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Supporting Information for

Tandem Prins/Wagner/Ritter process for the stereoselective synthesis of (3-oxabicyclo[4.2.0]octan-1-yl)amide and (1-(5-aryltetrahydrofuran-3-yl)cyclobutyl)amide derivatives

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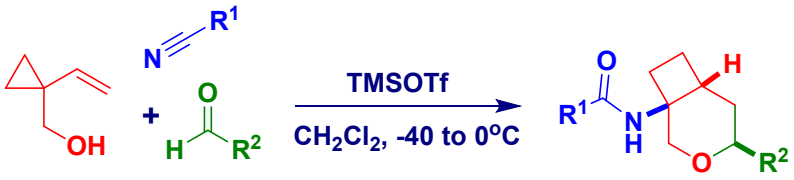

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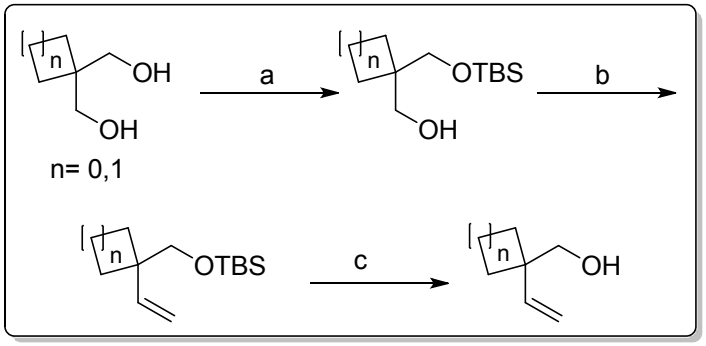
General methods

IR spectra were recorded on FT-IR spectrometer (KBr) and reported in reciprocal centimeters (cm^{-1}). $^{1}HNMR$ spectra were recorded at 500 MHz, 300 MHz and ^{13}C NMR at 125 MHz. For ^{1}H NMR, tetramethylsilane (TMS) was used as internal standard ($\delta = 0$) and the values are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), and the coupling constants in Hz. For ^{13}C NMR, $CDCl_3$ ($\delta = 77.27$) was used as internal standard and spectra were obtained with complete proton decoupling. Low-resolution MS and HRMS data were obtained using ESI ionization. Melting points were measured on micro melting point apparatus.

General procedure

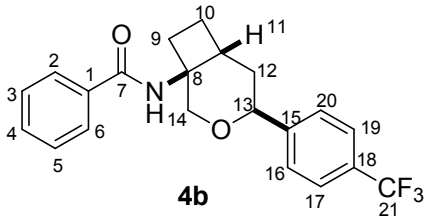
Scheme 1. Synthetic procedure



Reagents & conditions: (a) TBSCl, imidazole, DCM, 0 °C to rt (b) i) IBX, DMSO, 0° to rt, ii) $Ph_3P{=}CH_2$, THF, 0°C to rt (c) TBAF, THF.

4-Aryl-(3-oxabicyclo[4.2.0]octan-1-yl)amide (4):

To a mixture of aldehyde (1.2 mmol) and (1-vinylcyclopropyl)methanol (1.0 mmol), and nitrile (1.0 mmol), in dichloromethane (5.0 mL), was added TMSOTf (10% mol) slowly drop by drop at -40 °C. The resulting mixture was stirred at 0 °C for the specified time. The progress of the reaction was monitored by TLC using ethyl acetate and hexane as eluent. After completion, the mixture was treated with aqueous sodium bicarbonate solution and then the product was extracted with ethyl acetate. The organic layer was dried over Na_2SO_4 and concentrated in vacuo. The resulting crude material was purified by column chromatography over silica gel to give the 4-aryl-(3-oxabicyclo[4.2.0]octan-1-yl)amide.



4b

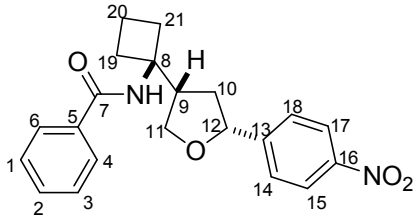
The relative stereochemistry of **4b** was established by 1D and 2D NMR experiments. The two aromatic rings were distinguished based on characteristic nOe correlations between H13 and H16/H20 as well as NH and H2/H6. Also the presence of nOe correlations between NH/H11, H12/H20, H14/H9, H13/H10 indicates their conformation as shown in the above figure.

^{1}H NMR: δ 7.78 (d, *J* =8.2 Hz, H17, H19), 7.60 (d, *J* = 8.2 Hz, H2, H6), 7.52-7.43 (m , H3, H4, H5, H16, H20), 6.43 (s, NH), 4.64 (d, *J* = 13 Hz, H14), 4.64 (dd, *J* = 1.3, 13 Hz, H13), 4.00 (d, *J* = 13 Hz, H14'), 2.93 (tt, *J* = 3.6, 9.8 Hz, H11), 2.40 (ddd, *J* = 9.0, 10.2, 11.5 Hz,

H9), 2.24 (ddd, *J* = 2.6, 7.7, 11.5 Hz, H9'), 2.11-2.03 (m , H10', H10), 1.79-1.75 (m, H12', H12).

(1-(5-Aryltetrahydrofuran-3-yl)cyclobutyl)benzamide (5):

To a mixture of aldehyde (1.2 mmol) and (1-vinylcyclobutyl)methanol (1.0 mmol), and nitrile(1.0 mmol), in dicloromethane (5.0 mL) was added TMSOTf (10% mol) slowly drop by drop at -40 ^{o}C. The resulting mixture was stirred at room temperature for the specified time. The progress of the reaction was monitored by TLC using ethyl acetate and hexane as eluent. After completion, the mixture was treated with aqueous sodium bicarbonate solution and then the product was extracted with ethyl acetate. The organic layer was dried over Na_2SO_4 and concentrated in vacuo. The resulting crude material was purified by column chromatography over silica gel to give the (1-(5-aryltetrahydrofuran-3-yl)cyclobutyl) benzamide.



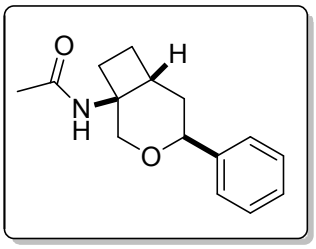
5a

The relative stereochemistry of **5a** was established by nOe correlations between amide proton and H4/H6 as well as H12 and H14/H18. The two aromatic rings were identified for compound **5a**. The presence of nOe correlation between H9 and H12 indicates that these two protons are in cis orientation. This observation is supported by the absence of nOe between H9 and H14/H18 as well as the presence of nOe between amide proton and H14/H18. The presence of J-correlations H9/H11, H9/H10, H19/H20 and H20/H21 confirms the structure as shown in the figure, which is supported by the nOe correlations shown in the above figure.

^{1}H NMR: δ 8.15 (d, *J* = 8.4 Hz, H15, H17), 7.65 (d, *J* = 7.6 Hz, H4, H6), 7.50 (d, *J* = 8.4 Hz, H14, H18), 7.48 (broad, H2), 7.40 (t, *J* = 7.6 Hz, H3, H1), 6.39 (s, NH), 4.97 (dd, *J* = 6.4, 10.0 Hz, H12), 4.06 (dd, *J* = 6.0, 9.0 Hz, H11), 4.10 (dd, *J* = 8.3, 9.0 Hz, H11'), 3.35 (dddd, *J* = 6.0, 8.3, 8.3, 8.3 Hz, H9), 2.63-2.56 (m, H21), 2.58 (ddd, *J* = 6.4, 8.3, 12.5 Hz ,H10), 2.52 (t, *J* = 10.4 Hz, H19), 2.24-2.13 (m, H19',H20), 2.11-2.02 (m, H21'), 1.87-1.77 (m, H20'), 1.66 (ddd, *J* = 8.3, 10.0, 12.5, H10').

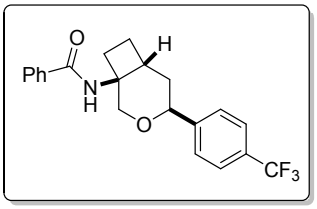
Characterization data of products:

_N_-(4-Phenyl-3-oxabicyclo[4.2.0]octan-1-yl)acetamide (4a)



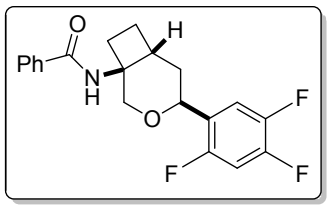
Pale yellow semi-solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38-7.26 (m, 5H), 5.83 (bs, 1H), 4.57-4.45 (m, 2H), 3.9 (d, J = 12.9 Hz, 1H), 2.82-2.75 (m, 1H), 2.14-1.93 (m, 7H), 1.79-1.66 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.6, 142.4, 128.3, 127.5, 125.6, 76.1, 74.0, 51.8, 37.1, 31.2, 30.0, 23.8, 18.7 ppm; IR (KBr): υ 3278, 2925, 1644, 1544, 1451, 105, 1088, 915, 752 cm^{-1}; HRMS (*m/z*) calcd for $C_{15}H_{19}O_2NNa$: 268.1308, found: 268.1303.

_N_-(4-(4-(Trifluoromethyl)phenyl)-3-oxabicyclo[4.2.0]octan-1-yl)benzamide (4b)



Colourless solid, m.p. 175-177 ^{o}C ; ^{1}H NMR: δ 7.78 (d, J =8.2 Hz, H17, H19), 7.60 (d, J = 8.2 Hz, H2, H6), 7.52-7.43 (m , H3, H4,H5, H16, H20), 6.43 (s, NH), 4.64 (d, J = 13 Hz, H14), 4.64 (dd, J = 1.3, 13 Hz, H13), 4.00 (d, J = 13 Hz, H14'), 2.93 (tt, J = 3.6, 9.8 Hz, H11), 2.40 (ddd, J = 9.0, 10.2, 11.5 Hz, H9), 2.24 (ddd, J = 2.6,7.7,11.5 Hz, H9'), 2.11-2.03 (m , H10', H10), 1.79-1.75 (m , H12', H12) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.9, 146.6, 134.6, 131.5, 128.5, 126.8, 125.8, 125.3, 125.2, 75.4, 73.9, 52.1, 37.1, 31.5, 30.2, 18.8 ppm; ^{13}C-DEPT: CH2: 73.9, 31.5, 30.2, 18.8 ppm; CH: 131.5, 128.8, 126.7, 125.7, 125.2, 75.4, 37.1 ppm; IR (KBr): υ 3380, 3328, 2923, 1639, 1528, 1324, 1123, 845, 709 cm^{-1}; HRMS (*m/z*) calcd for $C_{21}H_{21}O_2NF_3$: 376.1518, found: 376.1522.

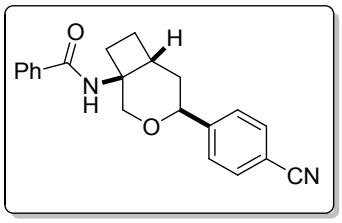
_N_-(4-(2,4,5-Trifluorophenyl)-3-oxabicyclo[4.2.0]octan-1-yl)benzamide (4c)



Pale yellow semi-solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81-7.77 (m, 2H), 7.54-7.43 (m, 3H), 7.35-7. 29 (m, 1H), 6.89 (m, 1H), 6.43 (bs, 1H), 4.84-4.79 (m, 1H), 4.62 (d, J = 12.9 Hz, 1H), 3.99 (d, J = 12.9 Hz, 1H), 2.93-2. 86 (m, 1H), 2.39-2. 32 (m, 1H), 2.26-2.21 (m, 1H), 2.1-2.03

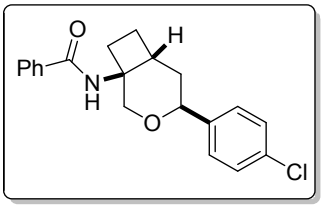
(m, 2H) 1.81-1.76 (m, 1H), 1.71-1.63 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.9, 134.6, 131.5, 128.5, 126.8, 115.2, 115.0, 105.4, 105.2, 105.0, 73.9, 69.6, 52.1, 37.0, 30.6, 30.2, 18.8 ppm; IR (KBr): υ 3319, 2924, 1639, 1528, 1087, 821, 713 cm^{-1}; HRMS (*m/z*) calcd for $C_{20}H_{19}O_2NF_3$: 362.1362, found: 362.1357.

***N*-(4-(4-Cyanophenyl)-3-oxabicyclo[4.2.0]octan-1-yl)benzamide (4d)**



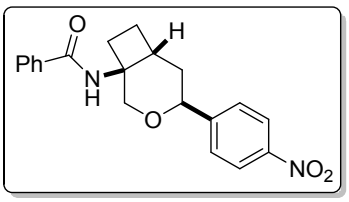
White solid, m.p. 125-127 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.80-7.77 (m, 2H), 7.65-7.62 (m, 2H), 7.54-7.41 (m, 5H), 6.43 (bs, 1H), 4.67-4.62 (m, 2H), 3.98 (d, J = 13.1 Hz, 1H), 2.96-2.89 (m, 1H), 2.42-2.34 (m, 1H), 2.28-2.22 (m, 1H), 2.13-1.99 (m, 2H), 1.8-1.69 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.8, 147.9, 134.5,132.1,131.4, 128.4, 126.7, 126.0, 118.6, 111.0, 75.1, 73.7, 51.9, 36.9, 31.3, 30.1, 18.7 ppm; IR (KBr): υ 3387, 2923, 2228, 1643, 1528, 1458, 1085, 830, 714 cm^{-1}; HRMS (*m/z*) calcd for $C_{21}H_{21}O_2N_2$: 333.1597, found: 333.1596.

***N*-(4-(4-Chlorophenyl)-3-oxabicyclo[4.2.0]octan-1-yl)benzamide (4e)**



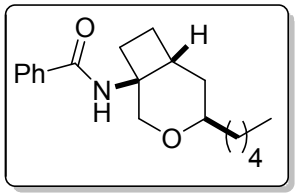
White solid, m.p. 152-154 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81-7.76 (m, 2H), 7.53-7. 42 (m, 3H), 7.31 (s, 4H), 6.45 (bs, 1H), 4.62 (d, J = 12.0 Hz, 1H), 4.59-4.52 (m, 1H), 3.98 (d, J = 12.8 Hz, 1H), 2.97-2.86 (m, 1H), 2.44-2.32 (m, 1H), 2.28-2.16 (m, 1H), 2.11-2.0 (m, 2H), 1.78-1.70 (m, 2H) ppm; ^{13}C NMR (125 MHz, CDCl3): δ 166.9, 141.0, 134.7, 133.1, 131.4, 128.5, 128.4, 127.0, 126.8, 75.4, 73.9, 52.1, 37.1, 31.4, 30.2, 18.8 ppm; IR (KBr): υ 3353, 2930, 1634, 1529, 1400, 1088, 695 cm^{-1} **;** HRMS (*m/z*) calcd for $C_{20}H_{21}O_2NCl$: 342.1255, found: 342.1252.

***N*-(4-(4-Nitrophenyl)-3-oxabicyclo[4.2.0]octan-1-yl)benzamide (4f)**



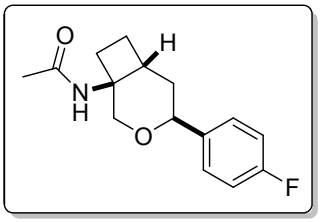
Yellow semi-solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.22-8.18 (m, 2H), 7.81-7.77 (m, 2H), 7.55-7.42 (m, 5H), 6.5 (bs, 1H), 4.71-4.65 (m, 2H), 4.0 (d, J = 12.9 Hz, 1H), 2.97-2.9 (m, 1H), 2.41-2.34 (m, 1H), 2.29-2.23 (m, 1H) 2.13-2.01 (m, 2H), 1.82-1.70 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.9, 150.0, 147.1, 134.5, 131.5, 128.5, 126.8, 126.2, 123.6, 75.1, 73.7, 52.0, 36.9, 31.5, 30.2, 18.8 ppm; IR (KBr): υ 3420, 2984, 1649, 1518, 1400, 1345, 1092, 851, 694 cm^{-1}; HRMS (*m/z*) calcd for $C_{20}H_{21}O_4N_2$: 353.1495, found: 353.1493.

***N*-(4-Pentyl-3-oxabicyclo[4.2.0]octan-1-yl)benzamide (4g)**



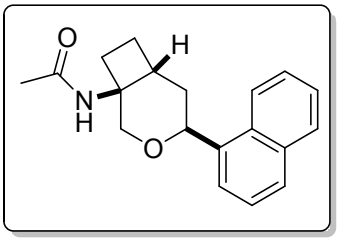
Colourless solid, m.p. 140-142 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.76-7.73 (m, 2H), 7.5-7.39 (m, 3H), 6.40 (bs, 1H), 4.47-4.43 (dd, J = 1.2 Hz, 1H), 3.79-3.75 (d, J = 13.2 Hz, 1H) 3.5-3.44 (m, 1H), 2.81-2.74 (m, 1H), 2.35-2.28 (m, 1H), 2.18-2.12 (m, 1H), 2.0-1.83 (m, 2H), 1.58-1.25 (m, 10H), 0.89 (t, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.8, 134.7, 131.3, 128.4, 126.8, 74.3, 73.5, 52.4, 36.9, 36.4, 31.8, 30.1,29.7, 29.6, 25.3, 22.6, 18.9, 14.0 ppm; IR (KBr): υ 3418, 2925, 1643, 1400, 1262, 1174, 1038, 802 cm^{-1}; HRMS (*m/z*) calcd for $C_{19}H_{27}O_2NNa$: 324.1934, found: 324.1924.

***N*-(4-(4-Fluorophenyl)-3-oxabicyclo[4.2.0]octan-1-yl)acetamide (4h)**



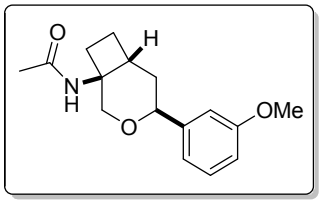
Pale yellow semi-solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35 -7.3 (m, 2H), 7.05-7.0 (m, 2H), 5.81 (bs, 1H), 4.57-4. 46 (m, 2H), 3.89 (d, J = 12.9 Hz, 1H), 2.81-2.75 (m, 1H), 2.29-2.21 (m, 1H), 2.13-2.08 (m, 1H), 2.03-1.93 (m, 5H), 1.76-1.64 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.9, 138.1, 127.4, 127.3, 115.2, 115.0, 75.4, 74.0, 51.7, 37.0, 31.2, 30.0, 23.8, 18.7 ppm; IR (KBr): υ 3325, 2925, 1648, 1455, 1369, 1224, 1088, 833, 741 cm^{-1}; HRMS (*m/z*) calcd for $C_{15}H_{18}O_2NFNa$: 286.1213, found: 286.1214.

***N*-(4-(Naphthalen-1-yl)-3-oxabicyclo[4.2.0]octan-1-yl)acetamide (4i)**



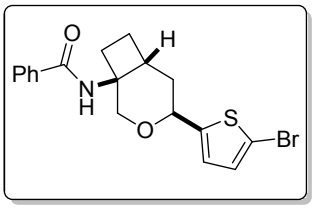
Pale yellow semi-solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.0 (d, J = 7.7 Hz, 1H), 7.9-7.75 (m, 2H), 7.67-7.43 (m, 4H), 5.93 (bs, 1H), 5.32-5.23 (m, 1H), 4.59 (d, J = 12.8 Hz, 1H), 4.08 (d, J = 13.0 Hz, 1H), 2.9-2.78 (m, 1H), 2.05-1.78 (m, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.6, 138.0, 133.7, 130.2, 128.9, 128.0, 125.9, 125.48, 125.46, 123.0, 122.7, 74.4, 73.3, 52.0, 37.3, 30.6, 30.1, 23.8, 18.8 ppm; IR (KBr): υ 3292, 3057, 2926, 1645, 1456, 1304, 1090, 781, 735 cm^{-1}; HRMS (*m/z*) calcd for $C_{19}H_{22}O_2N$: 296.1645, found: 296.1644.

_N_-(4-(3-Methoxyphenyl)-3-oxabicyclo[4.2.0]octan-1-yl)acetamide (4j)



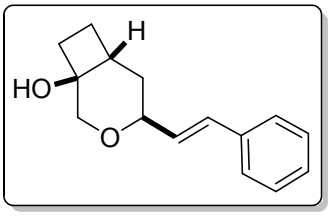
Pale yellow liquid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27 -7.23 (m, 1H), 6.94-6.90 (m, 2H), 6.83-6.80 (m, 1H) 5.83 (bs, 1H), 4.53-4.46 (m, 2H), 3.89 (d, J = 12.8 Hz, 1H),3.81(s, 3H), 2.80-2.74 (m, 1H), 2.29-2.22 (m, 1H), 2.13-2.08 (m, 1H), 2.01-1.94 (m, 4H), 1.77-1.63 (m, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.9, 159.6, 144.0, 129.4, 117.9, 113.0, 111.2, 76.0, 73.9, 55.2, 51.7, 37.1. 31.2, 30.0, 23.8, 18.7 ppm; IR (KBr): υ 3325, 2925, 1648, 1455, 1369, 1214, 1078, 833, 741 cm^{-1}; HRMS (*m/z*) calcd for $C_{16}H_{22}O_3N$: 276.1594, found: 276.1586.

_N_-(4-(5-Bromothiophen-2-yl)-3-oxabicyclo[4.2.0]octan-1-yl)benzamide (4k)



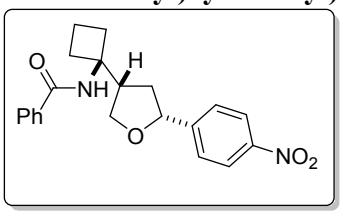
Pale yellow semi-solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78 -7.73 (m, 2H), 7.51-7.40 (m, 3H), 6.91 (d, J = 3.7 Hz, 1H), 6.74 (d, J = 2.9 Hz, 1H)6.41 (bs, 1H), 4.74 (d, J = 3.05 Hz, 1H), 4.55 (d, J = 13.2 Hz, 1H), 3.97 (d, J = 12.9 Hz, 1H), 2.99-2.90 (m, 1H), 2.45-2.32 (m, 1H), 2.25-2.17 (m, 1H), 2.11-1.90 (m, 3H), 1.87-1.81 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.3, 147.2, 131.7, 131.4, 129.2, 128.7 128.5, 126.8, 123.9, 123.8, 73.7, 72.1, 71.2, 52.2, 36.7, 30.6, 29.6, 18.9 ppm; IR (KBr): υ 3325, 2954, 1640, 1535, 1369, 1124, 1058, 833, 741 cm^{-1}; HRMS (*m/z*) calcd for $C_{18}H_{19}O_2NBrS$: 392.0314, found: 392.0310.

_N_-(4-((_E_)-styryl)-3-oxabicyclo[4.2.0]octan-1-yl)benzamide (4l)



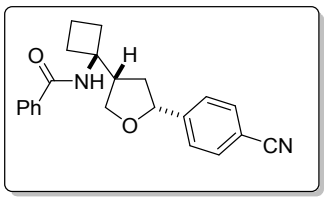
Pale yellow semi-solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41 -7.20 (m, 10H), 6.63(d, J = 16.0 Hz, 1H), 6.21(dd, J = 5.7 Hz, 1H) 4.13-4. 06 (m, 2H), 3.82 (d, J = 12.9 Hz, 1H), 2.58-2.50 (m, 1H), 1.93-1.68 (m, 4H), 1.6-1.5 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 136.8, 130.3, 130.0, 128.5, 127.5, 126.4, 75.3, 74.6, 68.9, 41.2, 32.1, 29.3, 15.6 ppm; IR (KBr): υ 3355, 3025, 2945,1455, 1369, 1223, 1078, 833, 714 cm^{-1}; HRMS (*m/z*) calcd for $C_{15}H_{18}O_2NNa$: 253.1204, found: 253.1202.

***N*-(1-(5-(4-Nitrophenyl)tetrahydrofuran-3-yl)cyclobutyl)benzamide (5a)**



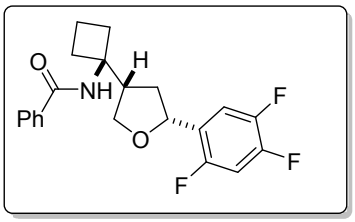
Pale yellow solid, m.p. 184-186 ^{o}C; ^{1}H NMR: δ 8.15 (d, J = 8.4 Hz, H15, H17), 7.65 (d, J = 7.6 Hz, H4, H6), 7.50 (d, J = 8.4 Hz, H14, H18), 7.48 (broad, H2), 7.40 (t, J = 7.6 Hz, H3, H1), 6.39 (s, NH), 4.97 (dd, J = 6.4, 10.0 Hz, H12), 4.06 (dd, J = 6.0, 9.0 Hz, H11), 4.10 (dd, J = 8.3, 9.0 Hz, H11'), 3.35 (dddd, J = 6.0, 8.3, 8.3, 8.3 Hz, H9), 2.63-2.56 (m, H21), 2.58 (ddd, J = 6.4, 8.3, 12.5 Hz ,H10), 2.52 (t, J = 10.4 Hz, H19), 2.24-2.13 (m, H19',H20), 2.11-2.02 (m, H21'), 1.87-1.77 (m, H20'), 1.66 (ddd, J = 8.3, 10.0, 12.5, H10') ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.9, 149.4, 147.1, 134.9, 131.5, 128.5, 126.6, 126.1, 123.6, 80.4, 70.0, 59.1, 45.8, 36.6, 30.8, 30.5, 14.2 ppm; ^{13}C-DEPT: CH2: 70.2, 36.8, 31.0, 30.7, 14.4 ppm; CH: 131.7, 128.7, 126.8, 126.3, 123.8, 80.6, 46.6 ppm; IR(KBr): υ 3418, 2953, 1636, 1516, 1400, 1347, 1079, 854 cm^{-1}; HRMS (*m/z*) calcd for $C_{21}H_{23}O_4N_2$: 367.1652, found: 367.1653.

***N*-(1-(5-(4-Cyanophenyl)tetrahydrofuran-3-yl)cyclobutyl)benzamide (5b)**



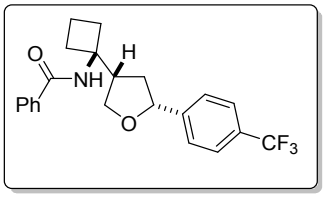
White solid, m.p. 202-204 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.67-7.63 (m, 2H), 7.61-7.57 (m, 2H), 7.53-7.38 (m, 5H), 6.37 (bs, 1H), 4.92 (dd, J = 6.4 Hz, 1H), 4.11-4.02 (m, 2H), 3.37-3.28 (m, 1H), 2.66-2.51 (m, 3H), 2.24-2.02 (m, 3H), 1.87-1.77 (m, 1H), 1.68-1.6 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.9, 147.3, 135.0, 132.2, 131.4, 128.5, 126.6, 126.1, 118.5, 111.1, 80.5, 69.9, 59.2, 45.8, 36.5, 30.8, 30.5, 14.2 ppm; IR (KBr): υ 3396, 2930, 2232, 1640, 1519, 1400, 1124, 1067, 837 cm^{-1}; HRMS (*m/z*) calcd for $C_{22}H_{23}O_2N_2$: 347.1754, found: 347.1763.

***N*-(1-(5-(2,4,5-Trifluorophenyl)tetrahydrofuran-3-yl)cyclobutyl)benzamide (5c)**



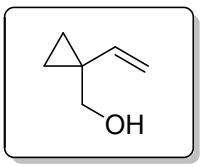
Pale yellow semi-solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73-7.65 (m, 2H), 7.55-7.27 (m, 4H), 6.94-6.83 (m, 1H), 6.4 (bs, 1H), 4.98 (dd, J = 6.2 Hz, 1H), 4.1-3.96 (m, 2H), 3.36-3.23 (m, 1H), 2.69-2.51 (m, 2H), 2.25-1.96 (m, 4H), 1.89-1.73 (m, 1H), 1.63-1.5 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.0, 135.0, 131.4, 128.5, 126.6, 114.6(dd), 105(q), 75.2, 69.5, 59.1, 45.9, 35.4, 30.8, 30.5, 14.1 ppm; IR (KBr): υ 3334, 2936, 1631, 1512, 1400, 1114, 890, 716 cm^{-1} ; HRMS (*m/z*) calcd for $C_{21}H_{21}O_2NF_3$: 376.1518, found: 367.1513.

***N*-(1-(5-(4-(Trifluoromethyl)phenyl)tetrahydrofuran-3-yl)cyclobutyl)benzamide (5d)**



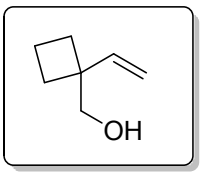
White solid, m.p. 162-164 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65-7.62 (m, 2H), 7.56 (d, J = 8.0 Hz, 2H), 7.5-7.44 (m, 3H), 7.41-7.36 (m, 2H), 6.42 (bs, 1H), 4.93 (dd, J = 6.5 Hz, 1H), 4.12-4.01 (m, 2H), 3.33-3.26 (m, 1H), 2.72-2.54 (m, 3H), 2.22-2.02 (m, 3H), 1.86-1.76 (m, 1H), 1.71-1.64 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.0, 145.8, 135.0, 131.4, 128.4, 126.6, 125.7, 125.3, 125.2, 80.7, 69.9, 59.3, 45.8, 36.4, 30.8, 13.9 ppm; IR (KBr): υ 3365, 3134, 2964, 1640, 1516, 1400, 1324, 1126, 1036, 718 cm^{-1}; HRMS (*m/z*) calcd for $C_{22}H_{23}O_2NF_3$: 390.1675, found: 390.1690.

(1-Vinylcyclopropyl)methanol:



Liquid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.65 (dd, J = 10.6 Hz, 1H), 5.13 (dd, J = 1.0 Hz, J = 1.2 Hz, 1H), 5.03 (dd, J = 1.0 Hz, 1H), 3.60 (s, 2H), 1.75 (bs, 1H), 0.74-0.66 (m, 4H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 141.1, 112.0, 67.7, 25.0, 12.1 ppm.

(1-Vinylcyclobutyl)methanol:



Liquid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.87 (dd, *J* = 10.5 Hz, 1H), 5.18 (dd, *J* = 1.5 Hz, *J* = 1.3 Hz, 1H), 5.11 (dd, *J* = 1.3 Hz, 1H), 3.58 (s, 2H), 2.05-1.82 (m, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.2, 113.7, 68.3, 46.4, 27.9, 25.6 ppm.

Crystallographic data for **4b**

X-ray data for the compound were collected at room temperature using a Bruker Smart Apex CCD diffractometer with graphite monochromated MoKα radiation (λ=0.71073Å) with ω-scan method.[1] Preliminary lattice parameters and orientation matrices were obtained from four sets of frames. Unit cell dimensions were determined using 3299 reflections for **4b**. Integration and scaling of intensity data were accomplished using SAINT program.[1] The structure was solved by Direct Methods using SHELXS97[2] and refinement was carried out by full-matrix least-squares technique using SHELXL97.[2] Anisotropic displacement parameters were included for all non-hydrogen atoms. All H atoms were positioned geometrically and treated as riding on their parent C atoms with C-H distances of 0.93--0.97 Å, and with U_{iso}(H) = 1.2U_{eq} (C) or 1.5U_{eq} for methyl atoms. Fluorine atoms in -CF_3 group were disordered over two sites - 69% site occupancy for atoms F1, F2, F3 (major component) and 31% site occupancy for atoms F1D, F2D, F3D (minor component). PART, DELU and SIMU instructions were used for disorder modeling of -CF_3 group and DFIX was used for fixing the C-F bond distance to 1.30Å with e.s.d value of 0.002Å.

Crystal data for **4b**: $C_{21}H_{20}F_3NO_2$, *M* = 375.38, colourless needle, 0.32 x 0.11 x 0.04 mm^3, monoclinic, space group *C*2/*c* (No. 15), *a* = 16.9345(13), *b* = 22.9721(13), *c* = 10.3059(7) Å, *β* = 108.212(2)°, *V* = 3808.4(4) Å^3, *Z* = 8, D_c = 1.309 g/cm^3, F_{000} = 1568, CCD area detector, MoKα radiation, λ = 0.71073 Å, *T* = 293(2)K, $2\theta_{max}$ = 50.0º, 18217 reflections collected, 3346 unique (R_{int} = 0.0373), Final *GoF* = 1.244, *R1* = 0.0978, *wR2* = 0.1977, *R* indices based on 2715 reflections with I >2*σ*(I) (refinement on F^2), 275 parameters, 42 restraints, μ = 0.104 mm^{-1}. CCDC 1009270 contains supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the

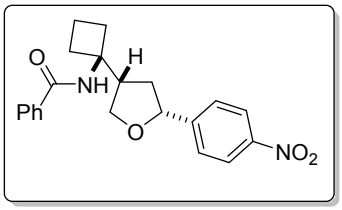
Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0) 1223 336 033; email: deposit@ccdc.cam.ac.uk.

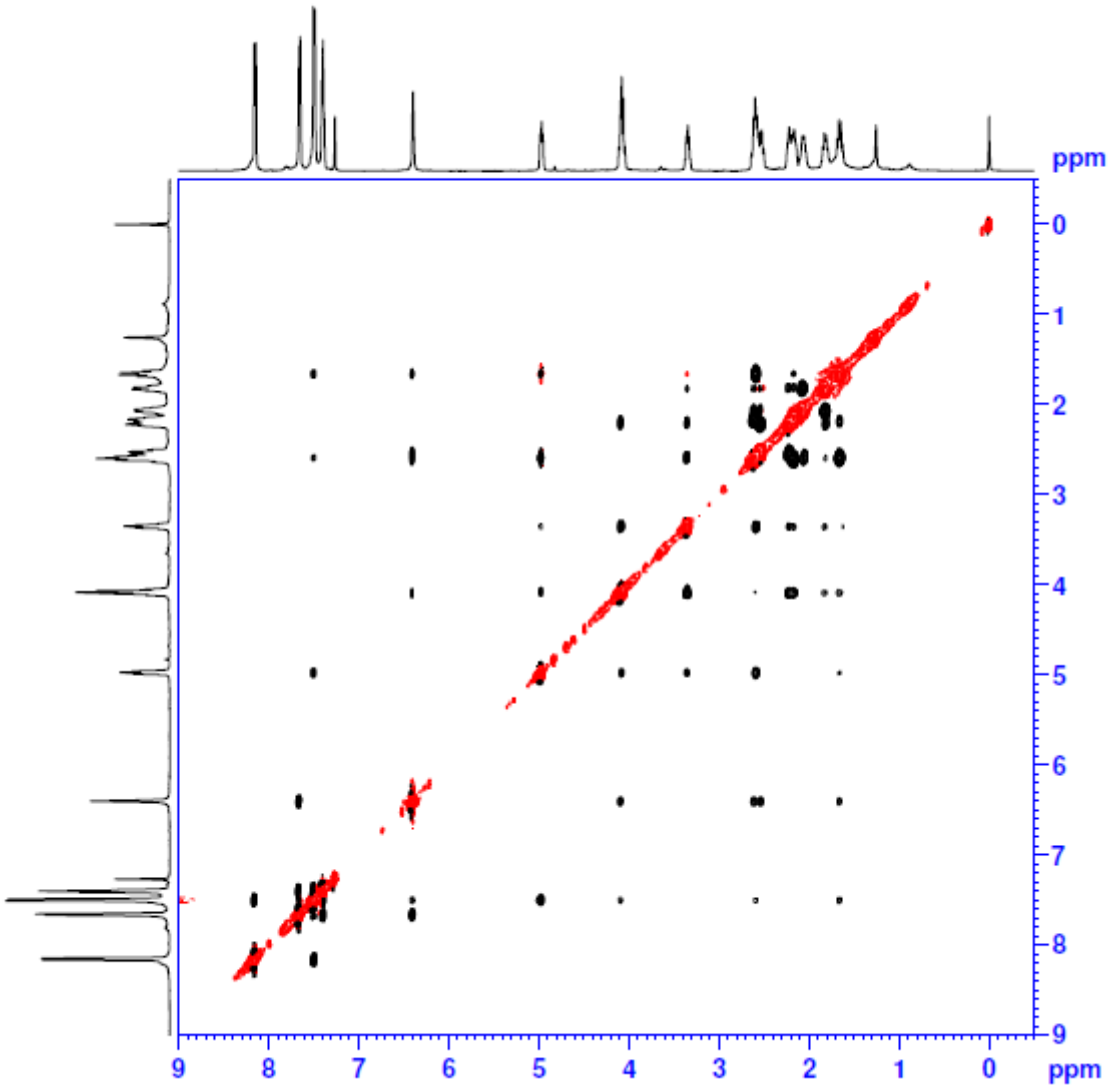
1. SMART & SAINT. Software Reference manuals. Versions 6.28a & 5.625, Bruker Analytical X-ray Systems Inc., Madison, Wisconsin, U.S.A., 2001.
2. Sheldrick, G. M. SHELXS97 and SHELXL97, Programs for crystal structure solution and refinement; University of Gottingen: Germany, 1997.

Figure caption: The molecular structure of **4b** with the atom-numbering scheme. Displacement ellipsoids are drawn at the 10% probability level and H atoms are shown as small spheres of arbitrary radius. Only major component of the disordered fluorine atoms in $-CF_3$ group is shown for clarity.

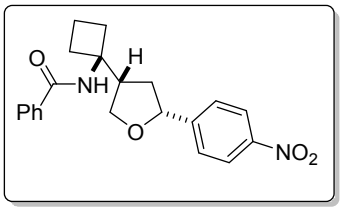
2D-NOESY spectrum of *N*-(1-(5-(4-nitrophenyl)tetrahydrofuran-3-yl)cyclobutyl) benzamide (5a)

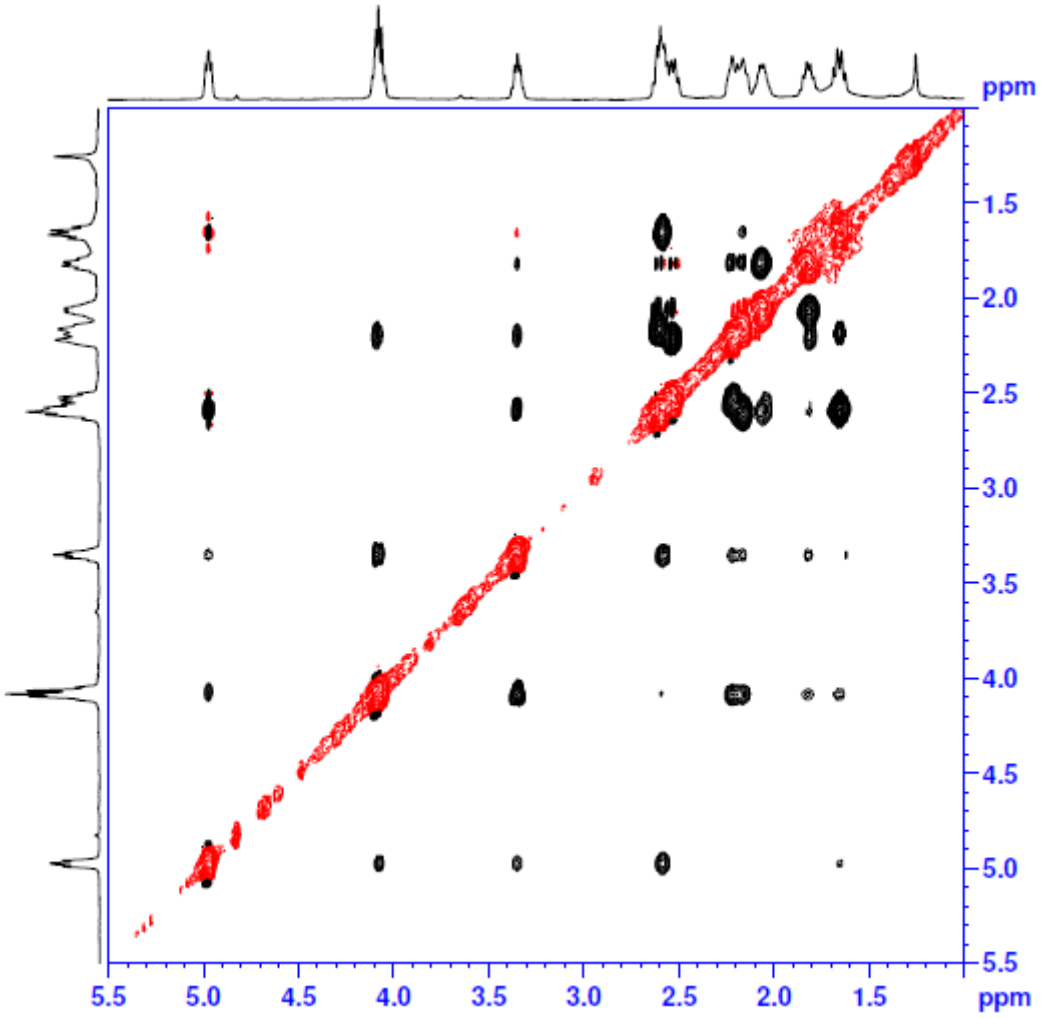
NOESY $CDCl_3$ AVANCE-500 MHz,17/06/2014





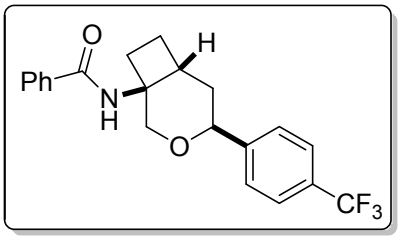
NOESY $CDCl_3$ AVANCE-500 MHz,17/06/2014 **5a**

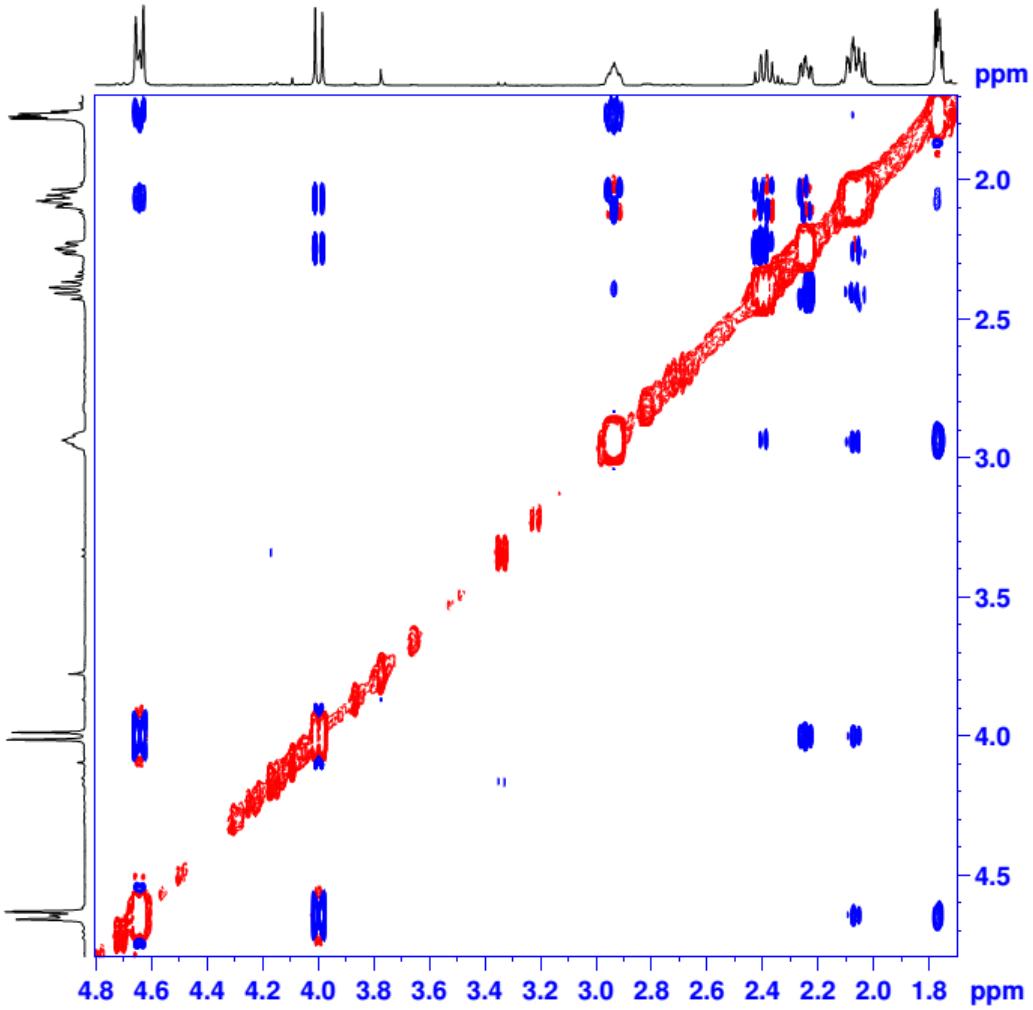




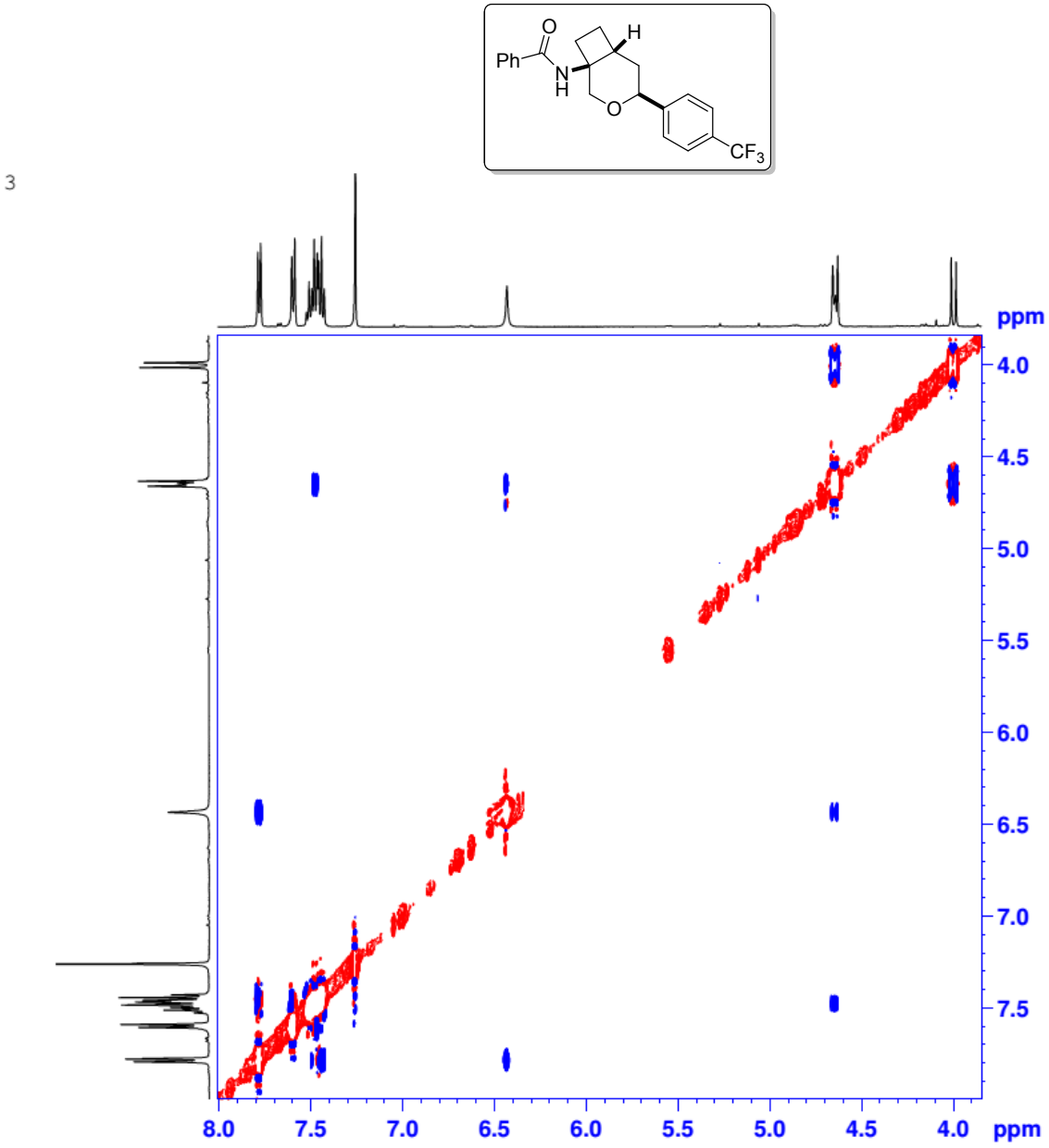
2D-NOESY spectrum of *N*-(4-(4-(trifluoromethyl)phenyl)-3-oxabicyclo[4.2.0]octan-1-yl)benzamide (4b)

NOESY $CDCl_3$ AVANCE-500 MHz,17/06/2014

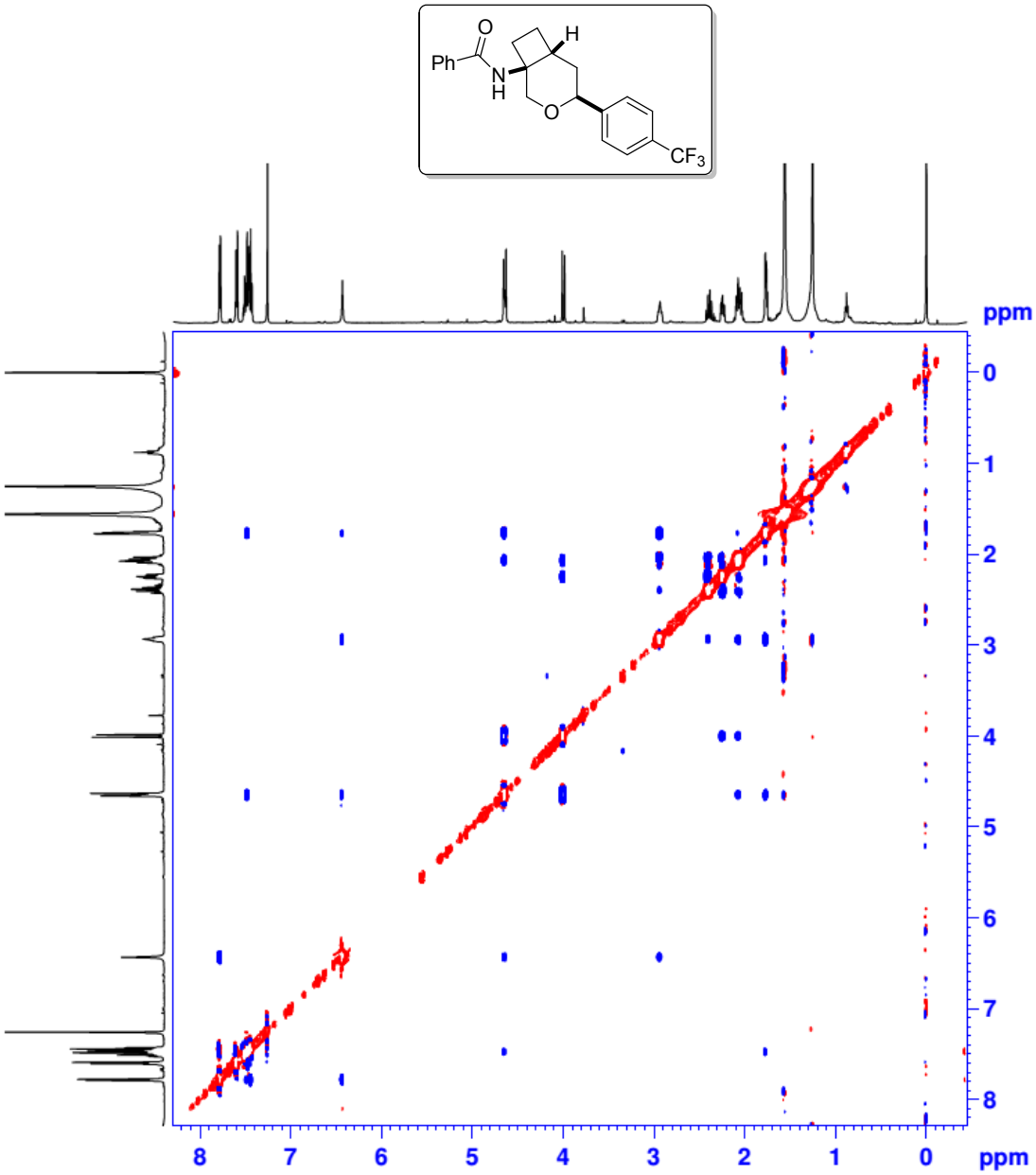




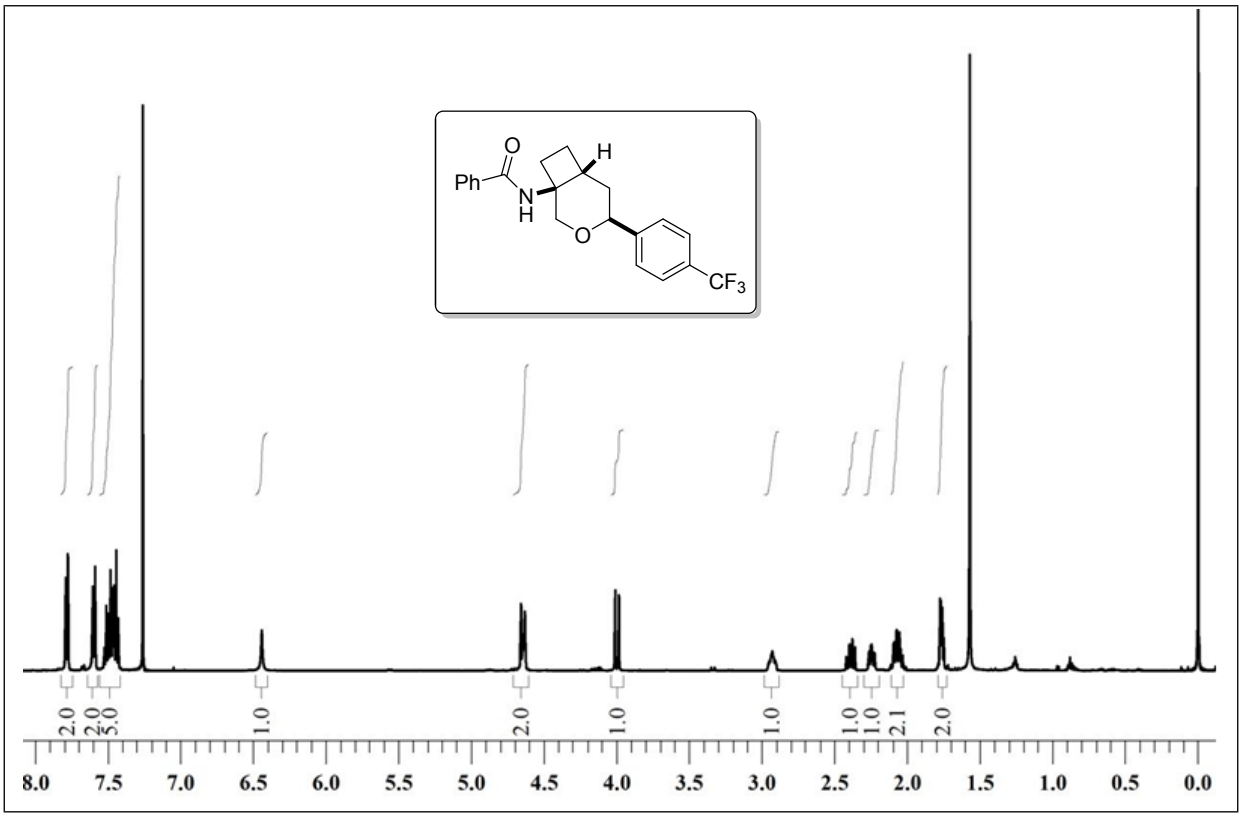
NOESY $CDCl_3$ AVANCE-500 MHz,17/06/2014 **4b**



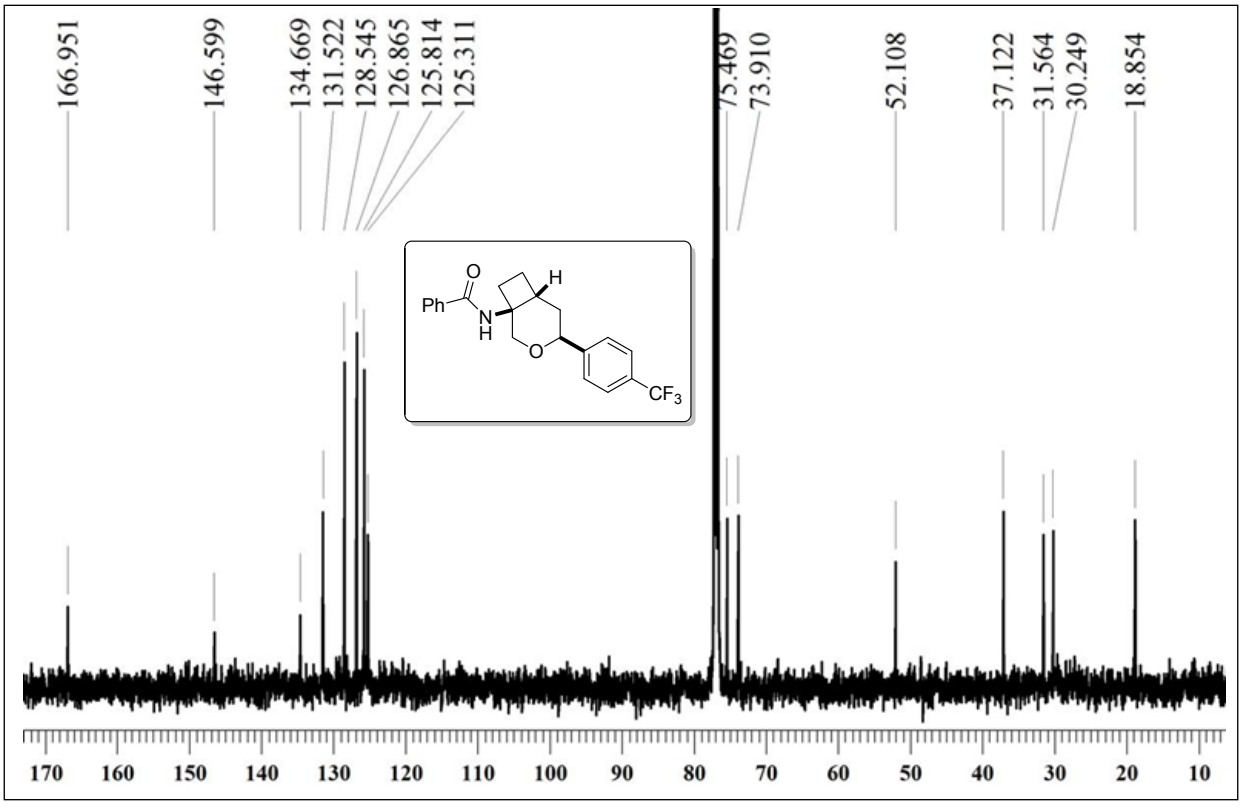
NOESY $CDCl_3$ AVANCE-500 MHz,17/06/2014 **4b**



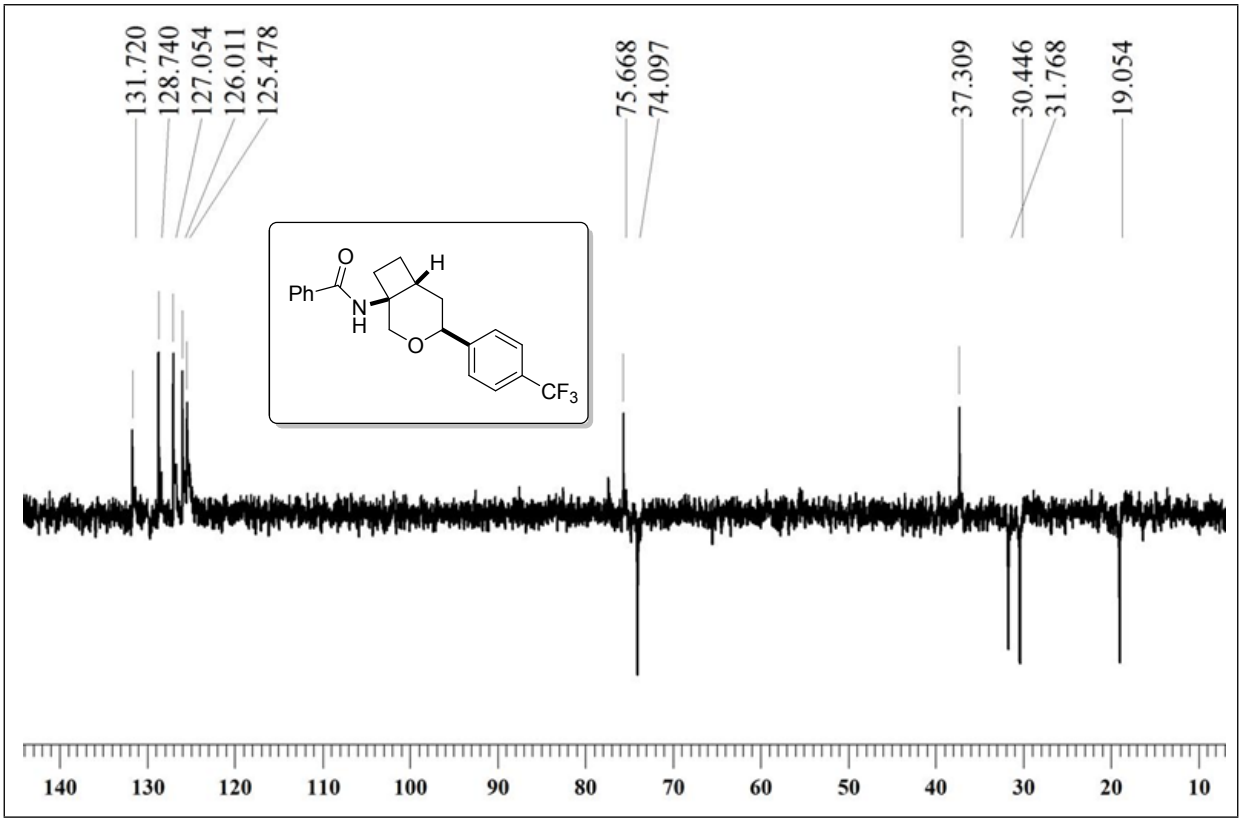
Copies of ^{1}H and ^{13}C NMR spectra



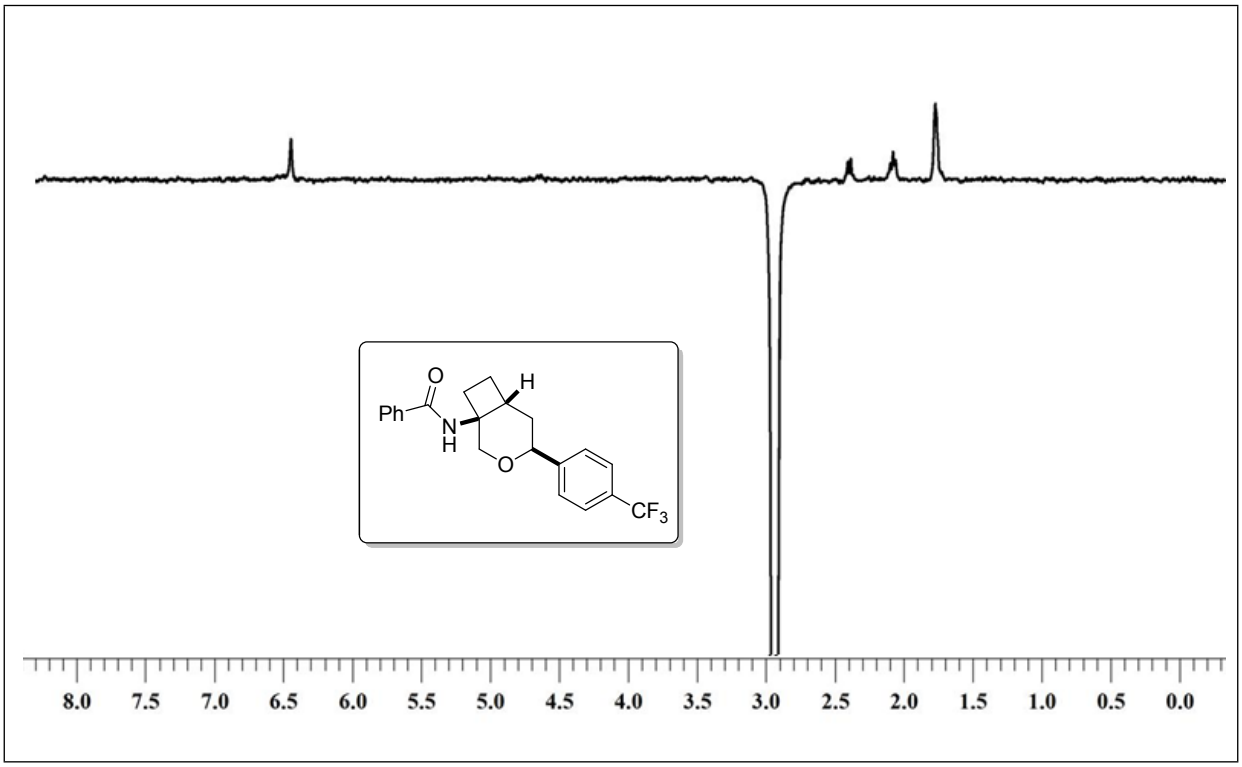
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 4b



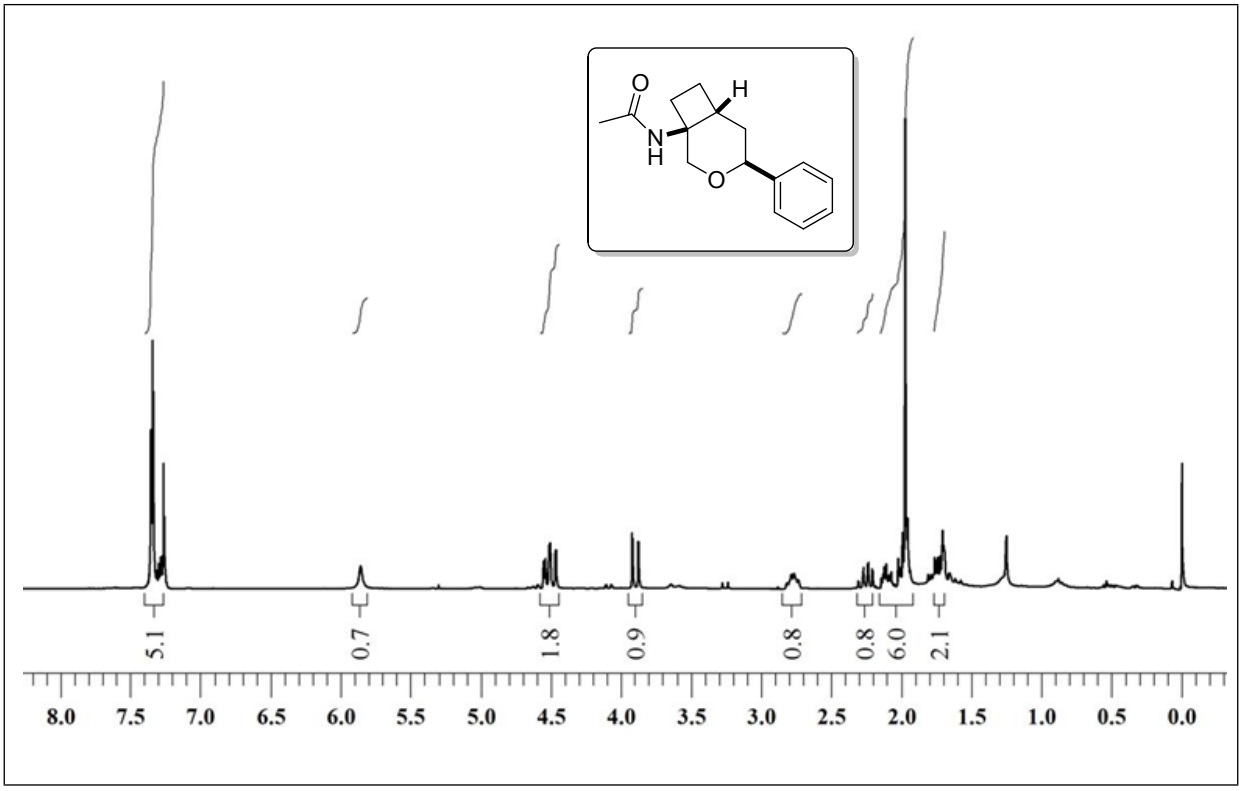
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 4b



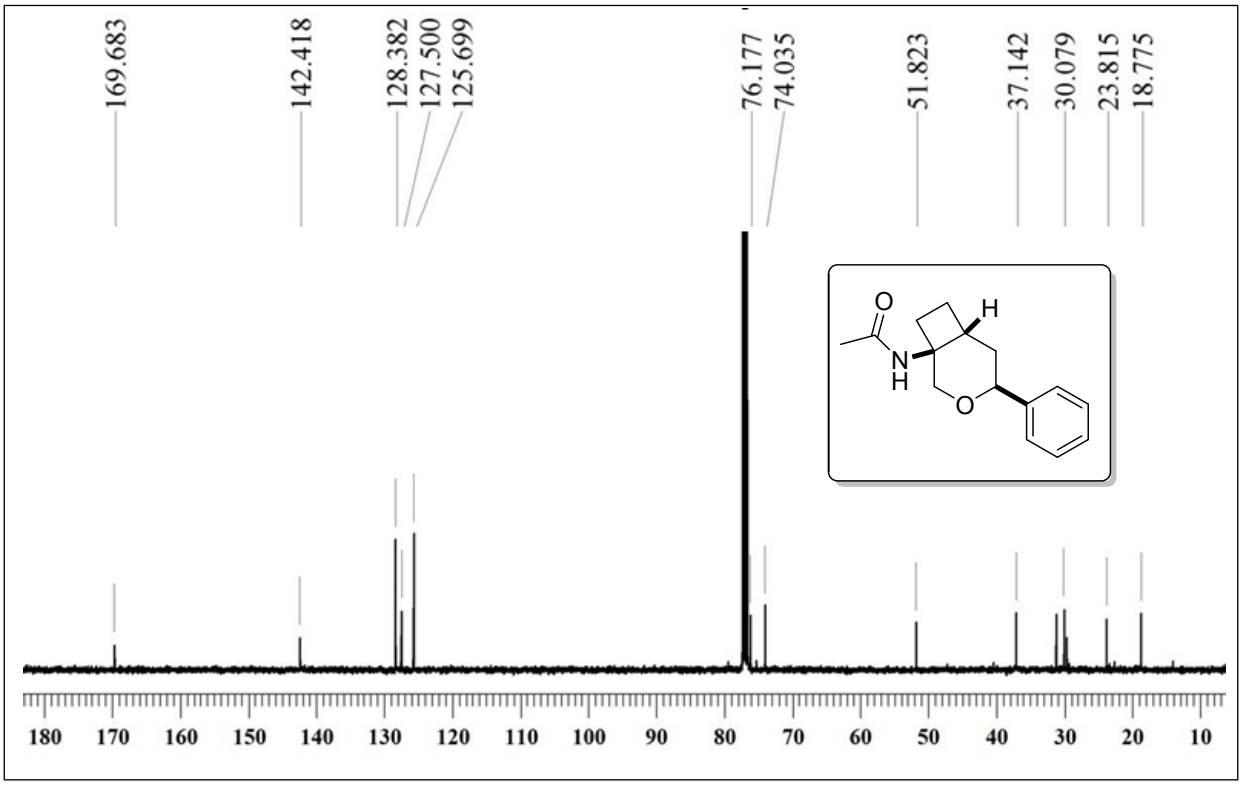
DEPT (135 MHz, $CDCl_3$) spectrum of 4b



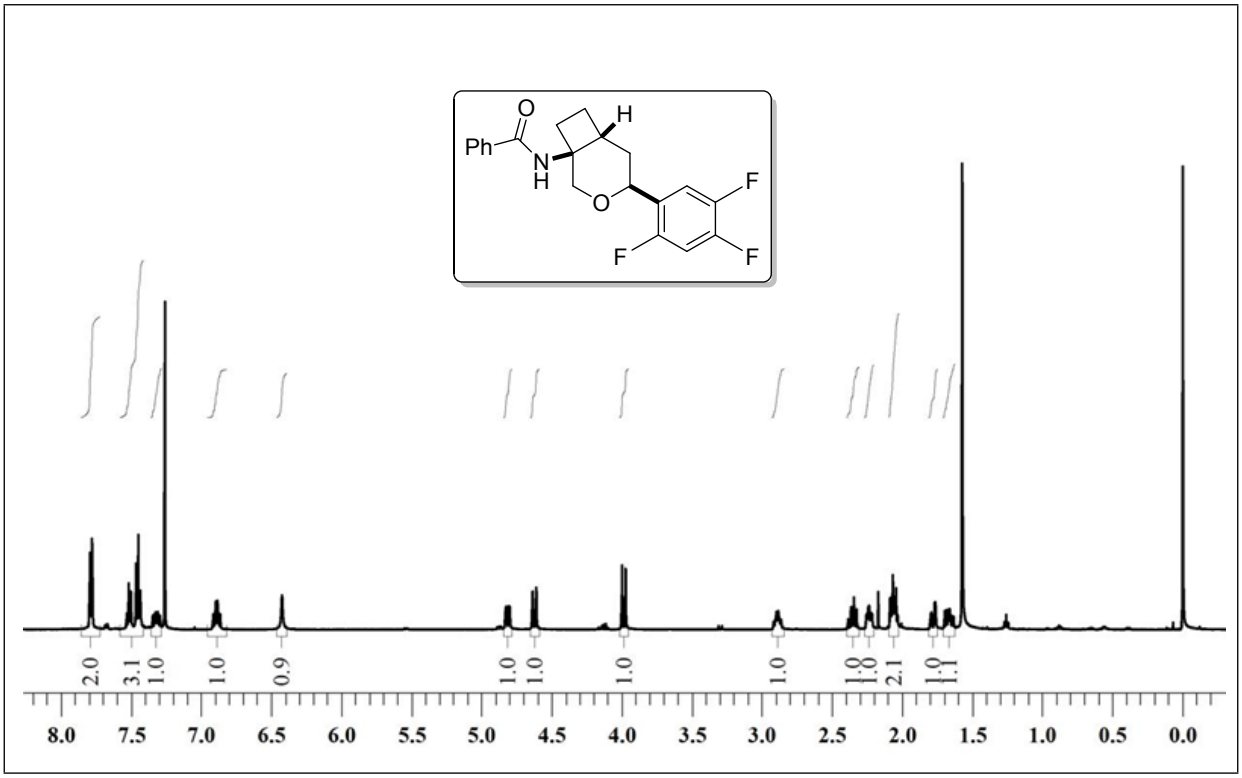
NOE (500 MHz, $CDCl_3$) spectrum of 4b



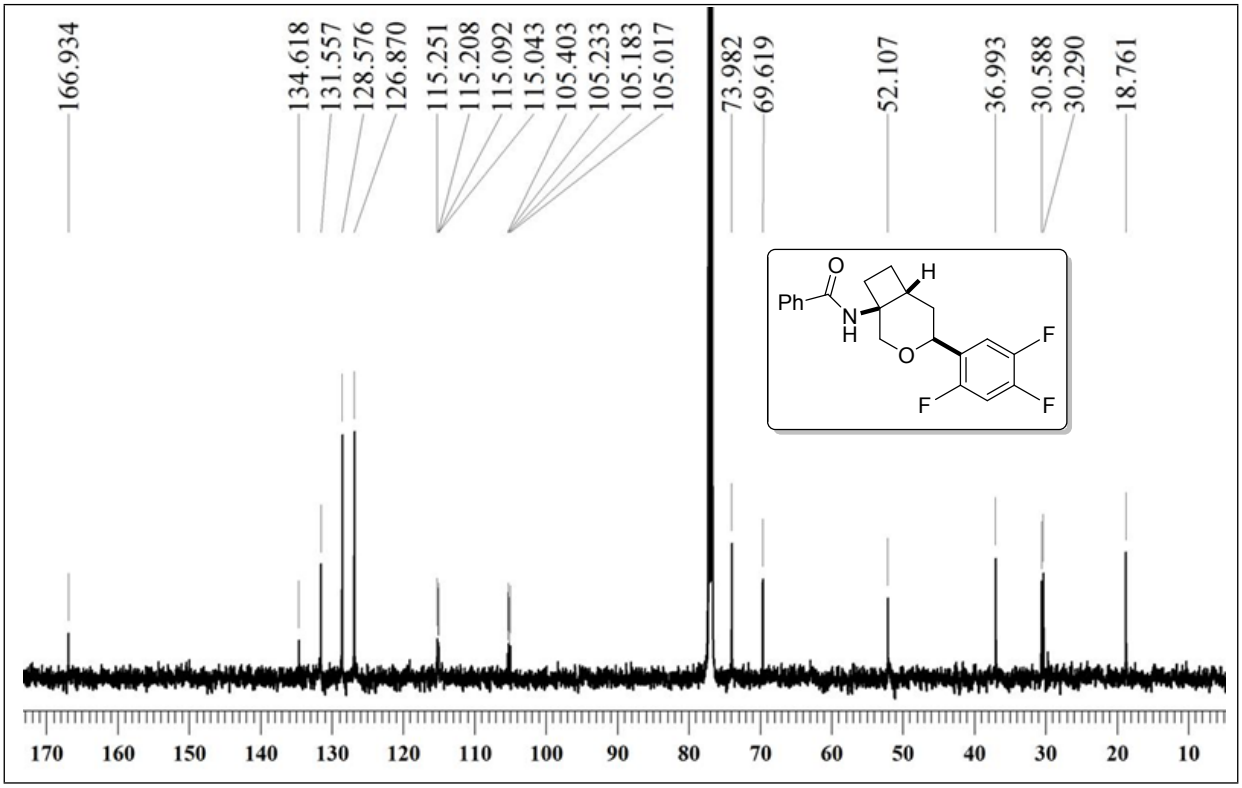
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 4a



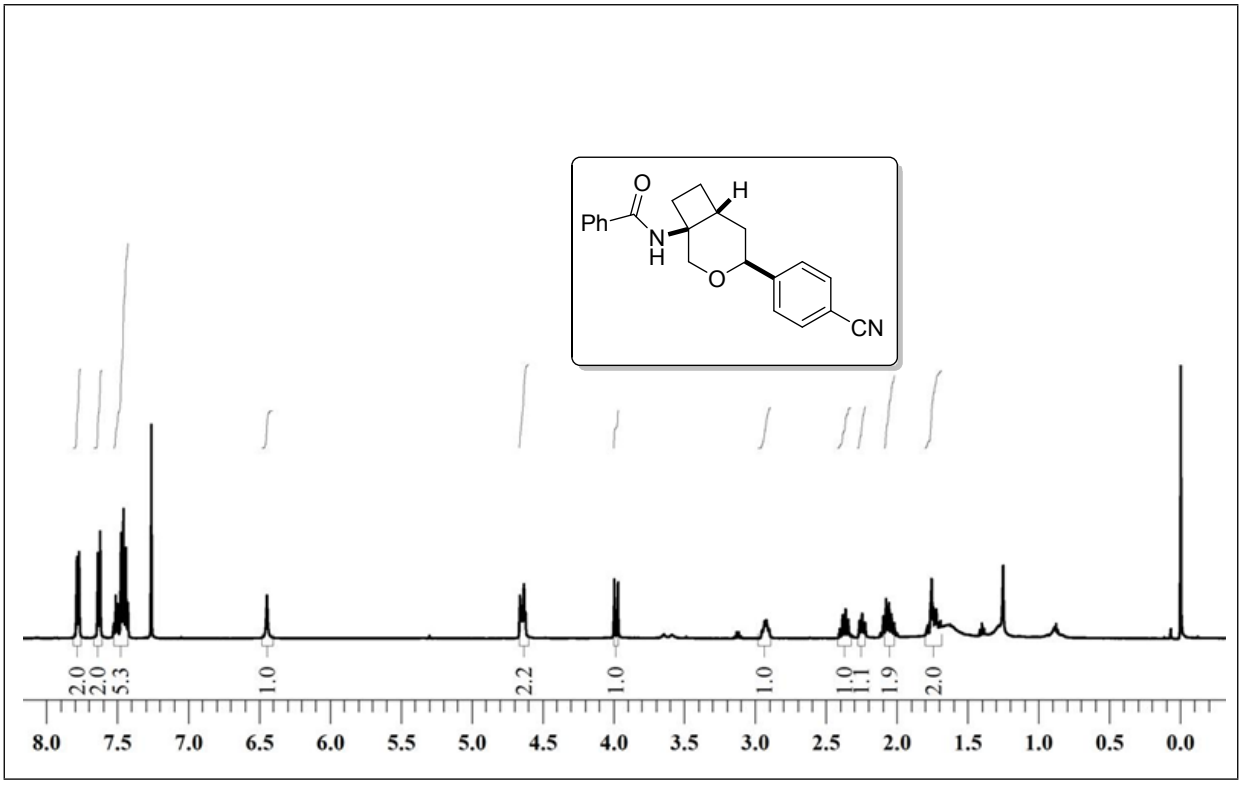
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 4a



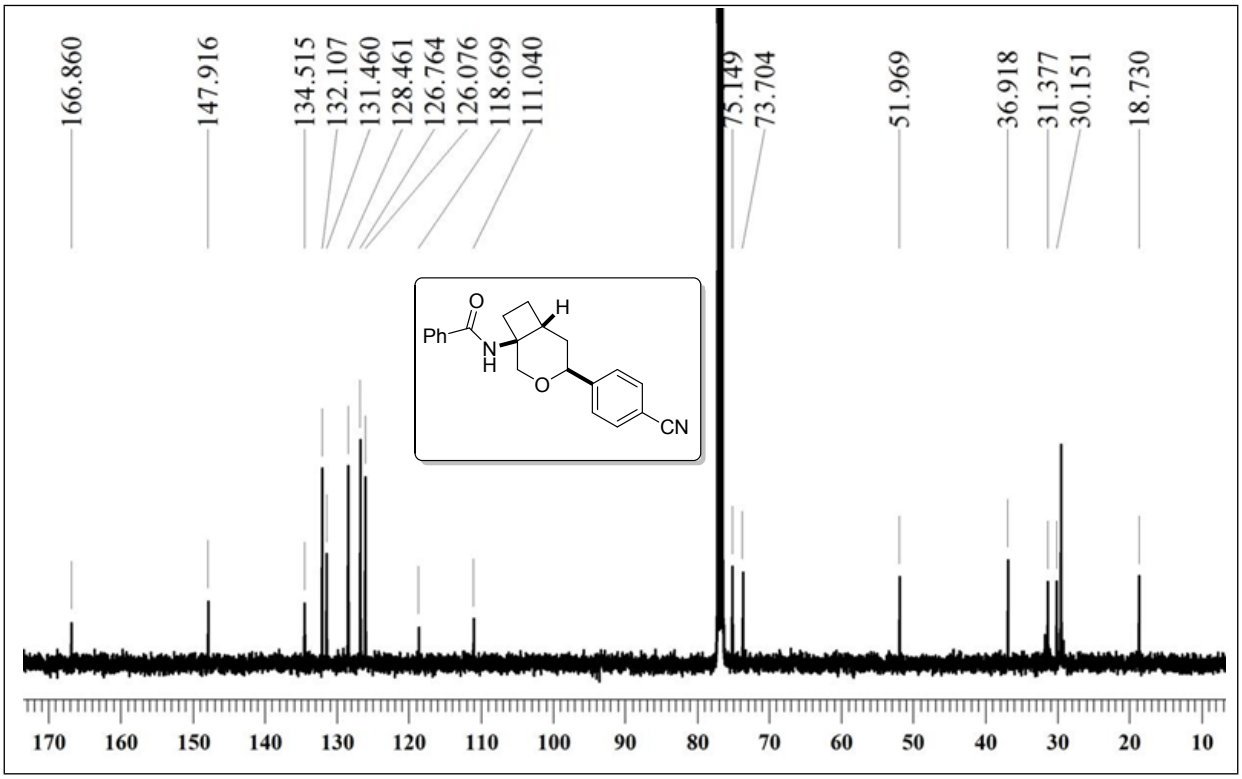
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 4c



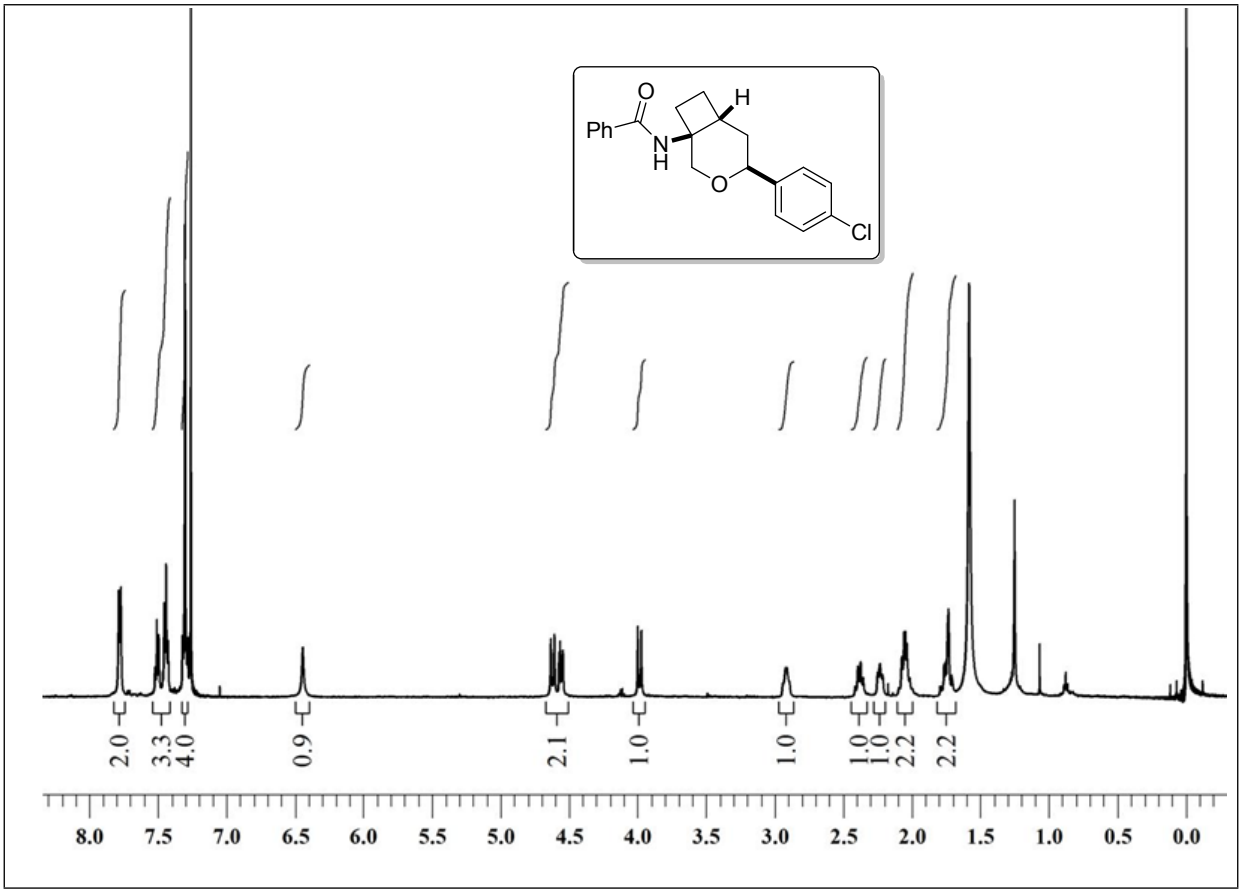
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 4c



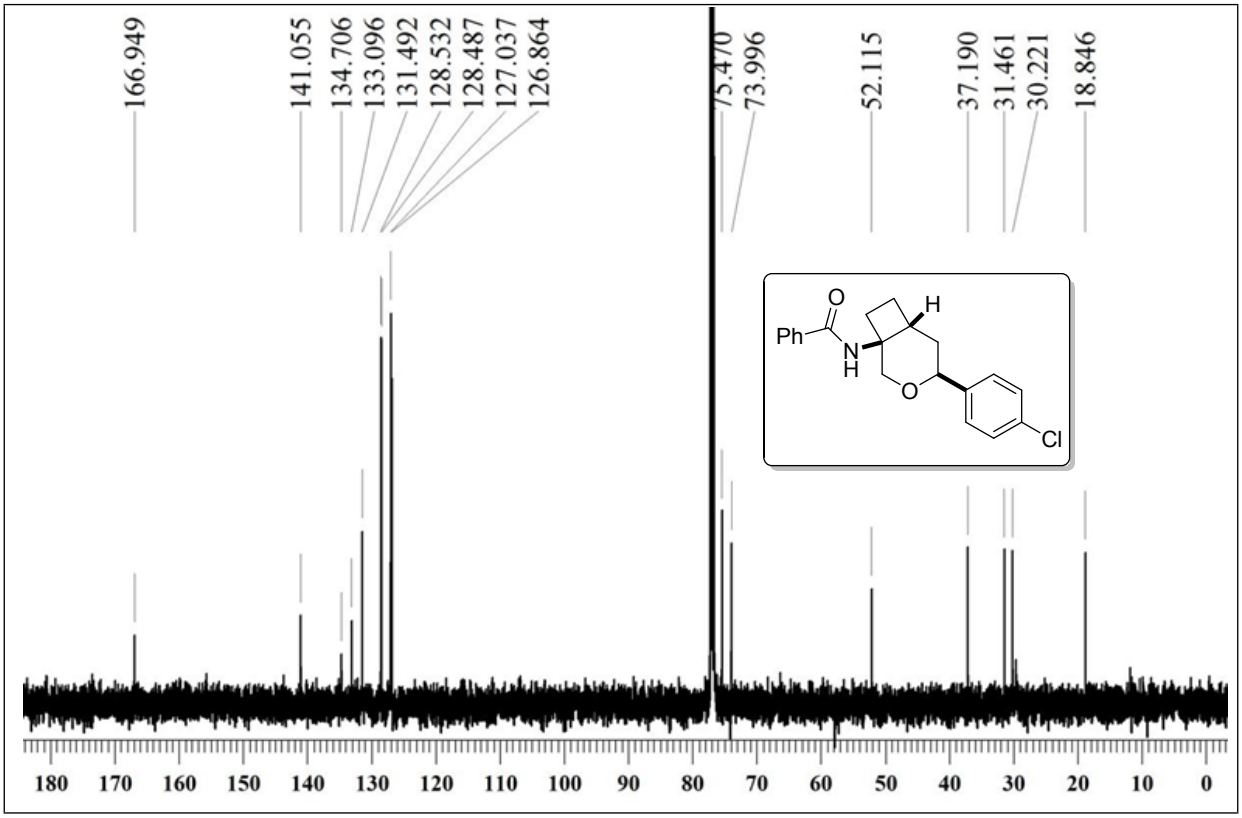
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 4d



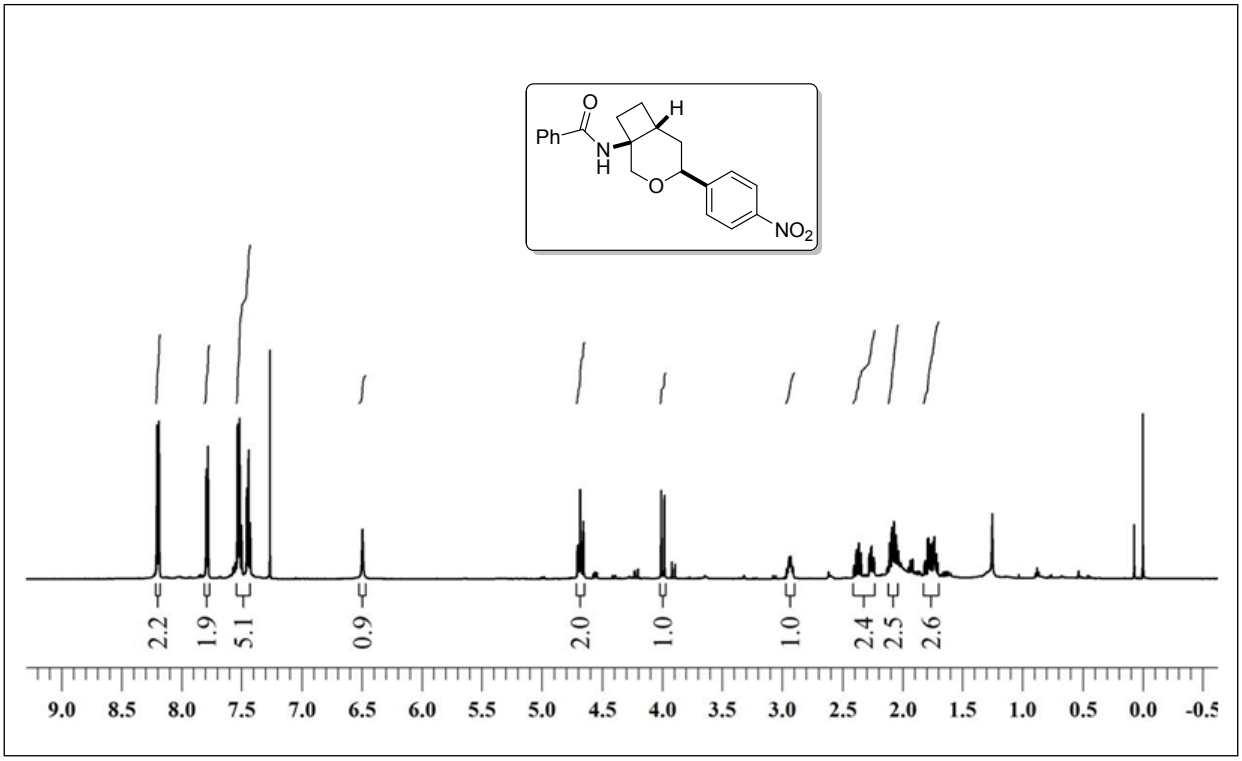
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 4d



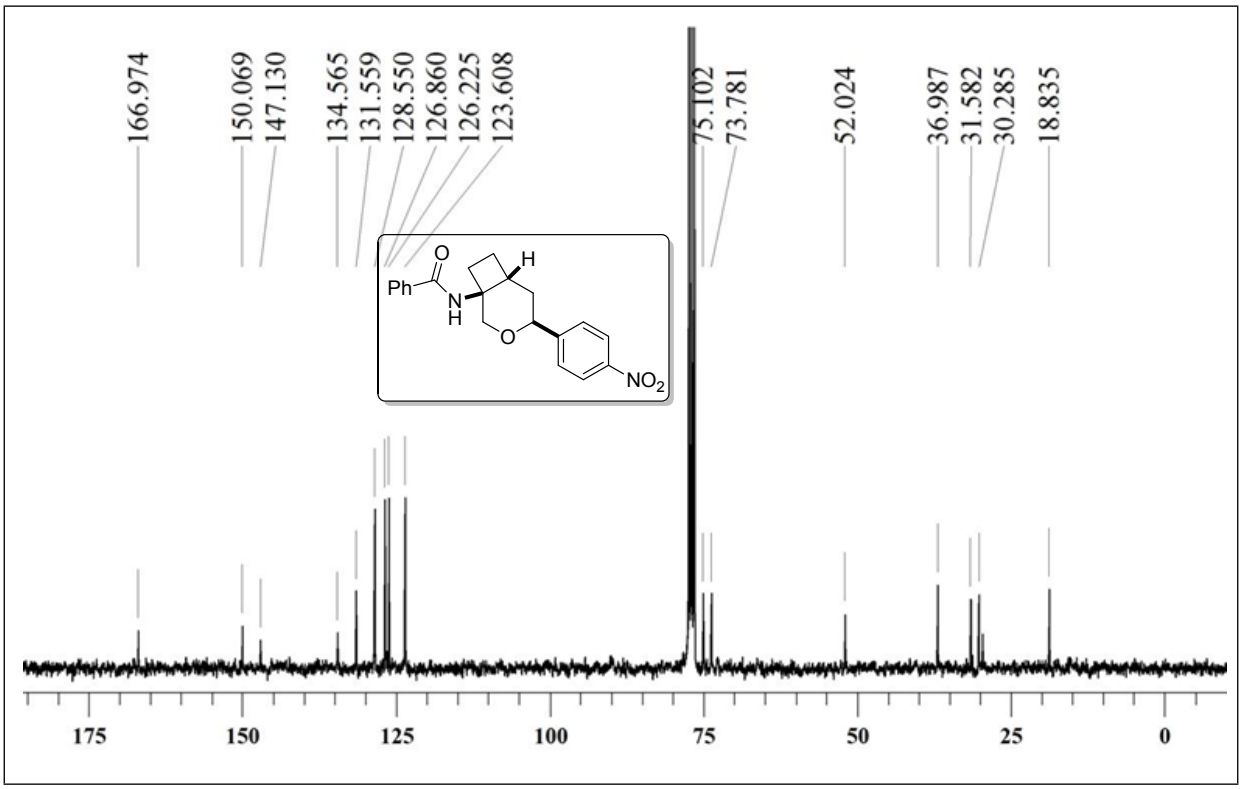
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 4e



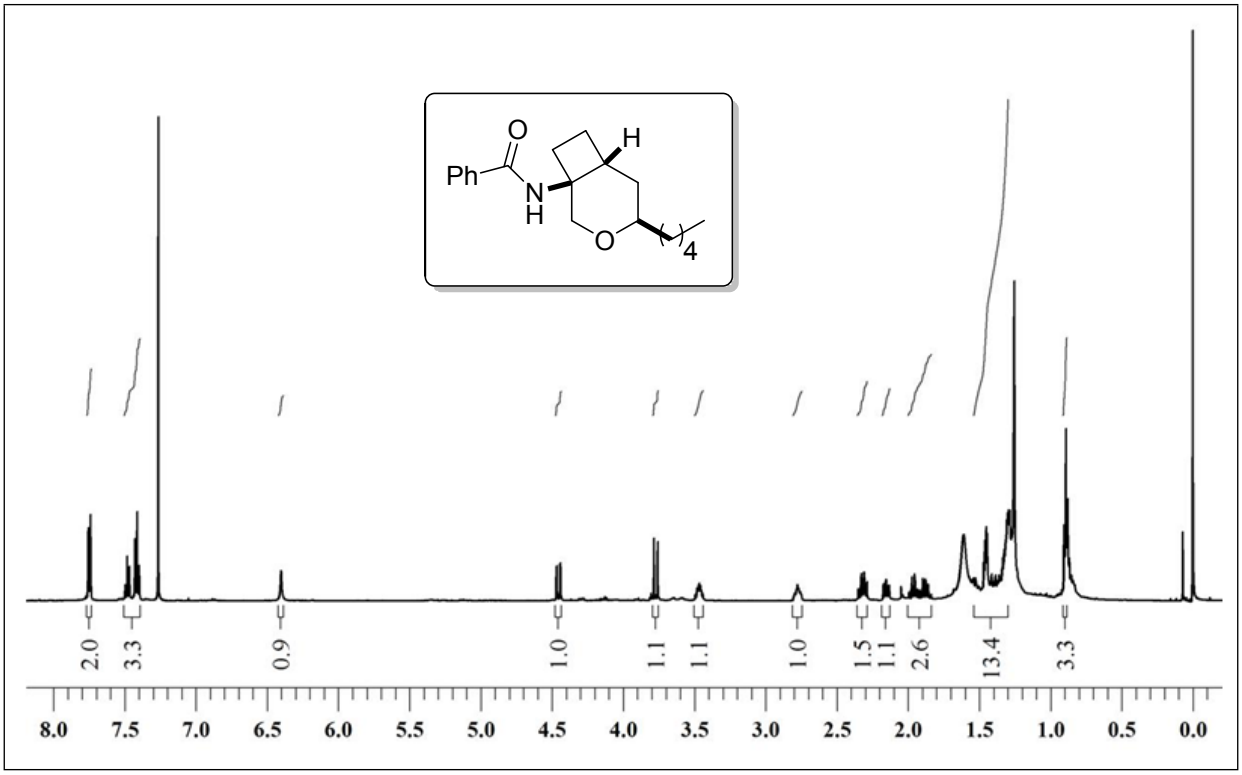
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 4e



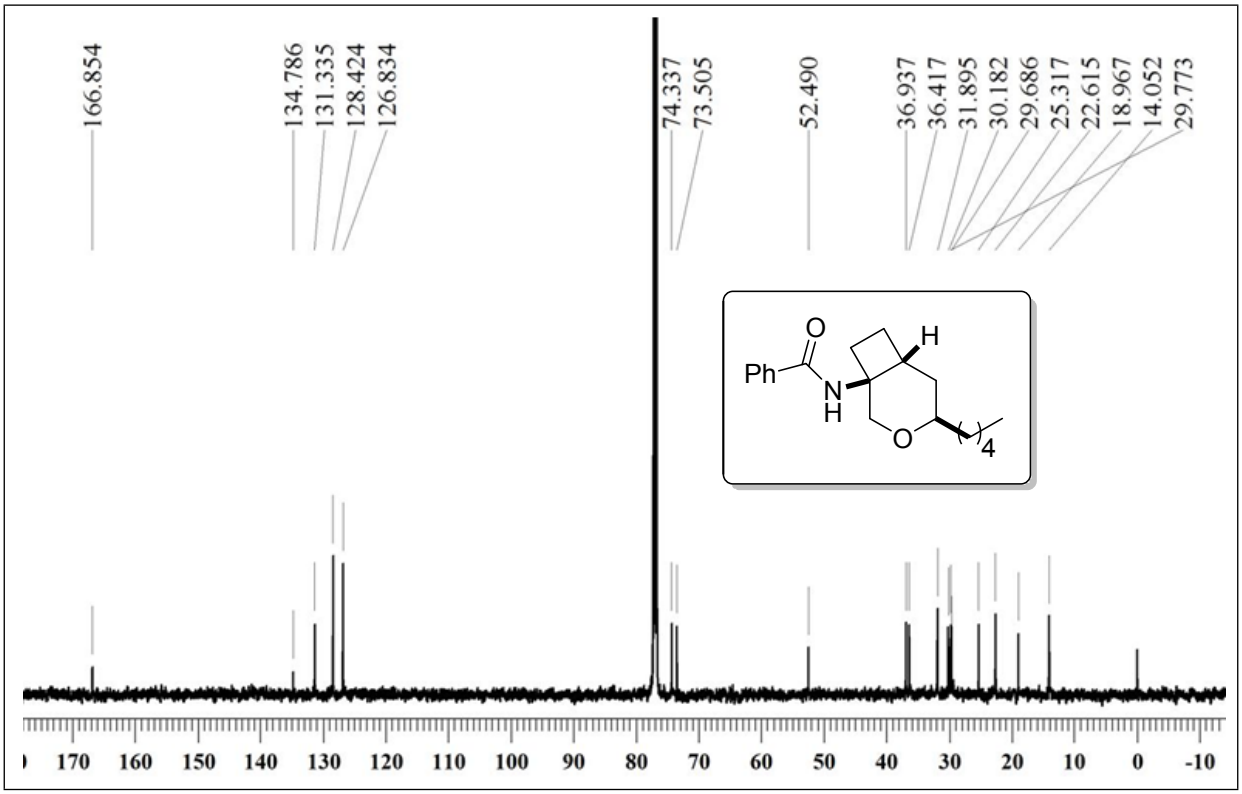
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 4f



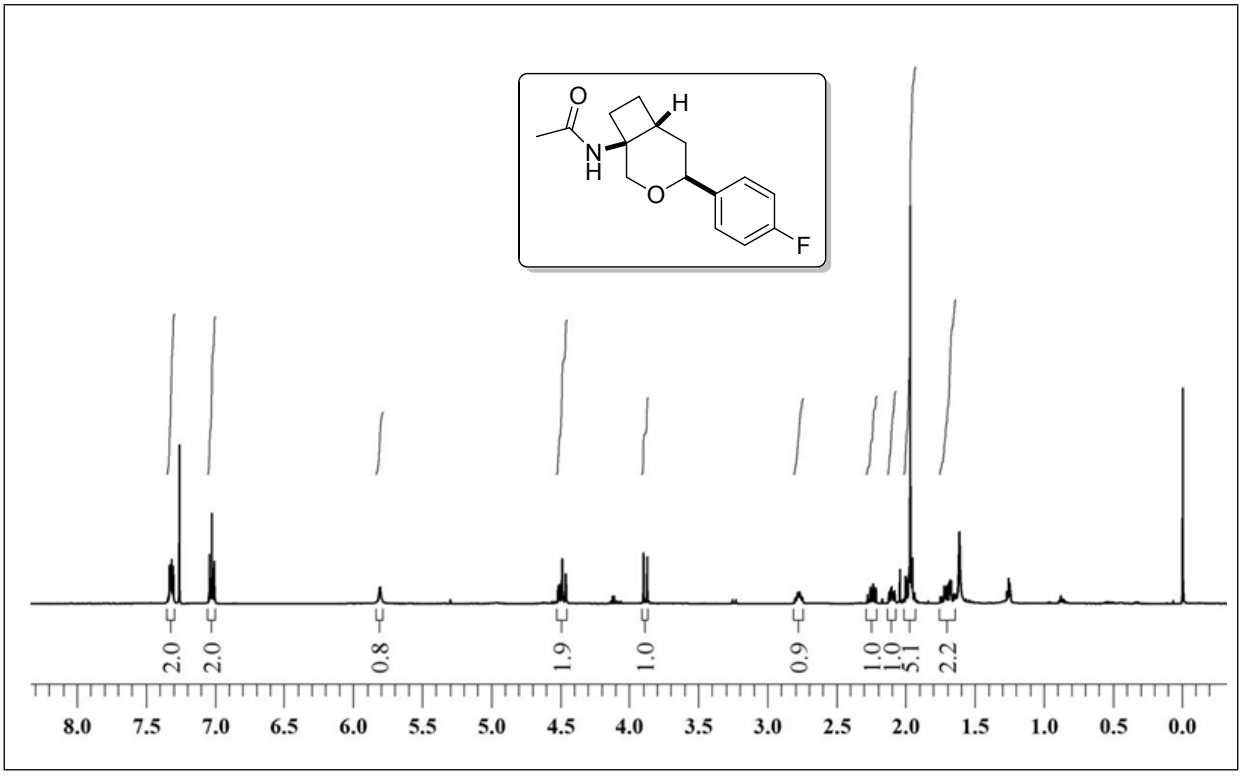
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 4f



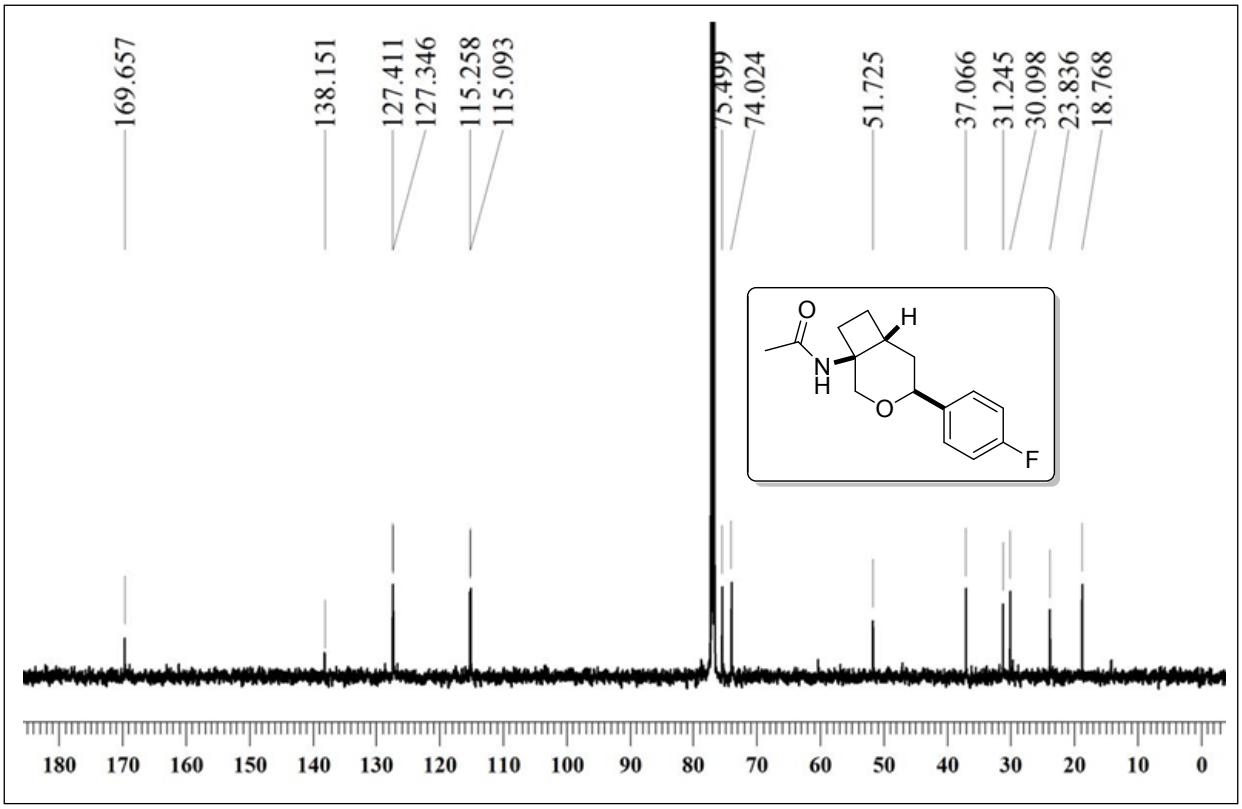
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 4g



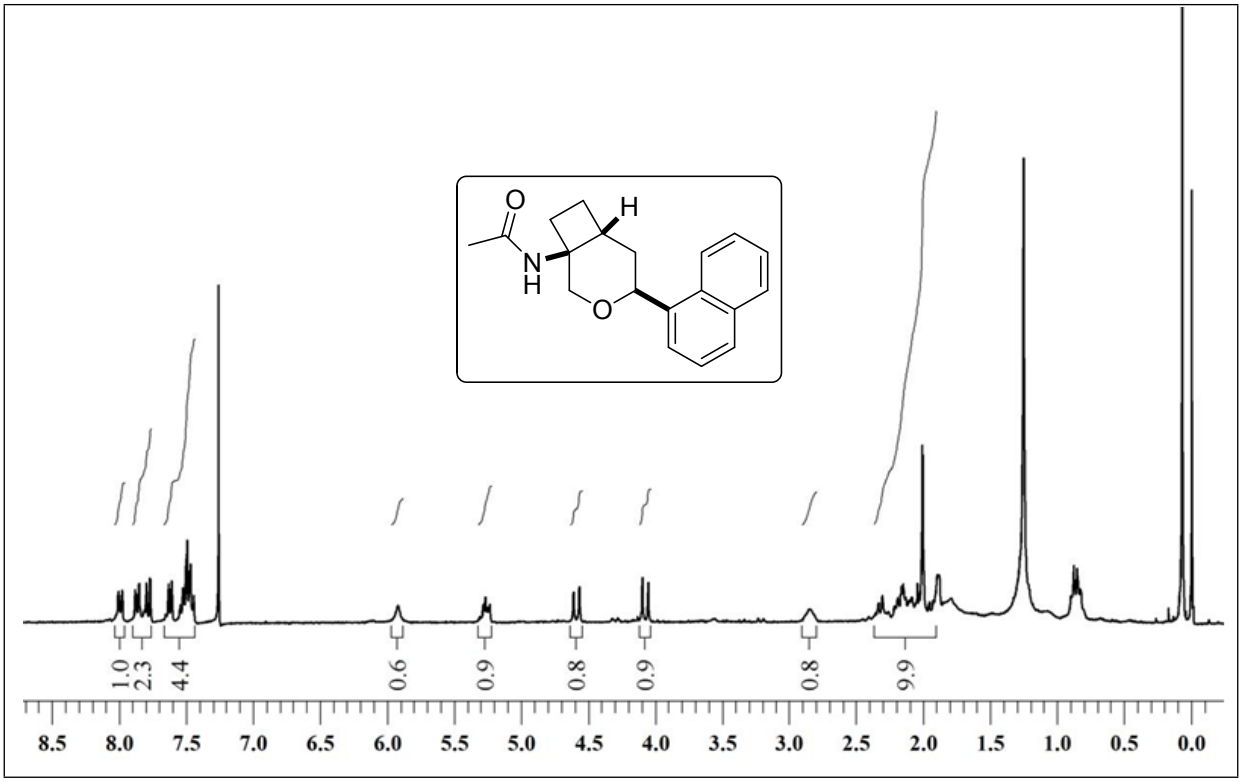
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 4g



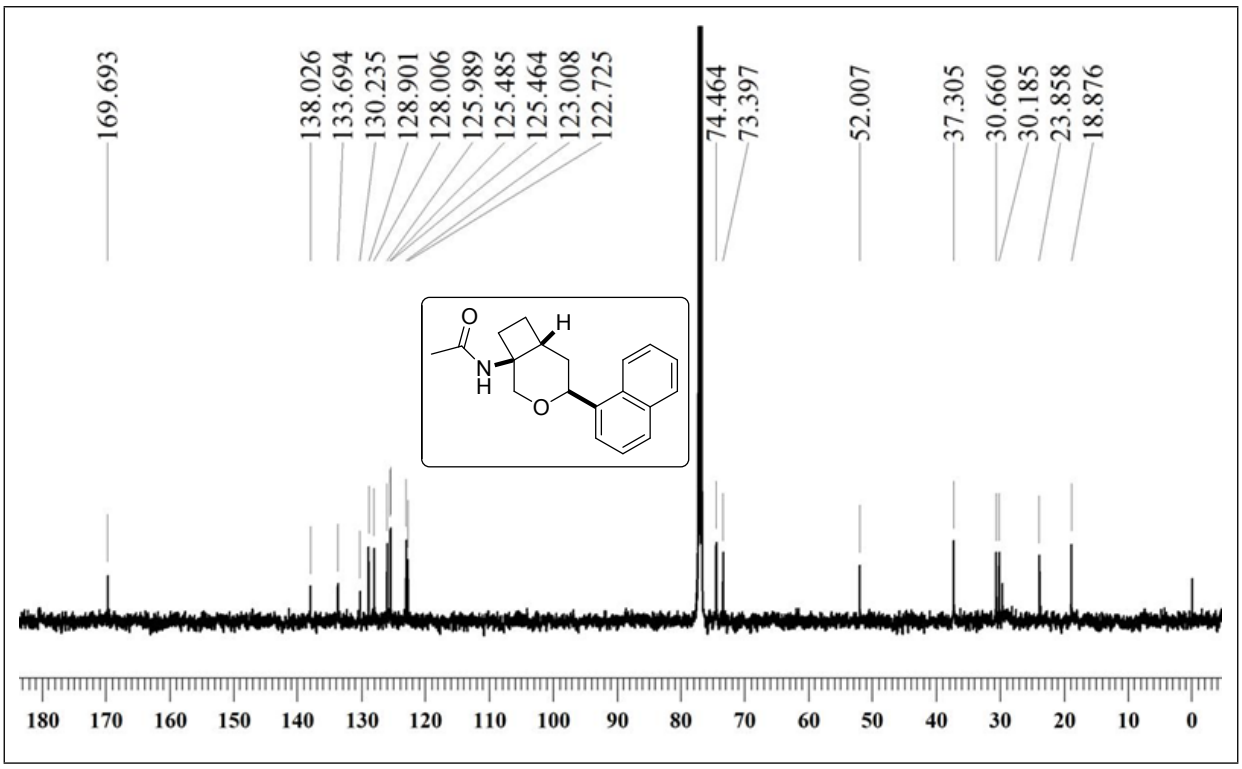
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 4h



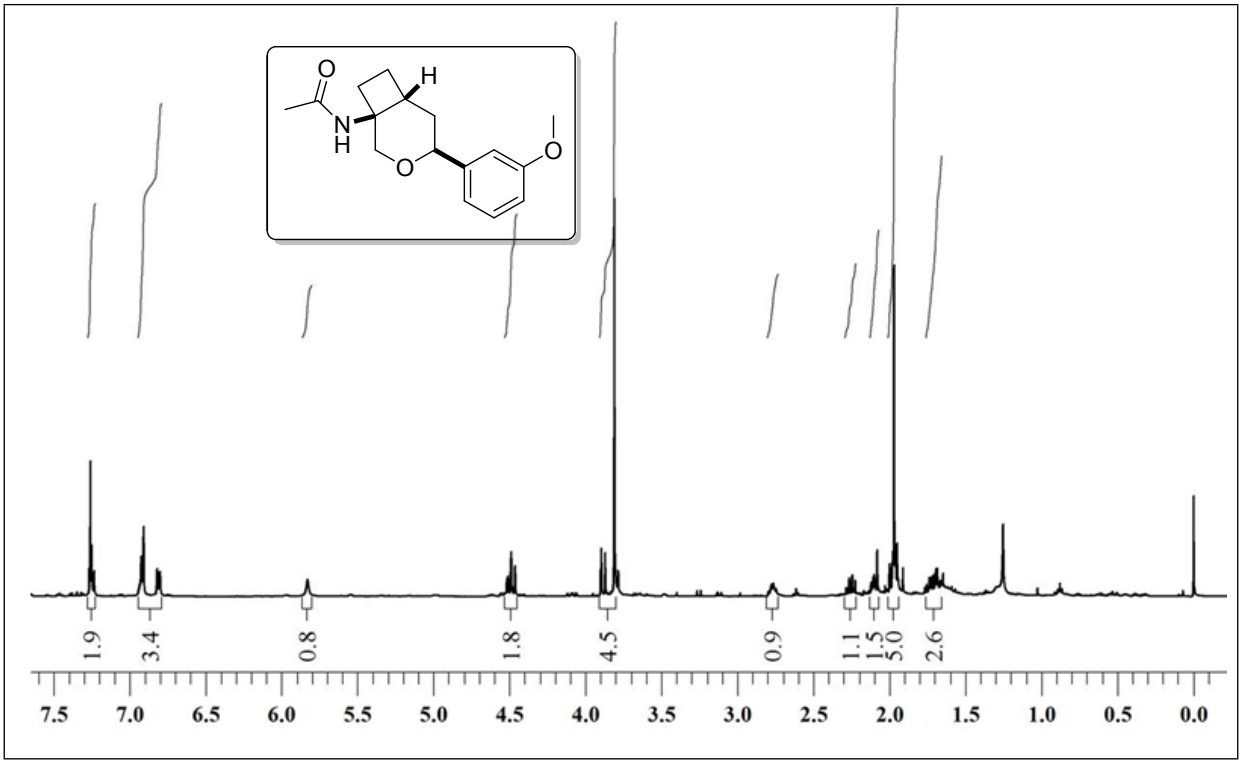
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 4h



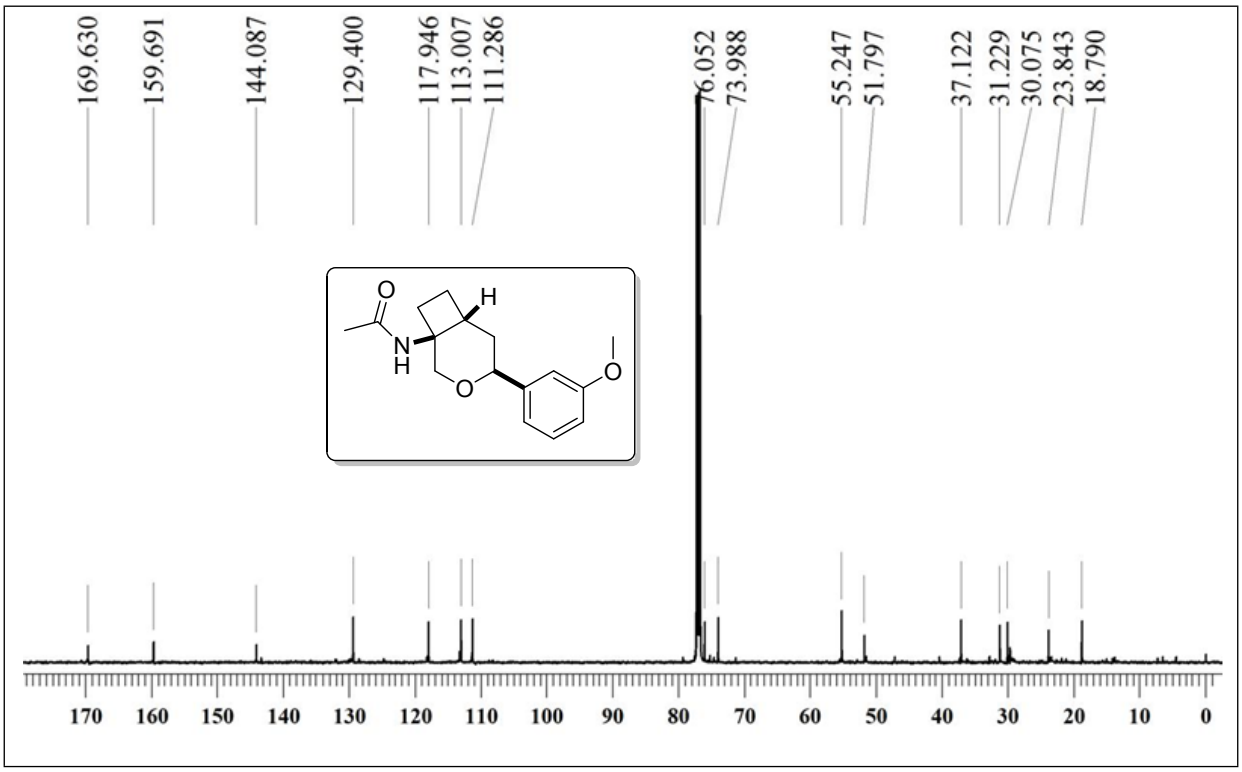
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 4i



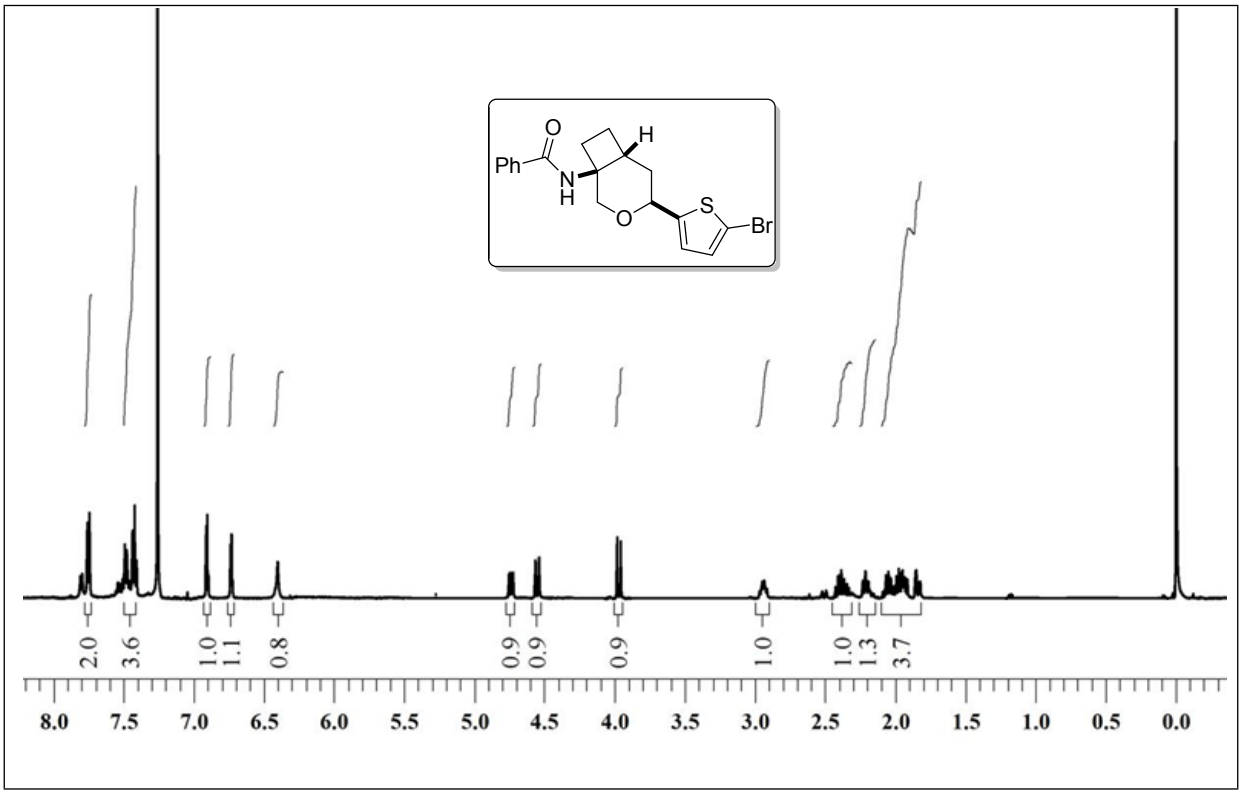
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 4i



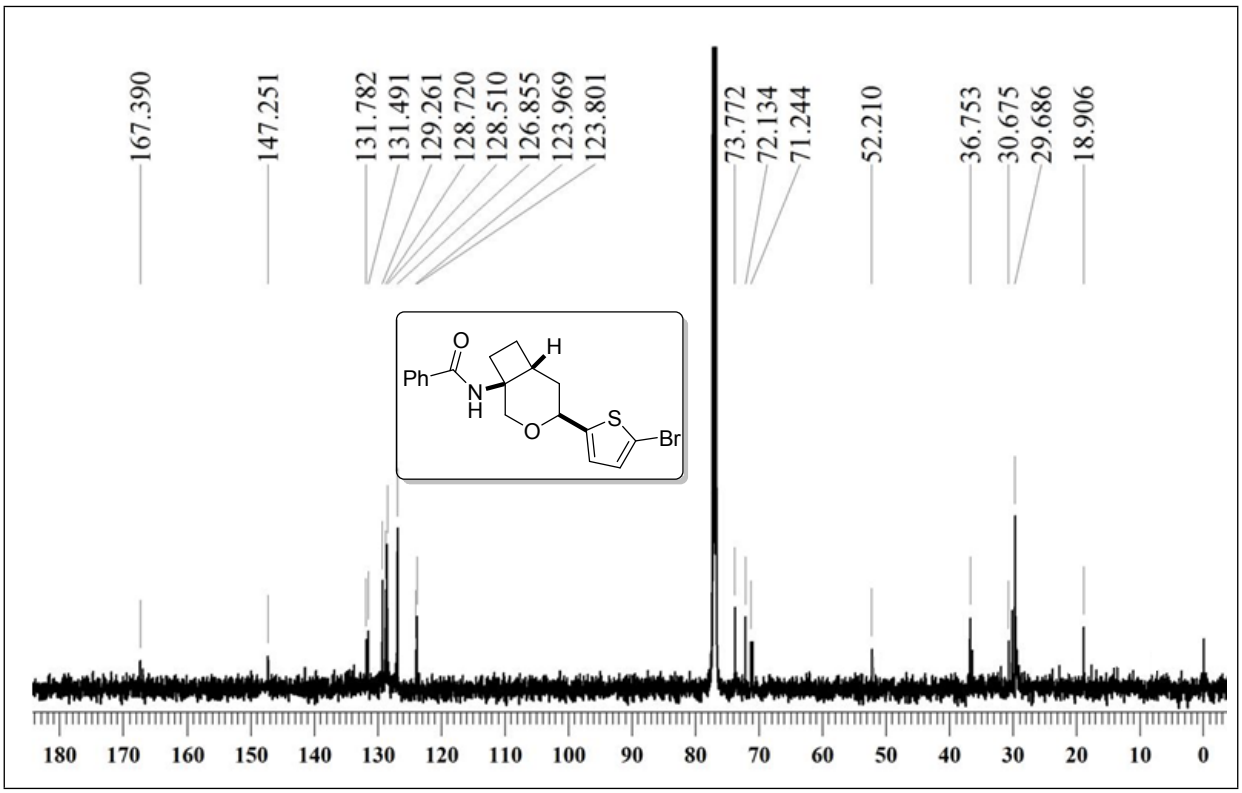
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 4j



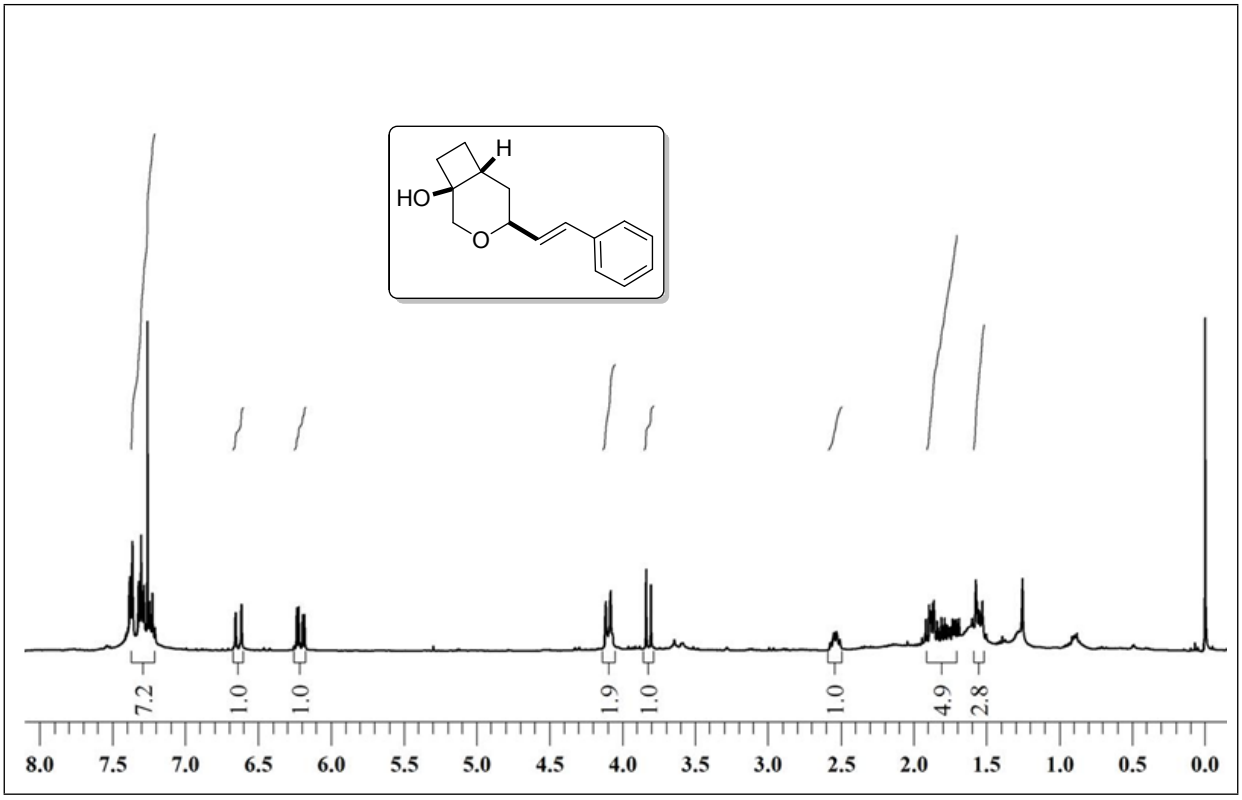
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 4j



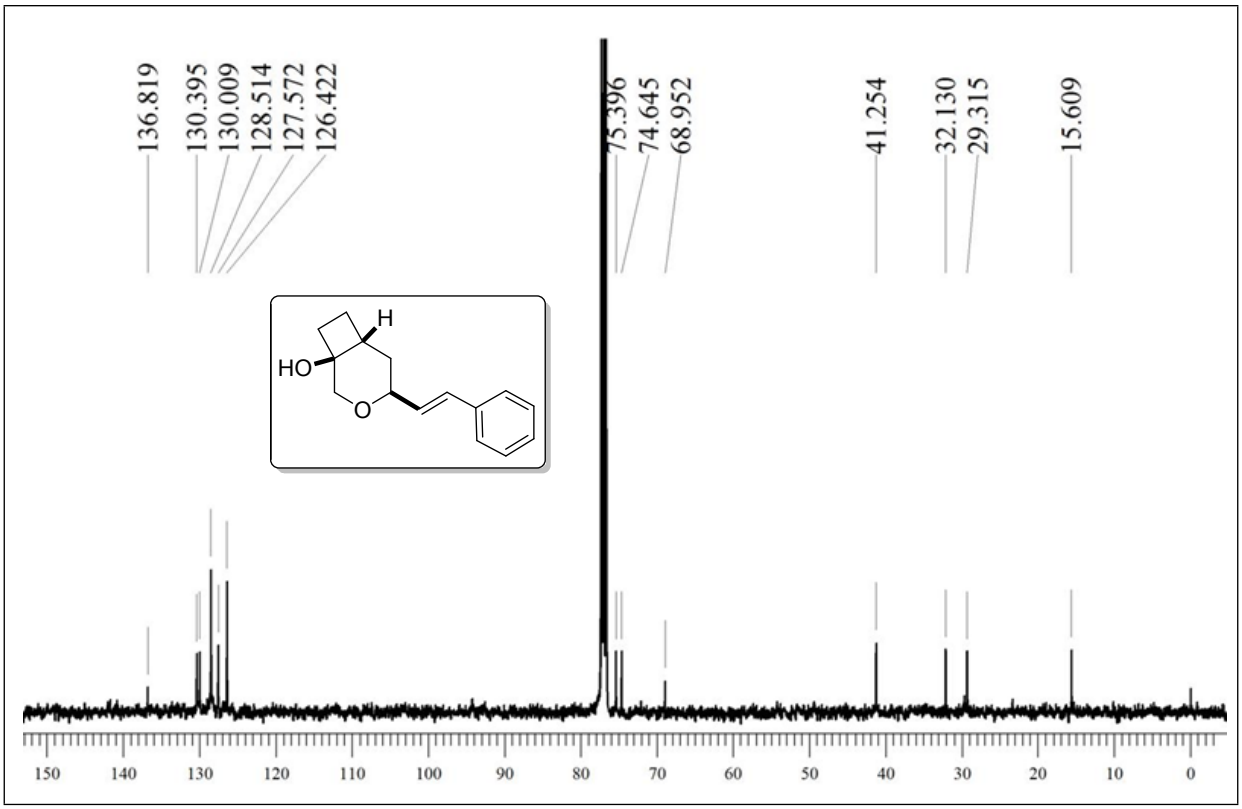
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 4k



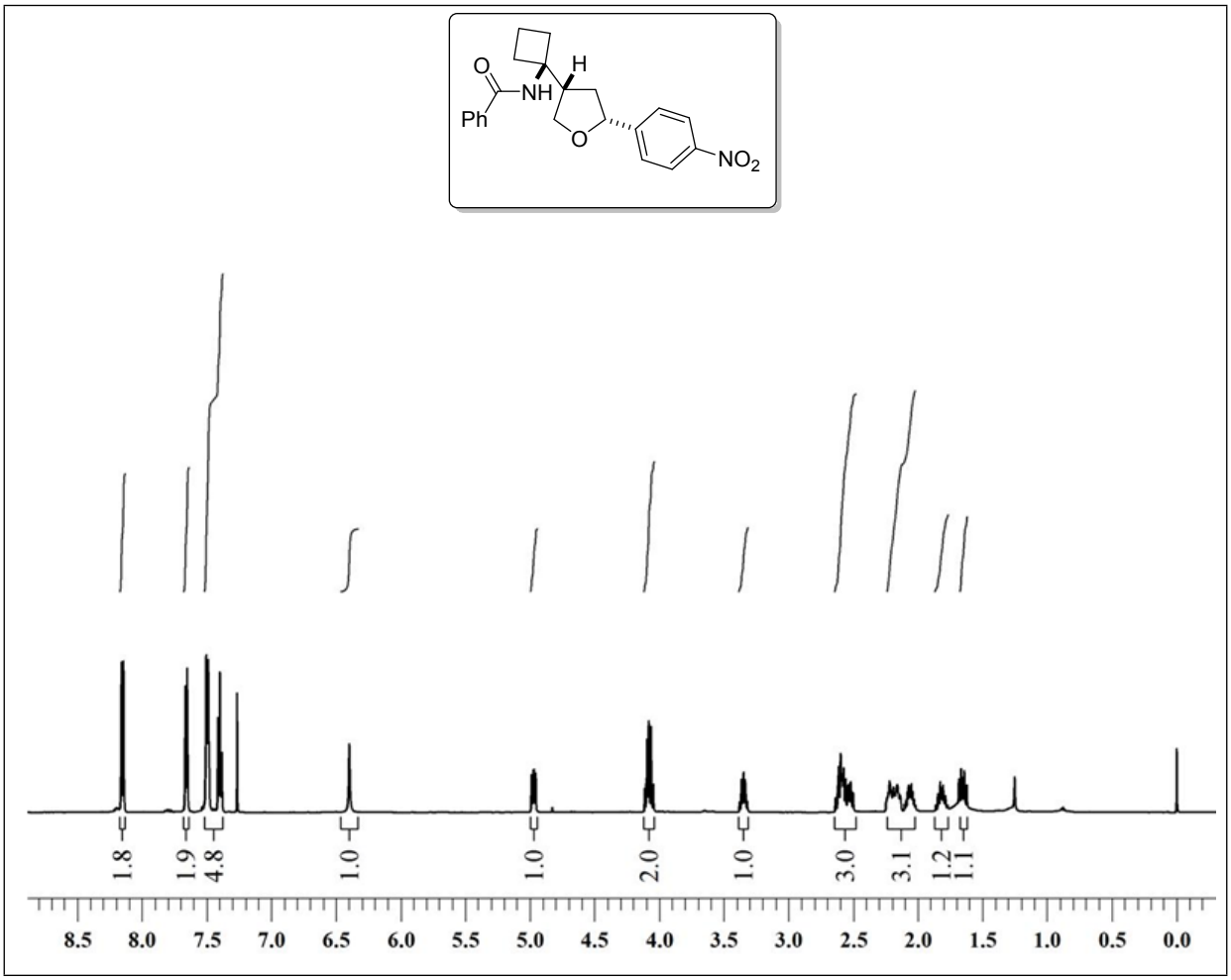
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 4k



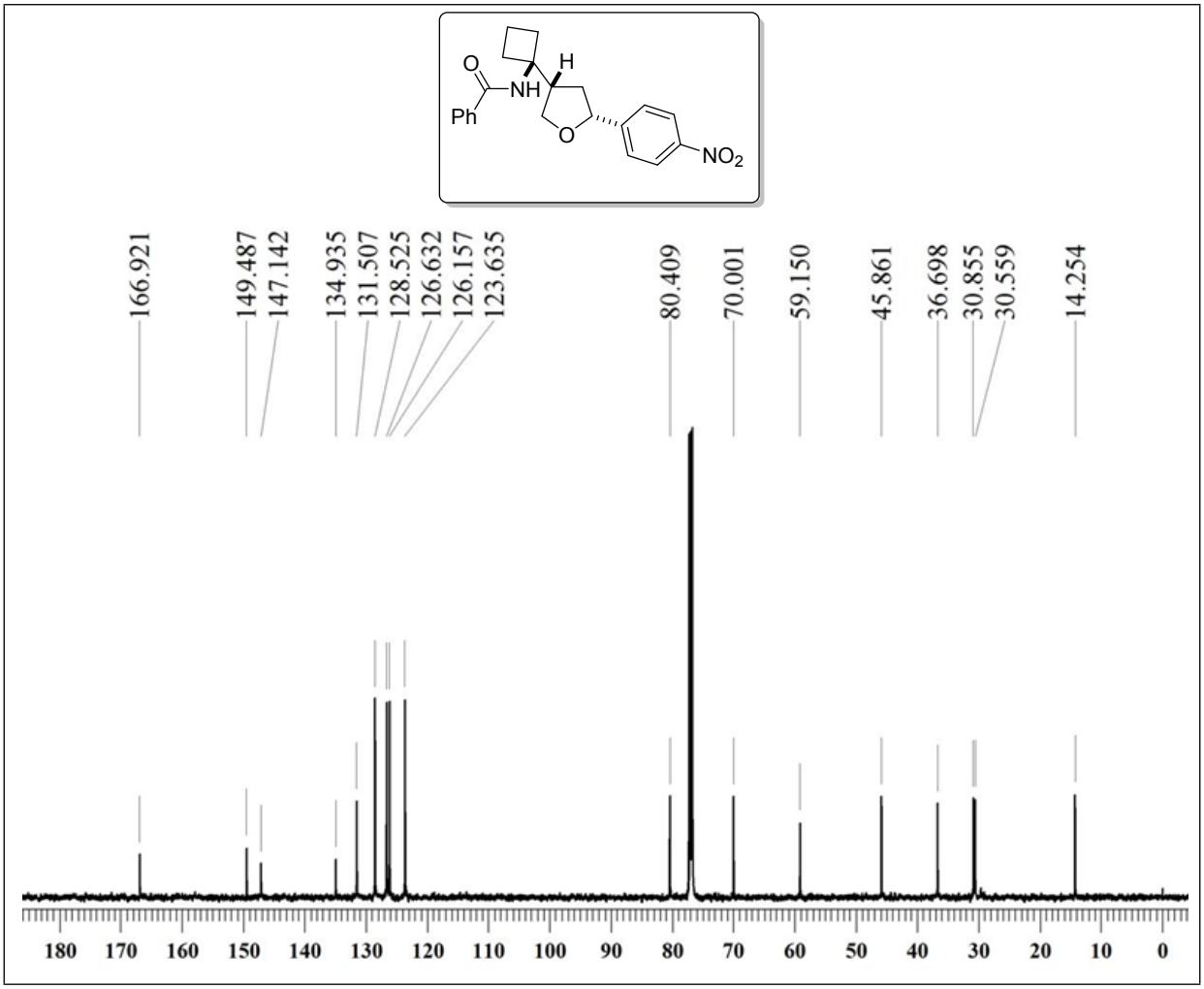
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 4l



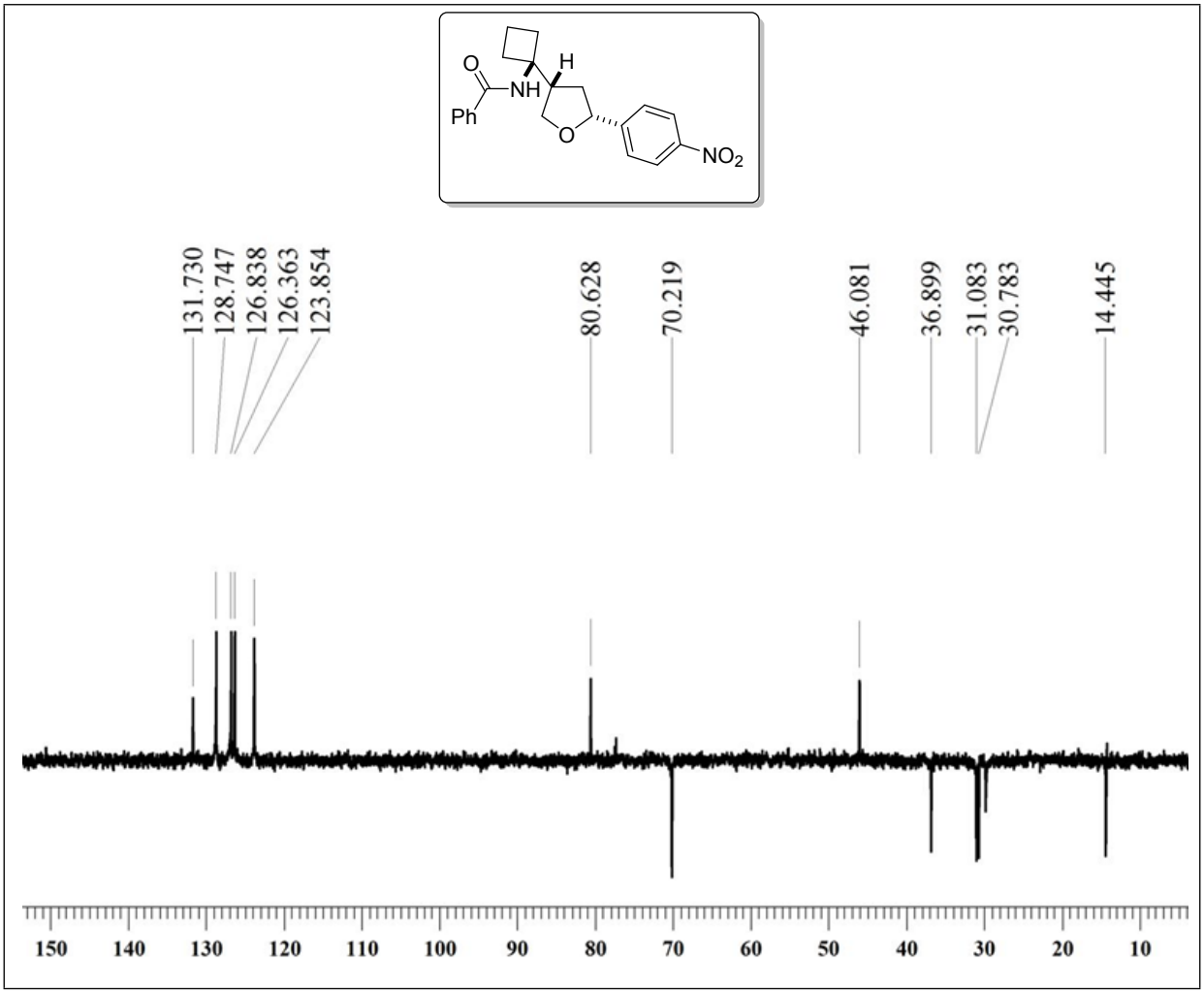
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 4l



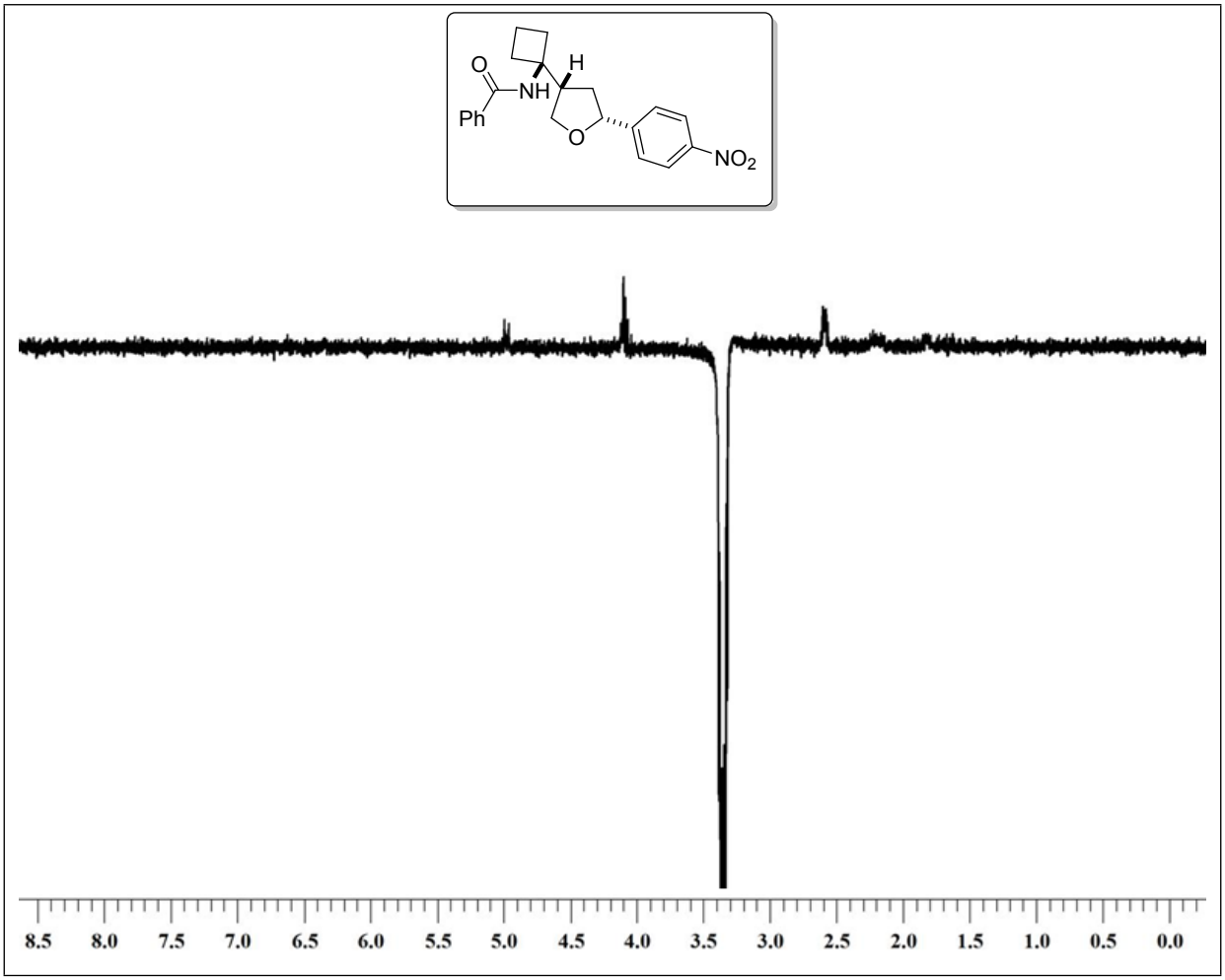
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 5a



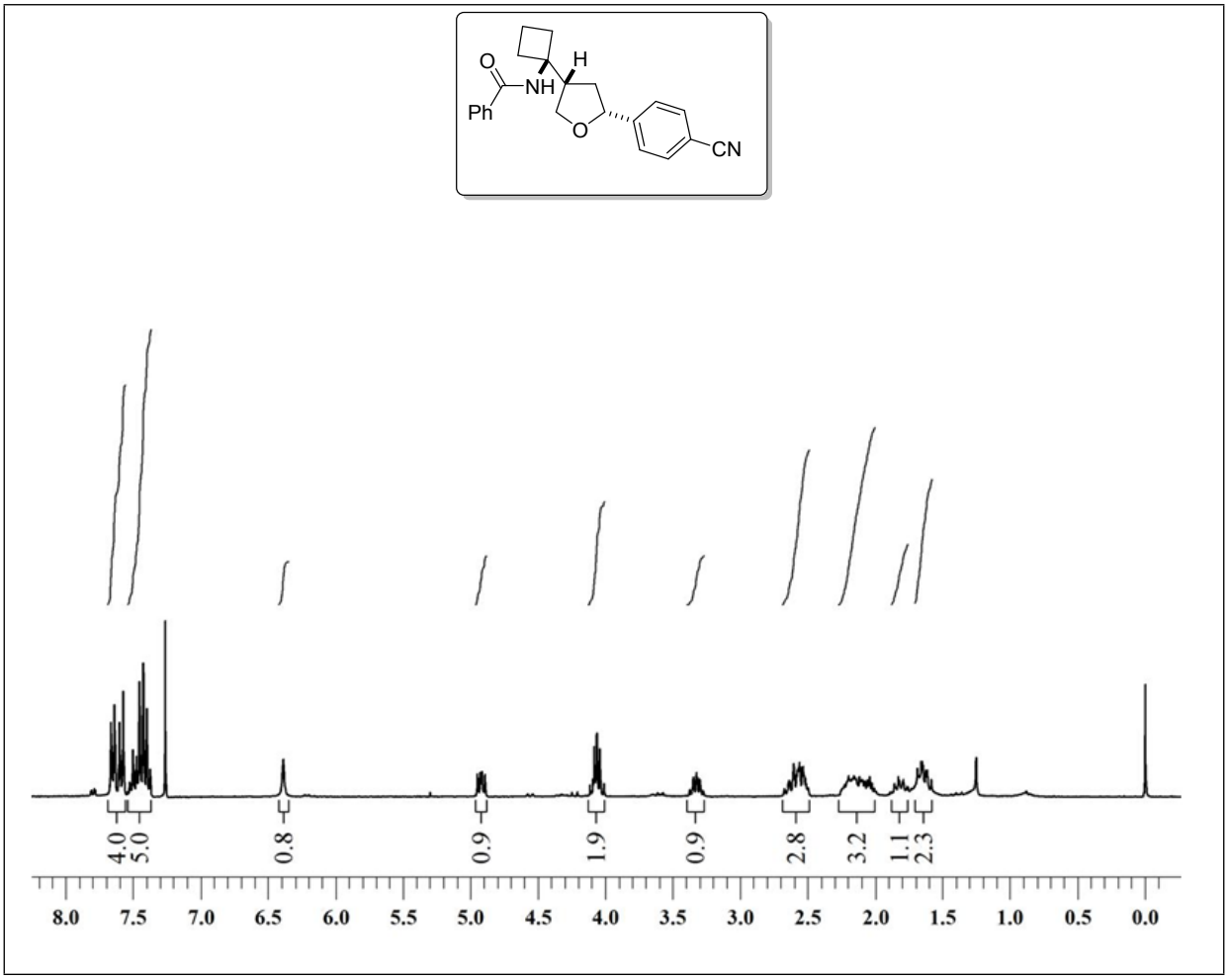
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 5a



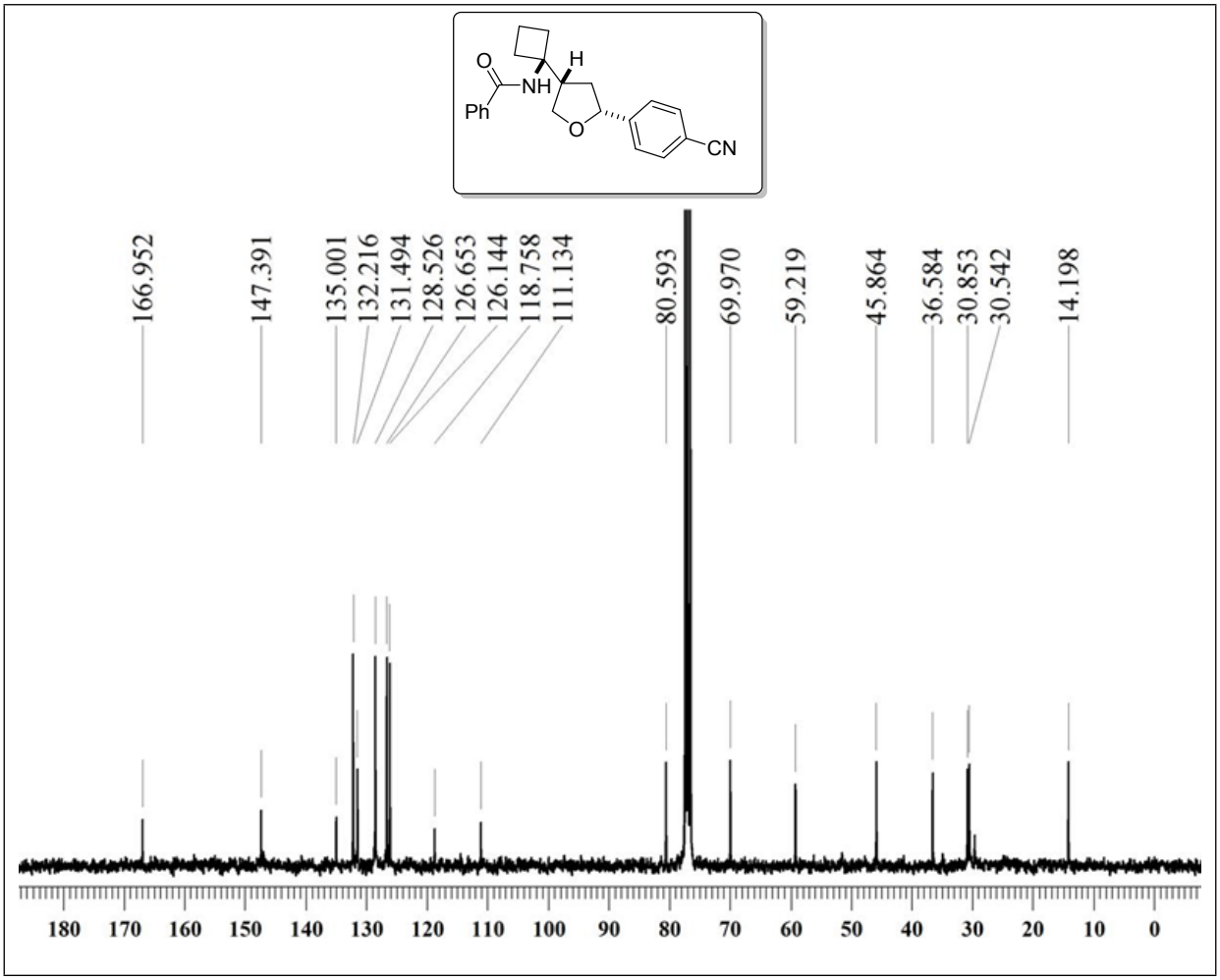
DEPT (135 MHz, $CDCl_3$) spectrum of 5a



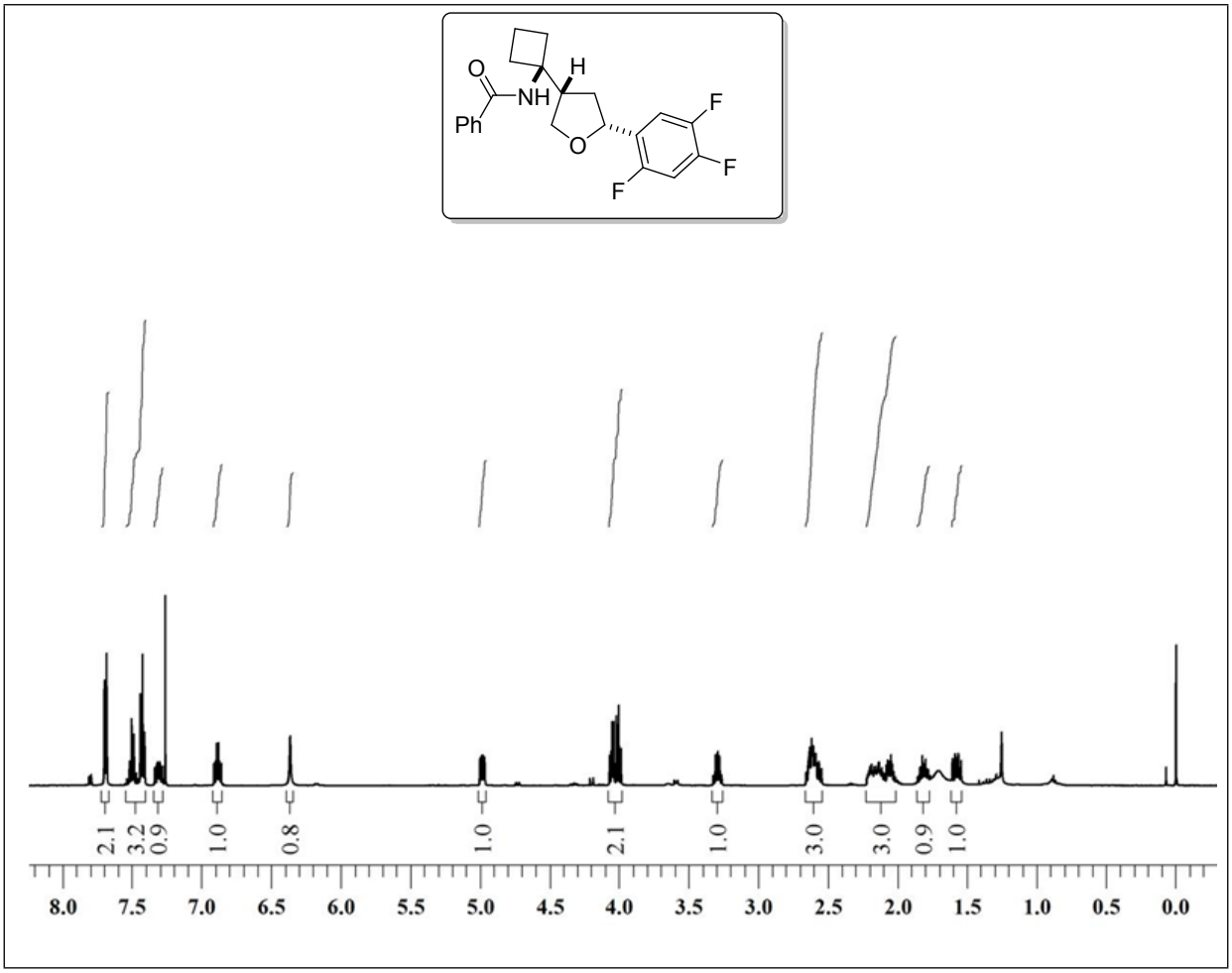
NOE (500 MHz, $CDCl_3$) spectrum of 5a



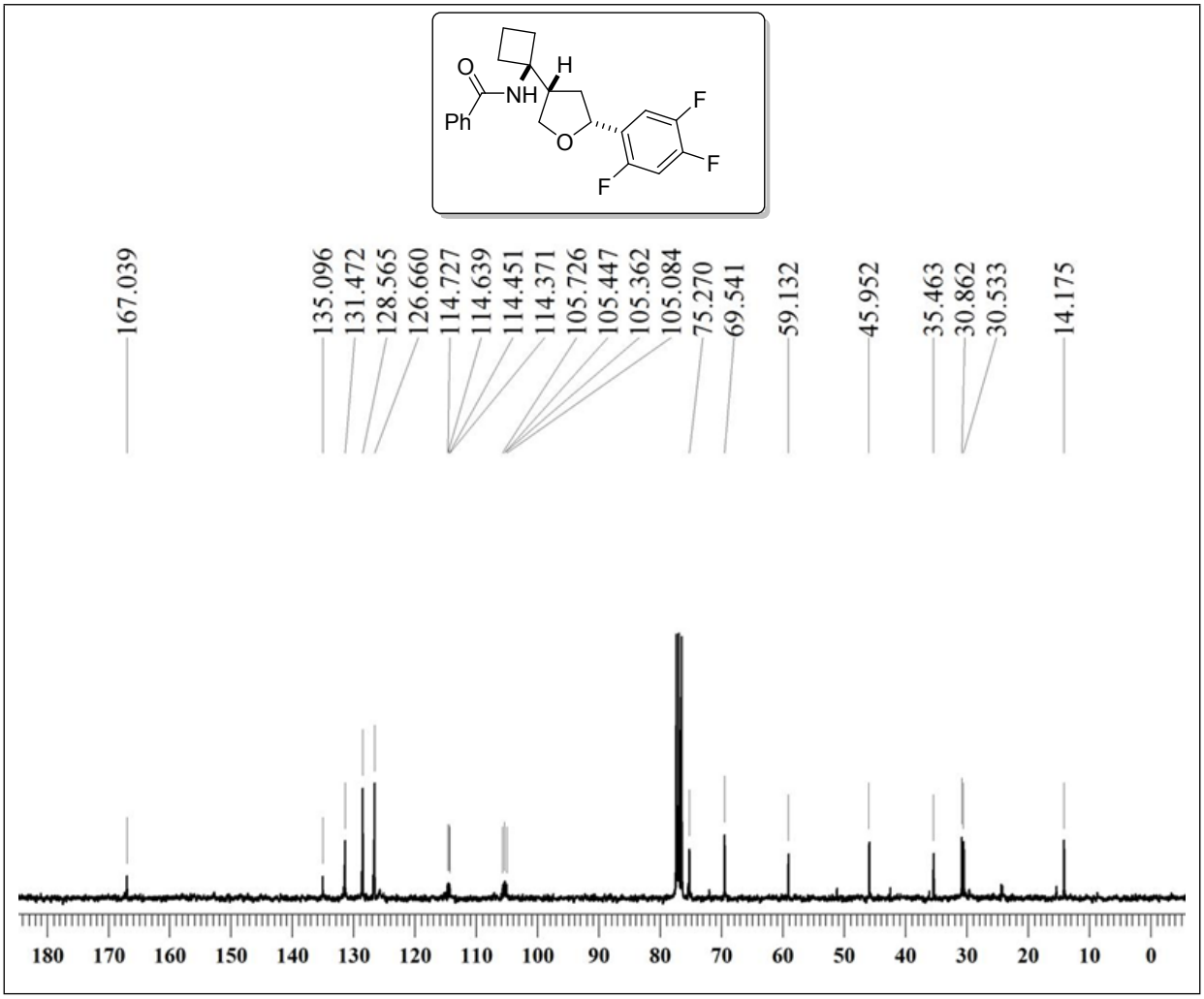
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 5b



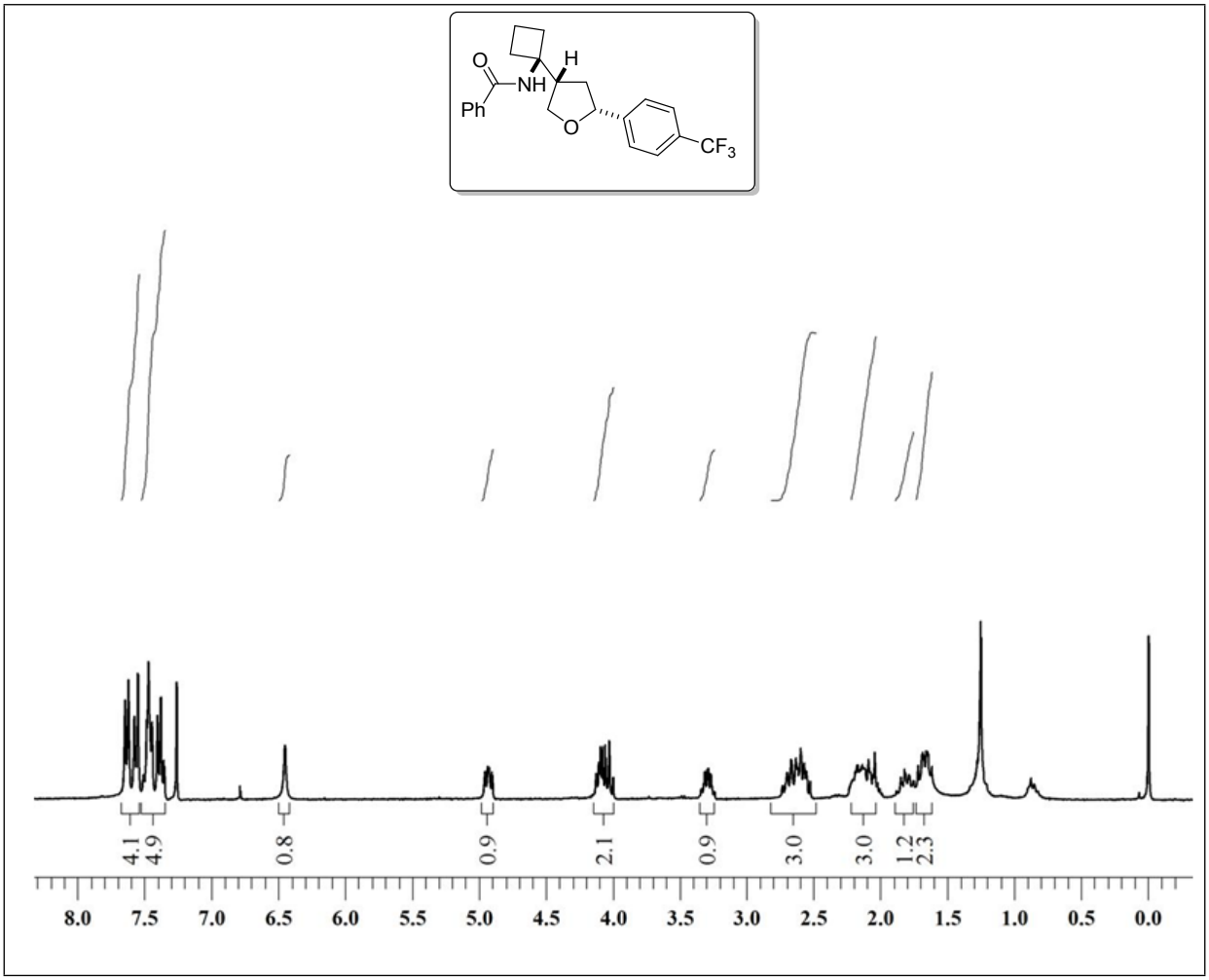
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 5b



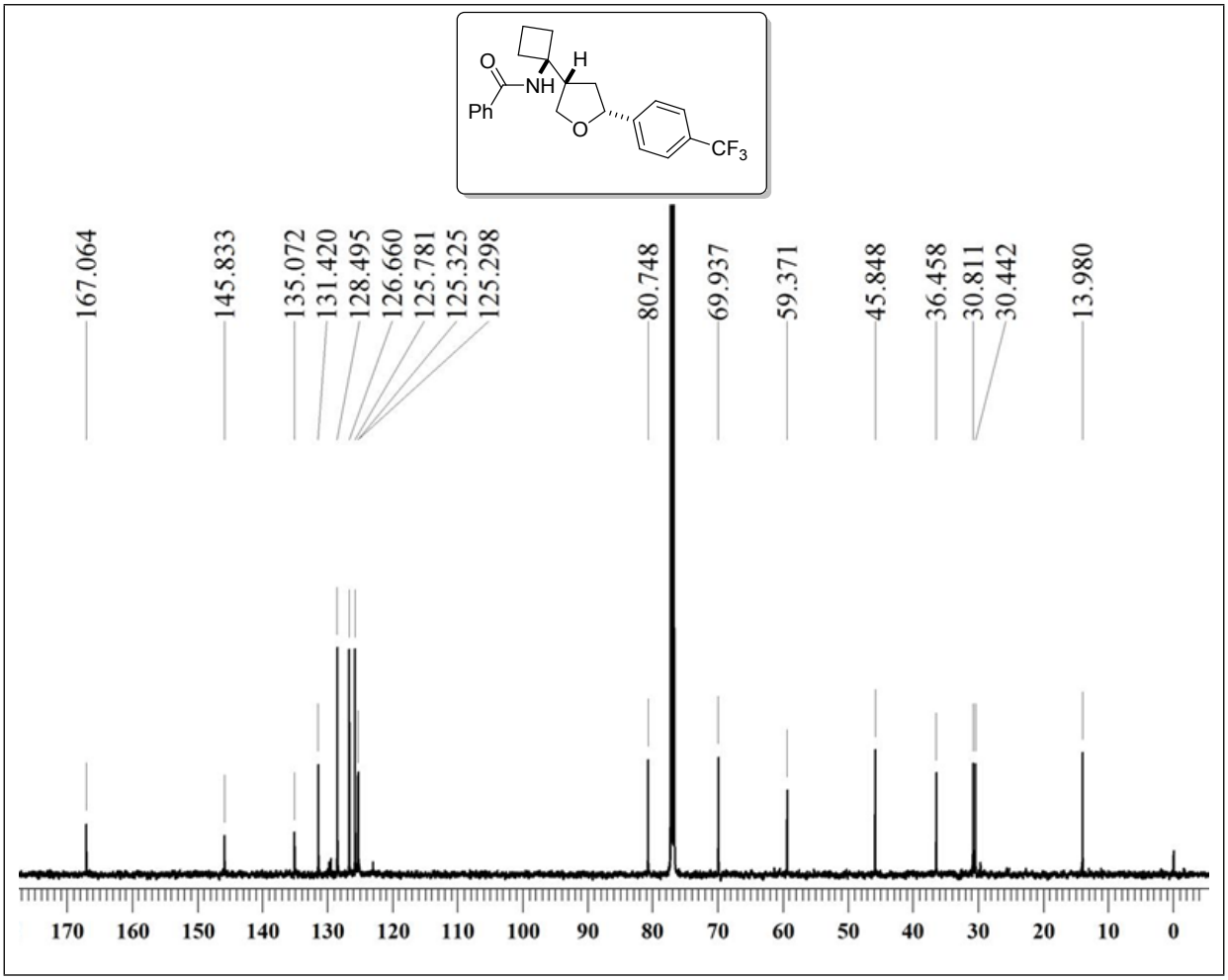
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 5c



^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 5c

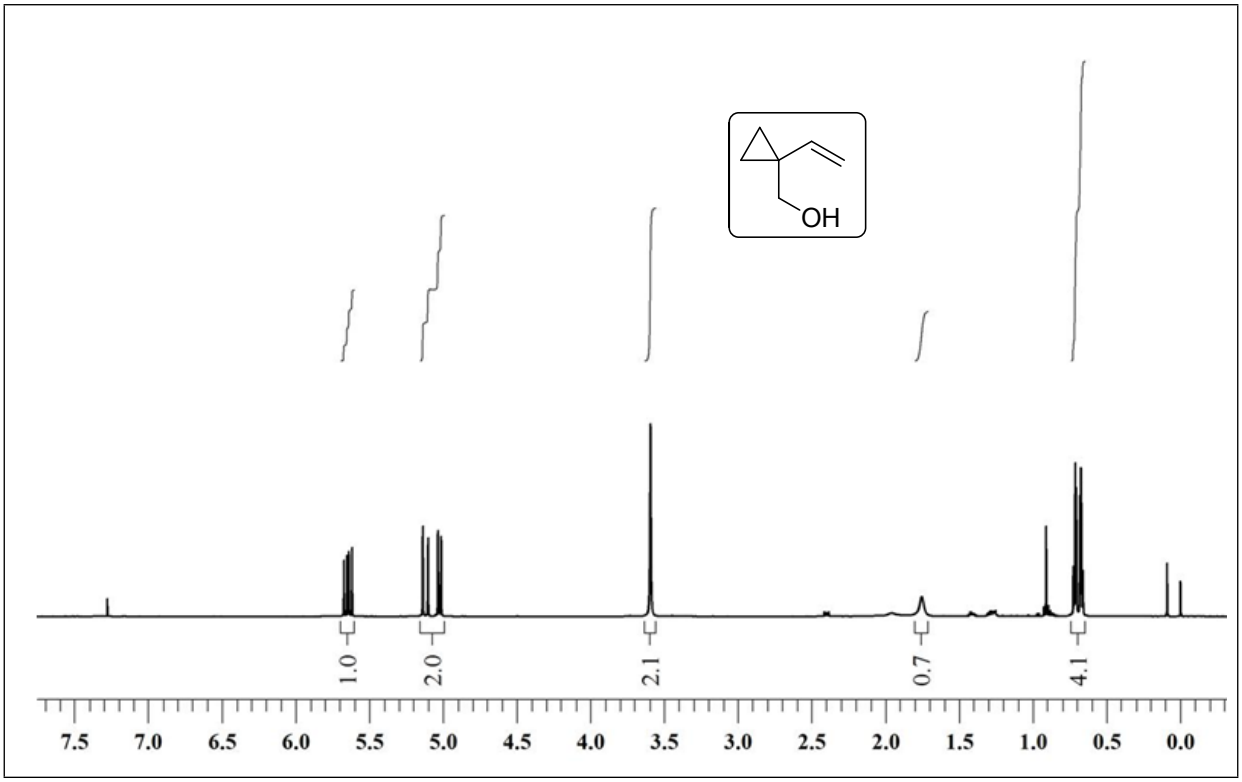


^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 5d

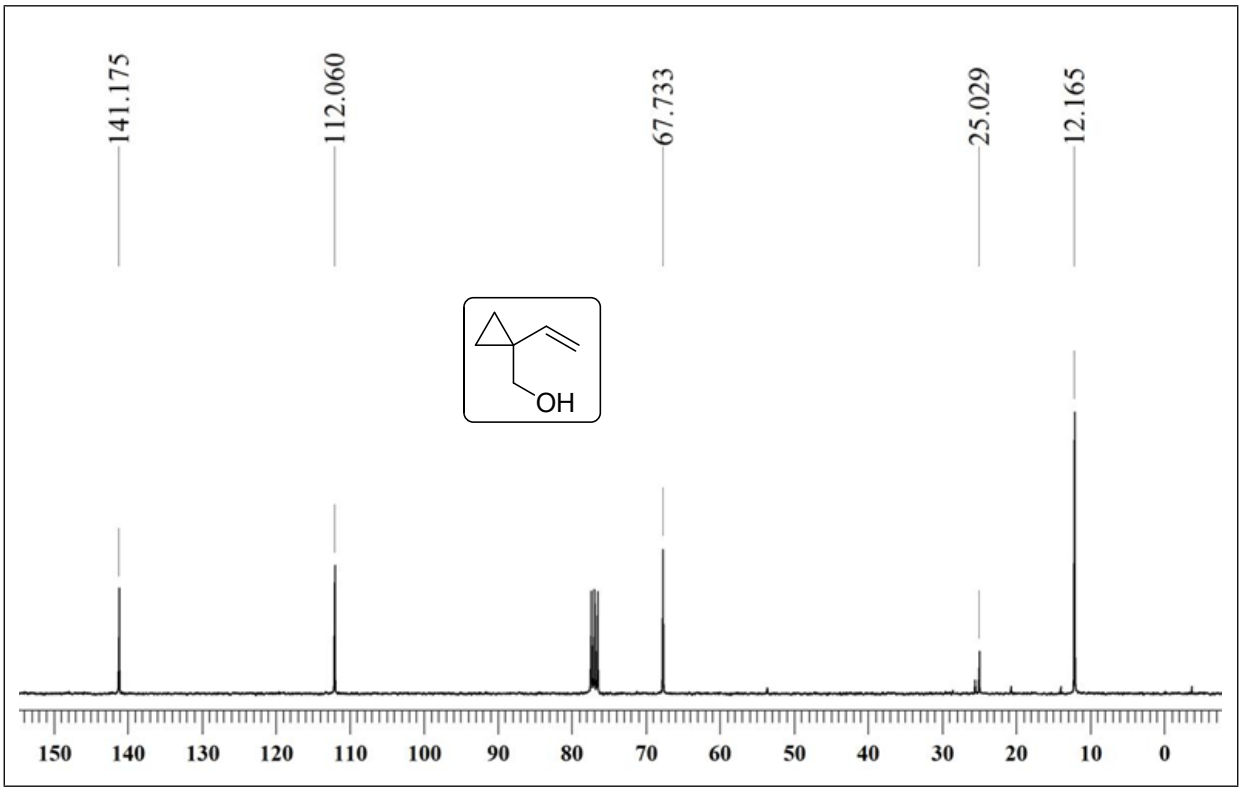


^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 5d

(1-Vinylcyclopropyl)methanol (1a)

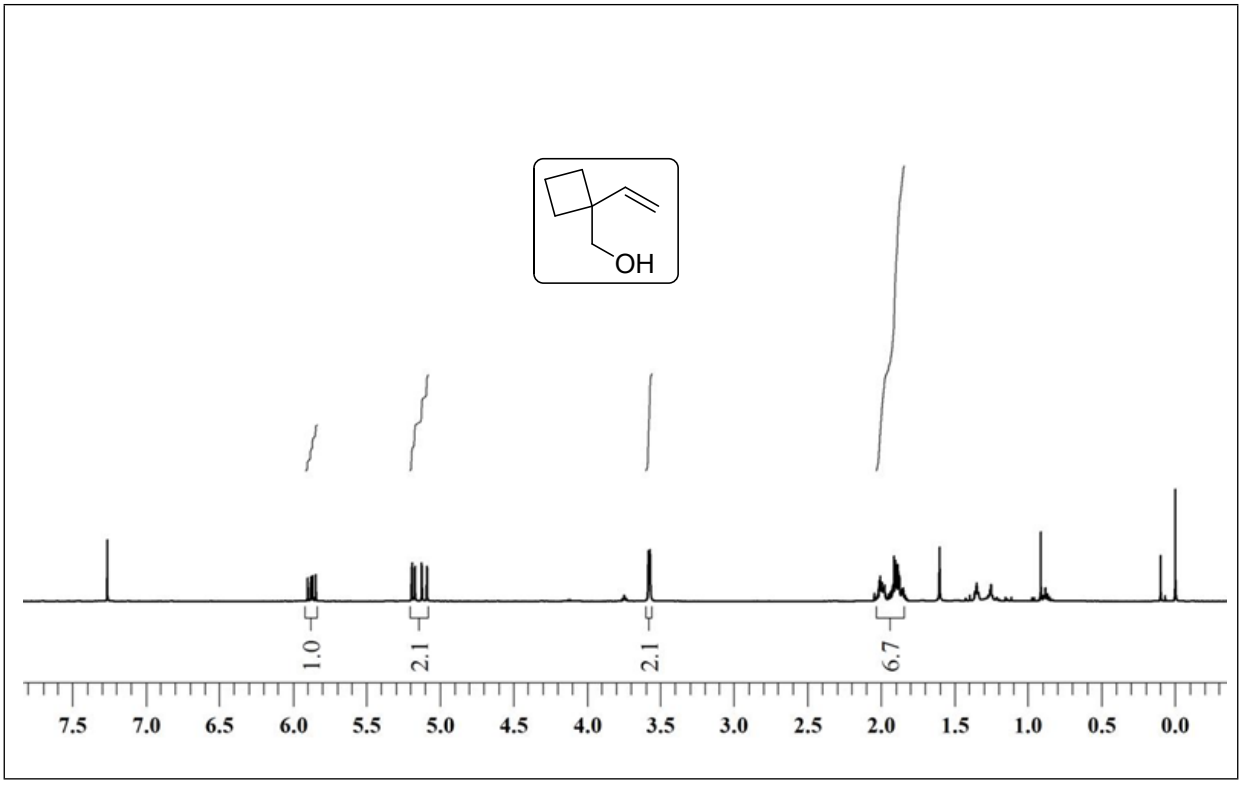


^{1}H NMR (500 MHz, $CDCl_3$) spectrum of compound (1a)

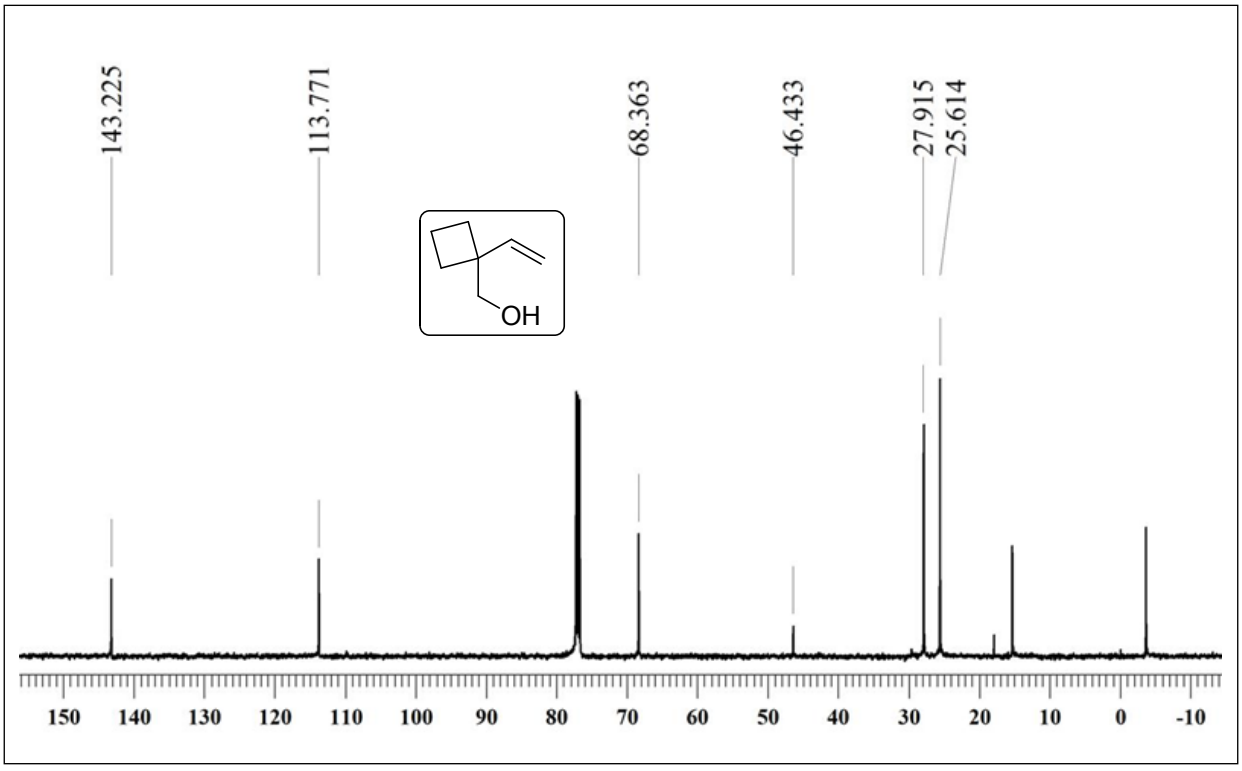


^{13}C NMR (125 MHz, $CDCl_3$) spectrum of compound (1a)

(1-Vinylcyclobutyl)methanol (1b):



^{1}H NMR (500 MHz, $CDCl_3$) spectrum of compound (1b)



^{13}C NMR (125 MHz, $CDCl_3$) spectrum of compound (1b)