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SUPPORTING INFORMATION

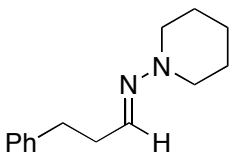
Title: Uncatalyzed Strecker-Type Reaction of *N*,*N*-Dialkylhydrazones in Pure Water
Author(s): Eugenia Marqués-López, Raquel P. Herrera, Rosario Fernández,* José M. Lassaletta*
Ref. No.: O200800297

General experimental methods. Purification of reaction products was carried out by flash chromatography using silica-gel (0.063-0.200 mm). Analytical thin layer chromatography was performed on 0.25 mm silica-gel 60-F plates. ^{1}H NMR spectra were recorded at 300 or 500 MHz; ^{13}C NMR spectra were recorded at 75 or 125 MHz in CD_3COCD_3 or $CDCl_3$ as the solvent. Chemical shifts were reported in the δ scale relative to residual CH_3COCH_3 (2.05 ppm) and $CHCl_3$ (7.26 ppm) for ^{1}H NMR and to the central line of CD_3COCD_3 (29.84 ppm) and $CDCl_3$ (77.16 ppm) for ^{13}C NMR. All commercially available solvents and reagents were used as received.

General procedure for the synthesis of aldehyde hydrazones 3a-g, 3a', and 5.

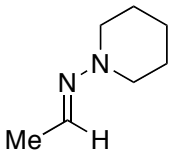
Na_2SO_4 and the corresponding aldehyde (20 mmol) were added to a solution of piperidin-1-amine (2.6 mL, 24 mmol) in CH_2Cl_2 (12 mL, 1.7 M). The mixture was stirred until total consumption of starting material, filtered and concentrated. Starting material, purification method, yields and spectral data for compounds **3a-g, 3a',** and **5** are as follows:

(*E*)-*N*-(3-Phenylpropylideneamino)piperidine (3a)



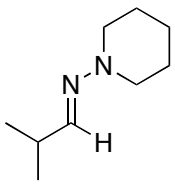
From dihydrocinamaldehyde, flash chromatography (1:4 → 1:1 Et_2O:hexane) gave 3.9 g (90%) of hydrazone **3a** as an oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.46-1.53 (m, 2H), 1.68-1.75 (m, 4H), 2.55-2.62 (m, 2H), 2.84 (t, J = 7.5 Hz, 2H), 2.93 (t, J = 5.7 Hz, 4H), 6.96 (t, J = 5.4 Hz, 1H), 7.19-7.33 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.3, 25.4, 34.0, 35.0, 52.9, 126.0, 128.5, 128.6, 139.6, 141.6. HRMS calcd for $C_{14}H_{21}N_2$ 217.1705; found 217.1701.

(*E*)-*N*-(Ethylideneamino)piperidine (3b)



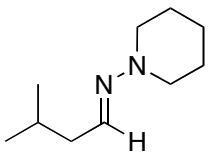
From acetaldehyde, flash chromatography (hexane → 1:9 EtOAc:hexane) gave 2.2 g (88%) of hydrazone **3b** as an oil. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 1.40-1.48 (m, 2H), 1.58-1.66 (m, 4H), 1.81 (d, J = 5.1 Hz, 3H), 2.82-2.86 (m, 4H), 6.88 (q, J = 5.1 Hz, 1H). ^{13}C NMR (75 MHz, CD_3COCD_3) δ 19.2, 25.0, 26.0, 53.3, 134.4. HRMS calcd for $C_7H_{15}N_2$ 127.1235; found 127.1231.

(*E*)-*N*-[(2-Methyl)propylideneamino]piperidine (3c)



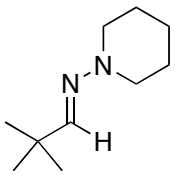
From isobutyraldehyde, flash chromatography (hexane) gave 2.8 g (90%) of hydrazone **3c** as an oil. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 1.01 (d, J = 6.9 Hz, 6H), 1.40-1.48 (m, 2H), 1.59-1.67 (m, 4H), 2.34-2.44 (m, 1H), 2.82-2.85 (m, 4H), 6.78 (d, J = 5.1 Hz, 1H). ^{13}C NMR (75 MHz, CD_3COCD_3) δ 21.0, 25.0, 26.0, 32.5, 53.2, 144.1. HRMS calcd for $C_9H_{18}N_2$ 154.1470; found 154.1476.

(*E*)-*N*-[(3-Methyl)butylideneamino]piperidine (3d)



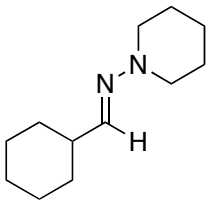
From isovaleraldehyde, flash chromatography (1:8 → 1:1 Et_2O:hexane) gave 3.3 g (98%) of hydrazone **3d** as an oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.92 (d, J = 6.7 Hz, 6H), 1.43-1.47 (m, 2H), 1.68 (m, 4H), 1.78 (m, 1H), 2.11 (dd, J = 7.0 Hz, J = 6.0 Hz, 2H), 2.55 (t, J = 6.0 Hz, 4H), 6.95 (t, J = 6.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.5, 24.3, 25.4, 27.5, 42.2, 53.2, 141.1. HRMS calcd for $C_{10}H_{21}N_2$ 169.1705; found 169.1704.

(*E*)-*N*-[(2,2-Dimethyl)propylideneamino]piperidine (3e)



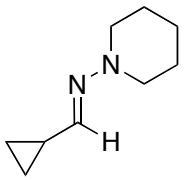
From pivalaldehyde, flash chromatography (hexane → 1:4 EtOAc:hexane) gave 2.9 g (85%) of hydrazone **3e** as an oil. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 1.03 (s, 9H), 1.43-1.49 (m, 2H), 1.59-1.67 (m, 4H), 2.82-2.85 (m, 4H), 6.81 (s, 1H). ^{13}C NMR (75 MHz, CD_3COCD_3) δ 25.1, 26.0, 28.6, 34.9, 53.3, 146.7. HRMS calcd for $C_{10}H_{21}N_2$ 169.1705; found 169.1696.

(*E*)-*N*-(Cyclohexylmethyleneamino)piperidine (3f)



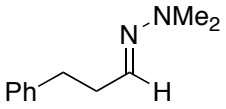
From cyclohexanecarbaldehyde, flash chromatography (hexane → 1:9 EtOAc:hexane) gave 3.4 g (87%) of hydrazone **3f** as an oil. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 1.14-1.38 (m, 5H), 1.40-1.48 (m, 2H), 1.59-1.76 (m, 9H), 2.07-2.16 (m, 1H), 2.81-2.85 (m, 4H), 6.76 (d, J = 5.4 Hz, 1H). ^{13}C NMR (75 MHz, CD_3COCD_3) δ 25.0, 26.0, 26.5, 26.9, 31.9, 42.0, 53.2, 143.2. HRMS calcd for $C_{12}H_{22}N_2$ 194.1783; found 194.1775.

(*E*)-*N*-(Cyclopropylmethyleneamino)piperidine (3g)



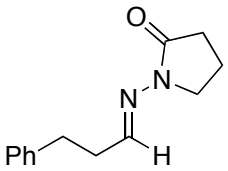
From cyclopropanecarbaldehyde, flash chromatography (hexane → 1:3 Et_2O:hexane) gave 2.6 g (84%) of hydrazone **3g** as an oil. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 0.50-0.55 (m, 2H), 0.69-0.75 (m, 2H), 1.39-1.47 (m, 2H), 1.50-1.65 (m, 5H), 2.79-2.82 (m, 4H), 6.46 (d, J = 7.0 Hz, 1H). ^{13}C NMR (75 MHz, CD_3COCD_3) δ 5.9, 14.7, 25.0, 26.0, 53.5, 142.5. HRMS calcd for $C_9H_{16}N_2$ 152.1313; found 152.1312.

(*E*)-Dihydrocinnamaldehyde *N*,*N*-dimethylhydrazone (3a')[1]



Following the general procedure for **3a-g**, but starting from dihydrocinamaldehyde (1.6 mL, 11 mmol) and *N*,*N*-dimethylhydrazine (775 μL, 10 mmol), flash chromatography (1:6 → 1:1 Et_2O:hexane) gave 1.7 g (95%) of hydrazone **3a'** as an oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.53-2.60 (m, 2H), 2.73 (s, 6H), 2.79-2.84 (m, 2H), 6.66 (t, J = 5.4 Hz, 1H), 7.17-7.32 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.2, 34.9, 43.4, 126.0, 128.5, 128.6, 138.1, 141.6. HRMS calcd for $C_{11}H_{16}N_2$ 176.1313; found 176.1310.

1-(3-Phenylpropylideneamino)pyrrolidin-2-one (5)[2]



Following the general procedure for **3a-g**, but starting from dihydrocinamaldehyde (570 μL, 3.9 mmol) and 1-amino-2-pyrrolidinone[3] (300 mg, 3 mmol), flash chromatography (EtAcO) gave 480 mg (74%) of hydrazone **5** as a white solid. Mp 60-62 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.10-2.20 (m, 2H), 2.52-2.58 (m, 2H), 2.71-2.80 (m, 2H), 2.85-2.92 (m, 2H), 3.52-3.57 (m, 2H), 7.18-7.46 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.0, 30.0, 33.2, 34.4, 44.5, 126.2, 128.4, 128.5, 136.7, 140.6, 148.3, 171.4. HRMS calcd for $C_{13}H_{17}N_2O$ 217.1341; found 217.1331.

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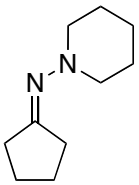
[1] S. E. Denmark, J. P. Edwards, O. Nicaise, *J. Org. Chem.* **1993**, *58*, 569.

[2] This product was synthesized in the frame of a different project: E. Martín-Zamora, E. Díez, E. Marqués-López, R. Fernández, J. M. Lassaletta, unpublished results.

[3] A. Zubek, *Z. Chem.* **1969**, *9*, 58.

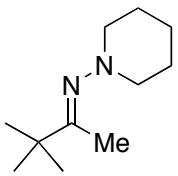
General procedure for the synthesis of ketone hydrazones 3h-k. To a stirred solution of ketone (15 mmol) in MeOH (3 mL) containing a drop of acetic acid was added 1-amino piperidine (1.7 mL, 15.8 mmol). The mixture was refluxed until total consumption of starting material (1 d aprox.), dried (Na_2SO_4), filtered and concentrated. Starting material, purification method, yields and spectral data for compounds **3h-k** are as follows:

***N*-(Cyclopentylideneamino)piperidine (3h)**



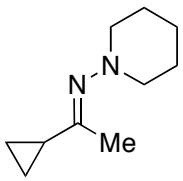
From cyclopentanone, flash chromatography (hexane → Et_2O → EtOAc) gave 1.9 g (75%) of hydrazone **3h** as an oil. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 1.36-1.42 (m, 2H), 1.57-1.77 (m, 8H), 2.23 (t, J = 6.9 Hz, 2H), 2.36 (t, J = 6.9 Hz, 2H), 2.57-2.60 (m, 4H). ^{13}C NMR (75 MHz, CD_3COCD_3) δ 24.7, 24.8, 25.4, 26.2, 29.5, 33.7, 56.7, 175.1. HRMS calcd for $C_{10}H_{18}N_2$ 166.1470; found 166.1478.

(*E*)-*N*-(3,3-Dimethyl)butan-2-ylideneamino)piperidine (3i)



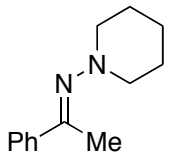
From 3,3-dimethylbutan-2-one, flash chromatography (hexane) gave 1.9 g (71%) of hydrazone **3i** as an oil. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 1.08 (s, 9H), 1.40-1.44 (m, 2H), 1.59-1.66 (m, 4H), 1.92 (s, 3H), 2.50-2.53 (m, 4H). ^{13}C NMR (75 MHz, CD_3COCD_3) δ 12.5, 24.8, 26.1, 28.4, 38.7, 56.6, 172.5. HRMS calcd for $C_{11}H_{22}N_2$ 182.1783; found 182.1785.

(*E*)-*N*-(1-Cyclopropylethylideneamino)piperidine (3j)



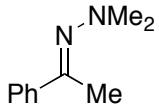
From 1-cyclopropylethanone, flash chromatography (hexane) gave 0.9 g (35%) of hydrazone **3j** (oil) as a 2.4:1 mixture of *E* and *Z* isomers. Data of *E* isomer: ^{1}H NMR (300 MHz, CD_3COCD_3) δ 0.64-0.79 (m, 4H), 1.37-1.43 (m, 2H), 1.54-1.65 (m, 5H), 1.82 (s, 3H), 2.47-2.50 (m, 4H). ^{13}C NMR (75 MHz, CD_3COCD_3) δ 5.7, 6.2, 18.0, 24.7, 26.1, 56.7, 167.7. HRMS calcd for $C_{10}H_{18}N_2$ 166.1470; found 166.1471.

(*E*)-*N*-(1-Phenylethylideneamino)piperidine (3k)



From acetophenone, flash chromatography (hexane) gave 2.0 g (65%) of hydrazone **3k** as an oil. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 1.44-1.52 (m, 2H), 1.67-1.75 (m, 4H), 2.34 (s, 3H), 2.72-2.75 (m, 4H), 7.34-7.38 (m, 3H), 7.79-7.84 (m, 2H). ^{13}C NMR (75 MHz, CD_3COCD_3) δ 15.2, 24.7, 26.1, 56.9, 127.2, 128.9, 129.9, 140.0, 161.9. HRMS calcd for $C_{13}H_{18}N_2$ 202.1470; found 202.1480.

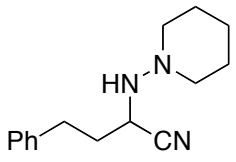
(*E*)-Acetophenone *N*,*N*-dimethylhydrazone (3k')



Following the general procedure for **3h-k**, but starting from acetophenone (2.3 mL, 20 mmol) and *N*,*N*-dimethylhydrazine (2.1 mL, 28 mmol), flash chromatography (hexane) gave 1.9 g (60%) of hydrazone **3k'** as an oil. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 2.34 (s, 3H), 2.53 (s, 6H), 7.35-7.38 (m, 3H), 7.79-7.82 (m, 2H). ^{13}C NMR (75 MHz, CD_3COCD_3) δ 15.1, 47.5, 127.1, 128.9, 129.9, 139.9, 161.6. HRMS calcd for $C_{10}H_{14}N_2$ 162.1157; found 162.1166.

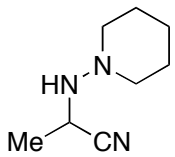
General procedure for the synthesis of hydrazino nitriles 4a-k, 4a', and 4k'. TMSCN (1.2-3.0 eq)[4] was added to a solution of hydrazone **3a-k**, **3a'**, or **3k'** (0.2 mmol) in H_2O (0.5 mL, 0.4 M) and the mixture was stirred until total consumption of starting material (5-72 h),[4] diluted with satd. $NaHCO_3$ (2 mL), extracted with AcOEt (3 × 1 mL), dried (Na_2SO_4), filtered, and concentrated. Starting material, yields and spectral data for compounds **4a-k**, **4a'**, and **4k'** are as follows:

4-Phenyl-2-(piperidin-1-ylamino)butanenitrile (4a)



From hydrazone **3a** (43.2 mg, 0.2 mmol), **4a** (43.8 mg, 90%) was obtained as an oil: ^{1}H NMR (300 MHz, CD_3COCD_3) δ 1.32-1.40 (m, 2H), 1.56-1.63 (m, 4H), 2.01-2.09 (m, 2H), 2.62-2.77 (m, 4H), 2.78-2.91 (m, 2H), 3.44 (d, J = 5.1 Hz, 1H), 3.74-3.80 (m, 1H), 7.19-7.34 (m, 5H). ^{13}C NMR (75 MHz, CD_3COCD_3) δ 24.3, 26.8, 32.4, 34.3, 50.9, 58.4, 121.8, 127.0, 129.2, 129.3, 141.8. HRMS calcd for $C_{15}H_{21}N_3$ 243.1735; found 243.1729.

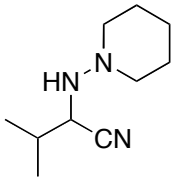
2-(Piperidin-1-ylamino)propanenitrile (4b)



From hydrazone **3b** (25.2 mg, 0.2 mmol), **4b** (27.5 mg, 90%) was obtained as an oil: ^{1}H NMR (300 MHz, CD_3COCD_3) δ 1.35 (d, J = 7.0 Hz, 3H), 1.28-1.39 (m, 2H), 1.54-1.61 (m, 4H), 2.58-2.75 (m, 4H), 3.31 (br s, 1H), 3.84-3.93 (m, 1H). ^{13}C NMR (75 MHz, CD_3COCD_3) δ 18.1, 24.4, 26.9, 46.3, 58.3, 122.6. HRMS calcd for $C_8H_{16}N_3$ 154.1344; found 154.1341.

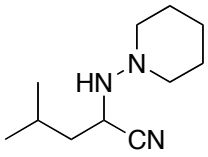
[4] See Table 2.

3-Methyl-2-(piperidin-1-ylamino)butanenitrile (4c)



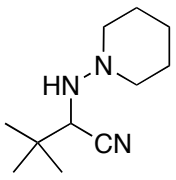
From hydrazone **3c** (30.8 mg, 0.2 mmol), **4c** (32.3 mg, 89%) was obtained as an oil : ^{1}H NMR (300 MHz, CD_3COCD_3) δ 1.03 (d, J = 6.9 Hz, 3H), 1.04 (d, J = 6.9 Hz, 3H), 1.29-1.39 (m, 2H), 1.53-1.61 (m, 4H), 1.89-2.05 (m, 1H), 2.62-2.73 (m, 4H), 3.20 (br s, 1H), 3.64 (t, J = 5.8 Hz, 1H). ^{13}C NMR (75 MHz, CD_3COCD_3) δ 18.5, 19.7, 24.5, 26.9, 30.7, 58.1, 58.2, 120.9. HRMS calcd for $C_{10}H_{18}N_3$ 180.1500; found 180.1486.

4-Methyl-2-(piperidin-1-ylamino)pentanenitrile (4d)



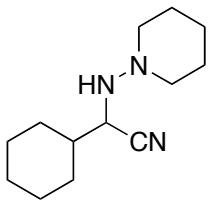
From hydrazone **3d** (33.6 mg, 0.2 mmol), **4d** (37.1 mg, 95%) was obtained as an oil: ^{1}H NMR (300 MHz, CD_3COCD_3) δ 0.93 (d, J = 6.6 Hz, 3H), 0.95 (d, J = 6.6 Hz, 3H), 1.29-1.41 (m, 2H), 1.54-1.61 (m, 6H), 1.79-1.92 (m, 1H), 2.56-2.83 (m, 4H), 3.30 (br s, 1H), 3.78-3.85 (m, 1H). ^{13}C NMR (75 MHz, CD_3COCD_3) δ 22.4, 22.8, 24.4, 25.6, 26.9, 41.2, 50.1, 58.4, 122.2. HRMS calcd for $C_{11}H_{20}N_3$ 194.1657; found 194.1653.

3,3-Dimethyl-2-(piperidin-1-ylamino)butanenitrile (4e)



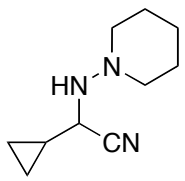
From hydrazone **3e** (33.6 mg, 0.2 mmol), **4e** (35.9 mg, 92%) was obtained as an oil: ^{1}H NMR (300 MHz, CD_3COCD_3) δ 1.04 (s, 9H), 1.29-1.38 (m, 2H), 1.53-1.61 (m, 4H), 2.56-2.84 (m, 4H), 3.12 (d, J = 7.0 Hz, 1H), 3.52 (d, J = 7.0 Hz, 1H). ^{13}C NMR (75 MHz, CD_3COCD_3) δ 24.4, 26.5, 26.9, 34.4, 58.0, 62.3, 121.3. HRMS calcd for $C_{11}H_{20}N_3$ 194.1657; found 194.1647.

2-Cyclohexyl-2-(piperidin-1-ylamino)acetonitrile (4f)



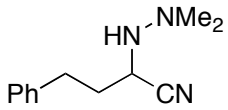
From hydrazone **3f** (33.8 mg, 0.2 mmol), **4f** (40.3 mg, 91%) was obtained as an oil: ^{1}H NMR (300 MHz, CD_3COCD_3) δ 1.03-1.41 (m, 7H), 1.53-1.93 (m, 10H), 2.60-2.74 (m, 4H), 3.18 (d, J = 5.8 Hz, 1H), 3.63 (t, J = 5.8 Hz, 1H). ^{13}C NMR (75 MHz, CD_3COCD_3) δ 24.4, 26.4, 26.5, 26.9, 27.0, 29.7, 30.4, 40.0, 57.5, 58.2, 121.1. HRMS calcd for $C_{13}H_{22}N_3$ 220.1814; found 220.1808.

2-Cyclopropyl-2-(piperidin-1-ylamino)acetonitrile (4g)



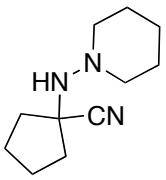
From hydrazone **3g** (30.4 mg, 0.2 mmol), **4g** (32.2 mg, 90%) was obtained as an oil: ^{1}H NMR (300 MHz, CD_3COCD_3) δ 0.36-0.65 (m, 4H), 1.13-1.25 (m, 1H), 1.29-1.38 (m, 2H), 1.53-1.61 (m, 4H), 2.59-2.75 (m, 4H), 3.28 (br s, 1H), 3.35 (dd, J = 8.2 Hz, J = 4.3 Hz, 1H). ^{13}C NMR (75 MHz, CD_3COCD_3) δ 3.0, 4.5, 13.2, 24.4, 26.9, 56.1, 58.1, 121.0. HRMS calcd for $C_{10}H_{16}N_3$ 178.1344; found 178.1338.

2-(2,2-Dimethylhydrazinyl)-4-phenylbutanenitrile (4a')



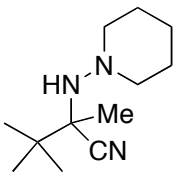
From hydrazone **3a'** (35.2 mg, 0.2 mmol), **4a'** (41.4 mg, 90%) was obtained as an oil: ^{1}H NMR (300 MHz, CD_3COCD_3) δ 1.99-2.06 (m, 2H), 2.45 (s, 6H), 2.77-2.84 (m, 2H), 3.34 (d, J = 4.8 Hz, 1H), 3.72-3.78 (m, 1H), 7.17-7.32 (m, 5H). ^{13}C NMR (75 MHz, CD_3COCD_3) δ 32.4, 34.2, 48.4, 51.1, 121.8, 127.0, 129.2, 129.3, 141.8. HRMS Calcd for $C_{12}H_{16}N_3$ 202.1344; found 202.1343.

1-(Piperidin-1-ylamino)cyclopentanecarbonitrile (4h)



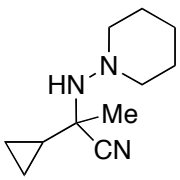
From hydrazone **3h** (33.2 mg, 0.2 mmol), **4h** (36.3 mg, 94%) was obtained as an oil: ^{1}H NMR (300 MHz, CD_3COCD_3) δ 1.28-1.39 (m, 2H), 1.55-1.63 (m, 4H), 1.65-2.06 (m, 8H), 2.61-2.79 (m, 4H), 3.38 (br s, 1H). ^{13}C NMR (75 MHz, CD_3COCD_3) δ 24.1, 24.4, 27.0, 38.1, 59.4, 62.1, 124.8. Mass spectrum (CI) *m/z* (rel intensity) 167 (M^+-CN, 27), 166 (M^+-HCN, 100), 84 (72). HRMS calcd for $C_{10}H_{18}N_2$ (M – HCN) 166.1470; found 166.1473.

2,3,3-Trimethyl-2-(piperidin-1-ylamino)butanenitrile (4i)



From hydrazone **3i** (36.4 mg, 0.2 mmol), **4i** (37.6 mg, 90%) was obtained as a white solid; M.p. 42-44 °C. ^{1}H NMR (300 MHz, C_6D_6, 70 °C) δ 0.90 (s, 9H), 1.11-1.18 (m, 2H), 1.28 (s, 3H), 1.45-1.52 (m, 4H), 2.33-2.45 (m, 4H), 2.78 (br s, 1H). ^{13}C NMR (75 MHz, C_6D_6, 70 °C) δ 19.6, 24.0, 25.2, 26.5, 36.2, 59.1, 64.0, 122.9. Mass spectrum (CI) *m/z* (rel intensity) 183 (M^+-CN, 39), 182 (M^+-HCN, 100), 84 (62). HRMS calcd for $C_{11}H_{22}N_2$ (M – HCN) 182.1783; found 182.1785.

2-Cyclopropyl-2-(piperidin-1-ylamino)propanenitrile (4j)

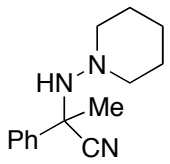


From hydrazone **3j** (33.2 mg, 0.2 mmol), **4j** (35.9 mg, 93%)[5] was obtained as an oil: ^{1}H NMR (300 MHz, CD_3COCD_3) δ 0.42-0.61 (m, 4H), 0.97-1.04 (m, 1H), 1.29-1.37 (m, 2H), 1.43 (s, 3H), 1.55-1.63 (m, 4H), 2.57-2.71 (m, 4H),

[5] **4j** was impurified with a 7% of unreacted hydrazone **3j**.

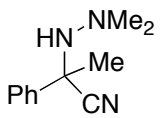
3.44 (br s, 1H). ^{13}C NMR (75 MHz, CD_3COCD_3) δ 1.2, 2.7, 18.6, 24.3, 24.8, 27.0, 59.3, 60.3, 121.8. Mass spectrum (CI) *m/z* (rel intensity) 167 (M^+-CN, 30), 166 (M^+-HCN, 100), 84 (43).

2-Phenyl-2-(piperidin-1-ylamino)propanenitrile (4k)



From hydrazone **3k** (40.4 mg, 0.2 mmol), **4k** (41.1 mg, 88%)[6] was obtained as an oil: ^{1}H NMR (300 MHz, CD_3COCD_3) δ 1.27-1.37 (m, 2H), 1.48-1.62 (m, 4H), 1.70 (s, 3H), 2.64-2.79 (m, 4H), 3.80 (br s, 1H), 7.32-7.49 (m, 3H), 7.51-7.64 (m, 2H). ^{13}C NMR (75 MHz, CD_3COCD_3) δ 24.3, 26.9, 28.2, 59.1, 61.7, 123.3, 127.0, 129.1, 129.2, 141.4. Mass spectrum (CI) *m/z* (rel intensity) 203 (M^+-CN, 38), 202 (M^+-HCN, 100), 84 (35). HRMS calcd for $C_{13}H_{18}N_2$ (M – HCN) 202.1470; found 202.1467.

2-(2,2-Dimethylhydrazinyl)-2-phenylpropanenitrile (4k')



From hydrazone **3k'** (32.5 mg, 0.2 mmol), flash chromatography (toluene) afforded **4k'** (26.8 mg, 71%) as an oil: ^{1}H NMR (300 MHz, CD_3COCD_3) δ 1.68 (s, 3H), 2.47 (s, 6H), 3.81 (br s, 1H), 7.35-7.44 (m, 3H), 7.61-7.63 (m, 2H). ^{13}C NMR (75 MHz, CD_3COCD_3) δ 28.5, 49.1, 61.8, 123.4, 126.8, 129.0, 129.2, 141.5. Mass spectrum (CI) *m/z* (rel intensity) 190 (M^+ + 1, 32), 163 (M^+ – CN, 84), 162 (M^+ – HCN, 100). HRMS cald for $C_{10}H_{14}N_2$ (M-HCN) 162.1157; found 162.1159.

'One-pot' reactions using TMSCN as the cyanide source. A mixture of hydrazine (130 μL, 1.2 mmol) and isovaleraldehyde or cyclopropanecarbaldehyde (1 mmol) was stirred for 10

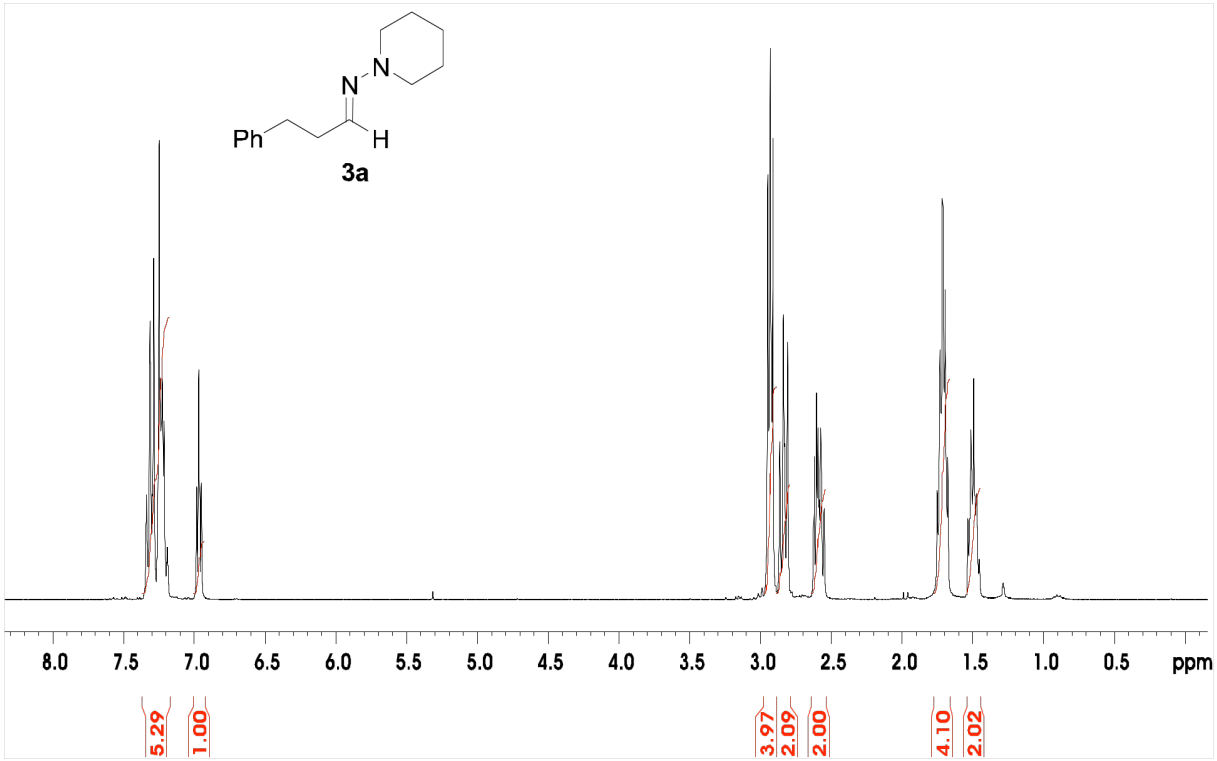
[6] **4k** was impurified with a 9% of unreacted hydrazone **3k**.

min. H_2O (2.5 mL) and TMSCN (268 μL, 2 mmol) were then added.[7] The mixture was stirred until total consumption of starting material (8 h), then satd. $NaHCO_3$ (2 mL) was added and the mixture was extracted with AcOEt (3 × 1 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated to afford compounds **4d** or **4g** as yellow oils in 94% and 84% yield, respectively.

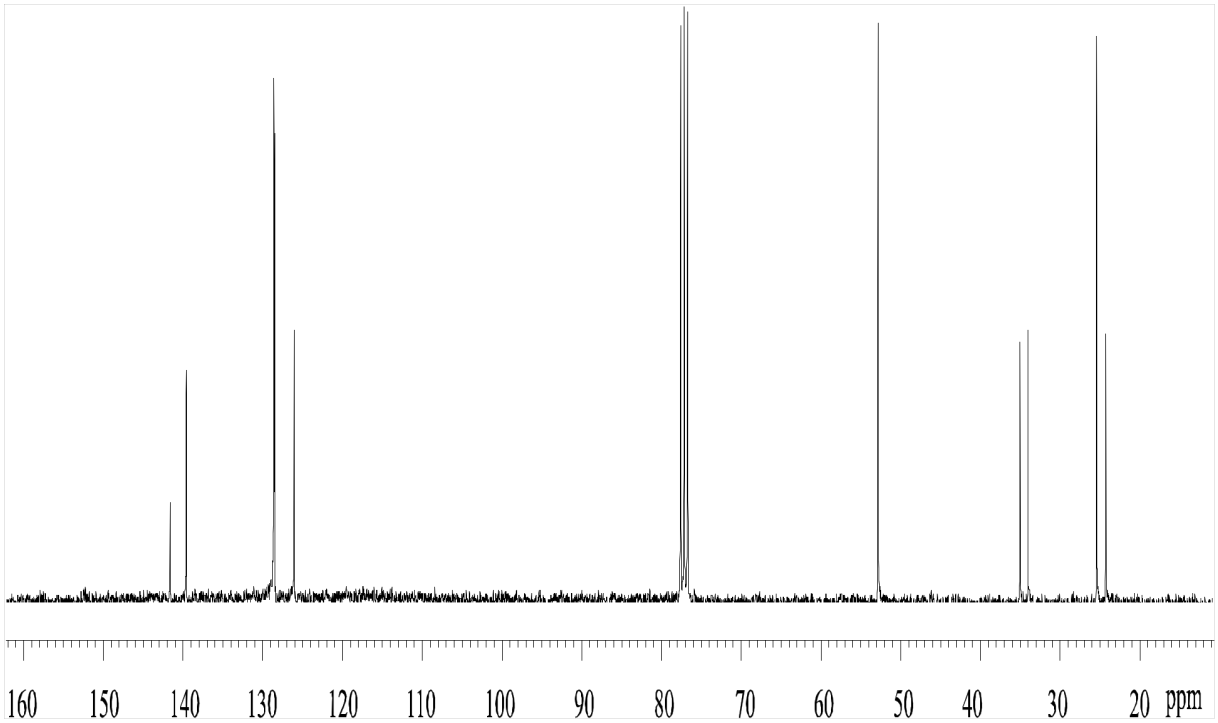
'One pot' reactions using KCN as the cyanide source. Hydrazine (130 μL, 1.2 mmol) and isovaleraldehyde or cyclopropanecarbaldehyde (1 mmol) were stirred for 10 minutes. H_2O (2.5 mL, 0.4 M), KCN (1.4 mmol or 2 mmol) and AcOH (1.4 mmol or 2 mmol) were consecutively added.[7] The mixture was stirred until total consumption of starting material (18 h), then satd. $NaHCO_3$ (2 mL) was added and the mixture was extracted with AcOEt (3 × 1 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated to afford compounds **4d** or **4g** as yellow oils in 90% and 80% yield, respectively.

[7] Reactions performed without a preliminary stirring of the aldehyde and the hydrazine also afforded products **4d** or **4g**, and no cyanohydrin resulting from the hydrocyanation of the aldehyde could be detected. The reactions, however, were not so clean under these conditions and the yields were lower. This can be attributed to a partial silylation or protonation of the hydrazine.

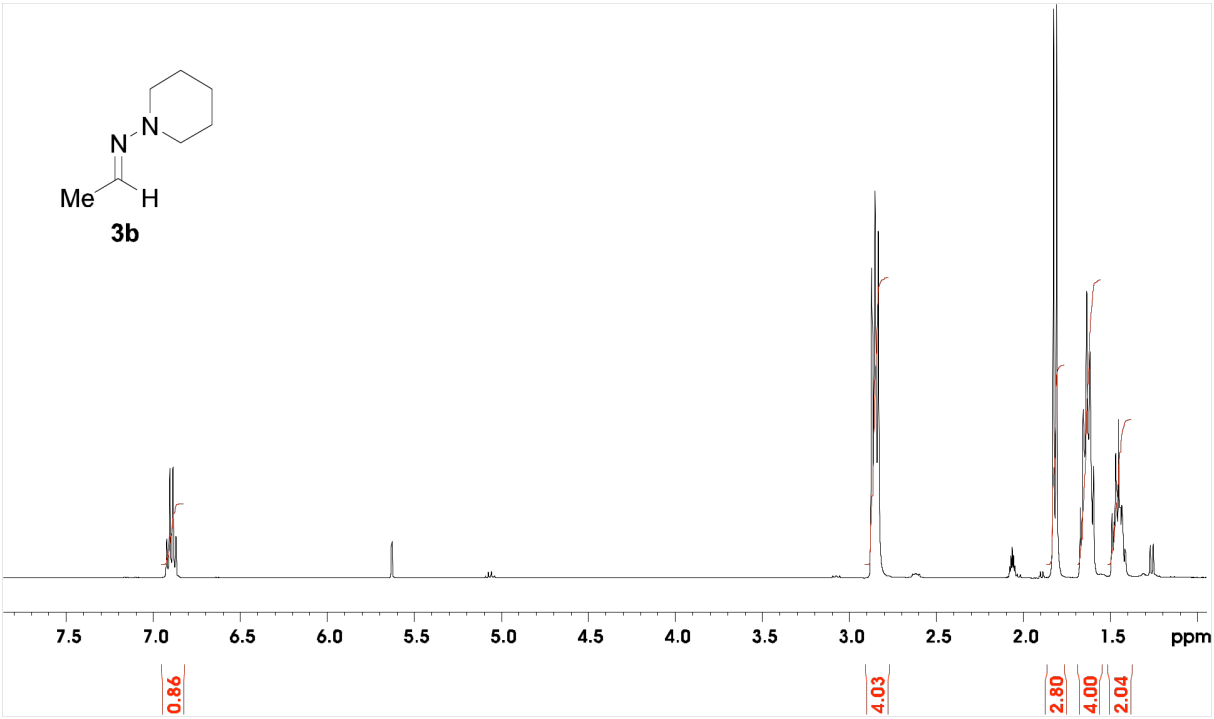
^{1}H NMR spectrum of **3a** (300 MHz, $CDCl_3$)



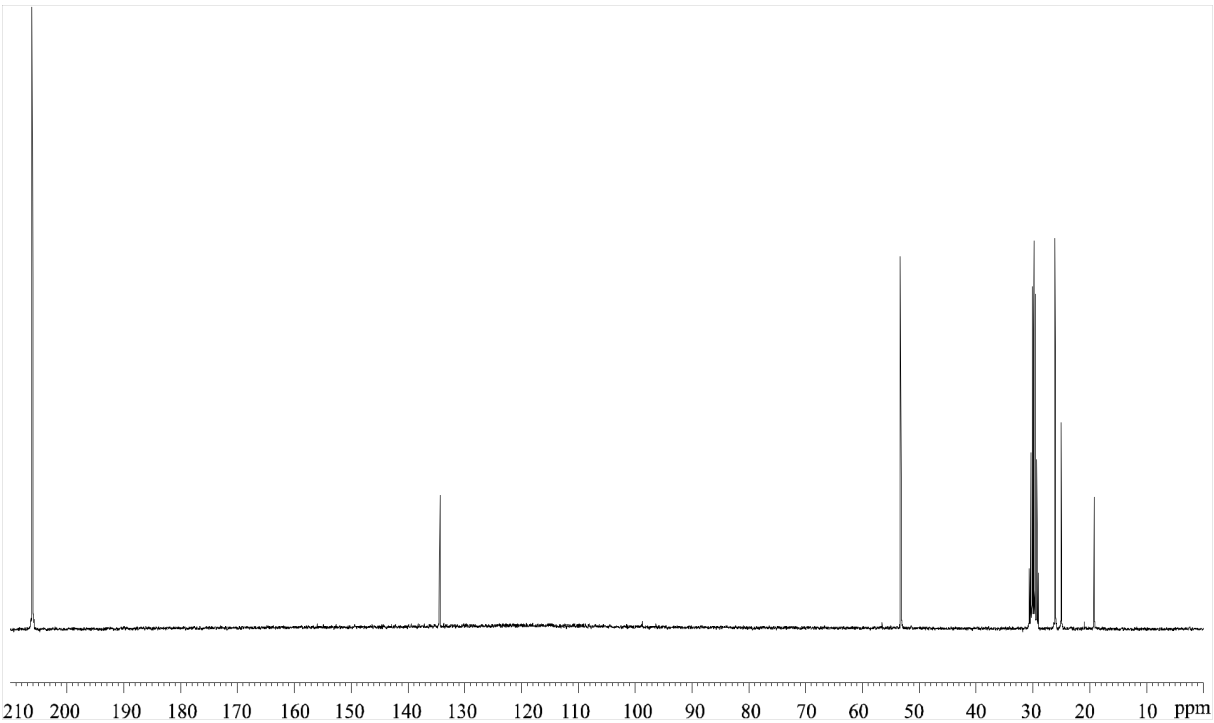
^{13}C NMR spectrum of **3a** (75 MHz, $CDCl_3$)



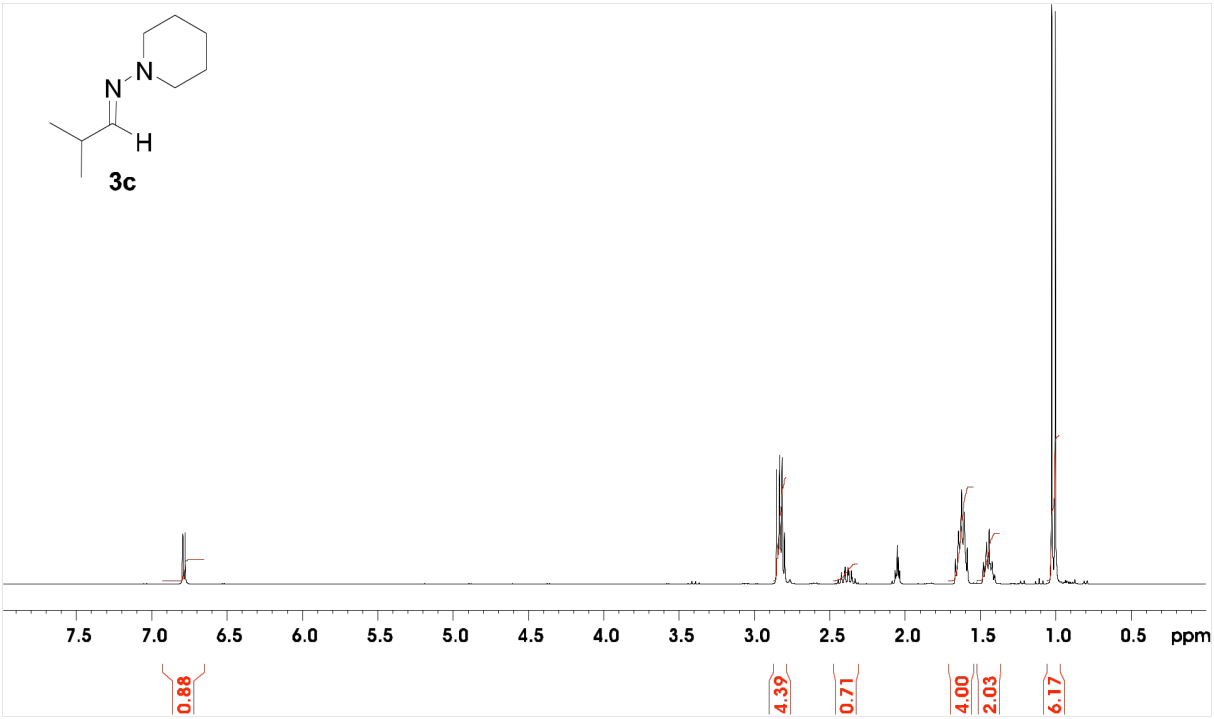
^{1}H NMR spectrum of **3b** (300 MHz, CD_3COCD_3)



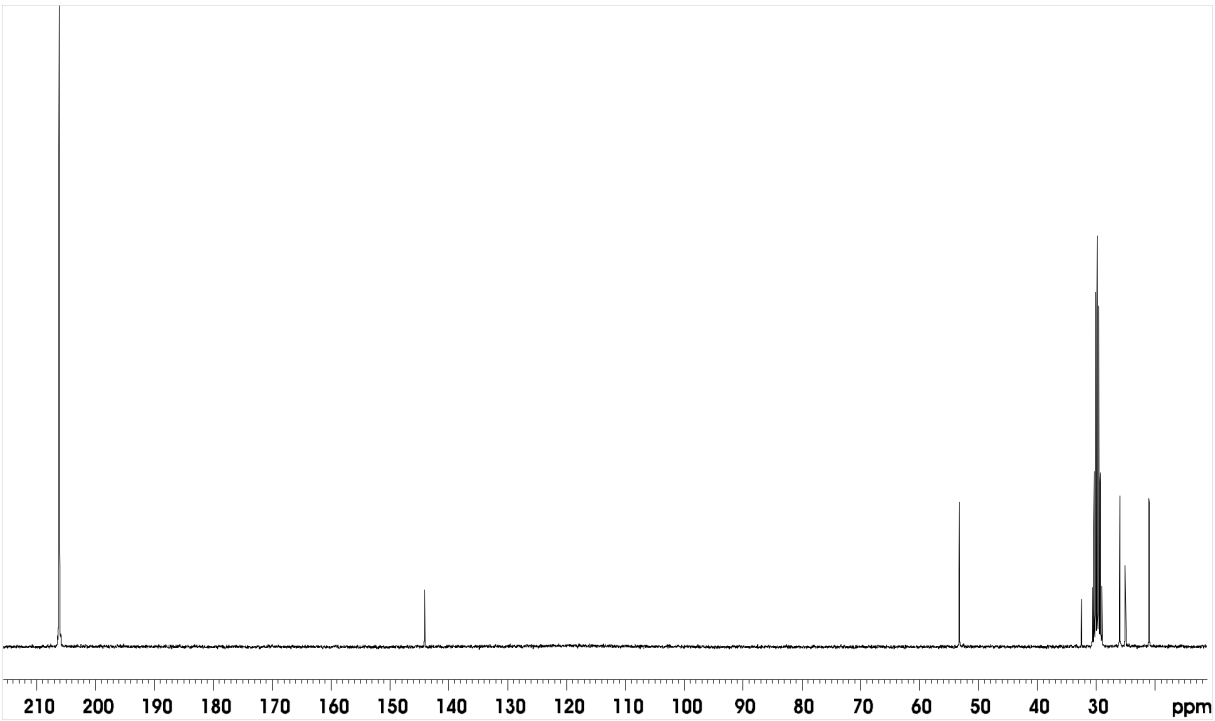
^{13}C NMR spectrum of **3b** (75 MHz, CD_3COCD_3)



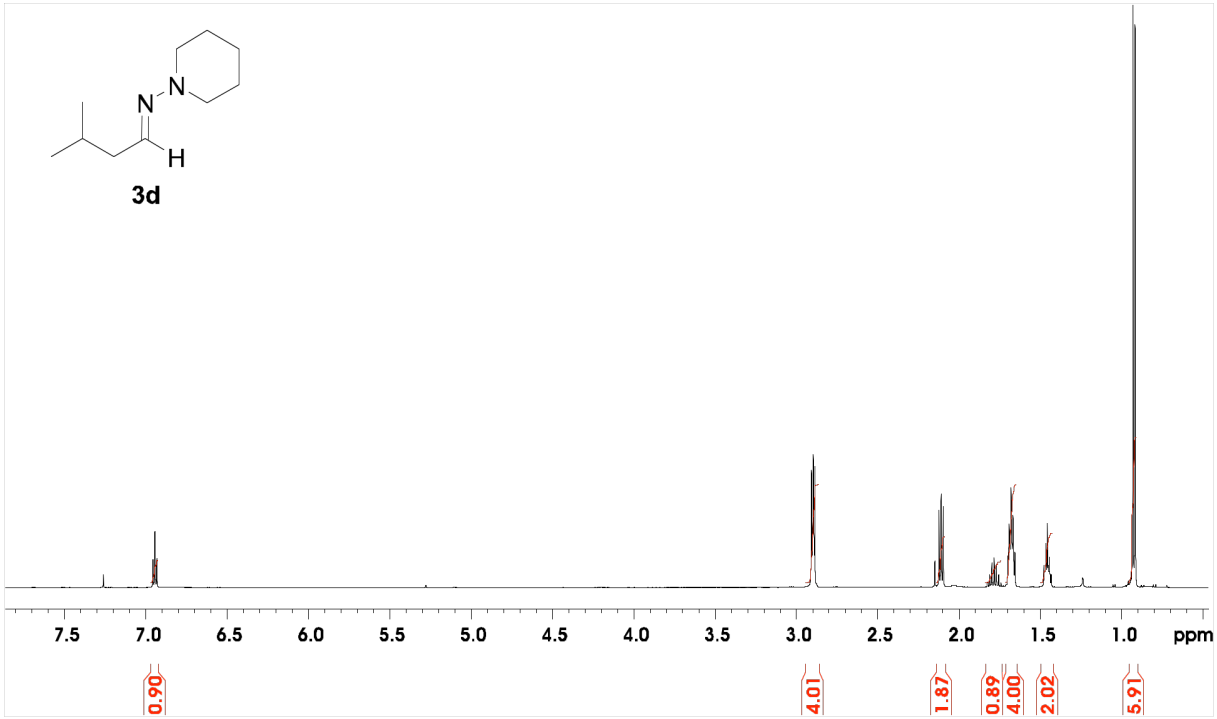
^{1}H NMR spectrum of **3c** (300 MHz, CD_3COCD_3)



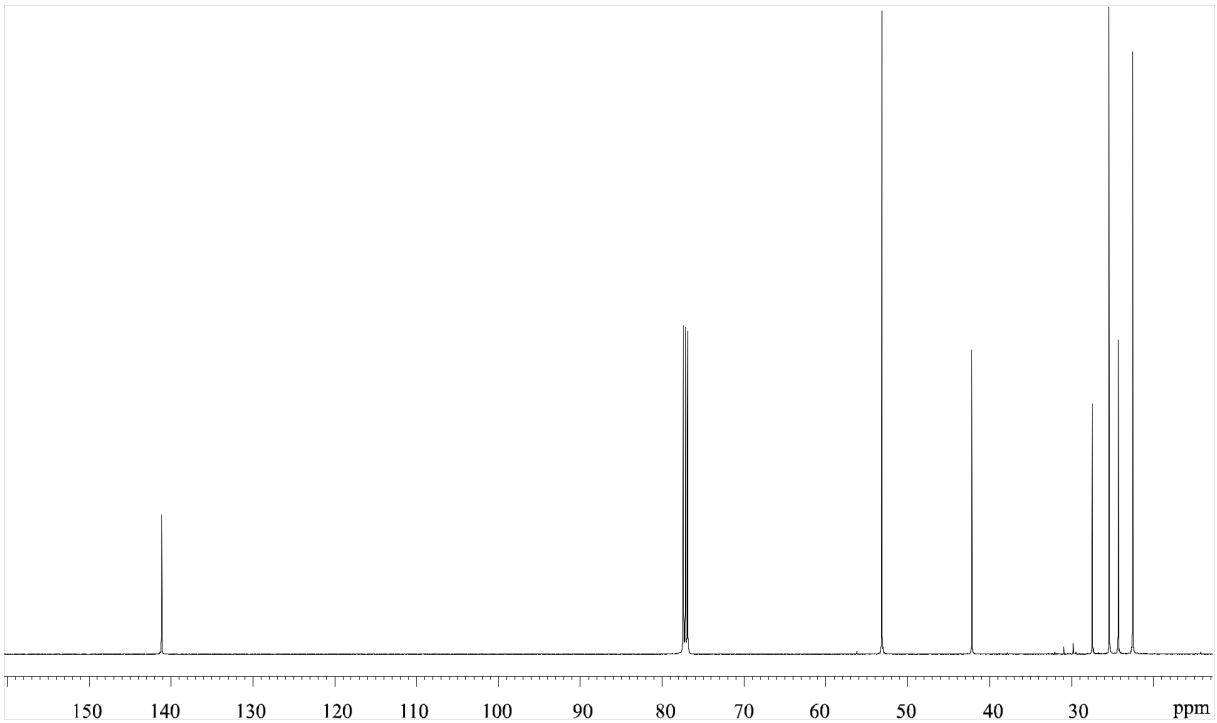
^{13}C NMR spectrum of **3c** (75 MHz, CD_3COCD_3)



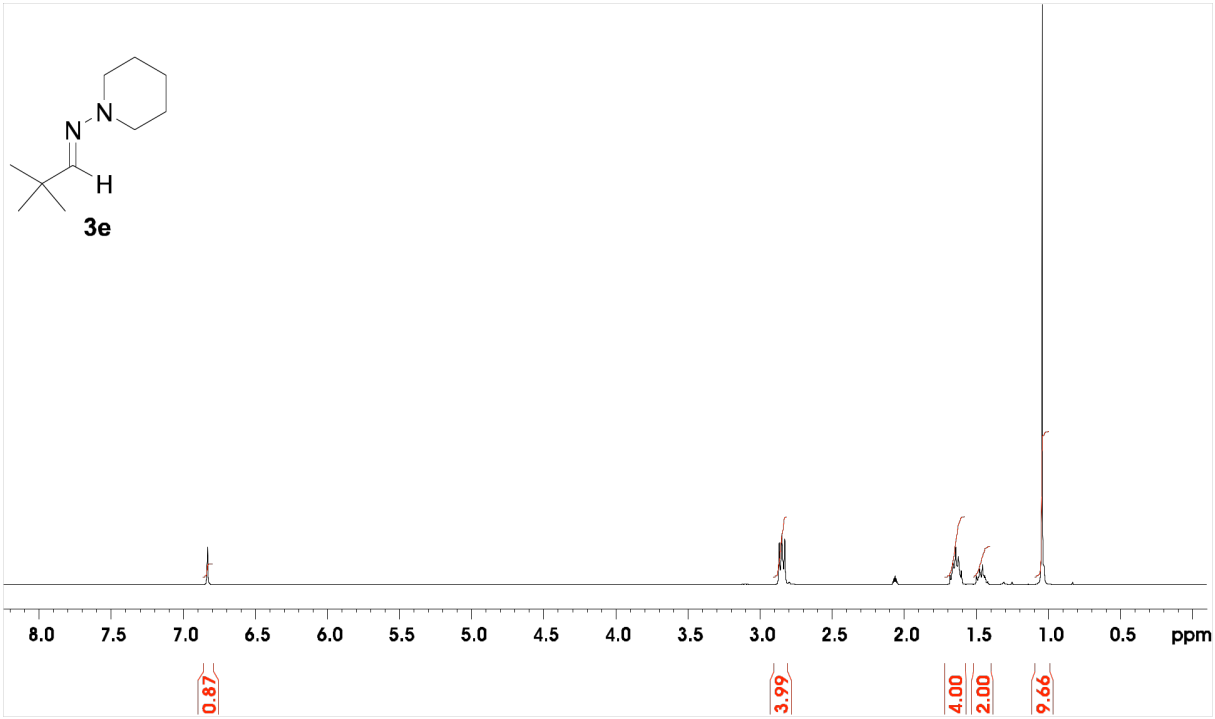
^{1}H NMR spectrum of **3d** (500 MHz, $CDCl_3$)



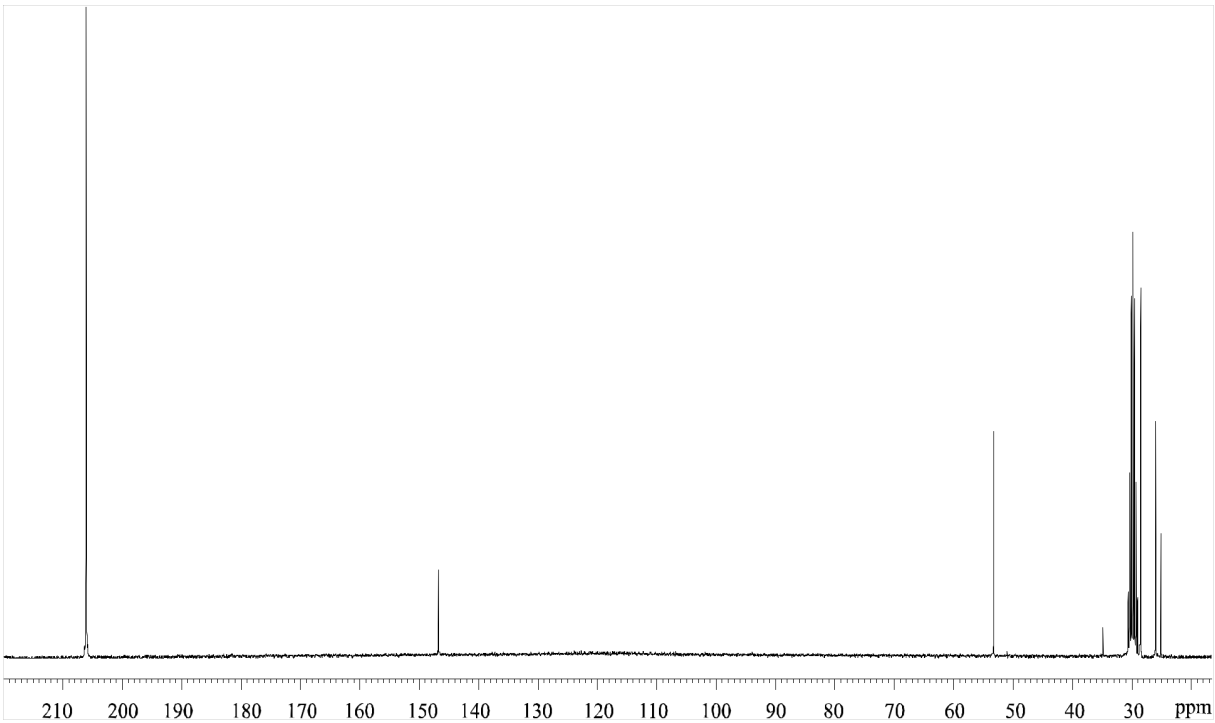
^{13}C NMR spectrum of **3d** (125 MHz, $CDCl_3$)



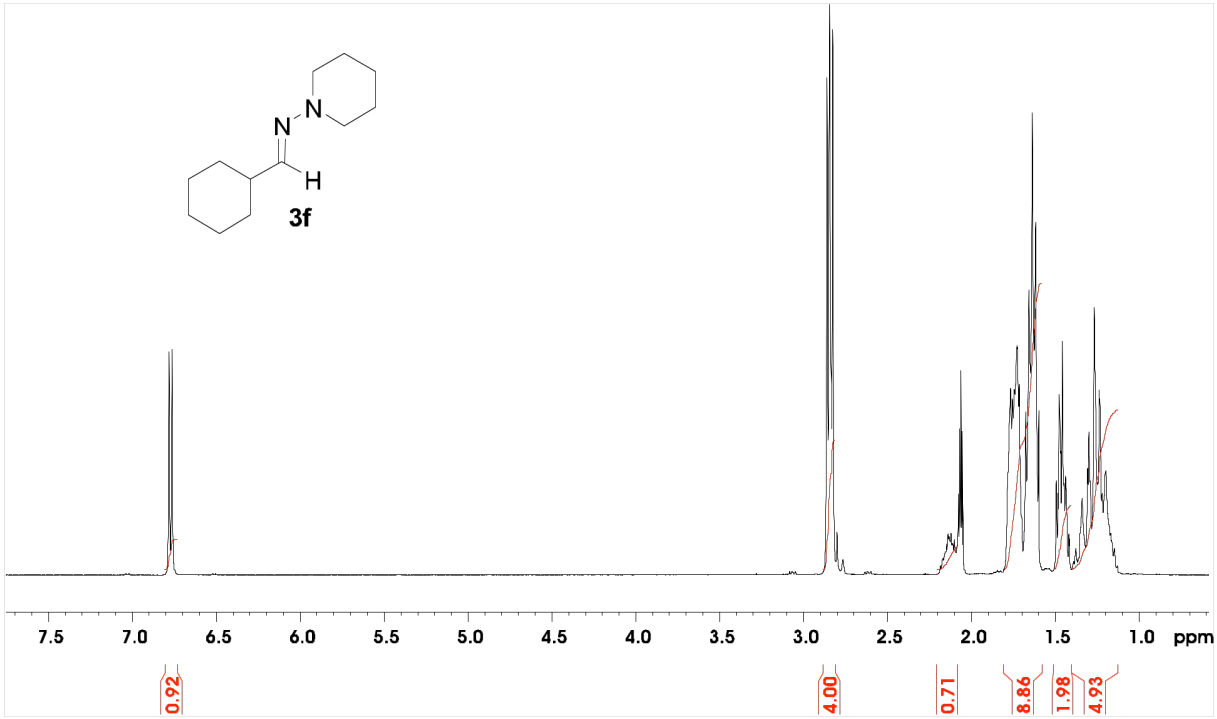
^{1}H NMR spectrum of **3e** (300 MHz, CD_3COCD_3)



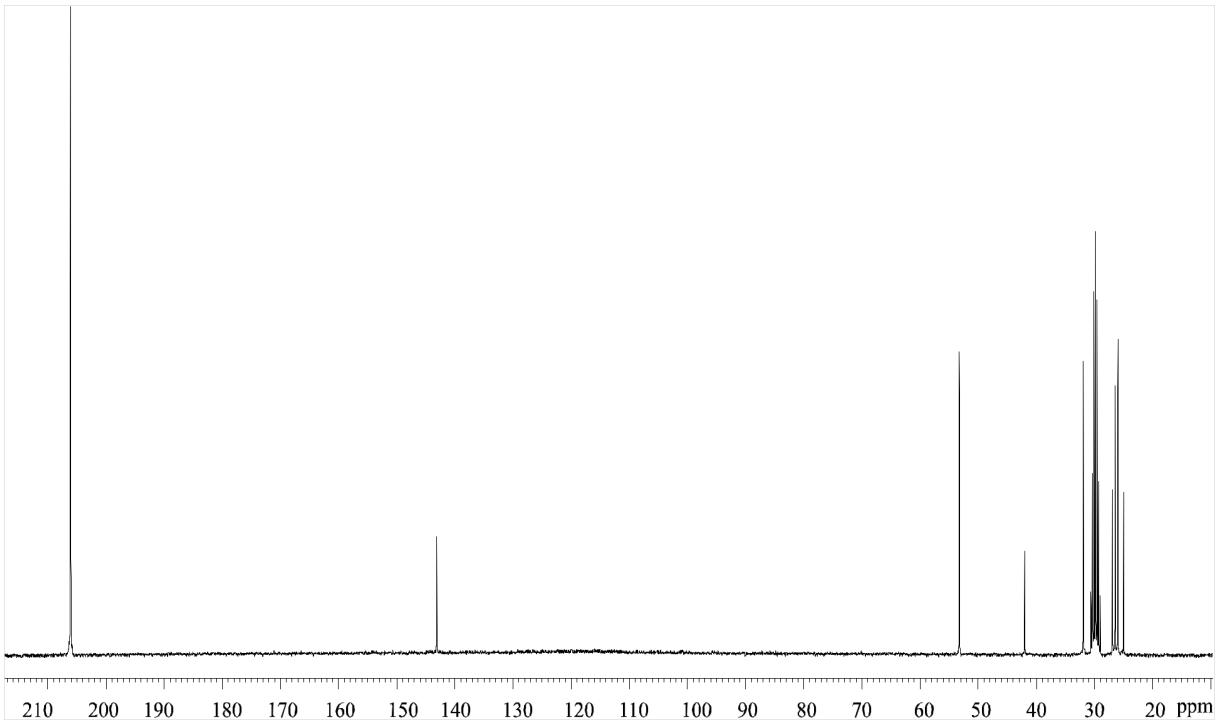
^{13}C NMR spectrum of **3e** (75 MHz, CD_3COCD_3)



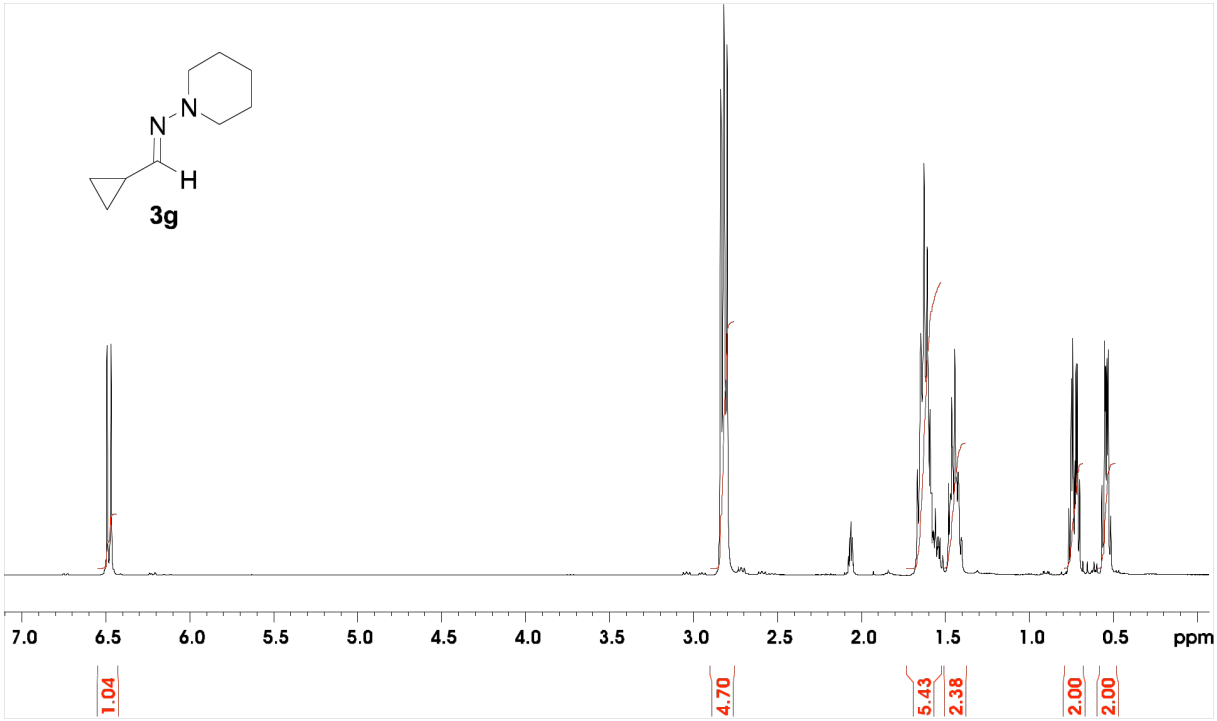
^{1}H NMR spectrum of **3f** (300 MHz, CD_3COCD_3)



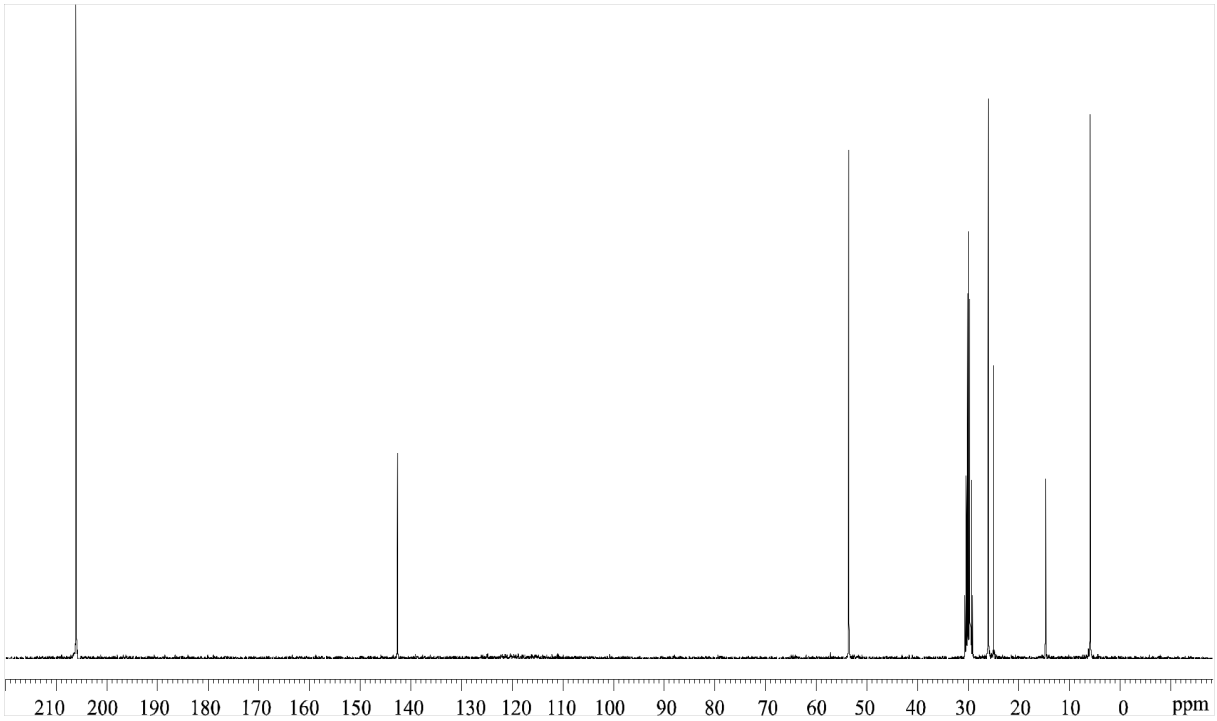
^{13}C NMR spectrum of **3f** (75 MHz, CD_3COCD_3)



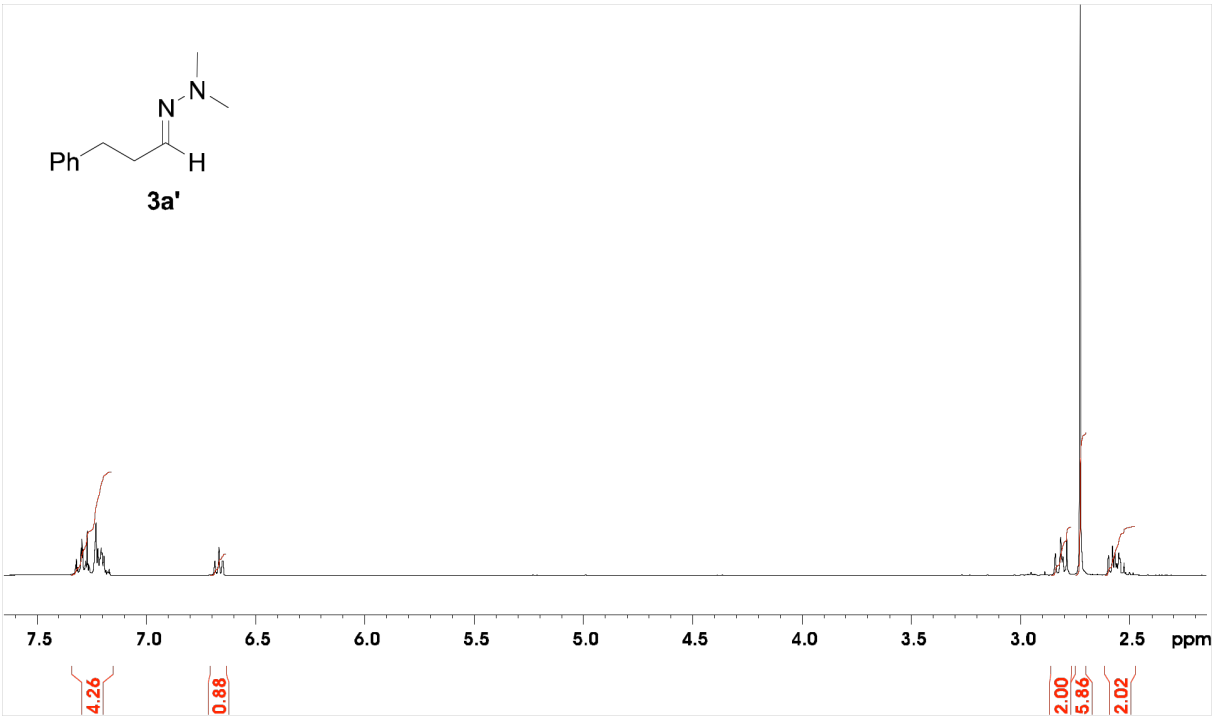
^{1}H NMR spectrum of **3g** (300 MHz, CD_3COCD_3)



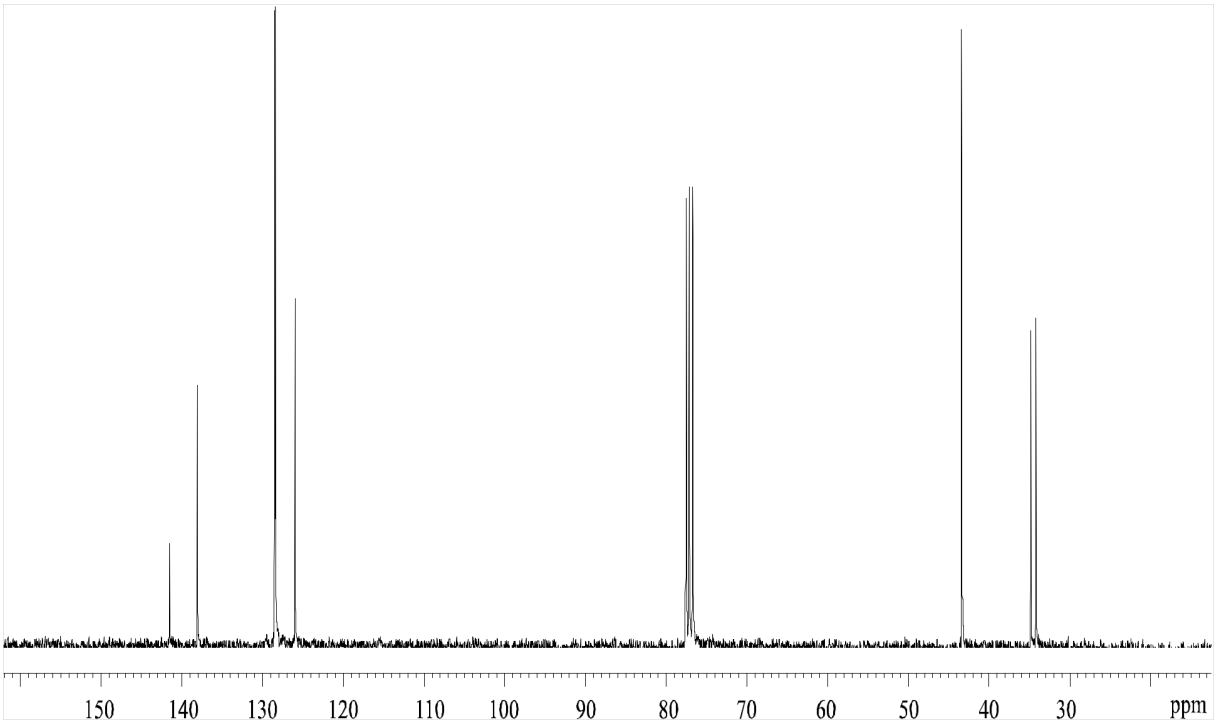
^{13}C NMR spectrum of **3g** (75 MHz, CD_3COCD_3)



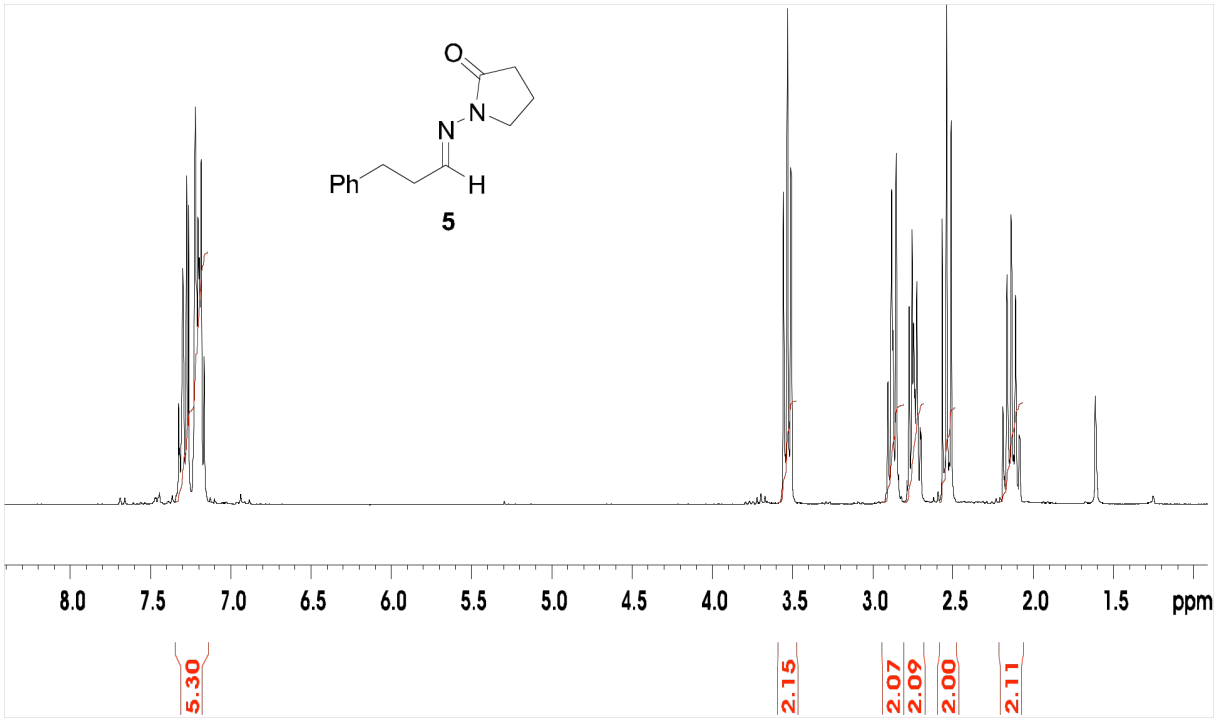
^{1}H NMR spectrum of **3a'** (300 MHz, $CDCl_3$)



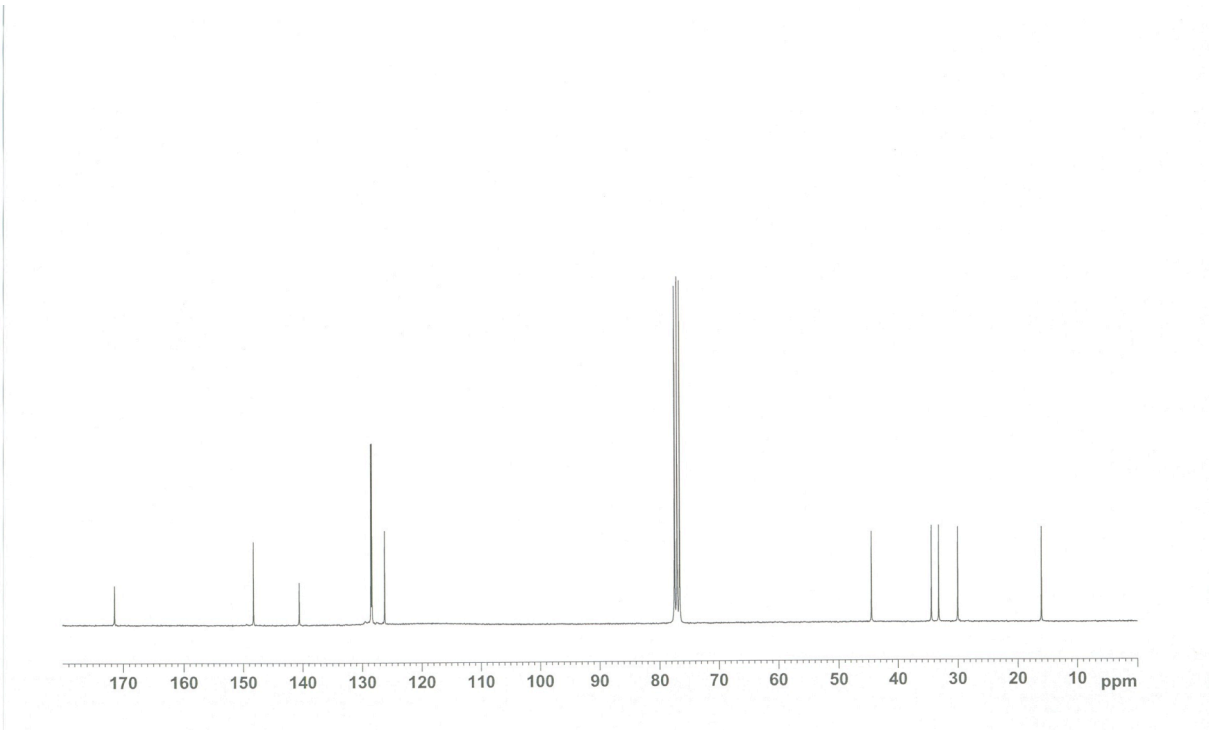
^{13}C NMR spectrum of **3a'** (75 MHz, $CDCl_3$)



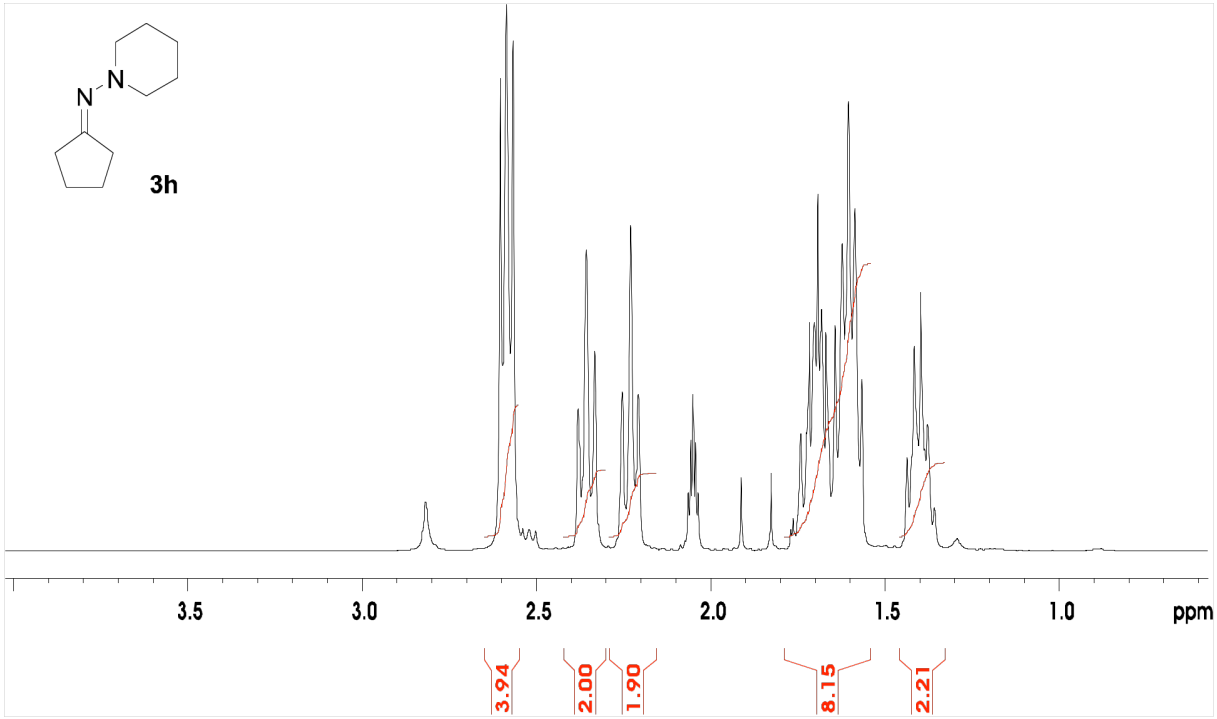
^{1}H NMR spectrum of **5** (300 MHz, $CDCl_3$)



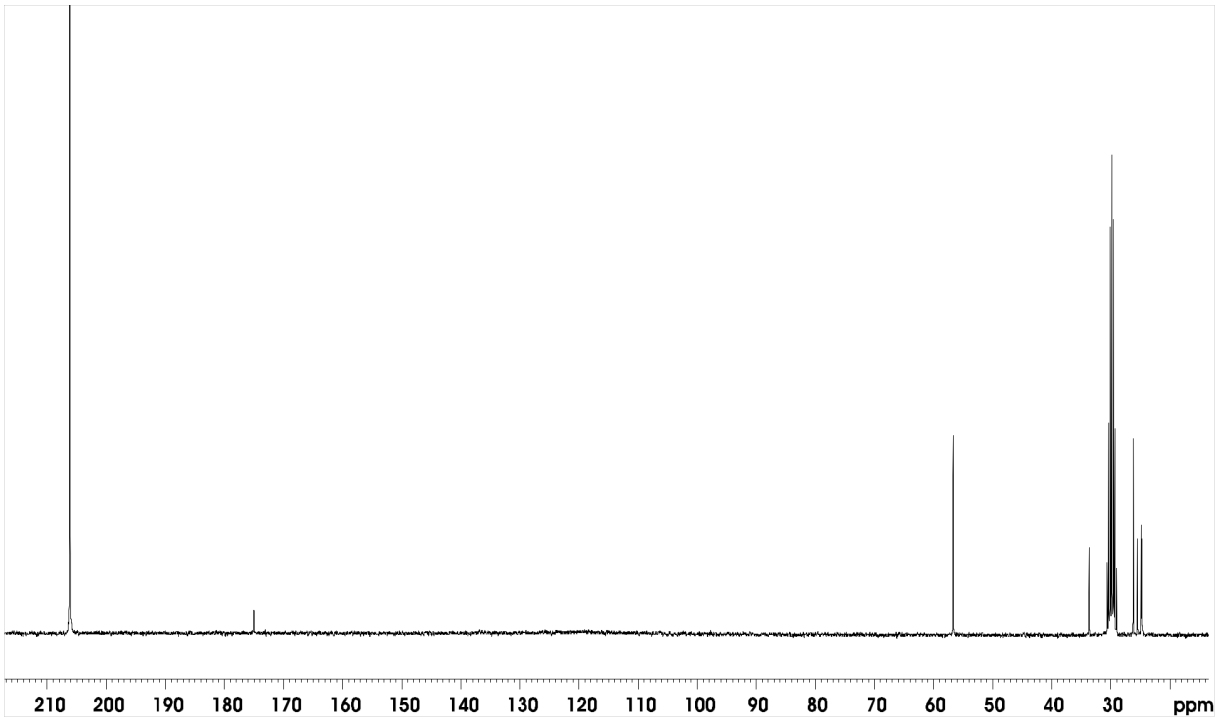
^{13}C NMR spectrum of **5** (75 MHz, $CDCl_3$)



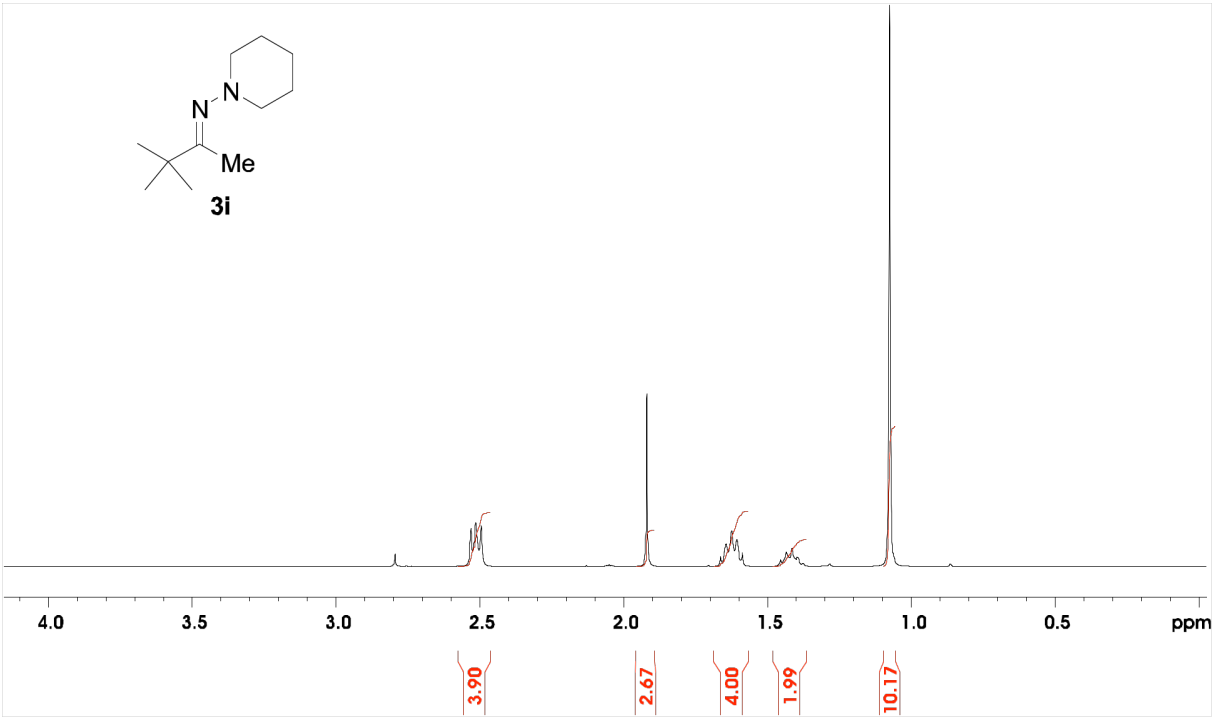
^{1}H NMR spectrum of **3h** (300 MHz, CD_3COCD_3)



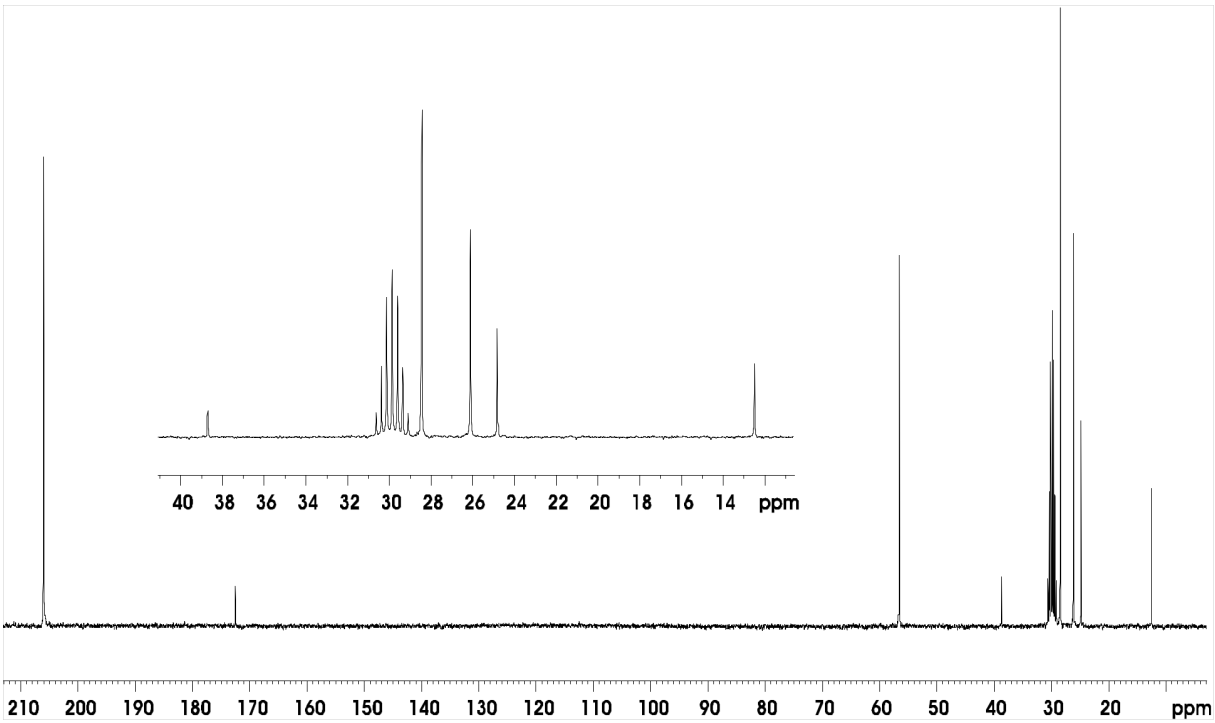
^{13}C NMR spectrum of **3h** (75 MHz, CD_3COCD_3)



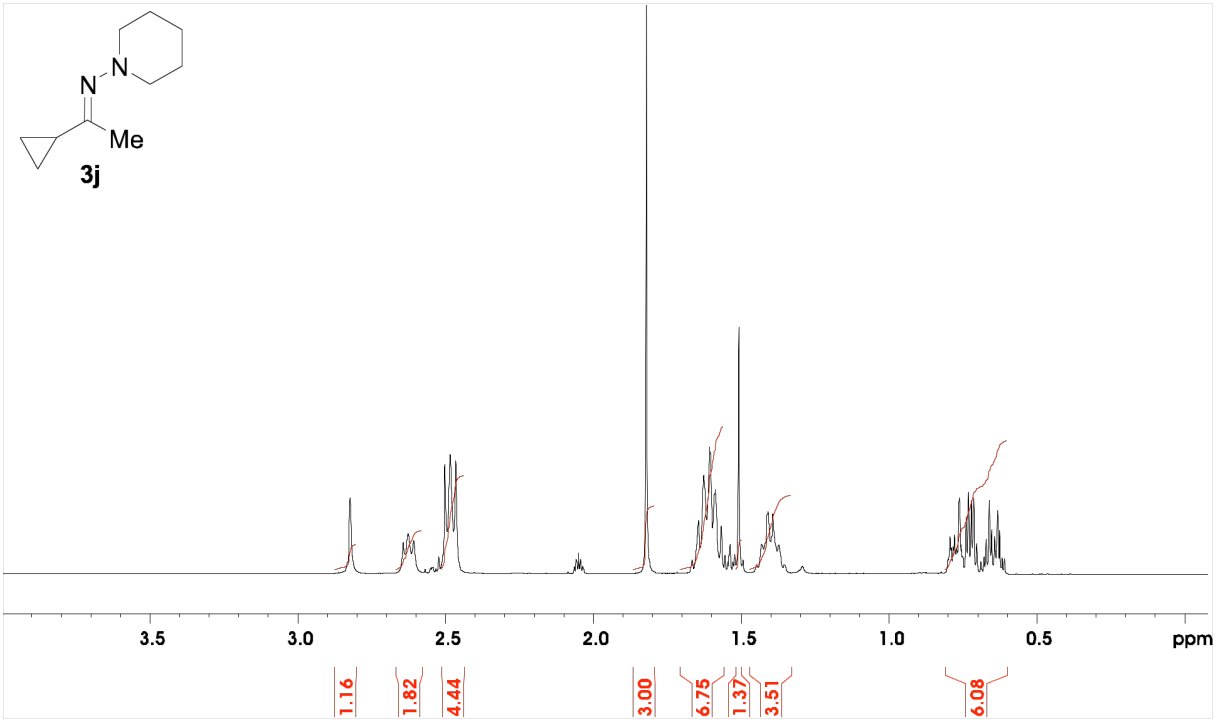
^{1}H NMR spectrum of **3i** (300 MHz, CD_3COCD_3)



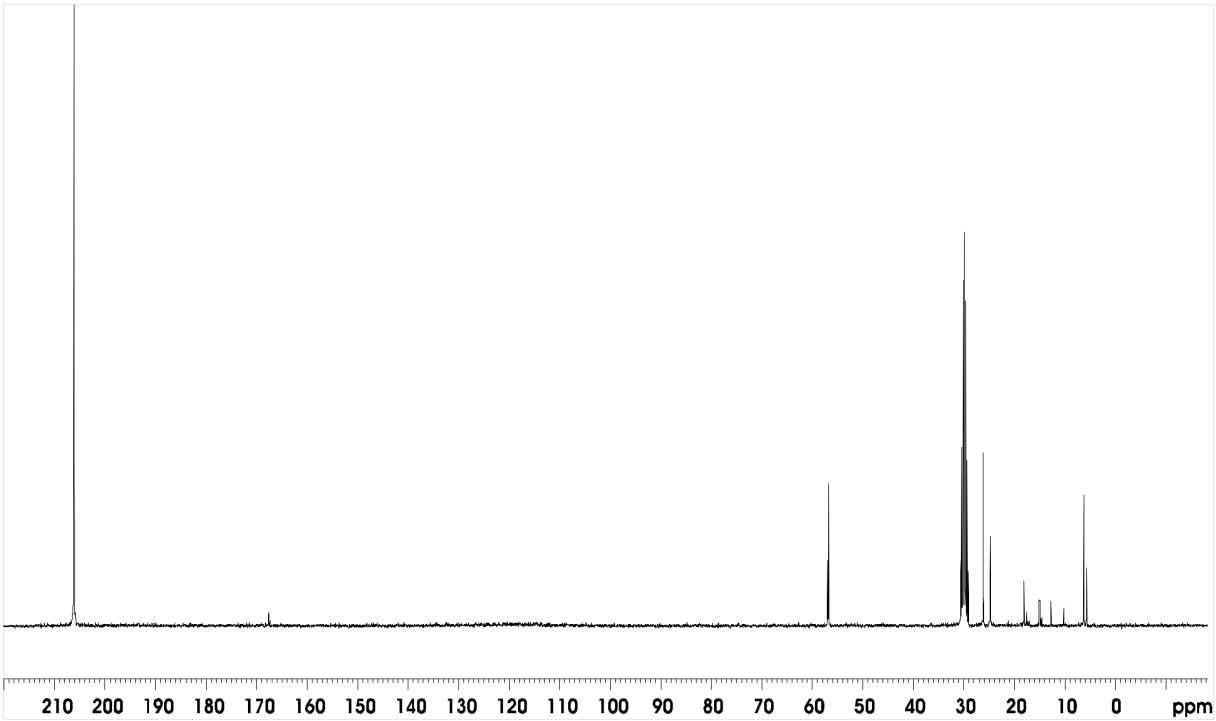
^{13}C NMR spectrum of **3i** (75 MHz, CD_3COCD_3)



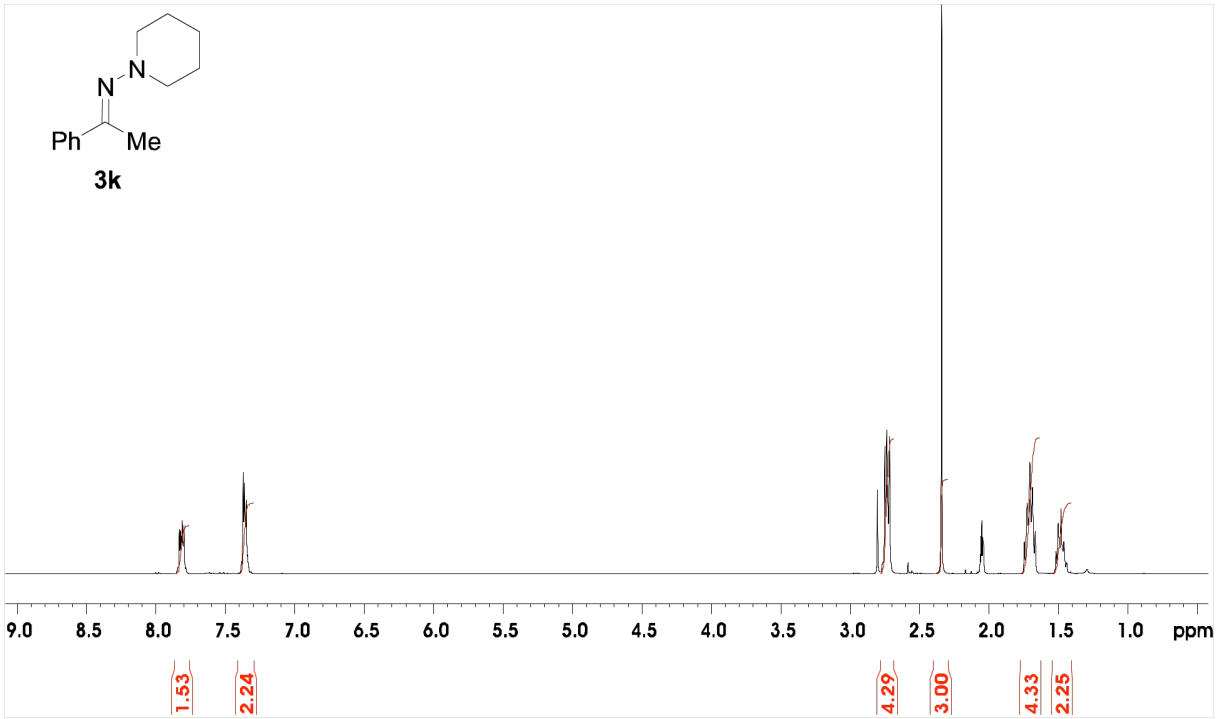
^{1}H NMR spectrum of **3j** (300 MHz, CD_3COCD_3)



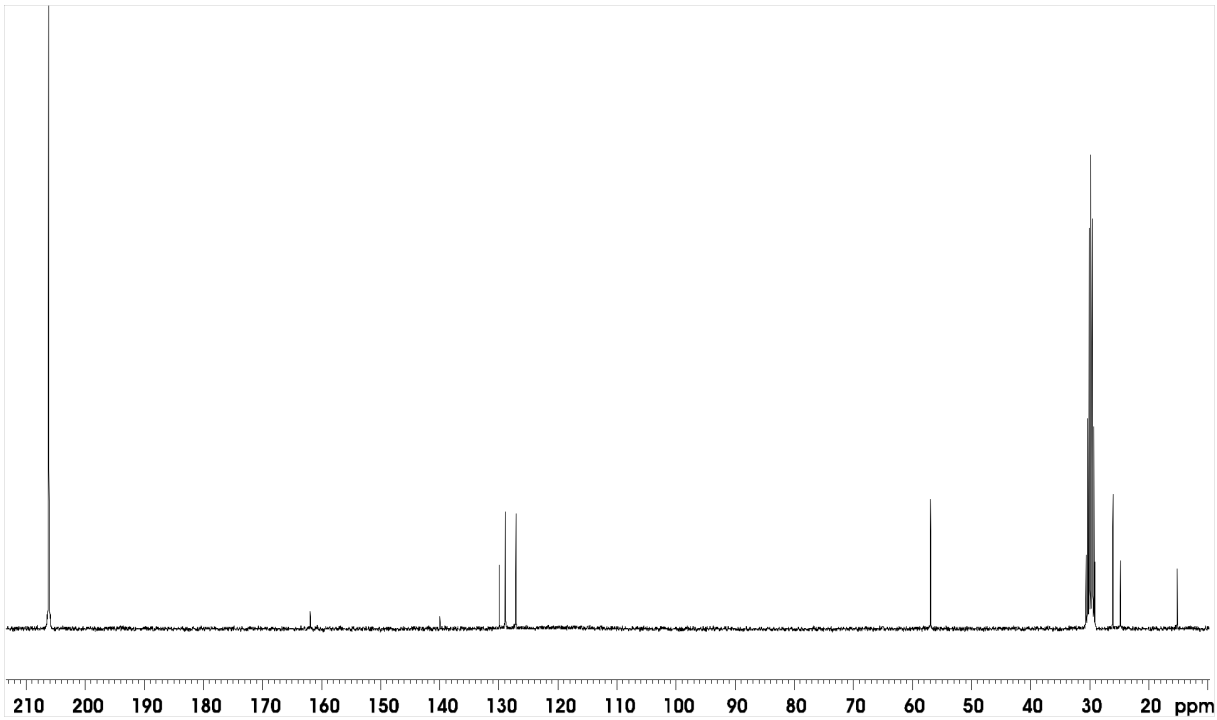
^{13}C NMR spectrum of **3j** (75 MHz, CD_3COCD_3)



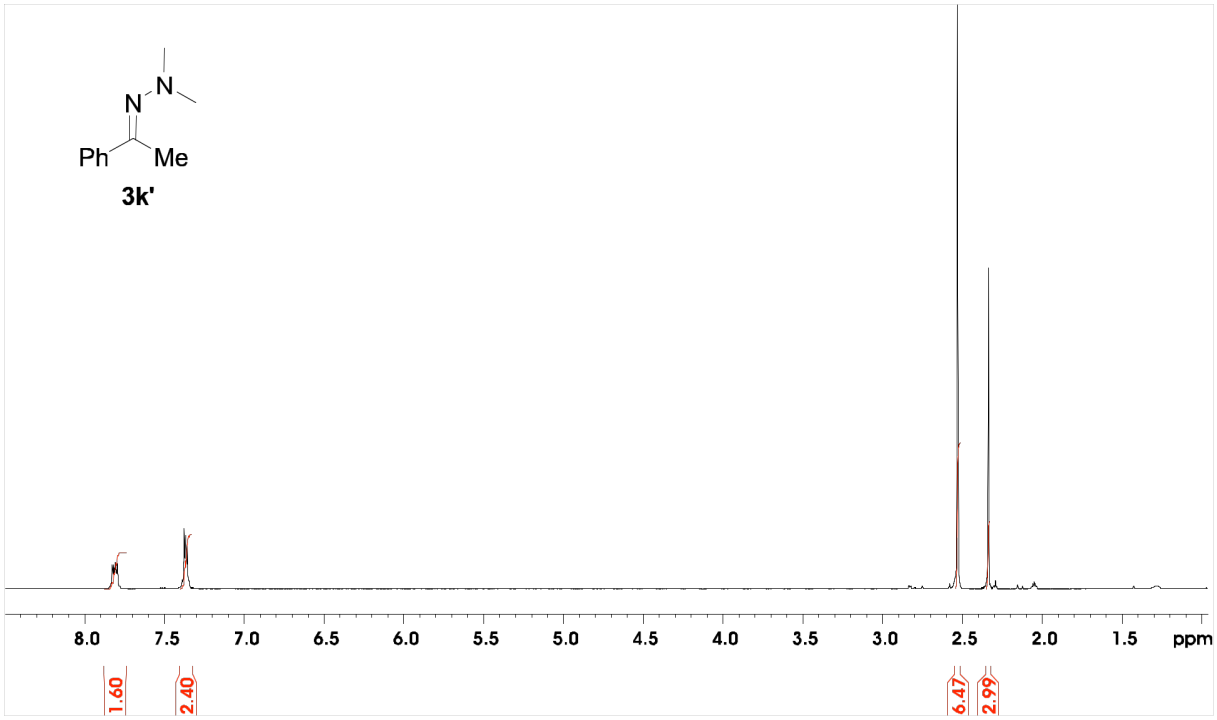
^{1}H NMR spectrum of **3k** (300 MHz, CD_3COCD_3)



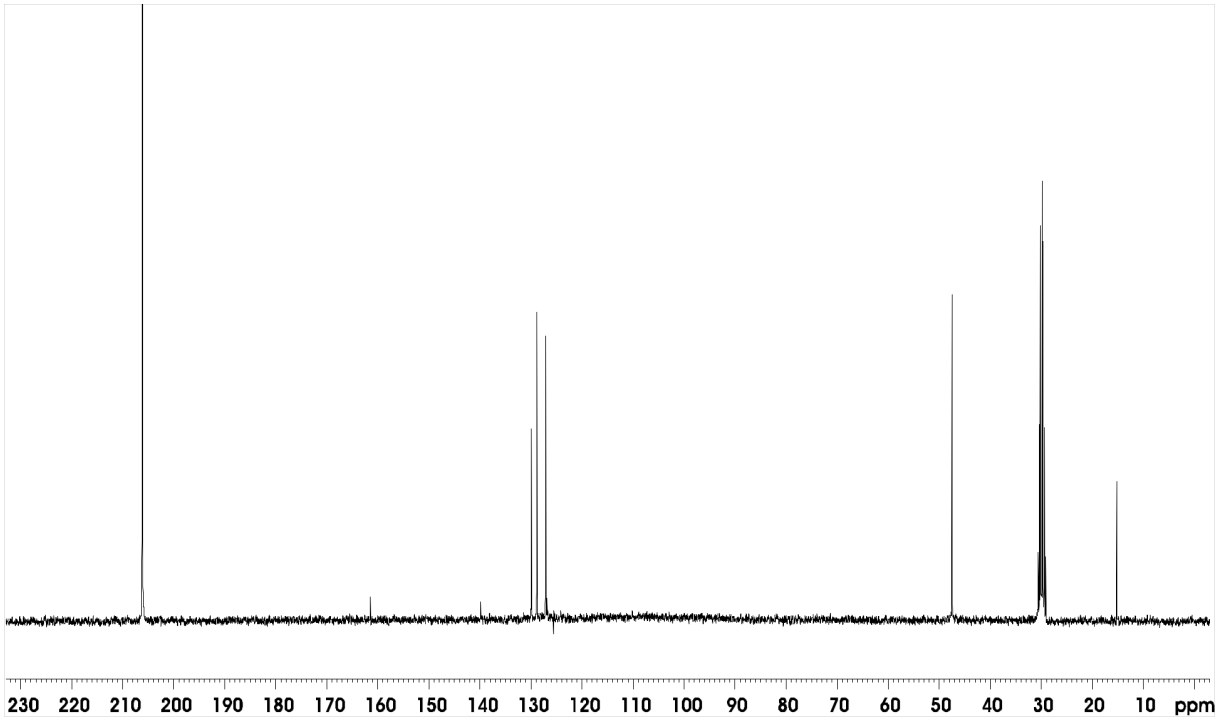
^{13}C NMR spectrum of **3k** (75 MHz, CD_3COCD_3)



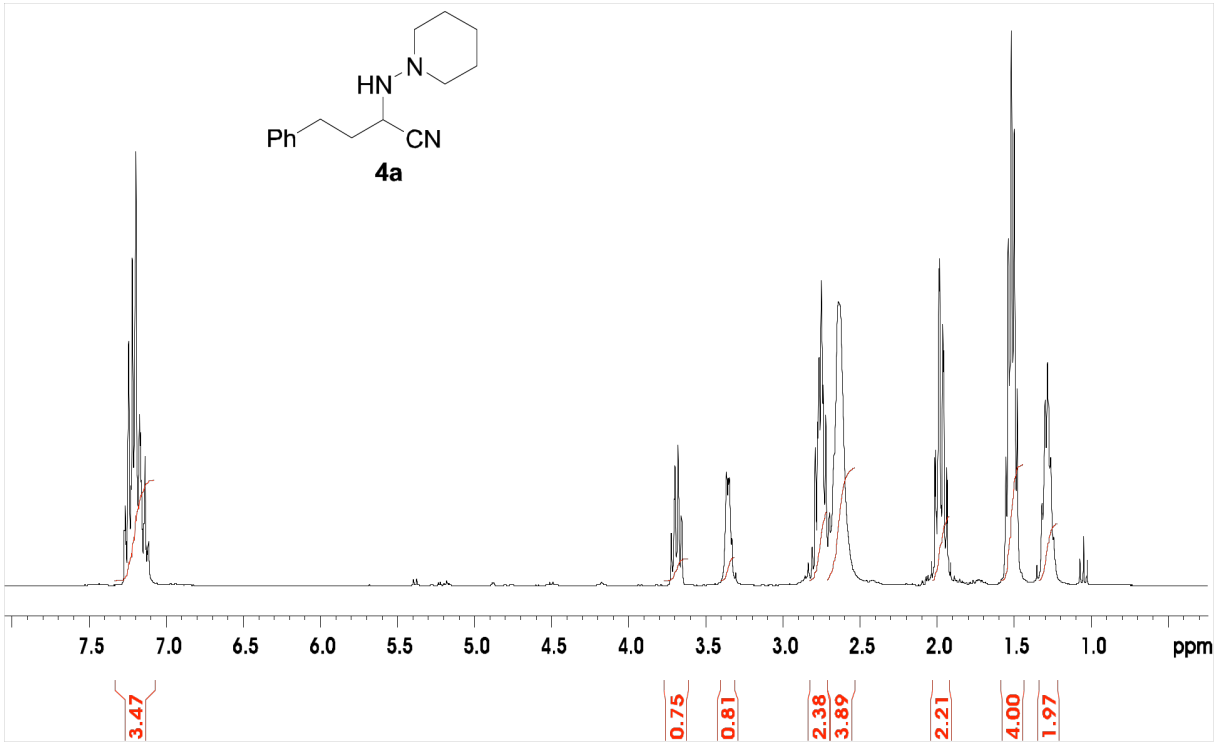
^{1}H NMR spectrum of **3k'** (300 MHz, CD_3COCD_3)



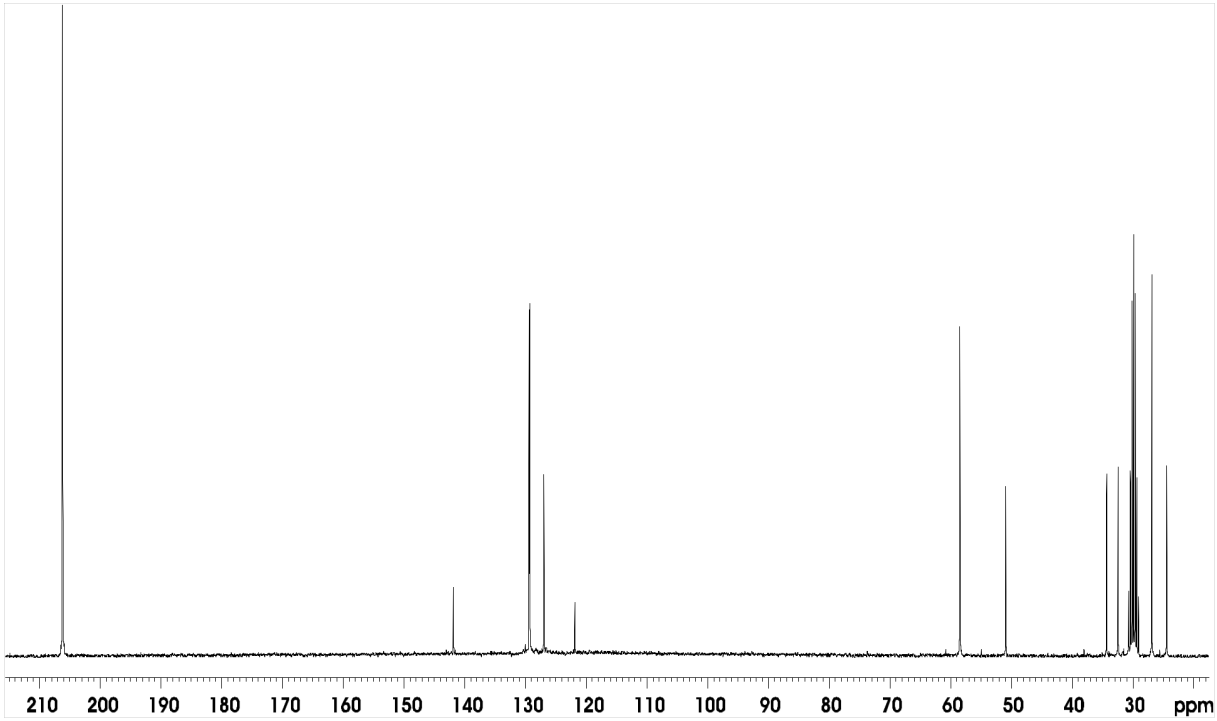
^{13}C NMR spectrum of **3k'** (75 MHz, CD_3COCD_3)



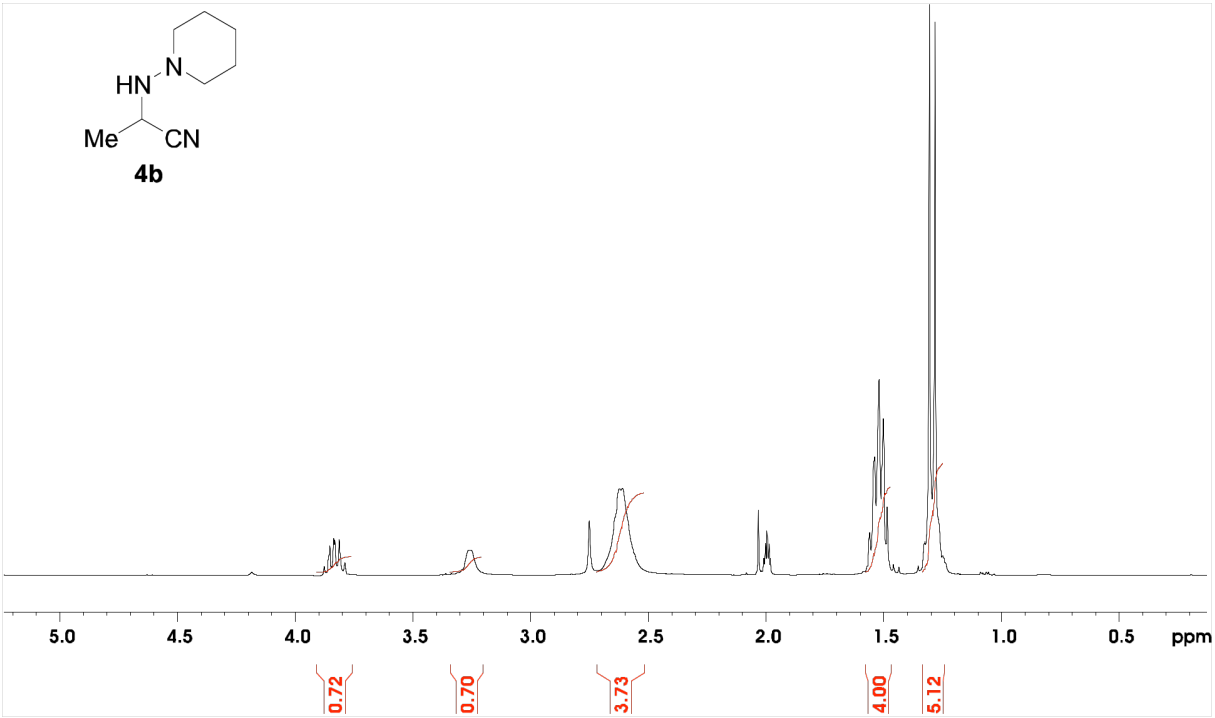
^{1}H NMR spectrum of **4a** (300 MHz, $CDCl_3$)



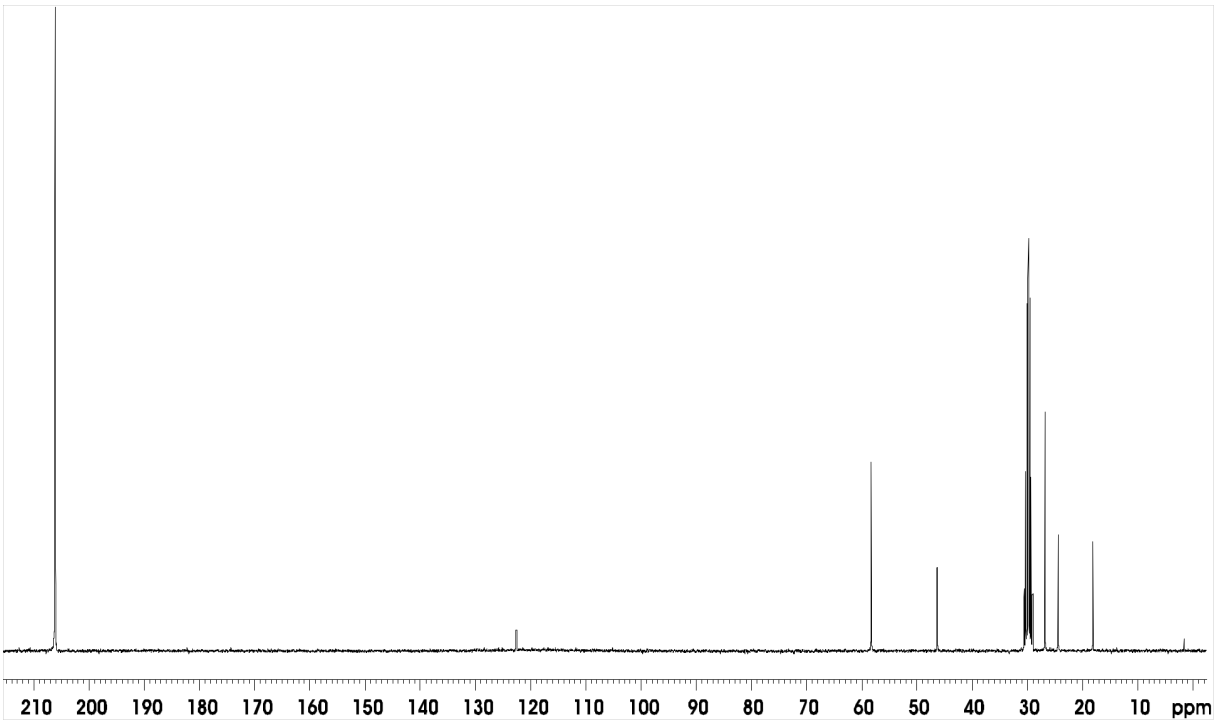
^{13}C NMR spectrum of **4a** (75 MHz, $CDCl_3$)



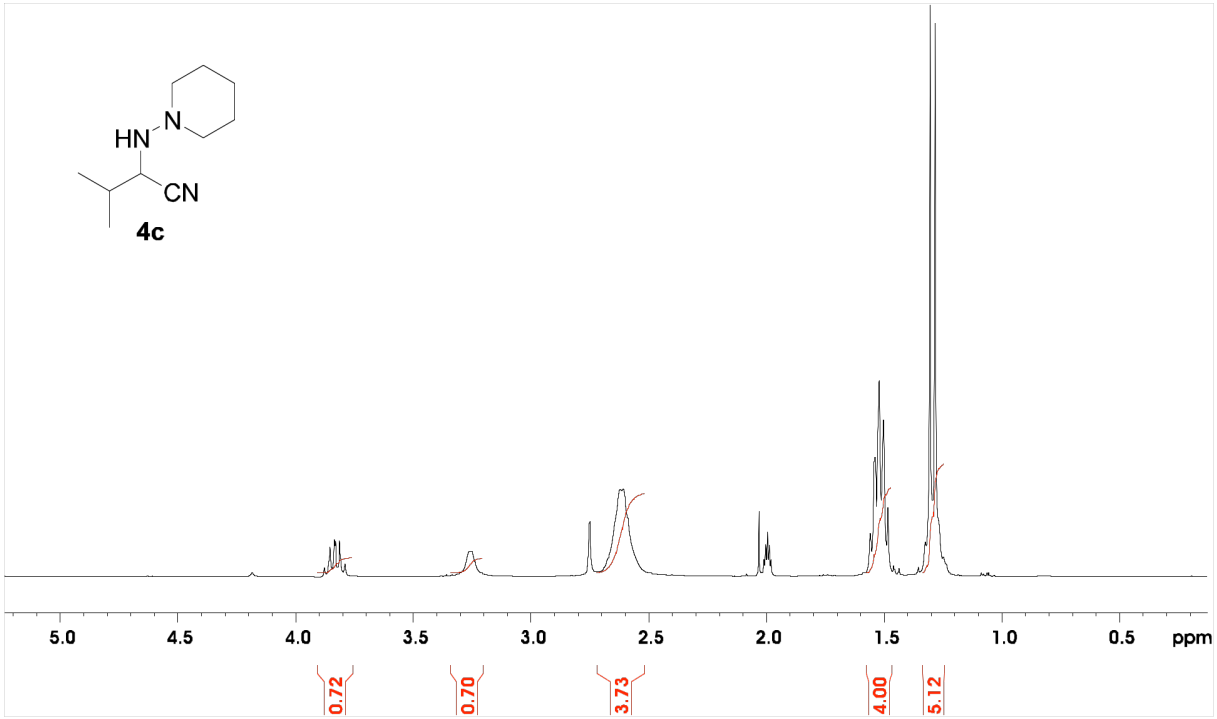
^{1}H NMR spectrum of **4b** (300 MHz, CD_3COCD_3)



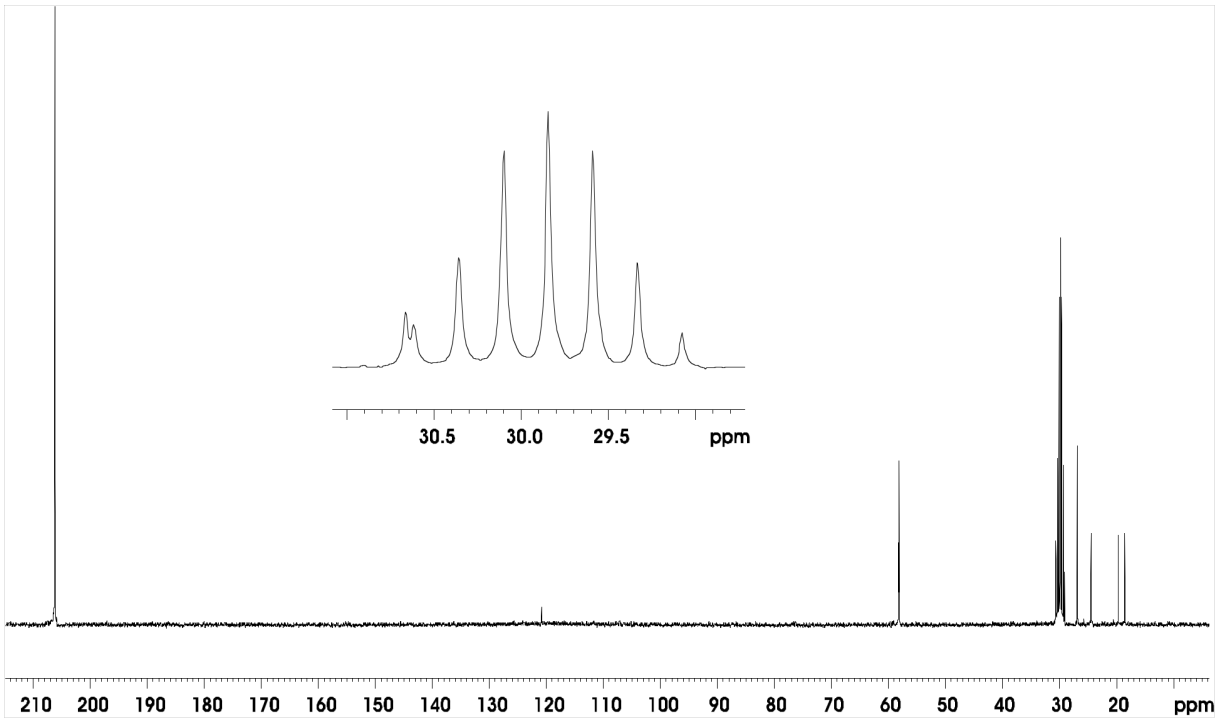
^{13}C NMR spectrum of **4b** (75 MHz, CD_3COCD_3)



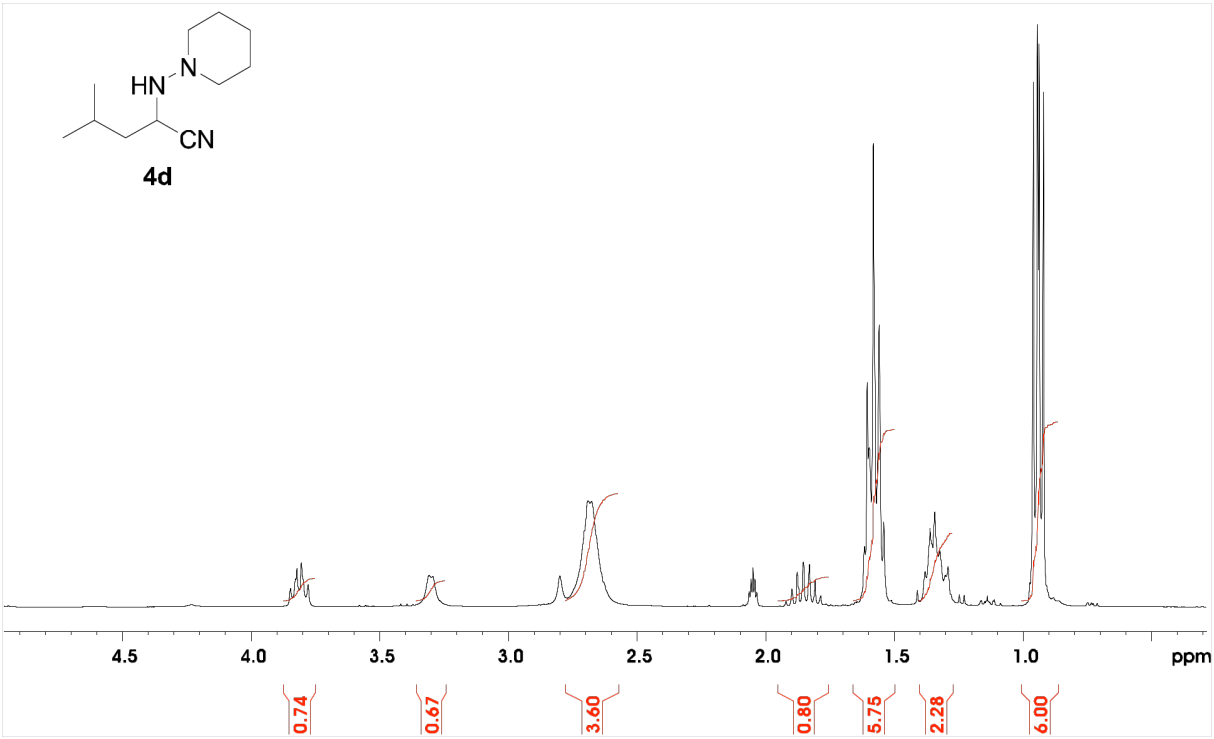
^{1}H NMR spectrum of **4c** (300 MHz, CD_3COCD_3)



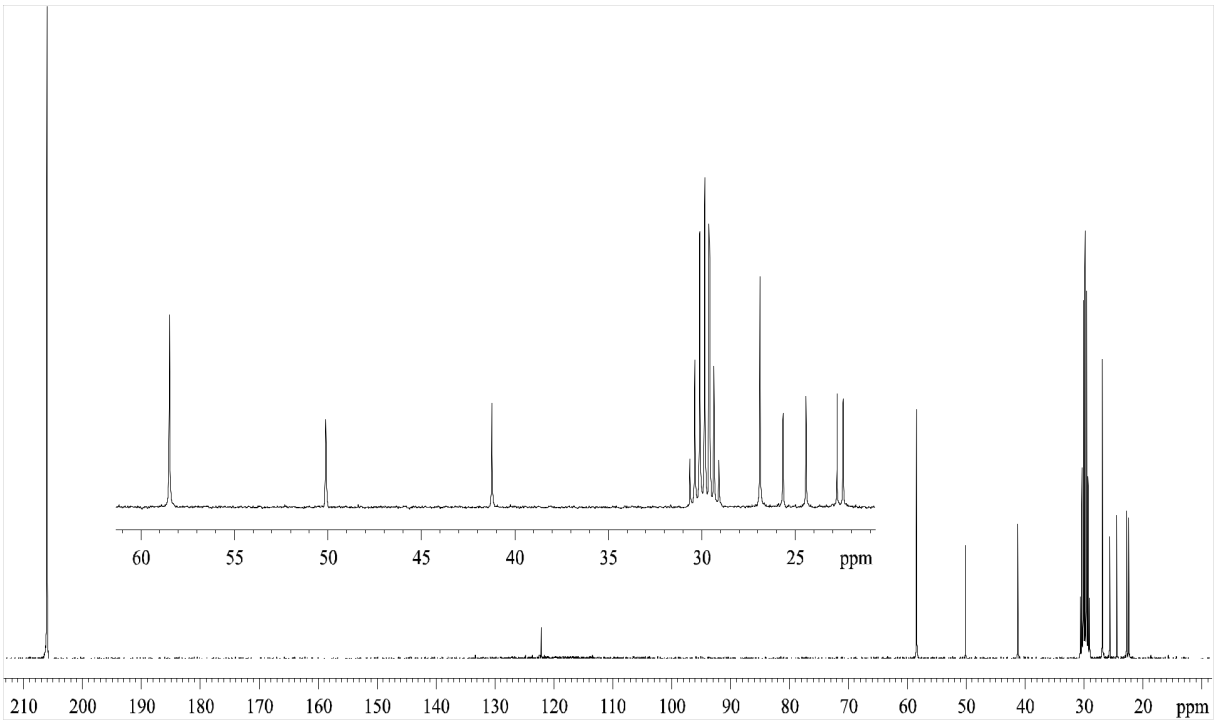
^{13}C NMR spectrum of **4c** (75 MHz, CD_3COCD_3)



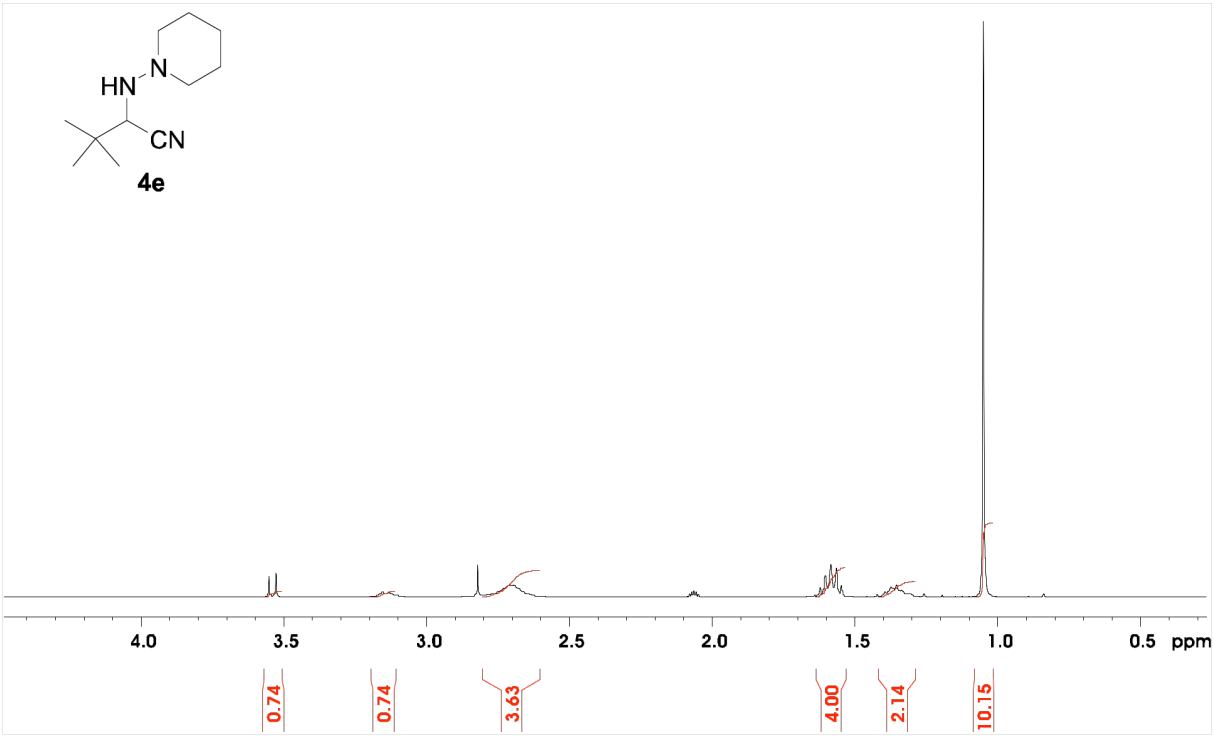
^{1}H NMR spectrum of **4d** (300 MHz, CD_3COCD_3)



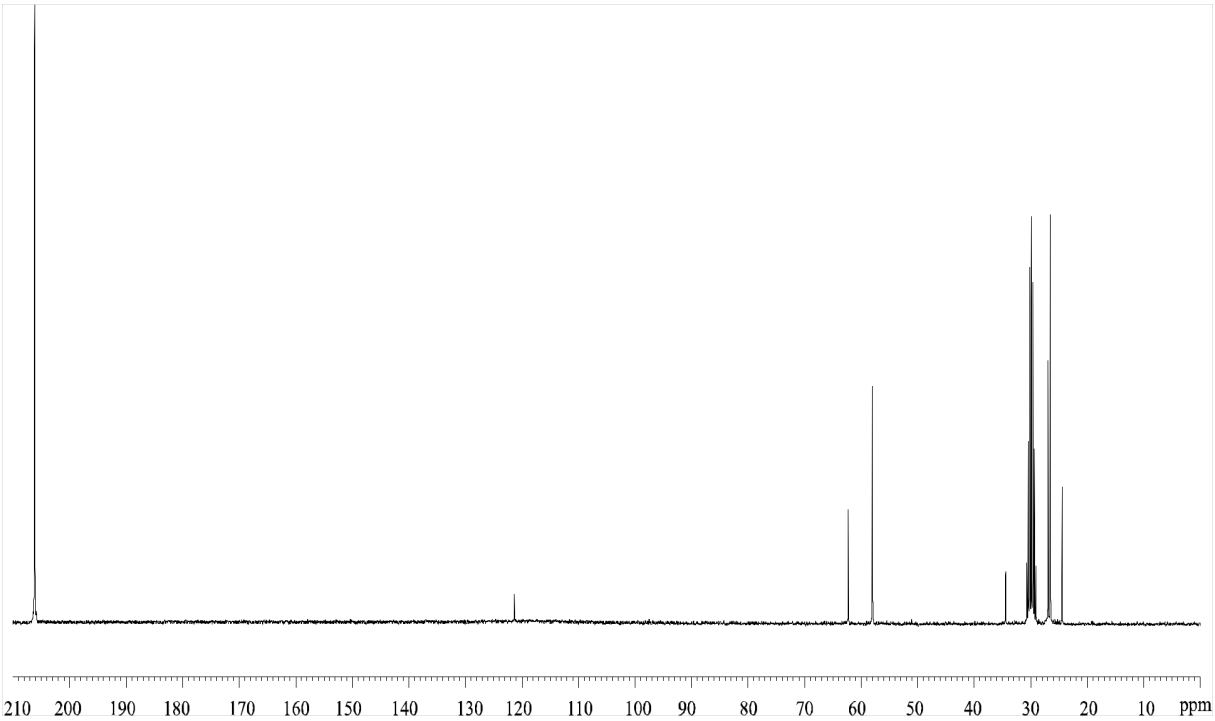
^{13}C NMR spectrum of **4d** (75 MHz, CD_3COCD_3)



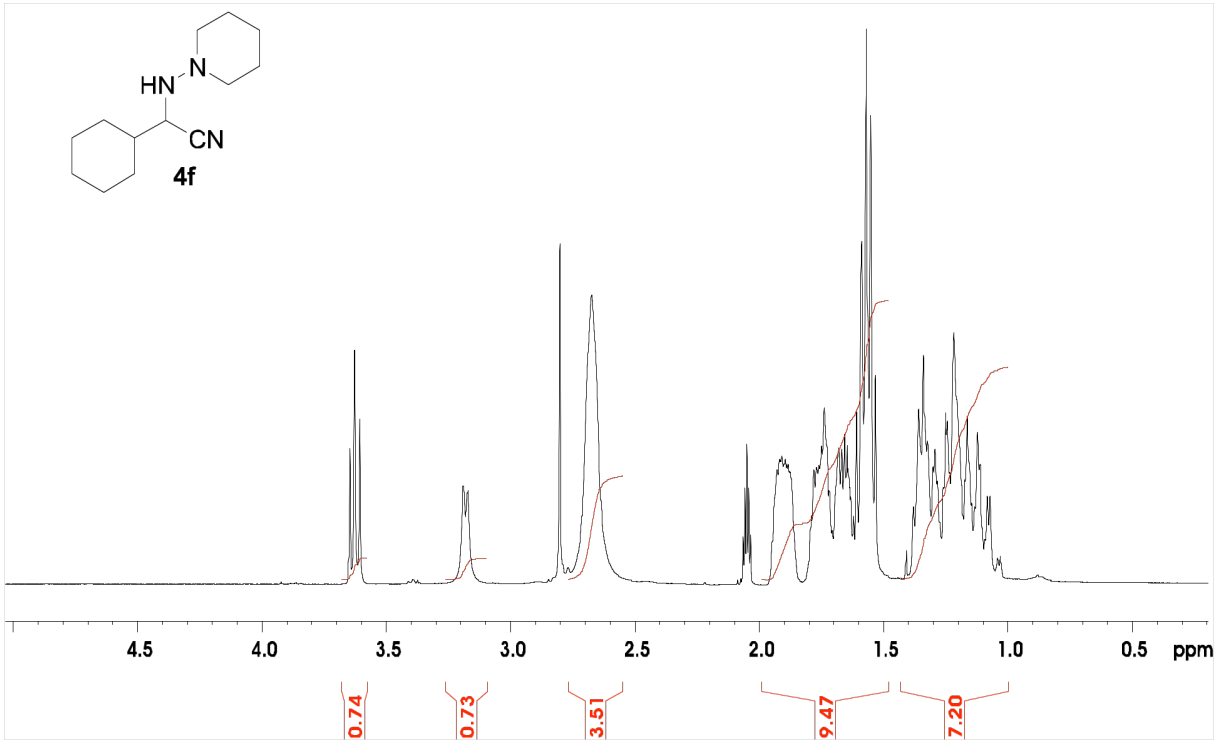
^{1}H NMR spectrum of **4e** (300 MHz, CD_3COCD_3)



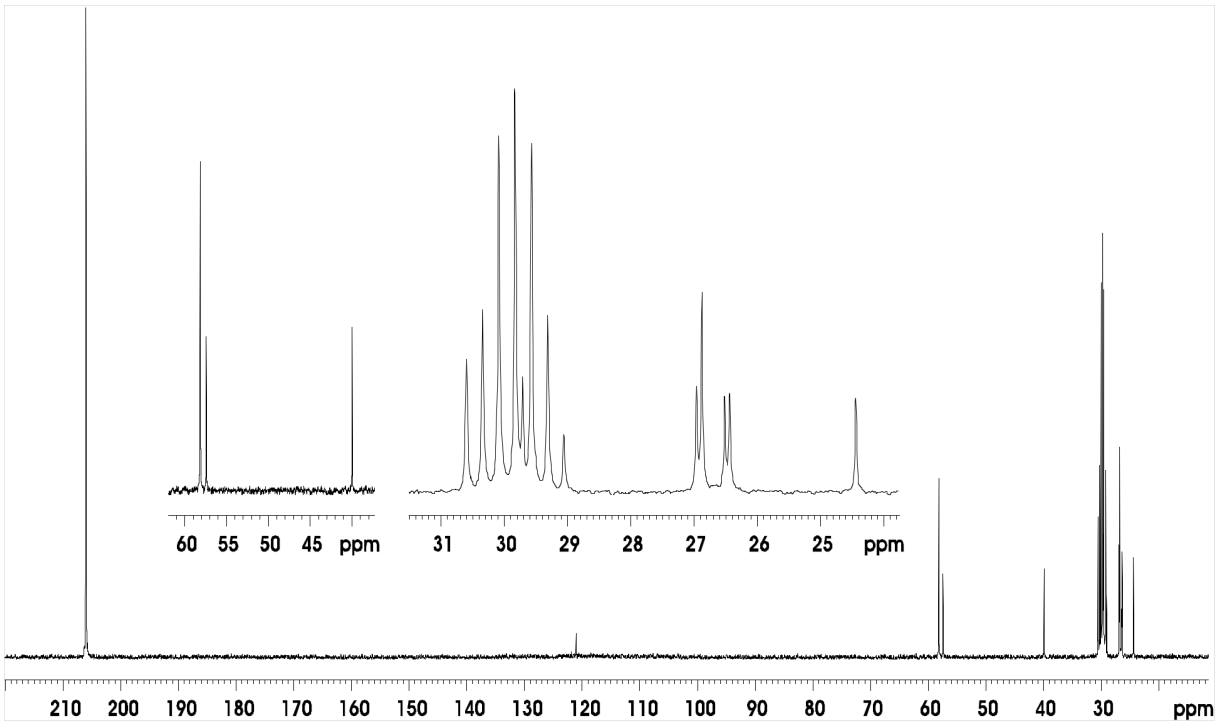
^{13}C NMR spectrum of **4e** (75 MHz, CD_3COCD_3)



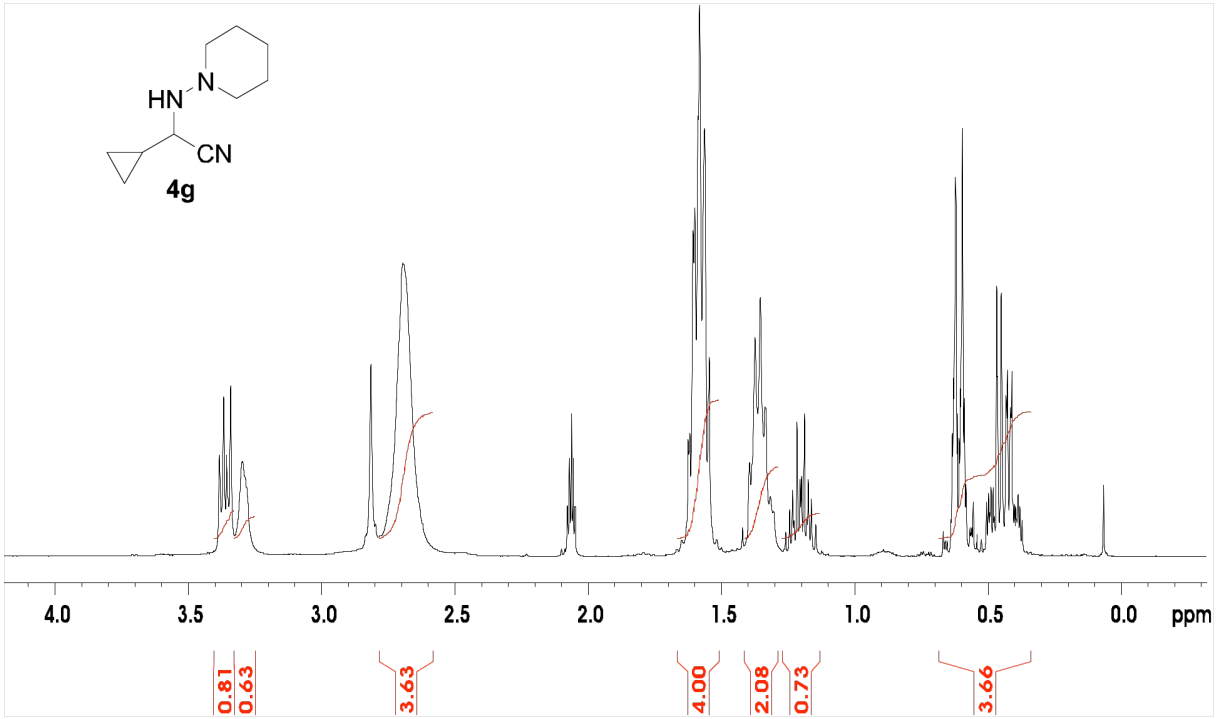
^{1}H NMR spectrum of **4f** (300 MHz, CD_3COCD_3)



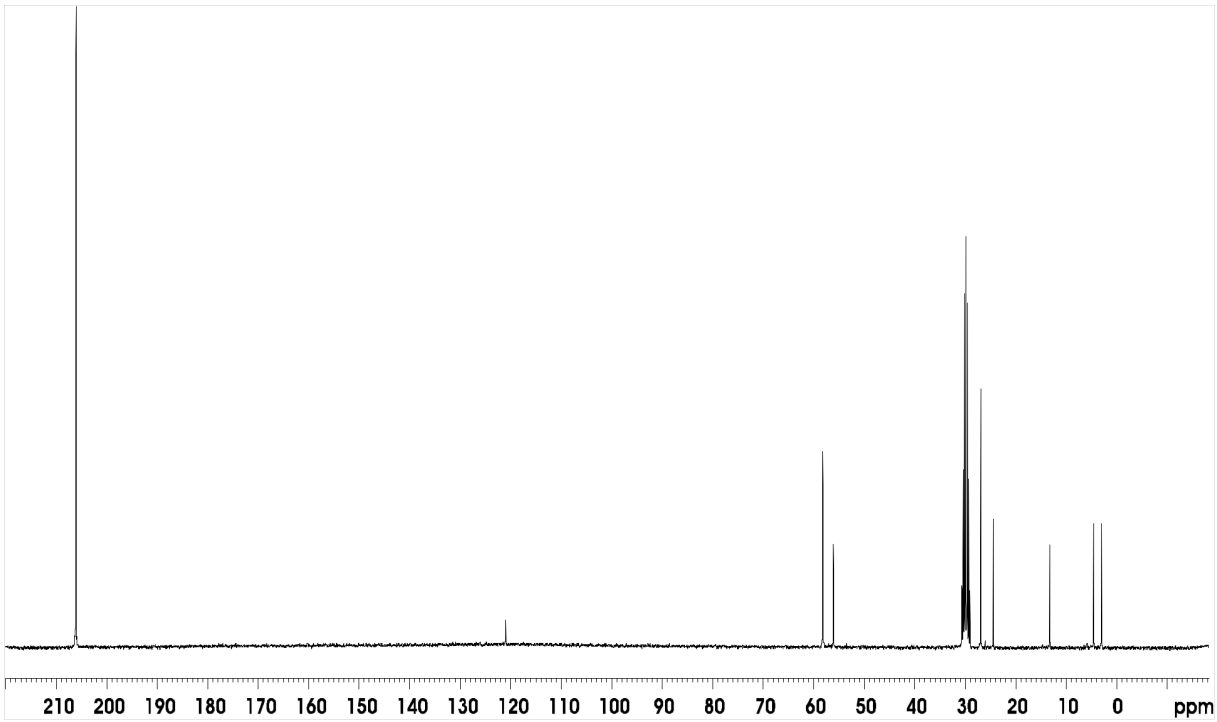
^{13}C NMR spectrum of **4f** (75 MHz, CD_3COCD_3)



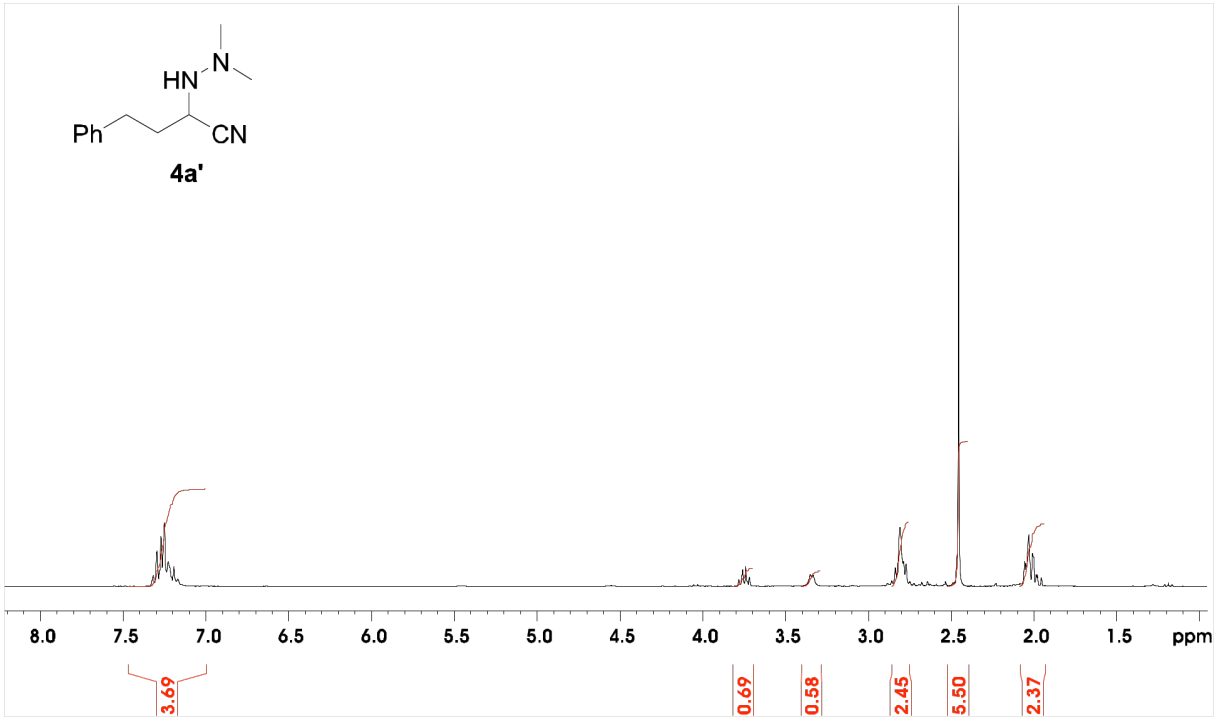
^{1}H NMR spectrum of **4g** (300 MHz, CD_3COCD_3)



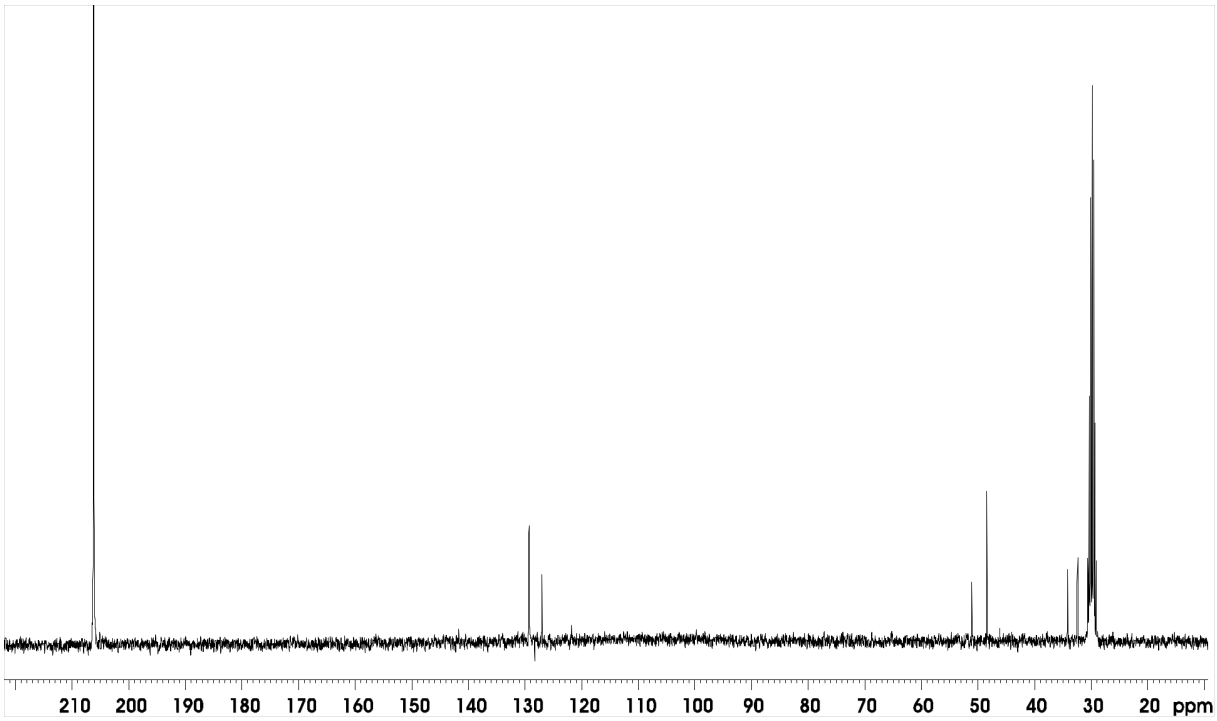
^{13}C NMR spectrum of **4g** (75 MHz, CD_3COCD_3)



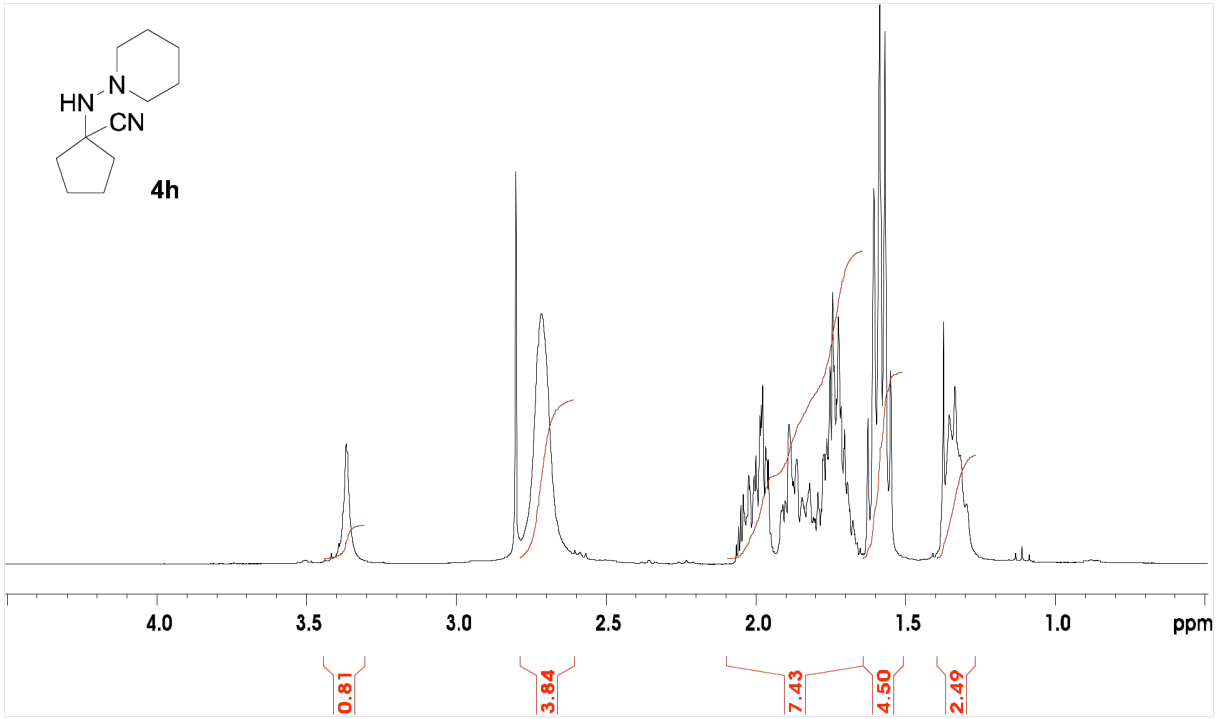
^{1}H NMR spectrum of **4a'** (300 MHz, CD_3COCD_3)



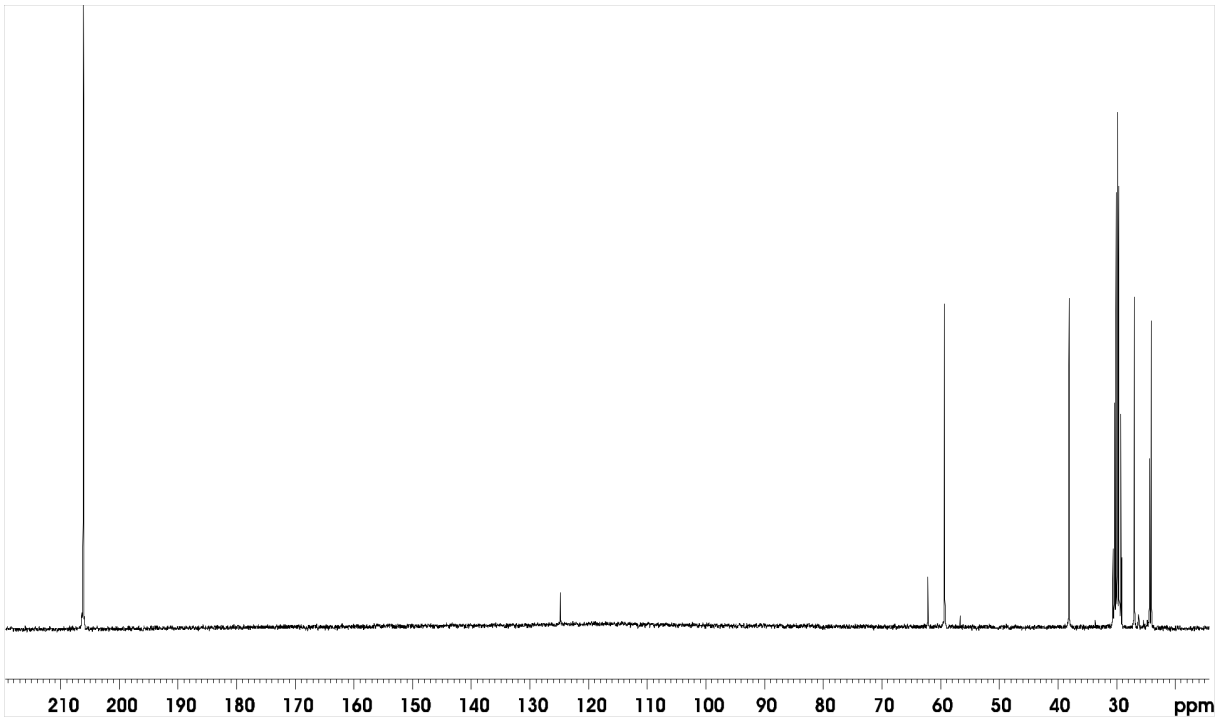
^{13}C NMR spectrum of **4a'** (75 MHz, CD_3COCD_3)



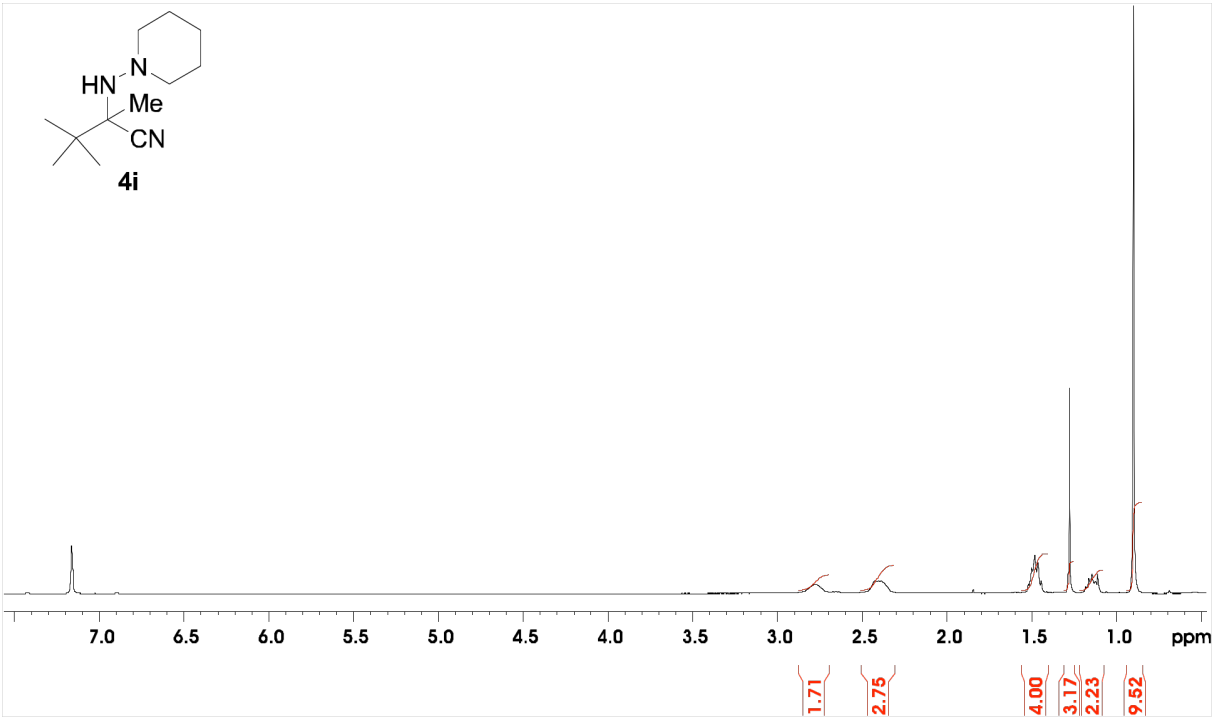
^{1}H NMR spectrum of **4h** (300 MHz, CD_3COCD_3)



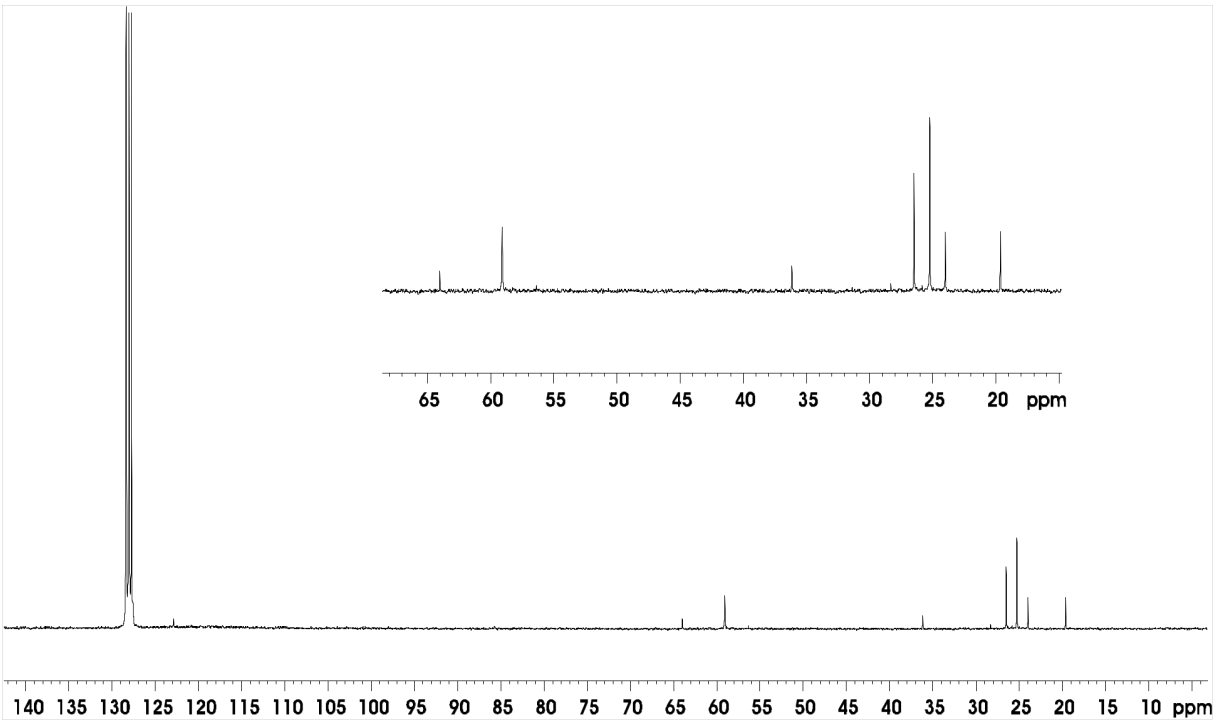
^{13}C NMR spectrum of **4h** (75 MHz, CD_3COCD_3)



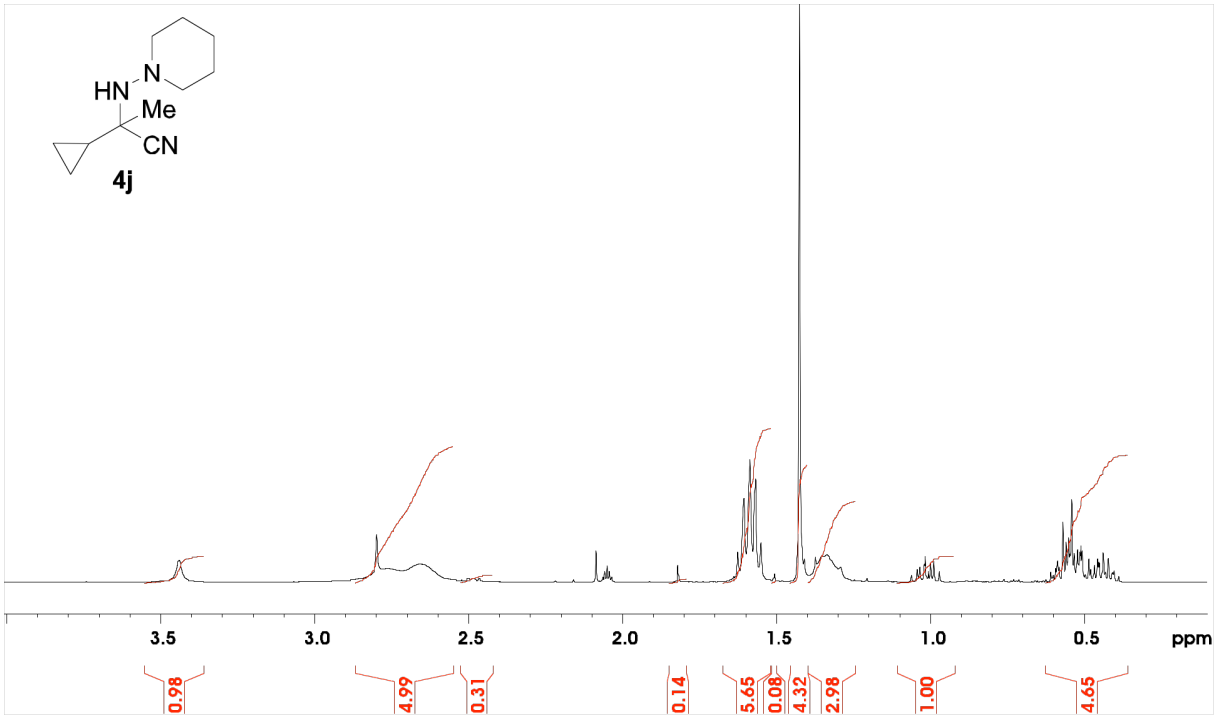
^{1}H NMR spectrum of **4i** (300 MHz, C_6D_6, 70 ºC)



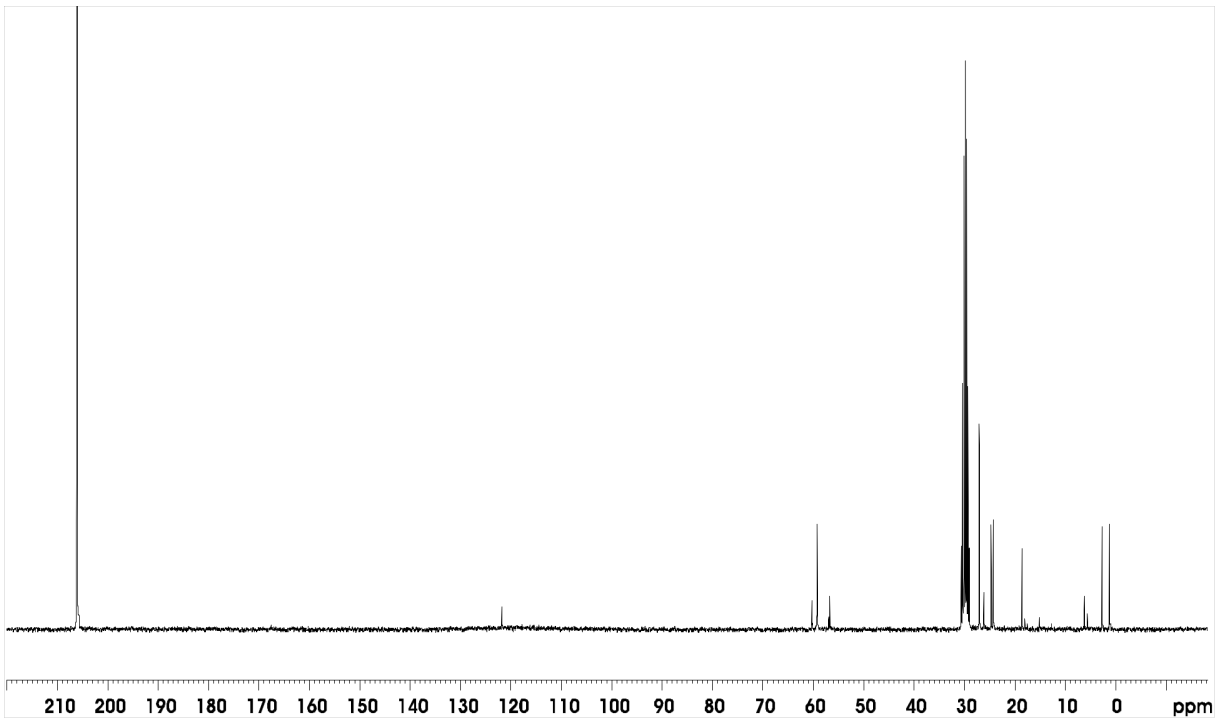
^{13}C NMR spectrum of **4i** (75 MHz, C_6D_6, 70 ºC)



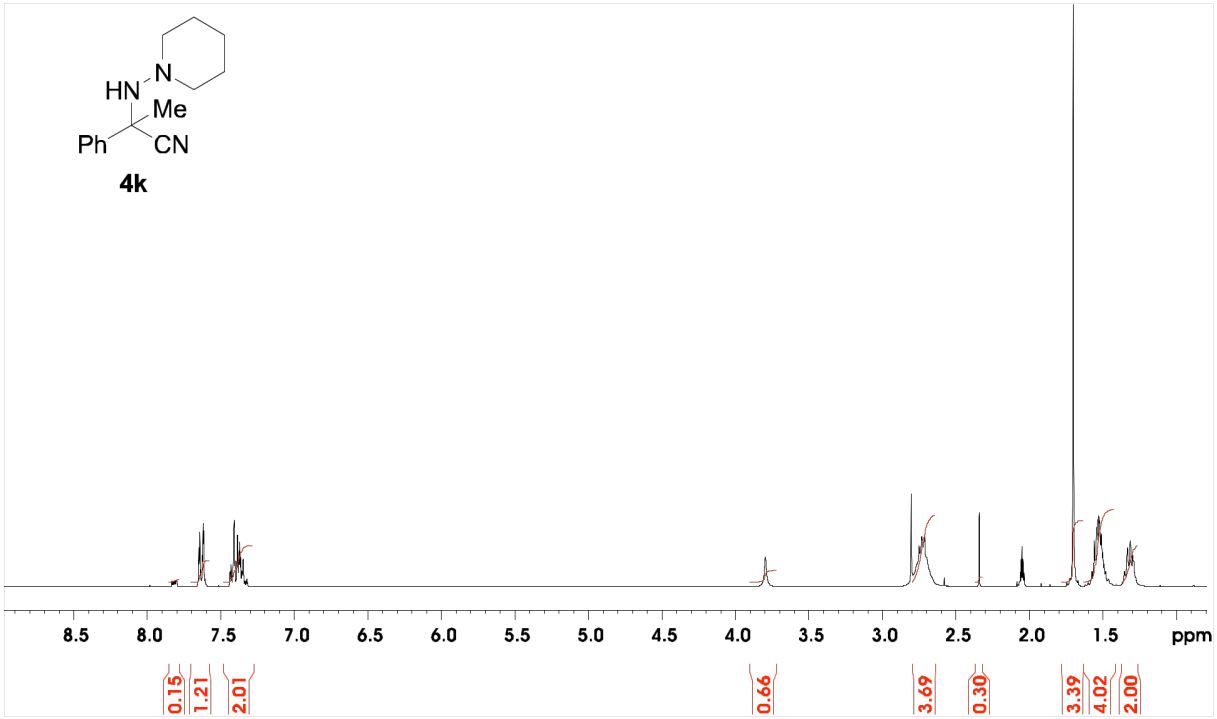
^{1}H NMR spectrum of **4j** (300 MHz, CD_3COCD_3)



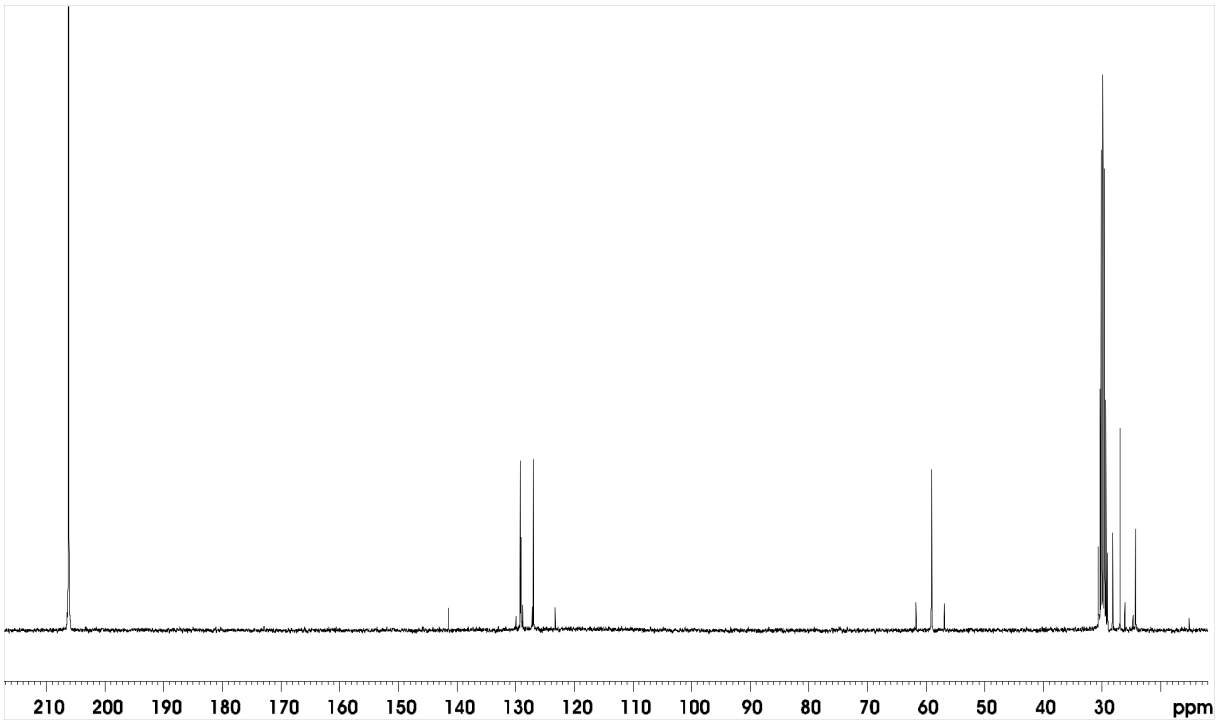
^{13}C NMR spectrum of **4j** (75 MHz, CD_3COCD_3)



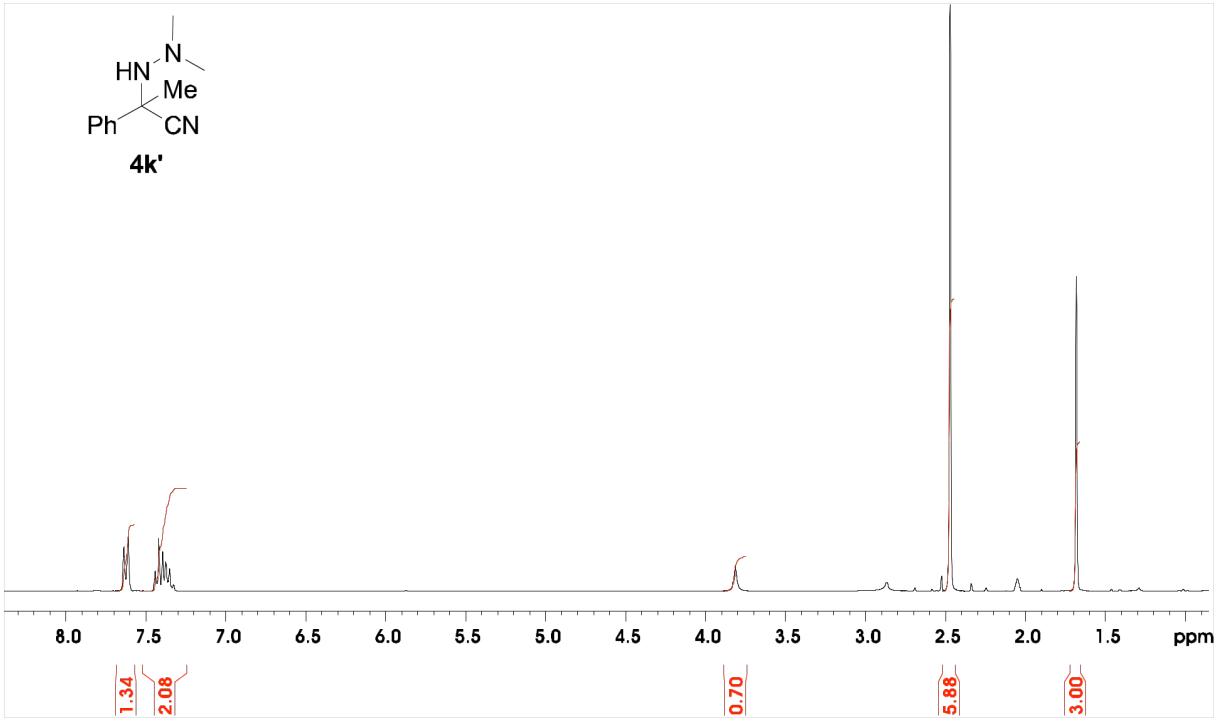
^{1}H NMR spectrum of **4k** (300 MHz, CD_3COCD_3)



^{13}C NMR spectrum of **4k** (75 MHz, CD_3COCD_3)



^{1}H NMR spectrum of **4k'** (300 MHz, CD_3COCD_3)



^{13}C NMR spectrum of **4k'** (75 MHz, CD_3COCD_3)