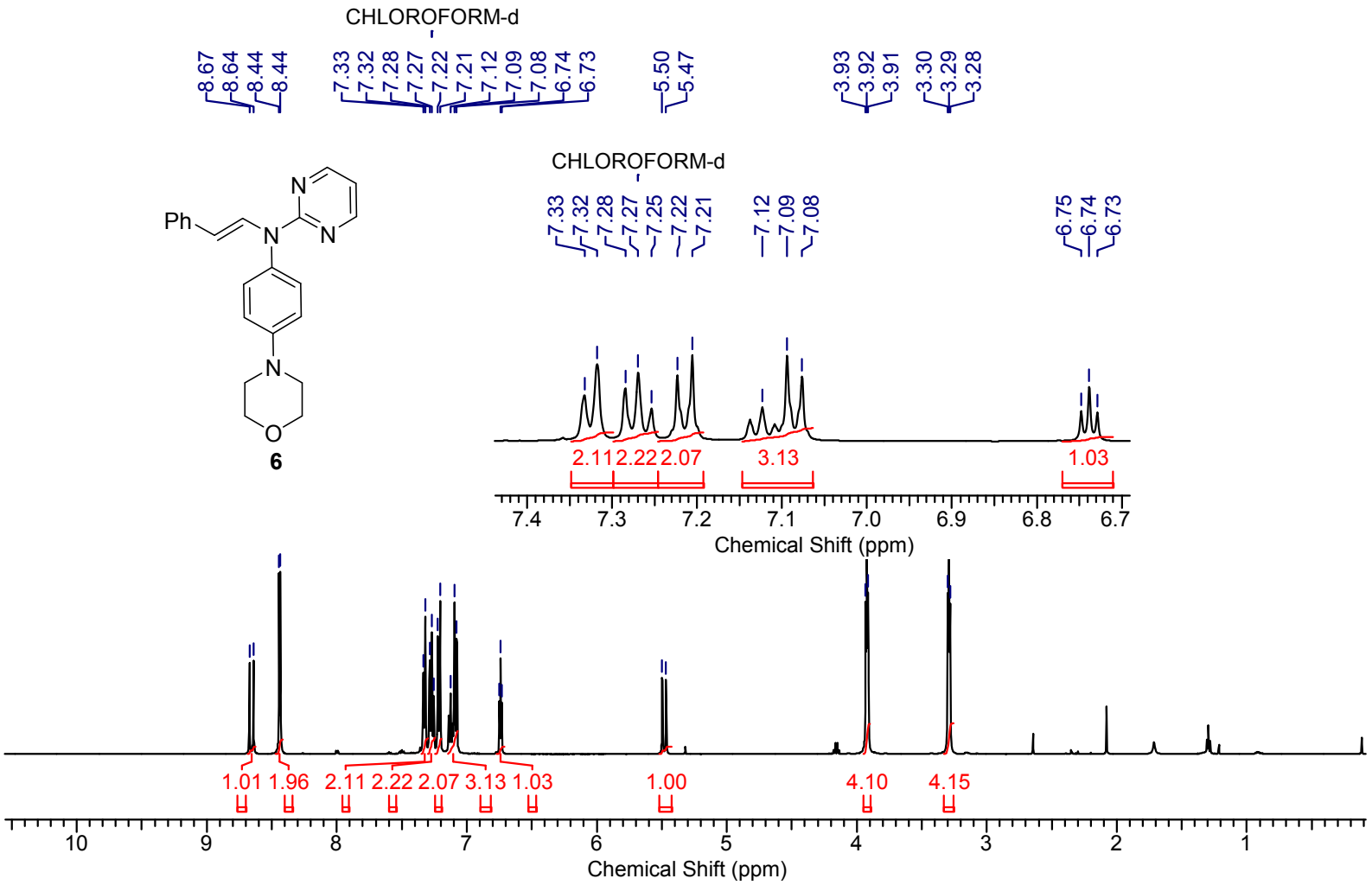

CHLOROFORM-d
159.92
157.87
140.15
139.98
132.47
129.81
128.90
128.38
126.26
126.13
125.74
125.48
125.43
123.79
113.02
108.01
77.25
77.00
76.74
134.93
133.71
132.47
131.18
129.81
129.77
128.90
128.38
126.26
126.13
125.74
125.48
125.43
123.79
122.34
21.47
N
N
N
Me
4f
140
135
130
125
Chemical Shift (ppm)
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

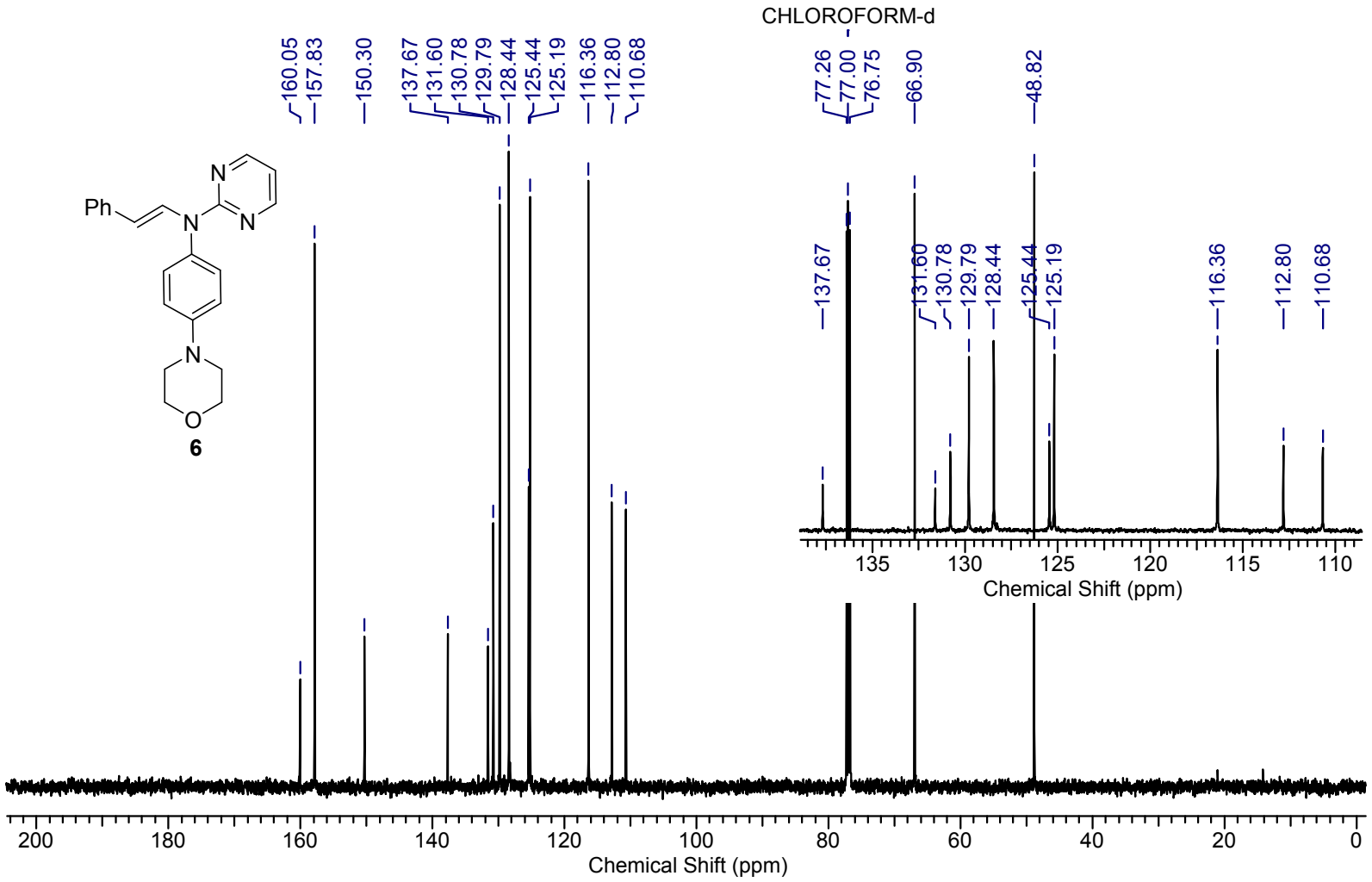

CHLOROFORM-d
8.56
8.53
8.44
8.43
7.47
7.46
7.29
7.27
7.09
7.08
6.99
6.77
6.77
6.76
5.31
5.28
2.44
CHLOROFORM-d
Br
F
N
N
N
Me
4g
7.47
7.46
7.44
7.29
7.27
7.20
7.20
7.19
7.18
7.18
7.17
7.17
7.09
7.08
7.01
6.99
6.98
6.77
6.77
6.76
2.03
1.37
1.12
2.14
1.01
1.15
7.50
7.25
7.00
6.75
Chemical Shift (ppm)
1.07
2.01
2.03
1.37
1.12
2.14
1.01
1.15
1.00
3.19
12
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


CHLOROFORM-d
159.73
158.01
157.88
140.00
139.61
135.50
131.28
129.78
129.67
129.00
126.07
125.34
125.29
116.36
116.18
113.25
109.06
108.89
108.24
77.25
77.00
76.74
21.44
Br
F
N
N
N
Me
4g
Chemical Shift (ppm)
Chemical Shift (ppm)


CHLOROFORM-d
8.65
8.62
8.46
8.45
7.76
7.74
7.63
7.61
7.47
7.40
7.39
7.32
7.27
7.13
6.77
6.77
5.53
5.50
1.61
Ph
N
N
N
Cl
5
CHLOROFORM-d
7.76
7.74
7.63
7.61
7.47
7.45
7.40
7.39
7.34
7.32
7.28
7.27
7.25
7.14
7.13
7.12
2.06
2.11
8.88
1.32
7.75
7.50
7.25
Chemical Shift (ppm)
1.06
2.08
2.06
2.11
8.88
1.32
1.12
1.00
11
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


CHLOROFORM-d
159.85
157.92
139.59
139.36
137.44
133.64
130.46
129.75
128.99
128.51
128.44
125.70
125.27
113.20
111.27
77.26
77.00
76.75
Ph
N
N
N
Cl
5
139.59
139.36
138.85
137.44
133.64
130.46
129.75
128.99
128.51
128.44
125.70
125.27
140
135
130
125
Chemical Shift (ppm)
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)


CHLOROFORM-d
8.67
8.64
8.44
8.44
7.33
7.32
7.28
7.27
7.22
7.21
7.12
7.09
7.08
6.74
6.73
5.50
5.47
3.93
3.92
3.91
3.30
3.29
3.28
Ph
N
N
N
N
O
6
CHLOROFORM-d
7.33
7.32
7.28
7.27
7.25
7.22
7.21
7.12
7.09
7.08
6.75
6.74
6.73
2.11 2.22 2.07
3.13
1.03
7.4
7.3
7.2
7.1
7.0
6.9
6.8
6.7
Chemical Shift (ppm)
1.01 1.96 2.11 2.22 2.07 3.13 1.03
1.00
4.10
4.15
10
9
8
7
6
5
4
3
2
1
Chemical Shift (ppm)


CHLOROFORM-d
160.05
157.83
150.30
137.67
131.60
130.78
129.79
128.44
125.44
125.19
116.36
112.80
110.68
77.26
77.00
76.75
66.90
48.82
Ph
N
N
N
N
O
6
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)
135
130
125
120
115
110
Chemical Shift (ppm)