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Electronic supporting information

Pd-catalyzed cascade reactions involving skipped dienes: from double carbopalladation to remote C–C cleavage

Hamid Azizollahi,[a,b] Vaibhav P. Mehta,*[a,c] and José-Antonio García-López*[a]

a. Grupo de Química Organometálica, Departamento de Química Inorgánica, Universidad de Murcia, Murcia 30100, Spain. E-mail: joangalo@um.es

b. Department of Chemistry, Faculty of Science, Ferdowsi University of Mashhad, 91775-1436, Mashhad, Iran.

c. Department of Chemistry, Marwadi University, Rajkot - Morbi Highway, Gauridad, Rajkot, Gujarat 360003 (India). E-mail: mehtavp.13@gmail.com

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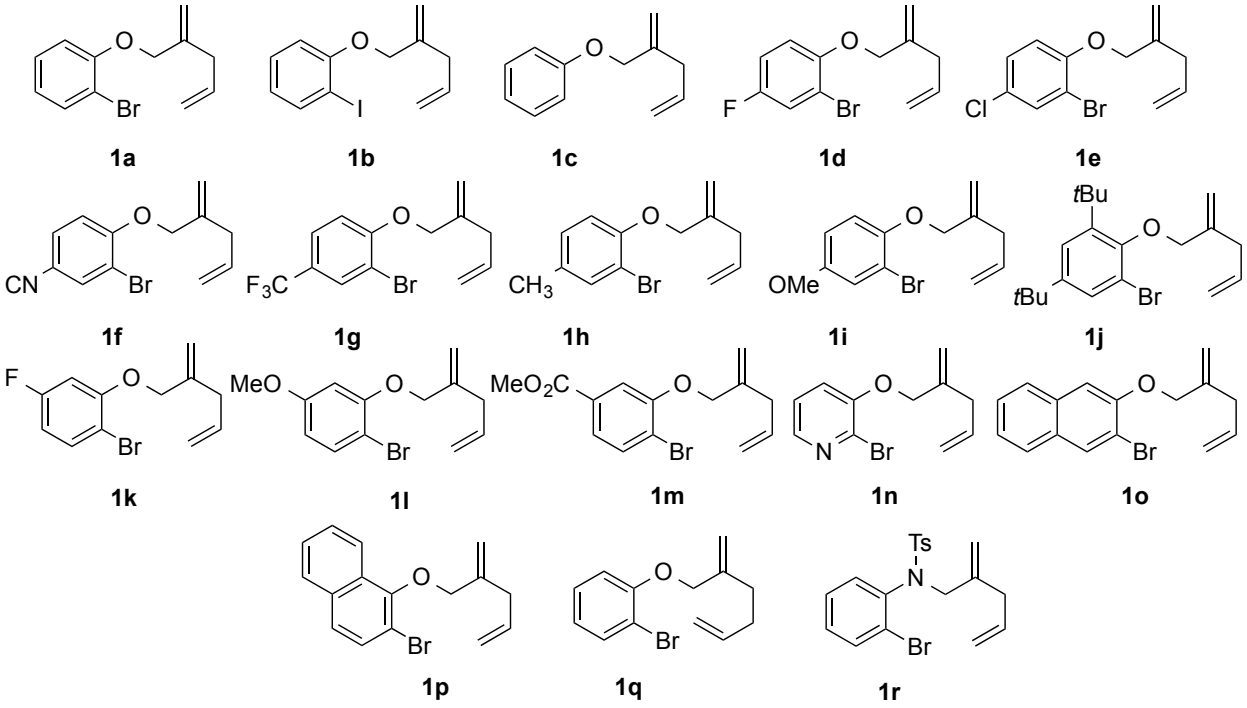
General Remarks

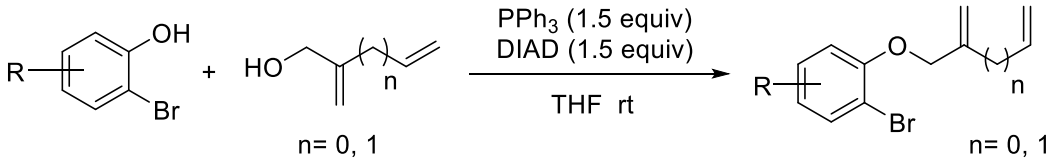
Nuclear Magnetic Resonance (NMR) spectra were recorded on a 400 or 300 MHz Bruker NMR spectrometers in $CDCl_3$ at 298 K (unless stated otherwise). All chemical shift values are reported in parts per million (ppm) relative to the solvent signal and were determined in $CDCl_3$, with coupling constant (*J*) values reported in Hz. All spectra were referenced to $CDCl_3$ the residual solvent peak $CHCl_3$ (δ = 7.26 ppm) for ^1H NMR and the $CDCl_3$ solvent peak (δ = 77.16 ppm) for $^{13}C\{^1H\}$ NMR. The notation of signals is: Proton: δ chemical shift in ppm (number of protons, multiplicity, *J* value(s), proton assignment). Carbon: δ chemical shift in ppm (carbon assignment). Fluorine: δ chemical shift in ppm (Fluorine assignment). Splitting patterns are assigned s =singlet, bd = broad doublet, d = doublet, td = triplet of doublet, dt = doublet of triplet, t = triplet, q = quartet, br= broad signal. IR spectra were recorded on a PelkinElmer Spectrum 65 spectrometer using the ATR technique (attenuated total reflection) on bulk material, and data are quoted in wavenumbers (cm^{-1}). Reagents were either purchased directly from commercial suppliers or prepared according to literature procedures. Unless otherwise noted, yields refer to isolated material on the basis of product purity (≥95%) by ^1H-NMR following silica gel chromatography. TLC plates Alugram® Sil G/UV254. Detection under UV light at 254 nm. Chromatography: Separations were carried out on Silica gel (Sigma Aldrich, 40-63 µ, 60 Å).

Chart of starting materials



Synthesis of starting materials.

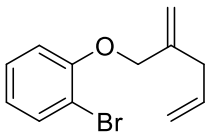
General procedure A for the synthesis of compounds 1a-q.



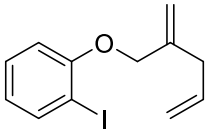
The starting 1,4-diene alcohol (2-methylenepent-4-en-1-ol) was prepared from propargyl alcohol and allylmagnesium bromide following a reported method in the literature.[1]

Procedure **A**. Starting materials **1** were prepared according to a procedure previously reported in the literature.[2] A solution of diisopropylazodicarboxylate (1 ml, 7.5 mmol, 1.5 eq) in dry THF (10 ml) was slowly added to a stirred solution of triphenylphospine (2 g, 7.5 mmol, 1.5 eq) under a nitrogen atmosphere, followed by the corresponding 2-bromophenol derivatives (5 mmol, 1eq) and 2-methylenepent-4-en-1-ol (0.49 g, 5 mmol), in THF (20 ml) at 0 ºC. The resulting mixture was stirred at room temperature overnight. After completion of the reaction, the reaction mixture was concentrated to approx. 5 ml and n-hexane (25 ml) was added. The resulting suspension was filtered and the solid was washed with n-hexane. The filtrate was evaporated to dryness and the crude was directly subjected to flash column chromatography using n-hexane as eluent to afford the pure products.

Compound 1a. Prepared according to procedure **A** from 2-bromophenol on a 10 mmol scale to afford the compound **1a** as a colorless oil in 78% yield (1.97 g, 7.79 mmol)**.** Rf (*n*-hexane) = 0.47. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.52 (dd, *J* = 7.8, 1.6 Hz, 1 H), 7.21 (m, 1 H), 6.87 – 6.78 (m, 2 H), 5.92– 5.79 (m, 1 H), 5.28 – 5.00 (m, 4 H), 4.50 (s, 2 H), 2.93 (d, *J* = 6.9 Hz, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 154.83 (s, C_q), 142.40 (s, C_q), 135.17 (s, CH), 133.25 (s, CH), 128.25 (s, CH), 121.83 (s, CH), 116.95 (s, CH_2), 113.32 (s, CH), 113.18 (s, CH_2), 112.17 (s, C_q), 71.02 (s, CH_2), 37.55 (s, CH_2). IR (cm^{-1}): 1584, 1477, 1441, 1275, 1244, 1050, 1031, 913, 743. HR-MS (+APCI) m/z calcd for $C_{12}H_{14}BrO$ $[M+H]^+$ 253.0223, found 253.0214.

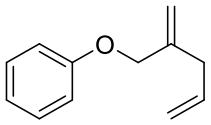


Compound 1b. Prepared according to procedure **A** from 2-iodophenol on a 10 mmol scale to afford the compound **1b** as a colorless oil in 73% yield (2.19 g, 7.3 mmol). Rf (*n*-hexane) = 0.51. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.77 (dd, *J* = 7.8, 1.6 Hz, 1



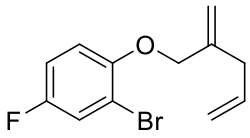
H), 7.30 – 7.22 (m, 1 H), 6.79 (dd, *J* = 8.3, 1.4 Hz, 1 H), 6.70 (ddd, *J* = 7.8, 7.4, 1.4 Hz, 1 H), 5.94– 5.80 (m, 1 H), 5.30 – 5.28 (m, 1 H), 5.20 – 5.04 (m, 3 H), 4.50 (s, 2 H), 2.97– 2.93 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 157.08 (s, C_q), 142.45 (s, C_q), 139.44 (s, CH), 135.26 (s, CH), 129.30 (s, CH), 122.56 (s, CH), 116.97 (s, CH_2), 113.31 (s, CH_2), 112.28 (s, CH), 86.53 (s, C_q), 71.19 (s, CH_2), 37.66 (s, CH_2). IR (cm^{-1}): 1580, 1472, 1438, 1276, 1243, 1050, 1015, 910, 745. HR-MS (+APCI) m/z calcd for $C_{12}H_{14}IO$ $[M+H]^+$ 301.0084, found 301.0079.

Compound 1c. Prepared according to procedure **A** from phenol on a 8 mmol scale to afford the compound **1c** as a colorless oil in 55% yield (0.77 g, 4.4 mmol). Rf (*n*-hexane) = 0.48.



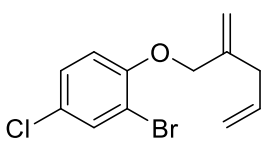
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.29 – 7.21 (m, 2 H), 6.96 – 6.87 (m, 3 H), 5.84 (m, 1 H), 5.24 – 4.97 (m, 4 H), 4.43 (s, 2 H), 2.88 (d, J = 6.8 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.69 (s, C_q), 143.18 (s, C_q), 135.30 (s, CH), 129.32 (s, CH), 120.75 (s, CH), 116.79 (s, CH_2), 114.72 (s, CH_2), 112.95 (s, CH), 70.26 (s, CH_2), 37.61 (s, CH_2). IR (cm^{-1}): 1568, 1470, 1441, 1275, 1244, 1030, 740. HR-MS (+APCI) m/z calcd for $C_{12}H_{15}O$ $[M+H]^+$ 175.1117, found 175.1115.

Compound 1d. Prepared according to procedure **A** from 2-bromo-4-fluorophenol on a 10 mmol scale to afford the compound **1d** as a colorless oil in 69% yield (1.87 g, 6.9 mmol)**.** Rf (*n*-hexane) = 0.46.



^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.28 (dd, *J* = 7.8, 3.0 Hz, 1 H), 6.96 – 6.90 (m, 1 H), 6.80 (dd, *J* = 9.1, 4.8 Hz, 1 H), 5.92– 5.78 (m, 1 H), 5.27 – 5.03 (m, 4 H), 4.46 (s, 2 H), 2.92 (d, *J* = 6.8, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 156.59 (d, *J* = 242.9 Hz, C_q), 151.56 (d, *J* = 2.8 Hz, C_q), 142.37 (s, C_q), 135.13 (s, CH), 120.34 (d, *J* = 25.7 Hz, CH), 116.97 (s, CH_2), 114.47 (d, *J* = 22.7 Hz, CH), 113.92 (d, *J* = 8.3 Hz, CH), 113.41 (s, CH_2), 112.33 (d, *J* = 9.8 Hz, C_q), 71.86 (s, CH_2), 37.53 (s, CH_2). ^{19}F NMR (282 MHz, $CDCl_3$) δ = -121.54 (s). IR (cm^{-1}): 1485, 1257, 1188, 1038, 912, 859, 784. HR-MS (+APCI) m/z calcd for $C_{12}H_{13}BrFO$ $[M+H]^+$ 271.0128, found 271.0116

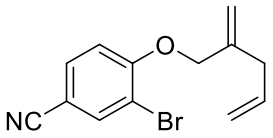
Compound 1e. Prepared according to procedure **A** from 2-bromo-4-chlorophenol on a 9.64 mmol scale to afford the compound **1e** as a colorless oil in 72% yield (1.99 g, 6.94 mmol)**.** Rf (*n*-hexane) = 0.52.



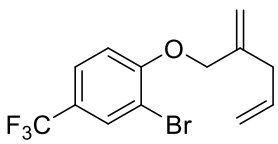
^{1}H NMR (300 MHz, CDCl3) δ = 7.50 (d, *J* = 2.5 Hz, 1 H), 7.20 - 7.10 (m, 1 H), 6.74 (d, *J* = 8.8 Hz, 1 H), 5.87– 5.78 (m, 1 H), 5.26 – 5.00 (m, 4 H), 4.45 (s, 2 H), 2.90 (d, *J* = 7.2 Hz, 2 H). ^{13}C NMR (75 MHz, CDCl3) δ = 153.69 (s, C_q), 142.01 (s, C_q), 134.98 (s, CH), 132.68 (s, CH), 128.01 (s, CH), 125.94 (s, C_q) 117.02 (s, CH_2), 113.87 (s, CH), 113.43 (s, CH_2), 112.63 (s, C_q), 71.33 (s, CH_2),

37.45 (s, CH_2). IR (cm^{-1}): 1475, 1286, 1263, 1246, 1046, 913, 868, 800, 733. HR-MS (+APCI) m/z calcd for $C_{12}H_{13}BrClO$ $[M+H]^+$ 286.9833, found 286.9820.

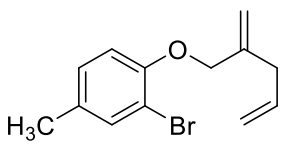
Compound 1f. Prepared according to procedure **A** from 3-bromo-4-hydroxybenzonitrile on a 10 mmol scale to afford the compound **1f** as a colorless oil in 71% yield (1.97 g, 7.1 mmol)**.** Rf (*n*-hexane/EtOAc, 10:1)= 0.58. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.81 (d, *J* = 2.0 Hz, 1 H), 7.56 (dd, *J* = 8.6, 2.0 Hz, 1 H), 6.92 (d, *J* = 8.6 Hz, 1 H), 5.91– 5.77 (m, 1 H), 5.29 – 5.06 (m, 4 H), 4.59 (s, 2 H), 2.92 (d, *J* = 6.9 Hz, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 158.33 (s, C_q), 141.21 (s, C_q), 136.53 (s, CH), 134.66 (s, CH), 132.82 (s, CH), 117.59 (s, C_q), 117.23 (s, CH_2), 113.97 (s, CH_2), 113.02 (s, CH), 112.56 (s, C_q), 105.04 (s, C_q), 71.28 (s, CH_2), 37.35 (s, CH_2). IR (cm^{-1}): 2227, 1596, 1490, 1294, 1256, 1194, 1051, 995, 913, 813. HR-MS (+APCI) m/z calcd for $C_{13}H_{13}BrNO$ $[M+H]^+$ 278.0175, found 278.0179.



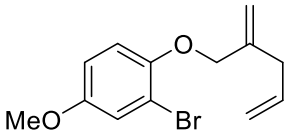
Compound 1g. Prepared according to procedure **A** from 2-bromo-4-(trifluoromethyl)phenol on a 4 mmol scale to afford the compound **1g** as a colorless oil in 69% yield (0.89 g, 2.76 mmol)**.** Rf (*n*-hexane) = 0.73. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.72 (dd, *J* = 2.2, 0.8 Hz, 1 H), 7.44 – 7.40 (m, 1 H), 6.83 (dd, *J* = 8.7, 0.9 Hz, 1 H), 5.84– 5.70 (m, 1 H), 5.26 – 4.89 (m, 4 H), 4.49 (s, 2 H), 2.97 – 2.71 (d, *J* = 6.9 Hz, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 157.46 (s, C_q), 141.75 (s, C_q), 134.95 (s, CH), 130.56 (q, *J* = 3.7 Hz, CH), 125.73 (q, *J* = 3.7 Hz, CH), 124.02 (q, J_{CF}= 32.9, C_q), 123.22 (q, J_{CF}= 272.4, C_q), 117.24 (s, CH), 113.83 (s, CH_2), 112.69 (s, CH_2), 112.33 (s, C_q), 71.32 (s, CH_2), 37.54 (s, CH_2). ^{19}F NMR (282 MHz, $CDCl_3$) δ = -61.71 (s). IR (cm^{-1}): 1609, 1501, 1406, 1322, 1268, 1120, 1079, 1049, 913, 813. HR-MS (+APCI) m/z calcd for $C_{13}H_{13}BrF_3O$ $[M+H]^+$ 321.0096, found 321.0102.



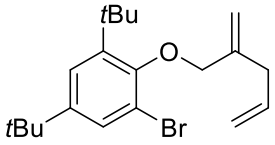
Compound 1h. Prepared according to procedure **A** from 2-bromo-4-methylphenol on a 16 mmol scale to afford the compound **1h** as a colorless oil in 65% yield (2.77 g, 10.4 mmol)**.** Rf (*n*-hexane) = 0.48. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.33 (dd, *J* = 2.2, 0.8 Hz, 1 H), 7.02 – 6.94 (m, 1 H), 6.74 (d, *J* = 8.3 Hz, 1 H), 5.91– 5.78 (m, 1 H), 5.26 – 5.01 (m, 4 H), 4.46 (s, 2 H), 2.91 (d, *J* = 6.9, 2 H), 2.23 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 152.76 (s, C_q), 142.65 (s, C_q), 135.24 (s, CH), 133.64 (s, CH), 131.51 (s, C_q), 128.64 (s, CH), 116.83 (s, CH_2), 113.39 (s, CH), 113.06 (s, CH_2), 111.92 (s, C_q), 71.28 (s, CH_2), 37.54 (s, CH_2), 20.08 (s, CH_3). IR (cm^{-1}): 1493, 1284, 1250, 1048, 995, 910, 868, 801, 670. HR-MS (+APCI) m/z calcd for $C_{13}H_{16}BrO$ $[M+H]^+$ 267.0379, found 267.0373.



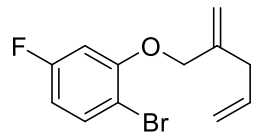
Compound 1i. Prepared according to procedure **A** from 2-bromo-4-methoxyphenol on a 5 mmol scale to afford the compound **1i** as a colorless oil in 71% yield (1.00 g, 3.55 mmol)**.** Rf (*n*-hexane/EtOAc, 10:1) = 0.51. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.11 (dd, *J* = 2.8, 0.5 Hz, 1 H), 6.88 – 6.67 (m, 2 H), 5.86 (m, 1 H), 5.36 – 4.95 (m, 4 H), 4.62 – 4.16 (m, 2 H), 3.74 (s, 3 H), 2.94 (d, *J* = 6.5, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 154.18 (s, C_q), 149.35 (s, C_q), 142.86 (s, C_q), 135.32 (s, CH), 118.83 (s, CH), 116.86 (s, CH_2), 114.79 (s, CH), 113.61 (s, CH), 113.21 (s, CH_2), 112.78 (s, C_q), 72.16 (s, CH_2), 55.83 (s, CH_3), 37.59 (s, CH_2). IR (cm^{-1}): 1491, 1459, 1438, 1271, 1210, 1037, 912, 779, 735. HR-MS (+APCI) m/z calcd for $C_{13}H_{16}BrO_2$ $[M+H]^+$ 283.0328, found 283.0331.



Compound 1j. Prepared according to procedure **A** from 2-bromo-4,6-di-tert-butylphenol on a 3 mmol scale to afford the compound **1j** as a colorless oil in 65% yield (0.71 g, 1.95 mmol)**.** Rf (*n*-hexane) = 0.72. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.41 (d, *J* = 2.4 Hz, 1 H), 7.29 (d, *J* = 2.4 Hz, 1 H), 5.95– 5.81 (m, 1 H), 5.38 – 4.97 (m, 4 H), 4.51 (s, 2 H), 2.93 (d, *J* = 6.8 Hz, 2 H), 1.39 (s, 9 H), 1.28 (s, 9 H).^{13}C NMR (75 MHz, $CDCl_3$) δ = 152.33 (s, C_q), 147.24 (s, C_q), 144.24 (s, C_q), 143.29 (s, C_q), 135.64 (s, CH), 128.89 (s, CH), 123.70 (s, CH), 117.83 (s, C_q), 116.57 (s, CH_2), 111.93 (s, CH_2), 74.37 (s, CH_2), 37.87 (s, CH_2), 35.76 (s, C_q), 34.53 (s, C_q), 31.37 (s, CH_3), 30.90 (CH_3). IR (cm^{-1}): 1490, 1282, 1251, 1048, 995, 905, 868, 673. HR-MS (+APCI) m/z calcd for $C_{20}H_{30}BrO$ $[M+H]^+$ 365.1475, found 365.1482.



Compound 1k. Prepared according to procedure **A** from 2-bromo-5-fluorophenol on a 10 mmol scale to afford the compound **1k** as a colorless oil in 65% yield (1.76 g, 6.5 mmol)**.** Rf (*n*-hexane) = 0.65. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.36 (dd, *J* = 8.6, 6.2 Hz, 1 H), 6.59 – 6.40 (m, 2 H), 5.82 – 5.66 (m, 1 H), 5.18 – 4.95 (m, 4 H), 4.38 (s, 2 H), 2.82 (d, *J* = 6.9 Hz, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.49 (d, J_{CF} = 246.2 Hz, C_q), 155.72 (d, J_{CF} = 10.1 Hz, C_q), 141.80 (s, C_q), 134.97 (s, CH), 133.38 (d, J_{CF} = 9.7 Hz, CH), 117.12 (s, CH_2), 113.57 (s, CH_2), 108.42 (d, *J* = 22.6 Hz, CH), 106.35 (d, J_{CF} = 3.7 Hz, C_q), 101.55 (d, J_{CF} = 26.8 Hz, CH), 71.19 (s, CH_2), 37.49 (s, CH_2). ^{19}F NMR (282 MHz, $CDCl_3$) δ = -111.82 (s). IR (cm^{-1}): 1604, 1581, 1481, 1420, 1290, 1280, 1164, 1110, 1040, 913, 829, 794. HR-MS (+APCI) m/z calcd for $C_{12}H_{13}BrFO$ $[M+H]^+$ 271.0128, found 271.0116.

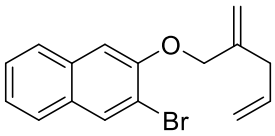


Compound 1l. Prepared according to procedure **A** from 2-bromo-5-methoxyphenol on a 2.95 mmol scale to afford the compound **1l** as a colorless oil in 72% yield (0.62 g, 2.12 mmol)**.** Rf (*n*-hexane/EtOAc, 20:1) = 0.53. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.40 (d, *J* = 8.7 Hz, 1 H), 6.50 – 6.33 (m, 2 H), 5.90 – 5.79 (m, 1 H), 5.27 – 5.03 (m, 4 H), 4.49 (s, 2 H), 3.77 (s, 3 H), 2.94 (d, *J* = 6.9 Hz, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 159.95 (s, C_q), 155.51 (s, C_q), 142.34 (s, C_q), 135.19 (s, CH), 133.06 (s, CH), 116.99 (s, CH_2), 113.27 (s, CH_2), 106.16 (s, CH), 102.95 (s, C_q), 101.14 (s, CH), 71.06 (s, CH_2), 55.48 (s, CH_3), 37.57 (s, CH_2). IR (cm^{-1}): 1584, 1485, 1305, 1201, 1166, 1061, 1021, 912, 830, 819, 785. HR-MS (+APCI) m/z calcd for $C_{13}H_{16}BrO_2$ $[M+H]^+$ 283.0328, found 283.0329.

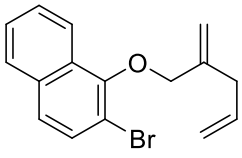
Compound 1m. Prepared according to procedure **A** from methyl 4-bromo-3-hydroxybenzoate on a 4.2 mmol scale to afford the compound **1m** as a colorless oil in 67% yield (0.87 g, 2.81 mmol)**.** Rf (*n*-hexane/EtOAc, 10:1) = 0.75. ^{1}H NMR (300 MHz, CDCl3) δ = 7.60 (d, *J* = 8.1 Hz, 1 H), 7.53 – 7.46 (m, 2 H), 5.93– 5.80 (m, 1 H), 5.36 – 5.03 (m, 4 H), 4.58 (s, 2 H), 3.90 (s, 3 H), 2.94 (d, *J* = 6.9 Hz, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.25 (s, C_q), 154.84 (s, C_q), 142.00 (s, C_q), 135.06 (s, CH), 133.22 (s, CH), 130.34 (s, C_q), 122.84 (s, CH), 117.92 (s, C_q), 117.04 (s, CH_2), 113.68 (s, CH), 113.57 (s, CH_2), 71.16 (s, CH_2), 52.25 (s, CH_3), 37.55 (s, CH_2). IR (cm^{-1}): 1719, 1576, 1433, 1411, 1287, 1233, 1104, 909, 757. HR-MS (+APCI) m/z calcd for $C_{14}H_{16}BrO_3$ $[M+H]^+$ 311.0277, found 311.0264.

Compound 1n. Prepared according to procedure **A** from methyl 2-bromopyridin-3-ol on a 3 mmol scale to afford the compound **1n** as a light yellow oil in 62% yield (0.47 g, 1.86 mmol)**.** The crude reaction mixture was purified by flash chromatography column (hexane/EtOAc, gradient from 0 to 50 % EtOAc). Rf (*n*-hexane/EtOAc, 10:1)= 0.44. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.97 (dd, *J* = 4.5, 1.7 Hz, 1 H), 7.19 (m, 1 H), 7.12 (dd, *J* = 8.1, 1.7 Hz, 1 H), 5.91– 5.78 (m, 1 H), 5.27 – 5.07 (m, 4 H), 4.55 (s, 2 H), 2.93 (d, *J* = 6.9 Hz, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 151.84 (s, C_q), 141.54 (s, C_q), 141.24 (s, CH), 134.82 (s, CH), 132.97 (s, C_q), 123.19 (s, CH), 119.89 (s, CH), 117.16 (s, CH_2), 113.88 (s, CH_2), 71.14 (s, CH_2), 37.40 (s, CH_2). IR (cm^{-1}): 1562, 1448, 1411, 1287, 1200, 1074, 1052, 994, 914, 793, 725. HR-MS (+ESI) m/z calcd for $C_{11}H_{13}BrNO$ $[M+H]^+$ 254.0175, found 254.0177.

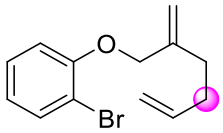
Compound 1o. Prepared according to procedure **A** from 3-bromonaphthalen-2-ol on a 2.5 mmol scale to afford the compound **1o** as a yellow oil in 60% yield (0.45 g, 1.5 mmol). Rf (*n*-hexane) = 0.5. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.04 (s, 1 H), 7.74 – 7.61 (m, 2 H), 7.38 (m, 2 H), 7.12 (s, 1 H), 5.94 – 5.82 (m, 1 H), 5.42 – 5.03 (m, 4 H), 4.61 (s, 2 H), 2.99 (d, *J* = 6.9, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 152.42 (s, C_q), 142.32 (s, C_q), 135.24 (s, CH), 133.36 (s, C_q), 132.19 (s, CH), 129.37 (s, C_q), 126.66 (s, CH), 126.58 (s, CH), 126.54 (s, CH), 124.44 (s, CH), 117.04 (s, CH_2), 113.77 (s, C_q), 113.31 (s , CH_2), 107.79 (s, CH), 71.03 (s, CH_2), 37.68 (s, CH_2). IR (cm^{-1}): 1590, 1496, 1450, 1326, 1248, 1213, 1180, 1031, 1018, 909, 859, 800, 743. HR-MS (+APCI) m/z calcd for $C_{16}H_{16}BrO$ $[M+H]^+$ 303.0379, found 303.0375.



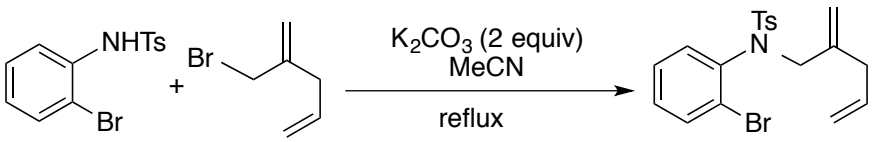
Compound 1p. Prepared according to procedure **A** from 2-bromonaphthalen-1-ol on a 2.5 mmol scale to afford the compound **1p** as a colorless oil in 59% yield (0.44 g, 1.47 mmol). Rf (*n*-hexane) = 0.48. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.12 – 8.04 (m, 1 H), 7.73 (m, 1 H), 7.56 – 7.37 (m, 4 H), 5.96 – 5.87 (m, 1 H), 5.43 – 5.05 (m, 4 H), 4.47 (s, 2 H), 3.05 (d, *J* = 6.8 Hz, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 151.88 (s, C_q), 143.34 (s, C_q), 135.42 (s, CH), 133.81 (s, C_q), 129.94 (s, CH), 129.11 (s, C_q), 127.90 (s, CH), 126.62 (s, CH), 126.42 (s, CH), 125.16 (s, CH), 121.94 (s, CH), 116.81 (s, CH_2), 113.45 (s, CH_2), 112.89 (s, C_q), 75.86 (s, CH_2), 37.78 (s, CH_2). IR (cm^{-1}): 1583, 1572, 1500, 1350, 1257, 1201, 1124, 1065, 911, 801, 780, 741. HR-MS (+APCI) m/z calcd for $C_{16}H_{16}BrO$ $[M+H]^+$ 303.0379, found 303.0384.



Compound 1q. Prepared according to procedure **A** from 2-bromo phenol on a 5 mmol scale and 2-methylenehex-5-en-1-ol to afford the compound **1q** as a colorless oil in 65 yield (0.87 g, 3.25 mmol). Rf (*n*-hexane) = 0.56. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.53 (dd, *J* = 7.8, 1.5 Hz, 1 H), 7.28 – 7.17 (m, 1 H), 6.92 – 6.76 (m, 2 H), 5.96 – 5.76 (m, 1 H), 5.28 – 4.95 (m, 4 H), 4.52 (s, 2 H), 2.29 (m, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 154.98 (s, C_q), 143.52 (s, C_q), 137.99 (s, CH), 133.33 (s, CH), 128.27 (s, CH), 121.88 (s, CH), 114.89 (s, CH_2), 113.42 (s, CH), 112.60 (s, CH_2), 112.28 (s, C_q), 71.64 (s, CH_2), 32.34 (s, CH_2), 31.77 (s, CH_2). IR (cm^{-1}): 1585, 1476, 1442, 1278, 1245, 1050, 1030, 906, 745, 666. HR-MS (+APCI) m/z calcd for $C_{13}H_{16}BrO$ $[M+H]^+$ 267.0379, found 267.0373.



Procedure B for the synthesis of compound 1r.



1r

Procedure **B.** To a stirred solution of N-(2-bromophenyl)-4-methylbenzenesulfonamide (1.2 mmol, 1 equiv) and K_2CO_3 (2 equiv) in MeCN (15 ml) was added 2-(bromomethyl)penta-1,4-diene (1 equiv), prepared according to the reported procedure,[1] under a nitrogen atmosphere. The resulting mixture was refluxed for 16 h. After completion of the reaction as checked by TLC, the reaction mixture was filtered and the filtrate was evaporated to dryness. The crude was directly subjected to flash column chromatography using n-hexane/ethyl acetate as eluent to afford the compound **1r**.

Compound 1r. Light yellow oil. 67% yield (0.33 g, 0.80 mmol)**.** The crude reaction mixture was purified by flash column chromatography (hexane/EtOAc, gradient from 0 to 35 % EtOAc). Rf (*n*-hexane/EtOAc, 20:1) = 0.23. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.63 – 7.54 (m, 3 H), 7.30 – 7.21 (m, 3 H), 7.19 – 7.05 (m, 2 H), 5.79 – 5.67 (m, 1 H), 5.11 – 4.98 (m, 2 H), 4.85 – 4.65 (m, 2 H), 4.36 – 3.97 (m, 2 H), 2.95 – 2.85 (d, *J* = 6.1, 2 H), 2.42 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 143.58 (s, C_q), 141.96 (s, C_q), 137.63 (s, C_q), 136.11 (s, C_q), 135.20 (s, CH), 133.94 (s, CH), 131.81 (s, CH), 129.53 (s, CH), 129.39 (s, CH), 127.90 (s, CH), 127.66 (s, CH), 125.45 (s, C_q), 116.82 (s, CH_2), 116.11 (s, CH_2), 55.50 (s, CH_2), 37.80 (s, CH_2), 21.50 (s, CH_3). IR (cm^{-1}): 1596, 1471, 1352, 1167, 1090, 1047, 911, 859, 813, 783, 715, 660. HR-MS (+ESI) m/z calcd for $C_{19}H_{21}BrNO_2S$ $[M+H]^+$ 406.0471, found 406.0472.

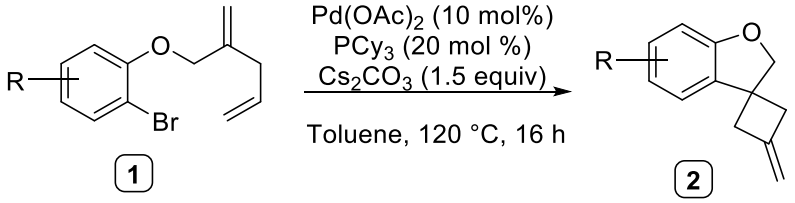
Optimization table for the cascade reaction leading to 2a and 3a.[a]

Pd source loading (mol%)	Ligand (mol%)	Base (equiv)	Solvent/ T (ºC)	Time (h)	Yield% (2a+3a)[b] Ratio 2a:3a[c]	observations
$Pd(OAc)_2$ (10)	PPh_3 (20)	Cs_2CO_3 1.5	DMF 80	16	-	complex mixture
$Pd(OAc)_2$ (10)	PPh_3 (20)	Cs_2CO_3 1.5	THF 80	16	-	complex mixture
$Pd(OAc)_2$ (10)	PPh_3 (20)	Cs_2CO_3 1.5	CH_3CN 80	16	20 (1:3)	
$Pd(OAc)_2$ (10)	PPh_3 (20)	Cs_2CO_3 1.5	HFIP 80	16	-	complex mixture
$Pd(OAc)_2$ (10)	PPh_3 (20)	Cs_2CO_3 1.5	Toluene 80	16	72 (1:2)	
$Pd(OAc)_2$ (2.5)	PPh_3 (5)	Cs_2CO_3 1.5	Toluene	16	45 (1:3)	
$Pd(OAc)_2$ (10)	Xantphos (20)	Cs_2CO_3 1.5	Toluene 80	16	52 (1:10)	
$Pd(OAc)_2$ (10)	DPPF (20)	Cs_2CO_3 1.5	Toluene 80	16	62 (traces:1)	intermediate **A** detected
$Pd(OAc)_2$ (10)	Johnphos (20)	Cs_2CO_3 1.5	Toluene 80	16	-	unreacted starting material
$Pd(OAc)_2$ (10)	IMes·HCl (20)	Cs_2CO_3 1.5	Toluene 80	16	46 (6:1)	
$Pd(OAc)_2$ (10)	Xantphos (20)	K_2CO_3 1.5	Toluene 80	16	35 (1:8)	intermediate **A** detected
$Pd(OAc)_2$ (10)	Xantphos (20)	Et_3N 1.5	Toluene 80	16	10	30% intermediate **A**
$Pd(OAc)_2$ (10)	Xantphos (20)	Cs_2CO_3 1.5	Toluene 80	1	traces	80% intermediate **A**
$Pd(OAc)_2$ (5)	Xantphos (10)	Cs_2CO_3 1.5	1,4-Dioxane 80	16	65 (1:10)	
$Pd(OAc)_2$ (10)	$P(Cy)_3$ (20)	Cs_2CO_3 1.5 eq	Toluene 80	16	90 (78)[d] (1:traces)	
$Pd(OAc)_2$ (10)	$P(Cy)_3$ (20)	Cs_2CO_3 1.5	Toluene 80	1	traces	unreacted starting material
$Pd(OAc)_2$ (10)	DPEphos (20)	Cs_2CO_3 1.5	Toluene 80	16	74 (66)[d] (traces:1)	
$Pd(OAc)_2$ (5)	DPPH (10)	Cs_2CO_3 1.5	Toluene 80	1	-	85% intermediate **A**
$Pd(OAc)_2$ (5)	DPEphos (10)	Cs_2CO_3 1.5	Toluene 80	1	10% (traces:1)	70% intermediate **A**
$Pd(OAc)_2$ (5)	$P(Cy)_3$ (10)	K_2CO_3 1.5	Toluene 80	6	25 (1:traces)	mainly unreacted starting material

$Pd(OAc)_2$ (5)	$P(Cy)_3$ (10)	K_2CO_3 1.5	Toluene 80	16	55 (1:traces)	
$Pd(OAc)_2$ (5)	DPEphos (10)	K_2CO_3 1.5	Toluene 80	6	65 (traces:1)	
$Pd(dba)_2$ (10)	DPEphos (20)	Cs_2CO_3 1.5	Toluene 80	1	10	85% intermediate **A**
$Pd(dba)_2$ (5)	-----	Cs_2CO_3 1.5	Toluene 80	16	0	unreacted s. material
$Pd(OAc)_2$ (10)	-----	Cs_2CO_3 1.5	Toluene 80	16	0	unreacted s. material
$PdCl_2(MeCN)_2$ (10)	------	Cs_2CO_3 1.5	Toluene 80	1	0	unreacted s. material
--------	----------	Cs_2CO_3 1.5	Toluene 80	1	0	unreacted s. material

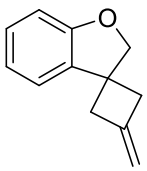
[a] Unless otherwise stated, the reactions were carried out with 0.2 mmol of **1a**, in toluene (3 mL) under N_2 atmosphere, at 80 ºC for 16 h. [b] Combined ^{1}H-NMR yield of **2a**+**3a** using trimethyl benzene-1,3,5-tricarboxylate as standard. [c] NMR ratio in the crude reaction mixture. [d] Isolated yield. Xantphos = 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene. DPPF = 1,1' bis(diphenylphosphino)ferrocene. DPEphos = bis-[2-(diphenylphosphino)phenyl]ether. DPPH = bis(diphenylphosphino)hexane. IMes·HCl= 1,3-Bis(2,4,6-trimethylphenyl)imidazolium chloride.

General procedure C for synthesis of [4,5]-spirocycles 2a-n.

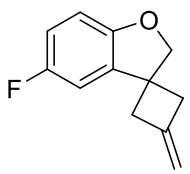


Procedure **C.** A solution of the corresponding compounds **1a-p** (0.5 mmol) in dry toluene (4 mL) under N_2 atmosphere was added to a mixture of $Pd(OAc)_2$ (11 mg, 10 mol%), PCy_3 (28 mg, 20 mol%) and Cs_2CO_3 (245 mg, 1.5 equiv) in a Schlenk tube under N_2 atmosphere. The reaction mixture was stirred at 120 °C for 16 hours. The resulting suspension was filtered through a Celite pad. The filtrate was evaporated to dryness and the crude was directly subjected to flash column chromatography using n-hexane/ethyl acetate as eluent to afford the pure products **2a-n**.

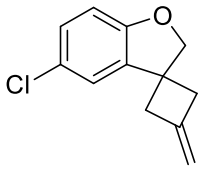
Compound 2a Prepared according to the procedure **C** from compound **1a** on a 0.3 mmol scale to afford the compound **2a** as a yellow oil in 78% yield (40 mg, 0.23 mmol)**.** Rf (*n*-hexane) = 0.2. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.35 (ddd, *J* = 7.4, 1.4, 0.6 Hz, 1 H), 7.14 (ddd, *J* = 8.0, 7.4, 1.4 Hz, 1 H), 6.91 (td, *J* = 7.4, 1.0 Hz, 1 H), 6.78 (dt, *J* = 8.0, 0.8 Hz, 1 H), 4.96 - 4.93 (m, 2 H), 4.56 (s, 2 H), 3.13 – 3.01 (m, 2 H), 3.01 – 2.91 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 159.44 (s, C_q), 142.80 (s, C_q), 134.32 (s, C_q), 128.32 (s, CH), 122.19 (s, CH), 120.88 (s, CH), 109.31 (s, CH), 107.49 (s, CH_2), 83.49 (s, CH_2), 45.53 (s, CH_2), 43.11 (s, C_q). IR (cm^{-1}): 1599, 1478, 1461, 1263, 1230, 1215, 971, 882, 828, 748, 740. HR-MS (+APCI) m/z calcd for $C_{12}H_{13}O$ $[M+H]^+$ 173.0961, found 173.0969.



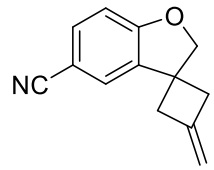
Compound 2b Prepared according to the procedure **C** from compound **1d** on a 0.5 mmol scale to afford the compound **2b** as a colorless oil in 71% yield (66 mg, 0.35 mmol)**.** Rf (*n*-hexane) = 0.3. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.03 (dd, *J* = 7.9, 2.7 Hz, 1 H), 6.80 (td, *J* = 8.8, 2.7 Hz, 1 H), 6.67 (dd, *J* = 8.6, 4.0 Hz, 1 H), 4.96 – 4.94 (m, 2 H), 4.56 (s, 2 H), 3.07 – 2.93 (m, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 157.87 (d, *J* = 237.4 Hz, C_q), 155.37 (s, C_q), 142.10 (s, C_q), 135.79 (d, *J* = 8.2 Hz, C_q), 114.49 (d, *J* = 24.2 Hz, CH), 109.49 (d, *J* = 8.5 Hz, CH), 109.27 (d, *J* = 24.7 Hz, CH), 107.86 (s, CH_2), 83.89 (s, CH_2), 45.33 (s, CH_2), 43.52 (s, C_q). ^{19}F NMR (188 MHz, $CDCl_3$) δ = -124.09 (s). IR (cm^{-1}): 1483, 1462, 1257, 1170, 973, 880, 863, 807, 778, 737, 713. HR-MS (+APCI) m/z calcd for $C_{12}H_{12}FO$ $[M+H]^+$ 191.0867, found 191.0872.



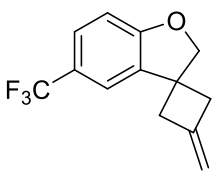
Compound 2c Prepared according to the procedure **C** from compound **1e** on a 0.5 mmol scale to afford the compound **2c** as a light yellow oil in 63% yield (65 mg, 0.31 mmol)**.** Rf (*n*-hexane) = 0.32. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.30 (dd, *J* = 2.2, 0.4 Hz, 1 H), 7.09 (dd, *J* = 8.5, 2.3 Hz, 1 H), 6.69 (dd, *J* = 8.4, 0.4 Hz, 1 H), 4.97– 4.96 (m, 2 H), 4.58 (s, 2 H), 3.08 – 2.93 (m, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.12 (s, C_q), 141.96 (s, C_q), 136.37 (s, C_q), 128.20 (s, CH), 125.51 (s, C_q), 122.43 (s, CH), 110.33 (s, CH), 108.01 (s, CH_2), 83.92 (s, CH_2), 45.46 (s, CH_2), 43.27 (s, C_q). IR (cm^{-1}): 1476, 1460, 1261, 1164, 1071, 969, 908, 878, 809, 731, 676. HR-MS (+APCI) m/z calcd for $C_{12}H_{12}ClO$ $[M+H]^+$ 207.0571, found 207.0508.



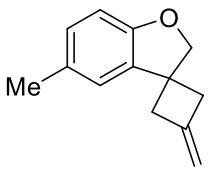
Compound 2d Prepared according to the procedure **C** from compound **1f** on a 0.5 mmol scale to afford the compound **2d** as a colorless oil in 53% yield (51 mg, 0.26 mmol)**.** Rf (*n*-hexane/EtOAc, 10:1) = 0.50. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.63 (dd, *J* = 1.8, 0.5 Hz, 1 H), 7.48 – 7.45 (m, 1 H), 6.82 (dd, *J* = 8.3, 0.5 Hz, 1 H), 5.01 – 4.96 (m, 2 H), 4.66 (s, 2 H), 3.03 (t, *J* = 2.4 Hz, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.08 (s, C_q), 141.14 (s, C_q), 136.24 (s, C_q), 133.71 (s, CH), 126.46 (s, CH), 119.47 (s, C_q), 110.34 (s, CH), 108.46 (s, CH_2), 84.27 (s, CH_2), 45.75 (s, CH_2), 42.71 (s, C_q), 30.89 (s, C_q). IR (cm^{-1}): 2227, 1606, 1482, 1286, 1261, 1104, 1079, 828, 732. HR-MS (+APCI) m/z calcd for $C_{13}H_{12}NO$ $[M+H]^+$ 198.0913, found 198.0919.



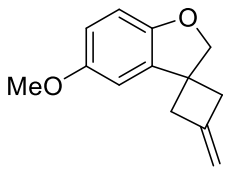
Compound 2e Prepared according to the procedure **C** from compound **1g** on a 0.5 mmol scale to afford the compound **2e** as a colorless oil in 75% yield (89 mg, 0.37 mmol). Rf (*n*-hexane) = 0.40. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.58 (dt, *J* = 1.9, 0.7 Hz, 1 H), 7.43 – 7.40 (m, 1 H), 6.87 – 6.77 (m, 1 H), 4.99– 4.97 (m, 2 H), 4.64 (s, 2 H), 3.13 – 2.96 (m, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 162.13 (s, C_q), 141.69 (s, C_q), 135.31 (s, C_q), 126.30 (q, *J* = 3.9 Hz, CH), 124.55 (q, *J* = 32.1 Hz, C_q), 123.37 (q, *J* = 271.05 Hz, C_q), 119.64 (q, *J* = 3.7 Hz, CH), 109.38 (s, CH), 108.21 (s, CH_2), 84.26 (s, CH_2), 45.61(s, CH_2) , 42.81 (s, C_q). ^{19}F NMR (188 MHz, $CDCl_3$) δ = -61.41(s). IR (cm^{-1}): 1619, 1496, 1334, 1317, 1274, 1156, 1112, 1057, 966, 883, 823, 732. HR-MS (+APCI) m/z calcd for $C_{13}H_{12}F_3O$ $[M+H]^+$ 241.0835, found 241.0846.



Compound 2f Prepared according to the procedure **C** from compound **1h** on a 1 mmol scale to afford the compound **2f** as a light yellow oil in 54% yield (100 mg, 0.54 mmol)**.** Rf (*n*-hexane) = 0.25. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.15 (dt, *J* = 2.0, 0.7 Hz, 1 H), 6.95 – 6.92 (m, 1 H), 6.67 (d, *J* = 8.1 Hz, 1 H), 4.95 – 4.92 (m, 2 H), 4.54 (s, 2 H), 3.09 – 3.00 (m, 2 H), 3.00 – 2.90 (m, 2 H), 2.31 (s, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 157.45 (s, C_q), 142.96 (s, C_q), 134.33 (s, C_q), 130.26 (s, C_q), 128.75 (s, CH), 122.70 (s, CH), 108.88 (s, CH), 107.44 (s, CH_2), 83.67 (s, CH_2), 45.45 (s, CH_2), 43.22 (s, C_q), 20.86 (s, CH_3). IR (cm^{-1}): 1489, 1266, 1230, 1209, 1197, 970, 875, 807, 737. HR-MS (+APCI) m/z calcd for $C_{13}H_{15}O$ $[M+H]^+$ 187.1117, found 187.1117.

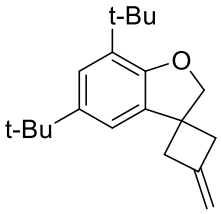


Compound 2g Prepared according to the procedure **C** from compound **1i** on a 0.2 mmol scale to afford the compound **2g** as a light yellow oil in 67% yield (27 mg, 0.13 mmol)**.** Rf (*n*-hexane/EtOAc, 20:1) = 0.40. ^{1}H NMR (300 MHz, $CDCl_3$) δ =



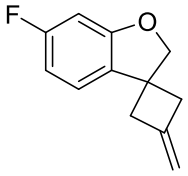
6.92 (m, 1 H), 6.68 (m, 2 H), 4.94 (m, 2 H), 4.54 (s, 2 H), 3.78 (s, 3 H), 3.21 – 2.83 (m, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ= 154.57 (s, C_q), 153.58 (s, C_q), 142.67 (s, C_q), 135.31 (s, C_q), 113.29 (s, CH), 109.27 (s, CH), 108.36 (s, CH), 107.59 (s, CH_2), 83.70 (s, CH_2), 56.06 (s, CH_3), 45.24 (s, CH_2), 43.61 (s, C_q). IR (cm^{-1}): 1487, 1466, 1201, 1176, 1039, 1024, 974, 880, 802. HR-MS (+APCI) m/z calcd for $C_{13}H_{15}O_2$ $[M+H]^+$ 203.1067, found 203.1062.

Compound 2h Prepared according to the procedure **C** from compound **1j** on a 0.3 mmol scale



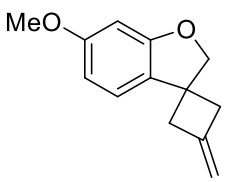
to afford the compound **2f** as a orange oil in 65% yield (55 mg, 0.2 mmol)**.** Rf (*n*-hexane) = 0.28. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.22 (d, *J* = 2.1 Hz, 1 H), 7.14 (d, *J* = 2.1 Hz, 1 H), 4.95 – 4.92 (m, 2 H), 4.55 (s, 2 H), 3.17 – 3.03 (m, 2 H), 3.00 – 2.87 (m, 2 H), 1.36 (s, 9 H), 1.32 (s, 9 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 155.35 (s, C_q), 143.49 (s, C_q), 143.47 (s, C_q), 134.01 (s, C_q), 131.90 (s, C_q), 122.32 (s, CH), 116.49 (s, CH), 107.29 (s, CH_2), 83.34 (s, CH_2), 45.62 (s, CH_2), 43.07 (s, C_q), 34.60 (s, C_q), 34.28 (s, C_q), 31.83 (s, CH_3), 29.40 (s, CH_3). IR (cm^{-1}): 1480, 1411, 1361, 1271, 1246, 1155, 980, 875, 818, 761. HR-MS (+APCI) m/z calcd for $C_{20}H_{29}O$ $[M+H]^+$ 285.2213, found 285.2199.

Compound 2i Prepared according to the procedure **C** from compound **1k** on a 1 mmol scale to



afford the compound **2i** as a colorless oil in 68% yield (129 mg, 0.68 mmol)**.** Rf (*n*-hexane) = 0.32. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.30 – 7.19 (m, 1 H), 6.65 – 6.55 (m, 1 H), 6.49 (dt, *J* = 9.5, 1.7 Hz, 1 H), 4.94 (m, 2 H), 4.60 (s, 2 H), 3.09 – 2.90 (m, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.27 (d, *J* = 243.3 Hz, C_q), 160.60 (d, *J* = 13.0 Hz, C_q), 142.4 (s, C_q), 130.10 (d, *J* = 2.5 Hz, C_q), 122.46 (d, *J* = 10.7 Hz, CH), 107.67 (s, CH_2), 107.45 (d, *J* = 23.0 Hz, CH), 97.76 (d, *J* = 26.5 Hz, CH), 84.61 (s, CH_2), 45.63 (s, CH_2), 42.61(s, C_q). ^{19}F NMR (188 MHz, $CDCl_3$) δ = -114.38 (s). IR (cm^{-1}): 1611, 1493, 1438, 1331, 1263, 1129, 1092, 980, 883, 838, 796, 736. HR-MS (+APCI) m/z calcd for $C_{12}H_{12}FO$ $[M+H]^+$ 191.0867, found 191.0872.

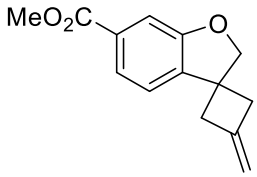
Compound 2j Prepared according to the procedure **C** from compound **1l** on a 0.3 mmol scale



to afford the compound **2j** as a light yellow oil in 72% yield (44 mg, 0.22 mmol). Rf (*n*-hexane/EtOAc, 20:1) = 0.49. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.22 (d, *J* = 8.3 Hz, 1 H), 6.47 (dd, *J* = 8.2, 2.3 Hz, 1 H), 6.37 (d, *J* = 2.3 Hz, 1 H), 4.94 – 4.91 (m, 2 H), 4.57 (s, 2 H), 3.77 (s, 3 H), 3.08 – 2.99 (m, 2 H), 2.99 – 2.90 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 160.79 (s, C_q), 160.58 (s, C_q), 142.97 (s,

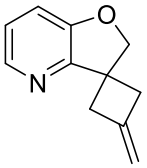
C_q), 126.53 (s, C_q), 122.33 (s, CH), 107.34 (s, CH_2), 106.54 (s, CH), 95.86 (s, CH), 84.44 (s, CH_2), 55.51 (s, CH_3), 45.64 (s, CH_2), 42.72 (s, C_q). IR (cm^{-1}): 1619, 1596, 1496, 1446, 1338, 1191, 1142, 1116, 1040, 979, 877, 823, 735. HR-MS (+APCI) m/z calcd for $C_{13}H_{15}O_2$ $[M+H]^+$ 203.1067, found 203.1068.

Compound 2k Prepared according to the procedure **C** from compound **1m** on a 1 mmol scale



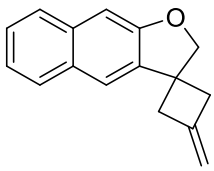
to afford the compound **2k** as a light yellow solid in 71% yield (164 mg, 0.71 mmol)**.** Rf (*n*-hexane/EtOAc, 20:1) = 0.34. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.64 (dd, *J* = 7.8, 1.4 Hz, 1 H), 7.42 – 7.36 (m, 2 H), 4.98 – 4.96 (m, 2 H), 4.61 (s, 2 H), 3.89 (s, 3 H), 3.12 – 2.96 (m, 4 H).^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.80 (s, C_q), 159.53 (s, C_q), 141.99 (s, C_q), 139.85 (s, C_q), 130.51 (s, C_q), 122.97 (s, CH), 121.82 (s, CH), 110.16 (s, CH), 107.94 (s, CH_2), 83.68 (s, CH_2), 52.07 (s, CH_3), 45.39 (s, CH_2), 43.03 (s, C_q). IR (cm^{-1}): 1715, 1590, 1435, 1280, 1249, 1208, 1081, 988, 881, 763, 733, 702. HR-MS (+APCI) m/z calcd for $C_{14}H_{15}O_3$ $[M+H]^+$ 231.1016, found 231.1008.

Compound 2l Prepared according to the procedure **C** from compound **1n** on a 1 mmol scale to



afford the compound **2l** as a light yellow oil in 78% yield (135 mg, 0.78 mmol)**.** Rf (*n*-hexane/EtOAc, 20:1) = 0.21. ^{1}H NMR (200 MHz, $CDCl_3$) δ = 8.15 (dd, *J* = 3.8, 2.4 Hz, 1 H), 7.05 – 7.00 (m, 2 H), 4.98 – 4.93 (m, 2 H), 4.68 (s, 2 H), 3.43 – 3.22 (m, 2 H), 3.04 – 2.80 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 154.85 (s, C_q), 153.00 (s, C_q), 142.29 (s, C_q), 141.76 (s, CH), 122.45 (s, CH), 115.54 (s, CH), 107.82 (s, CH_2), 83.34 (s, CH_2), 43.81 (s, CH_2), 42.40 (s, C_q). IR (cm^{-1}): 1603, 1576, 1426, 1271, 1159, 1106, 951, 877, 791, 763, 688. HR-MS (+ESI) m/z calcd for $C_{11}H_{12}NO$ $[M+H]^+$ 174.0913, found 174.0911.

Compound 2m. Prepared according to the procedure **C** from compound **1o** on a 0.33 mmol

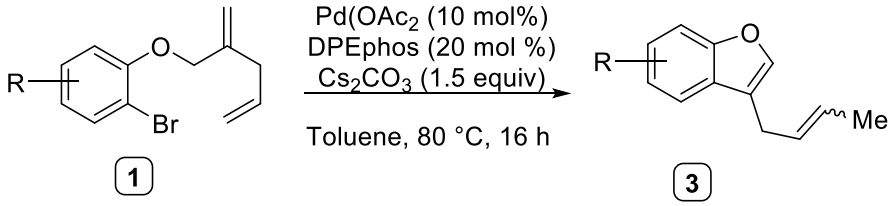


scale to afford the compound **2m** as a light yellow oil in 57% yield (41 mg, 0.18 mmol)**.** Rf (*n*-hexane) = 0.20. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.80 – 7.72 (m, 2 H), 7.69 – 7.66 (m, 1 H), 7.38 – 7.34 (m, 1 H), 7.30 – 7.26 (m, 1 H), 7.08 (s, 1 H), 5.01 – 4.99 (m, 2 H), 4.62 (s, 2 H), 3.19 – 3.11 (m, 2 H), 3.11 – 3.01 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.37 (s, C_q), 142.52 (s, C_q), 137.44 (s, C_q), 134.60 (s, C_q), 129.85 (s, C_q), 127.74 (s, CH), 126.80 (s, CH), 125.82 (s, CH), 123.27 (s, CH), 120.84 (s, CH), 107.88 (s, CH_2), 103.62 (s, CH), 83.67 (s, CH_2), 45.68 (s, CH_2), 42.70 (s, C_q). IR

(cm^{-1}): 1636, 1470, 1449, 1402, 1238, 1145, 1105, 1007, 962, 881, 865, 838, 745. HR-MS (+APCI) m/z calcd for $C_{16}H_{15}O$ $[M+H]^+$ 223.1117, found 223.1117.

Compound 2n. Prepared according to the procedure **C** (heating the reaction mixture at 105 ºC) from compound **1p** on a 0.5 mmol scale to afford the compound **2n** as a colorless oil in 56% yield (62 mg, 0.28 mmol)**.** Rf (*n*-hexane) = 0.30. ^{1}H NMR data for the (400 MHz, $CDCl_3$) δ = 7.98 – 7.95 (m, 1 H), 7.84 – 7.82 (m, 1 H), 7.52–7.43 (m, 4 H), 5.00 – 4.98 (m, 2 H), 4.80 (s, 2 H), 3.19 – 3.14 (m, 2 H), 3.07 – 3.03 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 154.75 (s, C_q), 143.0 (s, C_q), 134.16 (s, C_q), 127.88 (s, CH), 127.02 (s, C_q), 125.80 (s, CH), 125.45 (s, CH), 121.42 (s, CH), 120.91 (s, CH), 120.40 (s, C_q), 120.12 (s, CH), 107.49 (s, CH_2), 84.32 (s, CH_2), 45.67 (s, CH_2), 44.14 (s, C_q). IR (cm^{-1}): 1575, 1517, 1468, 1439, 1399, 1376, 1259, 1062, 957, 876, 803, 746. HR-MS (+APCI) m/z calcd for $C_{16}H_{15}O$ $[M+H]^+$ 223.1117, found 223.1114.

General procedure D for synthesis of compounds 3a-k.



Procedure **D.** A solution of the corresponding compounds **1a-m** (0.5 mmol) in dry toluene (4 mL) under N_2 atmosphere was added to a mixture of $Pd(OAc)_2$ (11 mg, 10 mol%), DPEphos (54 mg, 20 mol%) and Cs_2CO_3 (245 mg, 1.5 equiv) in a Schlenk tube under N_2 atmosphere. The reaction mixture was stirred at 80 °C for 16 hours. The resulting suspension was filtered through a Celite pad. The filtrate was evaporated to dryness and the crude was directly subjected to flash column chromatography using n-hexane/ethyl acetate as eluent to afford the pure products **3a-k**.

Compound 3a. Prepared according to the procedure **D** from compound **1a** on a 0.2 mmol scale (0.1 M solution) to afford the compound **3a** as a colorless oil in 66% yield (22 mg, 0.13 mmol)**.** Rf (*n*-hexane) = 0.30. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.54 – 7.51 (m, 1 H), 7.46 – 7.43 (m, 1 H), 7.38 (t, *J* = 1.2, 1 H), 7.30 – 7.19 (m, 2 H), 5.66 – 5.62 (m, 2 H), 3.43 – 3.40 (m, 2 H), 1.76 – 1.74 (m, 3 H). ^{13}C NMR (75

MHz, $CDCl_3$) δ = 155.49 (s, C_q), 141.23 (s, CH), 128.15 (s, C_q), 127.02 (s, CH), 125.65 (s, CH), 124.12 (s, CH), 122.20 (s, CH), 119.61 (s, CH), 119.39 (s, C_q), 111.39 (s, CH), 21.41 (s, CH_2), 12.81 (s, CH_3). IR (cm^{-1}): 1611, 1482, 1465, 1455, 1233, 1094, 1070, 749. HR-MS (+APCI) m/z calcd for $C_{12}H_{12}O$ $[M]^+$ 172.0882, found 172.0814.

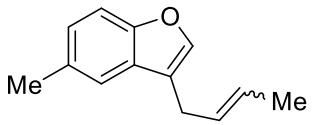
Compound 3b. Prepared according to the procedure **D** from compound **1d** on a 0.33 mmol scale to afford the compound **3b** as a light yellow oil in 53% yield (33 mg, 0.17 mmol)**.** Rf (*n*-hexane) = 0.51. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.42 (t, *J* = 1.3 Hz, 1 H), 7.37 (ddd, *J* = 8.9, 4.1, 0.5 Hz, 1 H), 7.17 (ddd, *J* = 8.6, 2.7, 0.5 Hz, 1 H), 6.99 (tdd, *J* = 9.1, 2.7, 0.5 Hz, 1 H), 5.73 – 5.55 (m, 2 H), 3.42 – 3.35 (m, 2 H), 1.79 – 1.74 (m, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 159.08 (d, *J* = 242.9 Hz, C_q), 151.68 (s, C_q), 143.03 (s, CH), 126.57 (s, CH), 128.96 (d, *J* = 10.2 Hz, C_q), 125.99 (s, CH), 119.68 (d, *J* = 3.9 Hz, C_q), 112.017 (d, *J* = 4.9 Hz, CH), 111.78 (d, *J* = 21.7 Hz, CH),105.25 (d, *J* = 24.8 Hz, CH), 21.36 (s, CH_2), 12.84 (s, CH_3). ^{19}F NMR (282 MHz, $CDCl_3$) δ = -121.49 (s). IR (cm^{-1}): 1480, 1449, 1264, 1162, 814, 733, 704. HR-MS (+APCI) m/z calcd for $C_{12}H_{12}FO$ $[M+H]^+$ 191.0867, found 191.0872.

Compound 3c. Prepared according to the procedure **D** from compound **1e** on a 0.5 mmol scale to afford the compound **3c** as a colorless oil in 62% yield (64 mg, 0.31 mmol)**.** Rf (*n*-hexane) = 0.50. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.49 (dd, *J* = 2.1, 0.6 Hz, 1 H), 7.40 (t, *J* = 1.3 Hz, 1 H), 7.36 (dd, *J* = 8.7, 0.6 Hz, 1 H), 7.26 – 7.20 (m, 1 H), 5.73 – 5.54 (m, 2 H), 3.41 – 3.35 (m, 2 H), 1.78 – 1.73 (m, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 153.83 (s, C_q), 142.63 (s, CH), 129.52 (s, C_q), 127.86 (s, C_q), 126.45 (s, CH), 126.10 (s, C_q), 124.33 (s, CH), 119.37 (s, CH), 119.21 (s, CH), 112.38 (s, CH), 21.26 (s, CH_2), 12.87 (s, CH_3). IR (cm^{-1}): 1469, 1450, 1263, 1185, 1086, 800, 734, 700. HR-MS (+APCI) m/z calcd for $C_{12}H_{12}ClO$ $[M+H]^+$ 207.0571, found 207.0504.

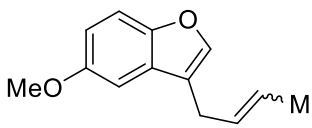
Compound 3d. Prepared according to the procedure **D** from compound **1f** on a 0.5 mmol scale to afford the compound **3d** as a light yellow oil in 57% yield (56 mg, 0.28 mmol)**.** Rf (*n*-hexane/EtOAc, 20:1) = 0.38. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.88 (dd, *J* = 1.6, 0.8 Hz, 1 H), 7.61 – 7.50 (m, 3 H), 5.78 – 5.54 (m, 2 H), 3.43 (m, 2 H), 1.77 (m, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 157.16 (s, C_q), 143.38 (s, CH), 128.86 (s, C_q), 127.89 (s, CH), 126.61 (s, CH), 125.94 (s, CH), 124.99 (s, CH), 119.60 (s, C_q), 112.60 (s, CH), 106.15 (s, C_q), 30.95 (s, C_q), 21.14 (s, CH_2),

12.91 (s, CH_3). IR (cm^{-1}): 2228, 1613, 1483, 1465, 1293, 1247, 1082, 900, 821, 733. HR-MS (+APCI) m/z calcd for $C_{13}H_{12}NO$ $[M+H]^+$ 198.0913, found 198.0906.

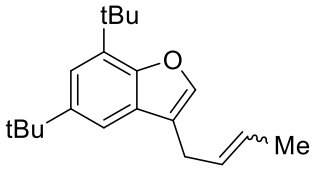
Compound 3e. Prepared according to the procedure **D** from compound **1h** on a 2 mmol scale to afford the compound **3e** as a color less oil in 76% yield (283 mg, 1.52 mmol)**.** Rf (*n*-hexane) = 0.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.36 – 7.34 (m, 1 H), 7.33 – 7.30 (m, 2 H), 7.09 (dd, *J* = 8.4, 1.8 Hz, 1 H), 5.72 – 5.57 (m, 2 H), 3.39 (m, 2 H), 2.45 (s, 3 H), 1.81 – 1.72 (m, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 153.84 (s, C_q), 141.36 (s, CH), 131.62 (s, C_q), 128.16 (s, C_q), 127.07 (s, CH), 125.59 (s, CH), 125.35 (s, CH), 119.40 (s, C_q), 119.08 (s, CH), 110.88 (s, CH), 21.41 (s, CH_2), 21.39 (s, CH_3), 12.86 (s, CH_3). IR (cm^{-1}): 1621, 1486, 1369, 1265, 1228, 1217, 1206, 813, 755, 703. HR-MS (+APCI) m/z calcd for $C_{13}H_{15}O$ $[M+H]^+$ 187.1117, found 187.1125.



Compound 3f. Prepared according to the procedure **D** from compound **1i** on a 0.2 mmol scale to afford the compound **3f** as a yellow oil in 66% yield (27 mg, 0.13 mmol)**.** Rf (*n*-hexane/EtOAc, 20:1) = 0.58. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.39 – 7.35 (m, 1 H), 7.33 (d, *J* = 0.5 Hz, 1 H), 6.97 (d, *J* = 2.6 Hz, 1 H), 6.89 (ddd, *J* = 8.9, 2.7, 0.5 Hz, 1 H), 5.74 – 5.56 (m, 2 H), 3.85 (s, 3 H), 3.43 – 3.36 (m, 2 H), 1.77 (m, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 155.62 (s, C_q), 150.42 (s, C_q), 142.13 (s, CH), 128.63 (s, C_q), 126.92 (s, CH), 125.67 (s, CH), 119.40 (s, C_q), 112.68 (s, CH), 111.81 (s, CH), 102.21 (s, CH), 55.92 (s, CH_3), 21.45 (s, CH_2), 12.86 (s, CH_3). IR (cm^{-1}): 1625, 1485, 1430, 1290, 1219, 1080, 1024, 933, 789, 734. HR-MS (+APCI) m/z calcd for $C_{13}H_{15}O_2$ $[M+H]^+$ 203.1067, found 203.1072.

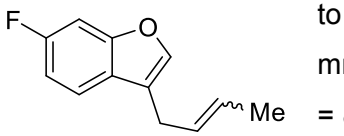


Compound 3g. Prepared according to the procedure **D** from compound **1j** on a 0.3 mmol scale to afford the compound **3g** as a light yellow oil in 58% yield (49 mg, 0.17 mmol)**.** Rf (*n*-hexane) = 0.41. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.38 – 7.35 (m, 2 H), 7.27 – 7.24 (m, 1 H), 5.72 – 5.57 (m, 2 H), 3.43 – 3.38 (m, 2 H), 1.77 (m, 3 H), 1.49 (s, 9 H), 1.38 (s, 9 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 152.00 (s, C_q), 145.04 (s, C_q), 140.46 (s, CH), 134.04 (s, C_q), 128.08 (s, C_q), 127.33 (s, CH), 125.35 (s, CH), 119.08 (s, C_q), 118.83 (s, CH), 113.35 (s, CH), 34.88 (s, C_q), 34.45 (s, C_q), 31.95 (s, CH_3), 29.92 (s, CH_3), 21.50 (s, CH_2), 12.83

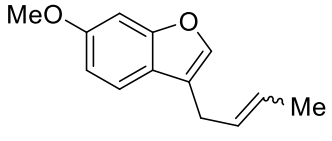


(s, CH_3). IR (cm^{-1}): 1481, 1460, 1363, 1264, 1242, 1174, 1081, 866, 735. HR-MS (+APCI) m/z calcd for $C_{20}H_{29}O$ $[M+H]^+$ 285.2213, found 285.2208.

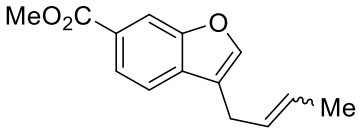
Compound 3h. Prepared according to the procedure **D** from compound **1k** on a 0.5 mmol scale to afford the compound **3h** as a colorless oil in 57% yield (54 mg, 0.28 mmol)**.** Rf (*n*-hexane) = 0.49. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.43 (dd, *J* = 8.5, 5.4 Hz, 1 H), 7.38 (t, *J* = 1.3 Hz, 1 H), 7.17 (dd, *J* = 9.1, 2.3, 1 H), 7.02 – 6.96 (m, 1 H), 5.70 – 5.58 (m, 2 H), 3.41 – 3.38 (m, 2 H), 1.77 – 1.74 (m, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 156.51 (d, *J* = 242.9 Hz, C_q), 150.78 (s, C_q), 142.13 (s, CH), 128.14 (s, CH), 125.68 (d, *J* = 10.2 Hz, C_q), 125.99 (s, CH), 119.68 (d, *J* = 3.9 Hz, C_q), 111.05 (d, *J* = 4.9 Hz, CH), 110.88 (d, *J* = 21.7 Hz, CH), 104.22 (d, *J* = 24.8 Hz, CH), 20.46 (s, CH_2), 11.94 (s, CH_3). IR (cm^{-1}): 1605, 1491, 1436, 1278, 1263, 1234, 1133, 1039, 963, 833, 736. HR-MS (+APCI) m/z calcd for $C_{12}H_{12}FO$ $[M+H]^+$ 191.0867, found 191.0870.



Compound 3i. Prepared according to the procedure **D** from compound **1l** on a 0.35 mmol scale to afford the compound **3i** as a yellow oil in 60% yield (42 mg, 0.21 mmol)**.** Rf(*n*-hexane/EtOAc, 20:1) = 0.60. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.39 (d, *J* = 8.4 Hz, 1 H), 7.30 (s, 1 H), 6.99 (d, *J* = 2.3 Hz, 1 H), 6.87 (dd, *J* = 8.5, 2.2 Hz, 1 H), 5.71 – 5.55 (m, 2 H), 3.85 (s, 3 H), 3.43 – 3.35 (m, 2 H), 1.76 (m, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 157.92 (s, C_q), 156.40 (s, C_q), 140.30 (s, CH), 127.07 (s, CH), 125.56 (s, CH), 121.52 (s, C_q), 119.69 (s, CH), 119.23 (s, C_q), 111.23 (s, CH), 95.96 (s, CH), 55.70 (s, CH_3), 21.44 (s, CH_2), 12.85 (s, CH_3). IR (cm^{-1}): 1627, 1491, 1439, 1288, 1219, 1141, 1080, 1024, 933, 802, 735. HR-MS (+APCI) m/z calcd for $C_{13}H_{15}O_2$ $[M+H]^+$ 203.1067, found 203.1068.

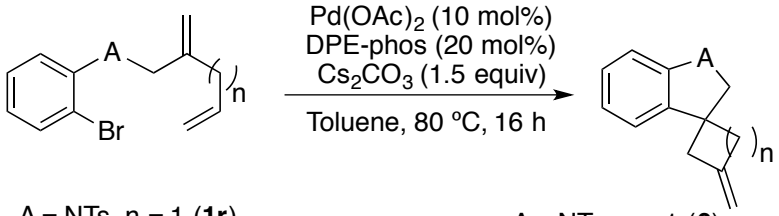


Compound 3j. Prepared according to the procedure **D** from compound **1m** on a 1 mmol scale to afford the compound **3j** as a light yellow oil in 61% yield (140 mg, 0.61 mmol)**.** Rf(*n*-hexane/EtOAc, 20:1) = 0.42. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.15 (dd, *J* = 1.4, 0.7 Hz, 1 H), 7.95 (dd, *J* = 8.2, 1.4 Hz, 1 H), 7.61 – 7.48 (m, 2 H), 5.76 – 5.54 (m, 2 H), 3.94 (s, 3 H), 3.48 – 3.38 (m, 2 H), 1.82 – 1.71 (m, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 167.32 (s, C_q), 154.88 (s, C_q), 144.24 (s, CH), 132.36 (s, C_q), 126.43 (s, CH), 126.17 (s, C_q), 126.11 (s, CH), 123.65 (s, CH), 119.71 (s, C_q), 119.27 (s, CH), 113.06 (s, CH), 52.16 (s, CH_3), 21.27 (s, CH_2), 12.87 (s, CH_3). IR (cm^{-1}): 1717,



1435, 1285, 1228, 1095, 980, 892, 759, 744. HR-MS (+APCI) m/z calcd for $C_{14}H_{15}O_3$ $[M+H]^+$ 231.1016, found 231.1006.

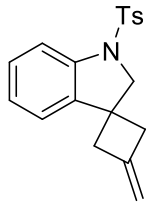
Synthesis of [4,5]-spirocycles 6 and 7.



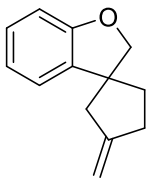
A = NTs, n = 1 (**1r**)
A = O, n = 2 (**1q**)

A = NTs, n = 1 (**6**)
A = O, n = 2 (**7**)

Compound 6. Prepared according to the procedure **D** from compound **1r** on a 0.2 mmol scale to afford the compound **6** as a colorless oil in 54% yield (35 mg, 0.10 mmol)**.** Rf (*n*-hexane/EtOAc, 20:1) = 0.25. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.70 – 7.59 (m, 3 H), 7.32 – 7.16 (m, 4 H), 7.05 (td, *J* = 7.5, 1.0 Hz, 1 H), 4.87 (m, 2 H), 3.94 (s, 2 H), 2.72 (m, 4 H), 2.36 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 144.03 (s, C_q), 142.02 (s, C_q), 141.18 (s, C_q), 139.01 (s, C_q), 133.82 (s, C_q), 129.55 (s, CH), 128.15 (s, CH), 127.25 (s, CH), 124.38 (s, CH), 122.14 (s, CH), 114.92 (s, CH), 107.75 (s, CH_2), 62.60 (s, CH_2), 45.35 (s, CH_2), 41.43 (s, C_q), 21.47 (s. CH_3). IR (cm^{-1}): 1595, 1474, 1456, 1353, 1248, 1163, 1093, 1033, 888, 819, 766, 681, 655. HR-MS (+ESI) m/z calcd for $C_{19}H_{20}NO_2S$ $[M+H]^+$ 326.1209, found 326.1211.

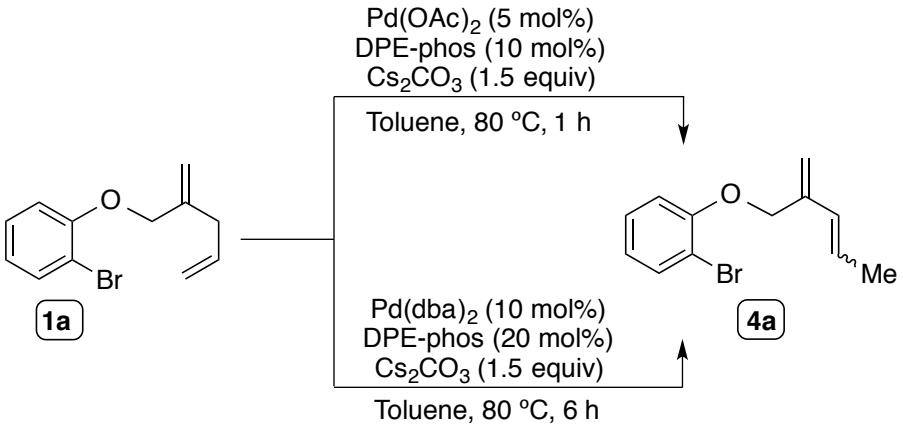


Compound 7. Prepared according to the procedure **D** from compound **1q** on a 0.4 mmol scale to afford the compound **7** as a light yellow oil in 76% yield (56 mg, 0.30 mmol)**.** Rf (*n*-hexane) = 0.20. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.13 (m, 2 H), 6.88 (td, *J* = 7.4, 1.0 Hz, 1 H), 6.80 (dd, *J* = 8.3, 1.0 Hz, 1 H), 4.96 (m, 2 H), 4.32 (s, 2 H), 2.71 – 2.52 (m, 2 H), 2.52 – 2.34 (m, 2 H), 2.13 – 1.89 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 159.73 (s, C_q), 149.92 (s, C_q), 133.75 (s, C_q), 128.17 (s, CH), 122.58 (s, CH), 120.62 (s, CH), 109.54 (s, CH), 107.09 (s, CH_2), 83.04 (s, CH_2), 52.51 (s, C_q), 46.12 (s, CH_2), 39.19 (s, CH_2), 31.34 (s, CH_2). IR (cm^{-1}): 1597, 1477, 1458, 1216, 1100, 1017, 963, 880, 831, 745. HR-MS (+APCI) m/z calcd for $C_{13}H_{15}O$ $[M+H]^+$ 187.1117, found 187.1117.



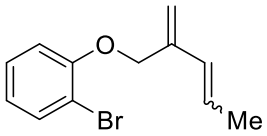
Isolation of intermediate 4a and mechanistic experiments

Isomerization of compound 1a to intermediate 4a.

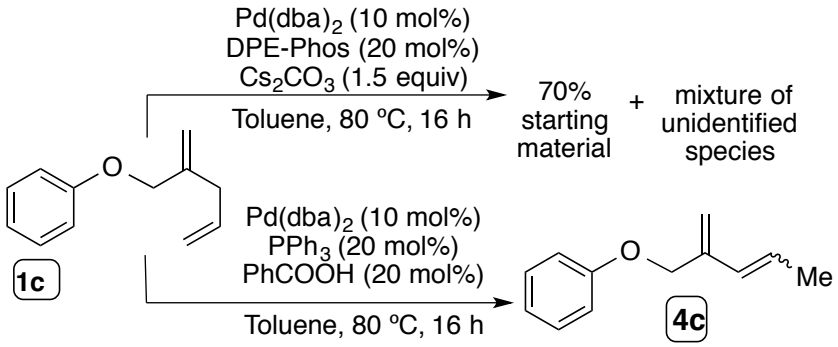


A solution of compound **1a** (50 mg, 0.2 mmol) in dry toluene (3 mL) under N_2 atmosphere was added to a mixture of $Pd(OAc)_2$ (2.2 mg, 5 mol%), DPE-Phos (11 mg, 10 mol%) and Cs_2CO_3 (98 mg, 1.5 equiv) in a Schlenk tube under N_2 atmosphere. The tube was sealed and the reaction mixture was stirred at 80 °C for 1 hour. The resulting suspension was filtered through a Celite pad. The filtrate was evaporated to dryness and the crude was directly subjected to flash column chromatography using n-hexane as eluent to afford the intermediate **4a** as a colorless oil in 59% isolated yield (28 mg, 0.11 mmol). The isomerization of the starting material **1a** also proceeded when using 10 mol% of $Pd(dba)_2$ instead of $Pd(OAc)_2$ as the catalyst, affording a 90% NMR yield.

Data for intermediate **4a:** Rf (*n*-hexane) = 0.47. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.99 (dd, *J* = 4.5, 1.7 Hz, 1 H), 7.20 (dd, *J* = 8.1, 4.5 Hz, 1 H), 7.13 (dd, *J* = 8.1, 1.7 Hz, 1 H), 6.19 – 6.10 (m, 2 H), 5.92 – 5.77 (m, 1 H), 5.27 (s, 1 H), 5.17 (dd, *J* = 1.5, 0.8 Hz, 1 H), 4.78 (s, 2 H), 1.83 - 1.80 (m, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 151.93 (s, C_q), 141.45 (s, CH), 139.44 (s, C_q), 133.17 (s, C_q), 130.13 (s, CH), 126.58 (s, CH), 123.22 (s, CH), 120.26 (s, CH), 115.37 (s, CH), 69.05 (s, CH_2), 18.57 (s, CH_3). IR (cm^{-1}): 1584, 1477, 1442, 1273, 1240, 1048, 1030, 742, 663. HR-MS (+APCI) m/z calcd for $C_{12}H_{14}BrO$ $[M+H]^+$ 253.0222, found 253.0227.



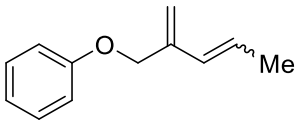
Isomerization of compound 1c to 1,3-diene 4c.



Isomerization via Pd(0). A solution of compound **1c** (35 mg, 0.2 mmol) in dry toluene (3 mL) under N_2 atmosphere was added to a mixture of $Pd(dba)_2$ (12 mg, 10 mol%), DPE-Phos (21 mg, 20 mol%) and Cs_2CO_3 (98 mg, 1.5 equiv) in a Schlenk tube under N_2 atmosphere. The tube was sealed and the reaction mixture was stirred at 80 °C for 16 hour. The resulting suspension was filtered through a Celite pad. The filtrate was evaporated to dryness. The ^{1}H-NMR spectrum of the crude mixture showed 70% of unreacted starting material plus a mixture of unidentified compounds.

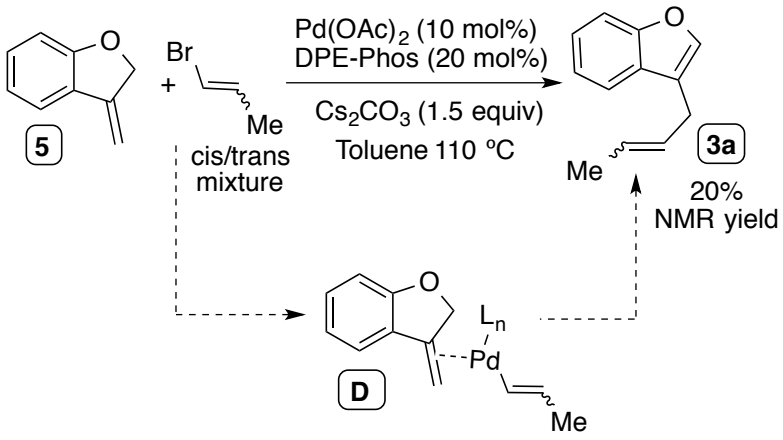
Isomerization via Pd–H generation. A solution of compound **1c** (52 mg, 0.3 mmol) in dry toluene (3 mL) under N_2 atmosphere was added to a mixture of $Pd(dba)_2$ (17 mg, 10 mol%), PPh_3 (16 mg, 20 mol%) and PhCOOH (7 mg, 20 mol%) in a Schlenk tube under N_2 atmosphere. The tube was sealed and the reaction mixture was stirred at 80 °C for 6 h. The resulting suspension was filtered through a Celite pad. The filtrate was evaporated to dryness. The 1H-NMR spectrum of the crude mixture nearly full conversion of the starting material into 1,3-diene **4c**. The crude mixture was subjected to flash column chromatography using n-hexane as eluent to afford the diene **4c** as a colorless oil in 57% isolated yield (30 mg, 0.17 mmol).

Data for 1,3-diene **4c:** Colorless oil. 57% yield (30 mg, 0.17 mmol). Rf (*n*-hexane) = 0.50. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.31 – 7.24 (m, 2 H), 7.00 – 6.90 (m, 3 H), 6.16 (dq, *J* = 15.9, 1.8 Hz, 2 H), 5.82 (dq, *J* = 16.0, 6.7 Hz, 1 H), 5.22 (s, 1 H), 5.13 (dd, *J* = 1.6, 0.8 Hz, 1 H), 4.66 (s, 1 H), 1.80 (dd, *J* = 6.7, 1.7 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.68 (s, C_q), 140.95 (s, C_q), 130.67 (s, CH),



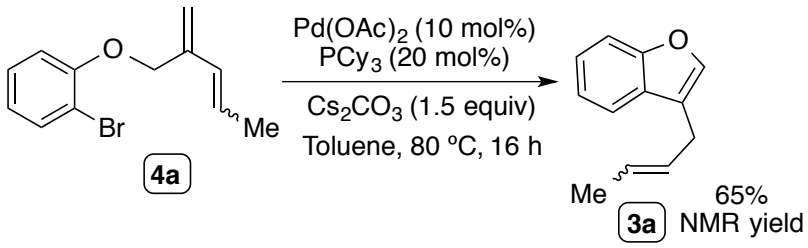
129.39 (s, CH), 126.28 (s, CH), 120.82 (s, CH), 115.29 (s, CH_2), 114.74 (s, CH), 68.13 (s, CH_2), 18.56 (s, CH_3). IR (cm^{-1}): 1598, 1493, 1235, 1170, 1031, 1011, 752, 690. HR-MS (+APCI) m/z calcd for $C_{12}H_{15}O$ $[M+H]^+$ 175.1117, found 175.1112.

Reaction of 3-methylene-2,3-dihydrobenzofuran with a mixture of cis-/trans-1-bromopropene.



A Schlenk tube was charged with $Pd(OAc)_2$ (10 mg, 0.044 mmol, 10 mol%), DPE-Phos (46 mg, 0.085 mmol, 20 mol%) and Cs_2CO_3 (210 mg, 0.65 mmol, 1.5 equiv) and 3-methylene-2,3-dihydrobenzofuran (57 mg, 0.432 mmol, 1 equiv) (prepared according to a previously reported procedure).[3] The tube was set under nitrogen atmosphere and dry toluene (3 mL) and cis-/trans-1-bromopropene (88 μL, 1 mmol, 2.4 equiv) were added. The tube was sealed and heated at 100 ºC for 16 h. The resulting suspension was filtered through a Celite pad. The filtrate was evaporated to dryness. The ^{1}H-NMR spectrum of the crude mixture showed 20% NMR yield of the benzofurane derivative **3a**.

Cyclization of intermediate 4a with catalytic amount of $Pd(OAc)_2$ and PCy_3.



A solution of compound **4a** (25 mg, 0.1 mmol, 1 equiv) in dry toluene (3 mL) under N_2 atmosphere was added to a mixture of $Pd(OAc)_2$ (2.5 mg, 10 mol%), PCy_3 (6 mg, 20 mol%) and Cs_2CO_3 (49 mg, 1.5 equiv) in a Schlenk tube under N_2 atmosphere. The tube was sealed and the reaction mixture was stirred at 80 °C for 16 hour. The resulting suspension was filtered through a Celite pad. The filtrate was evaporated to dryness. The ^{1}H-NMR spectrum of the crude mixture showed the formation of the benzofuran derivative **3a** in 65% NMR yield.

References

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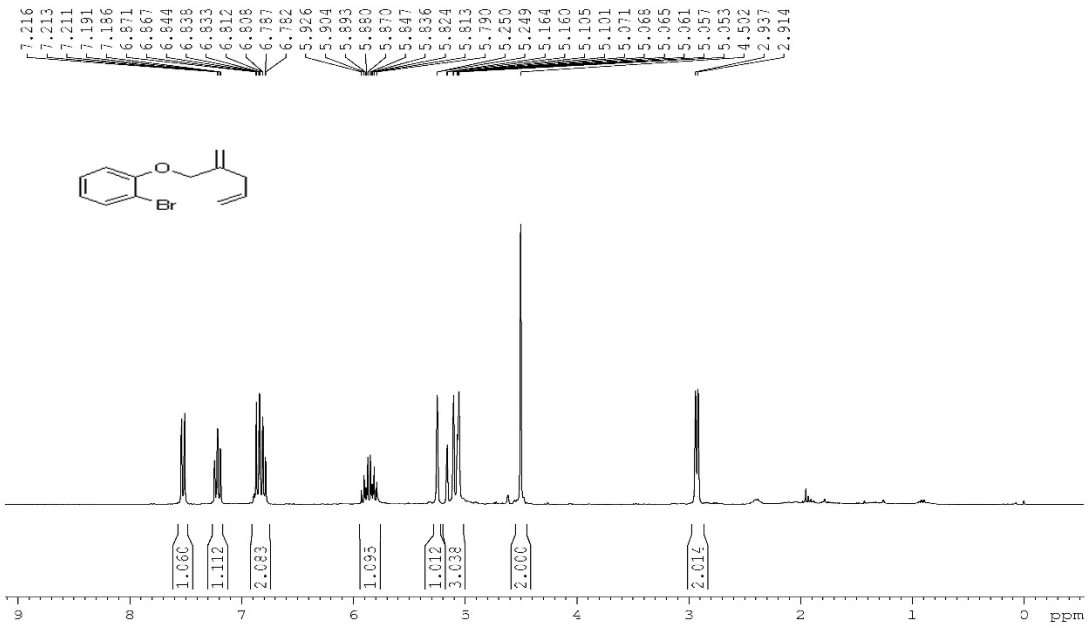
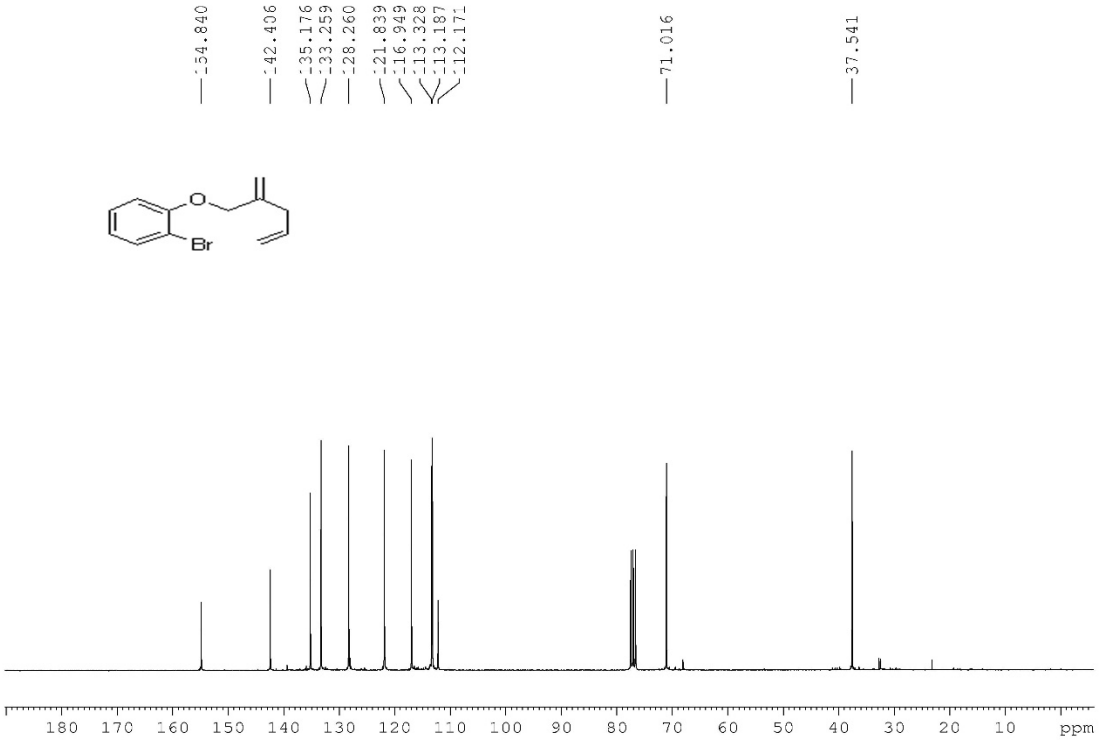
[2] (a) O. Mitsunobu, M. Yamada, *Bull. Chem. Soc. Jpn*. **1967,** *40*, 2380. (b) H. Zheng, Y. Zhu, Y. Shi, *Angew. Chem. Int. Ed.* **2014**, *53*, 11280 –11284. (c) J. Ye, Z. Shi, T. Sperger, Y. Yasukawa, C. Kingston, F. Schoenebeck, M. Lautens, *Nat. Chem.* **2017**, *9*, 361–368.

[3] T. W. Liwosz, S. R. Chemler, *Chem. Eur. J.* **2013**, *19*, 12771-12777.

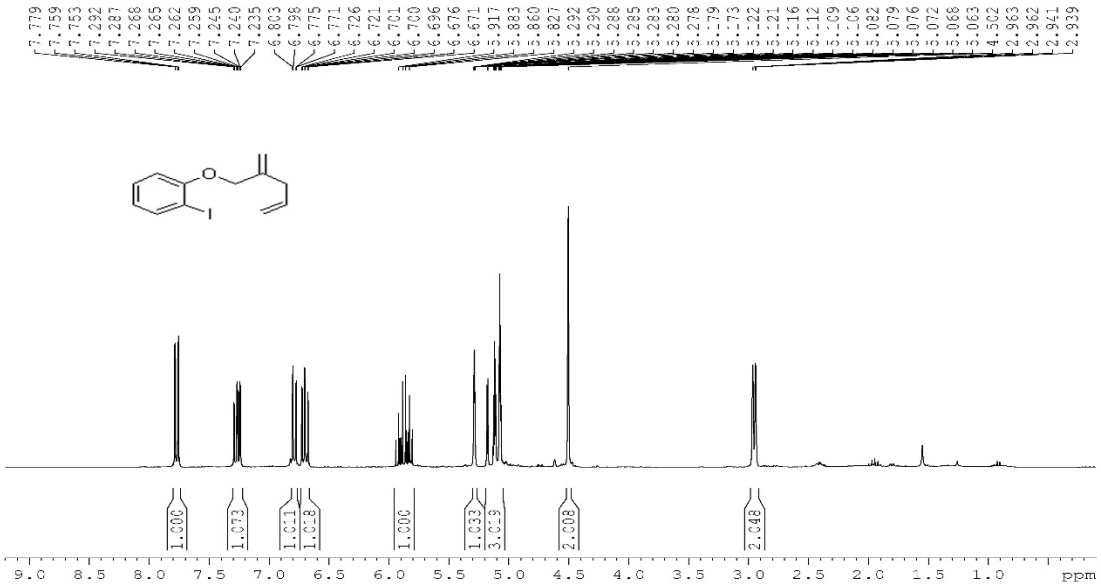
^{1}H NMR spectrum of compound **1a**



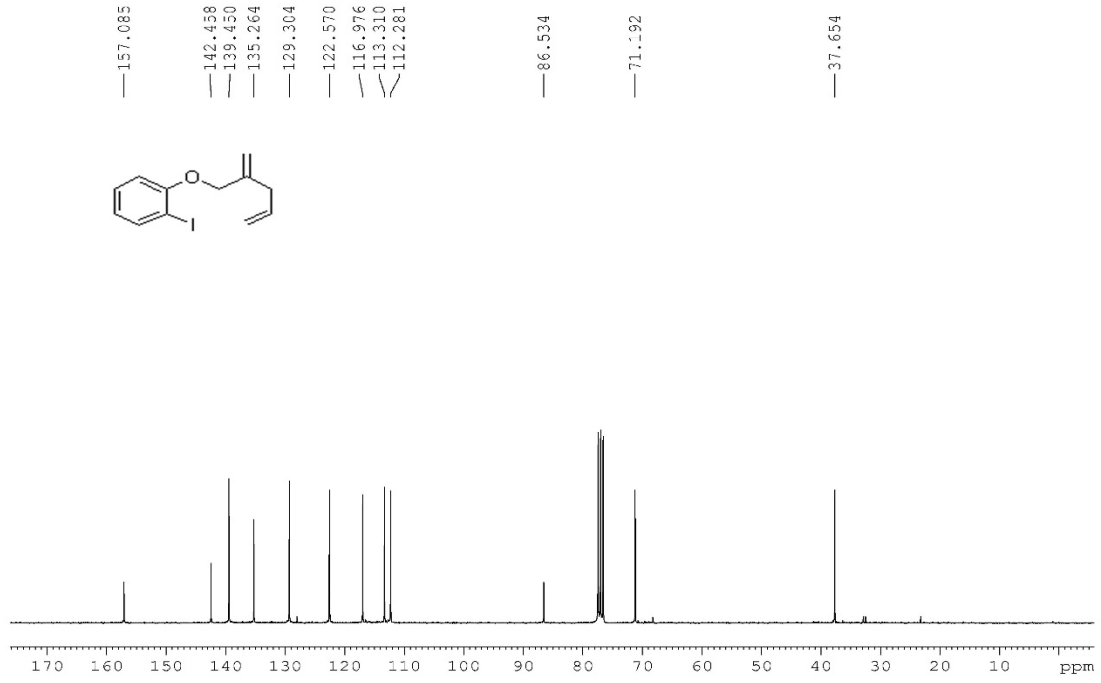
^{13}C NMR spectrum of compound **1a**



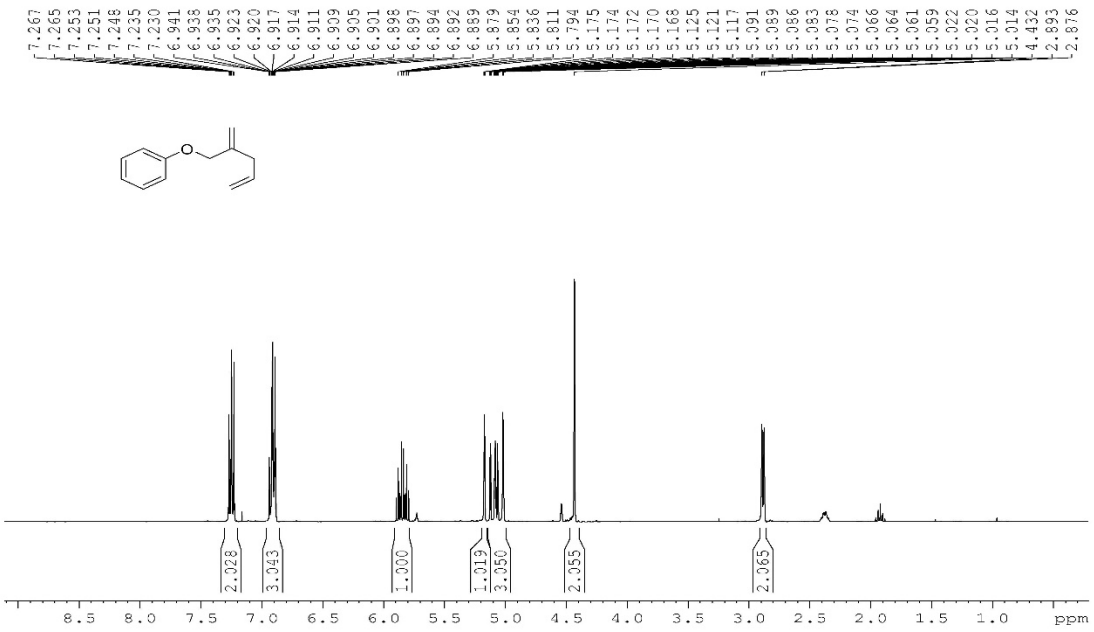
^{1}H NMR spectrum of compound **1b**



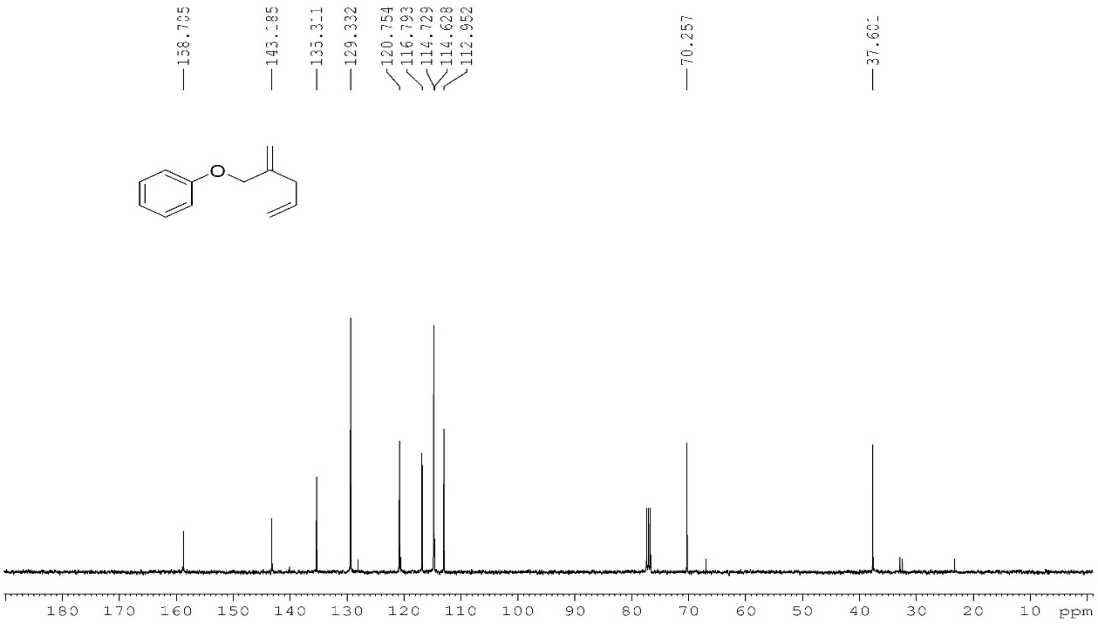
^{13}C NMR spectrum of compound **1b**



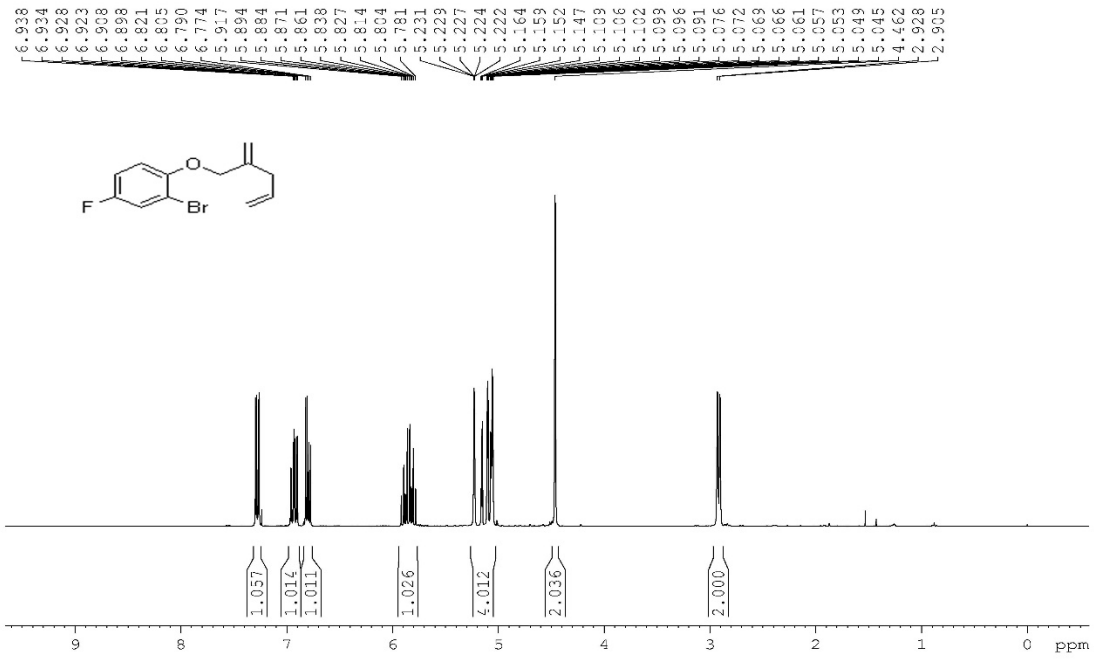
^{1}H NMR spectrum of compound **1c**



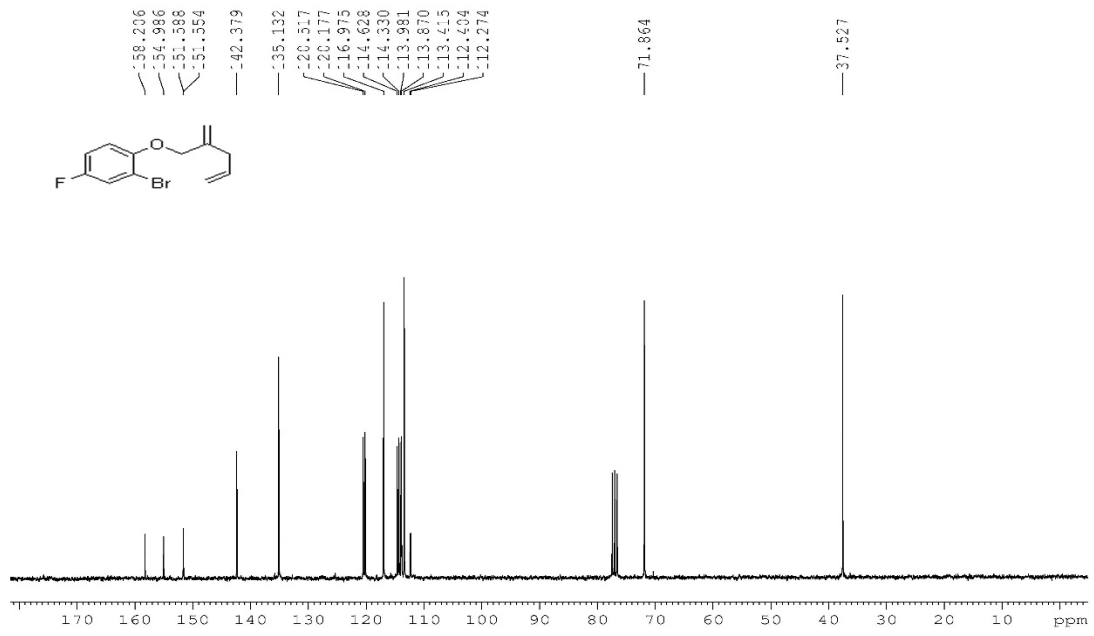
^{13}C NMR spectrum of compound **1c**



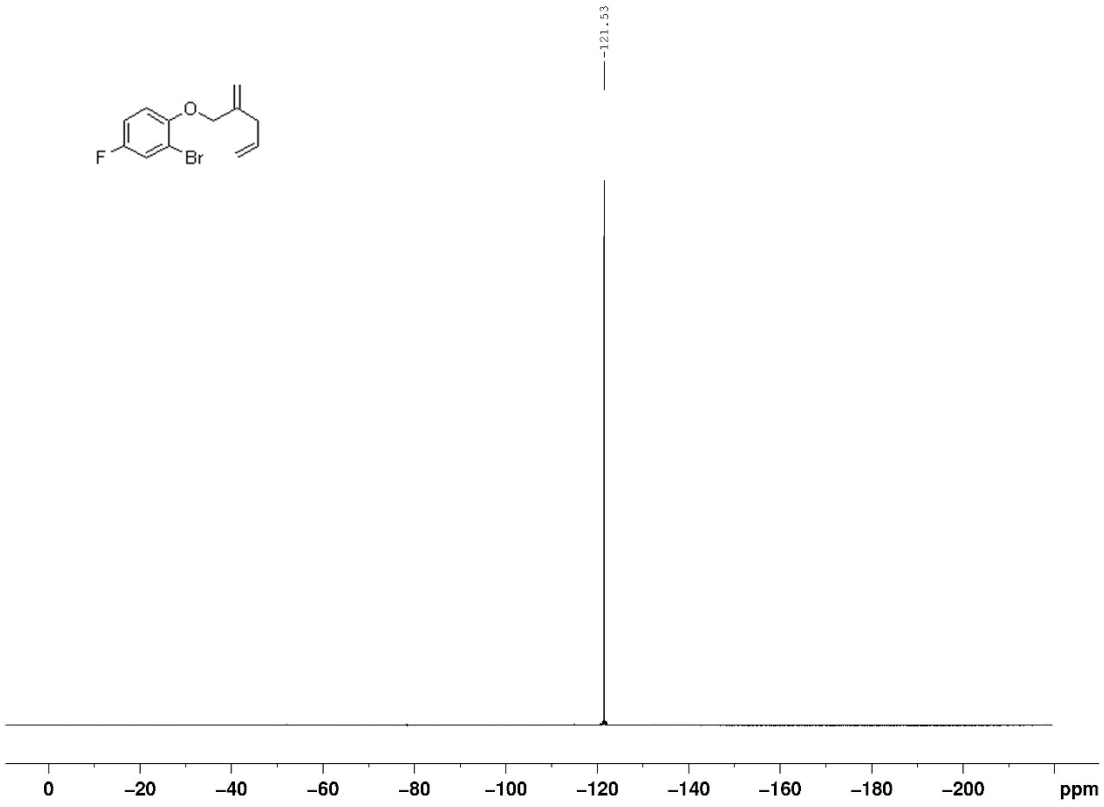
^{1}H NMR spectrum of compound **1d**



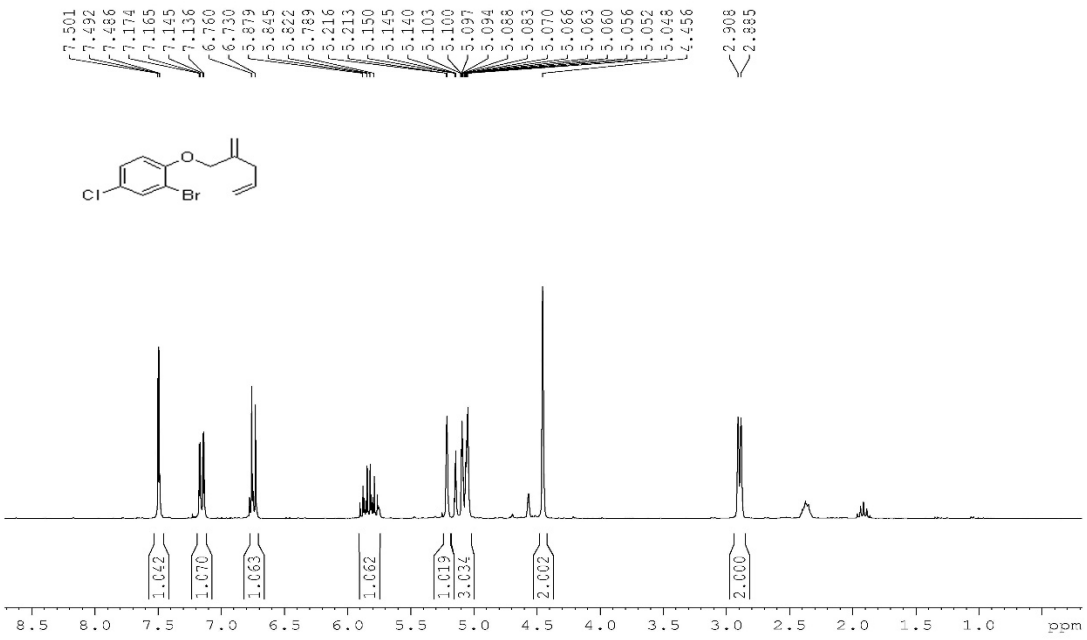
^{13}C NMR spectrum of compound **1d**



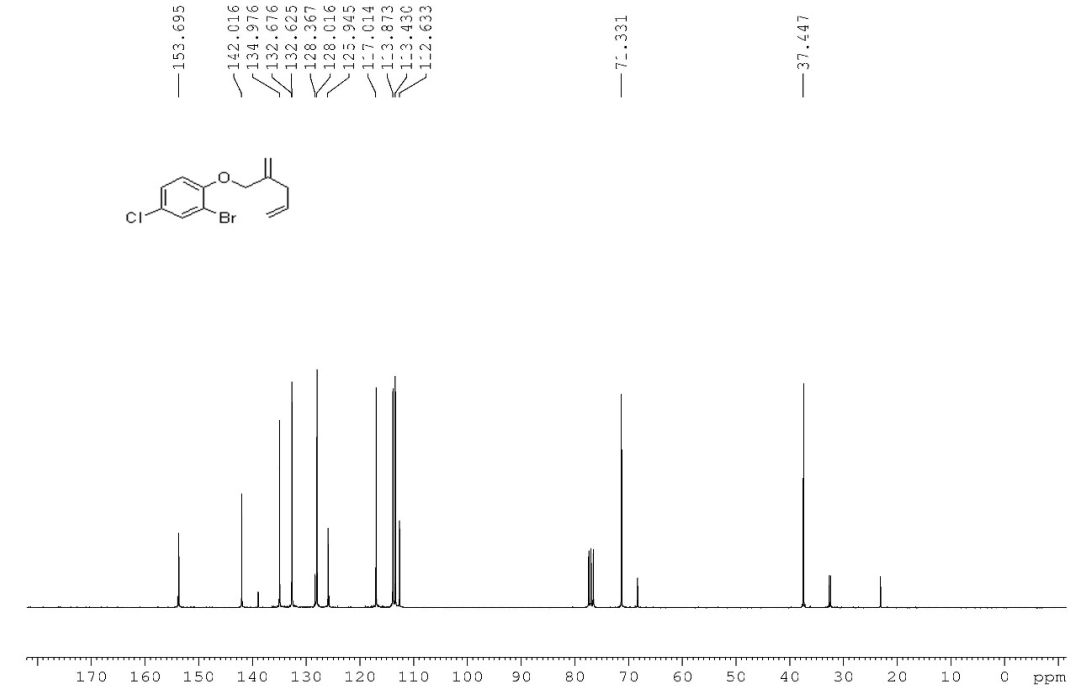
^{19}F NMR spectrum of compound **1d**



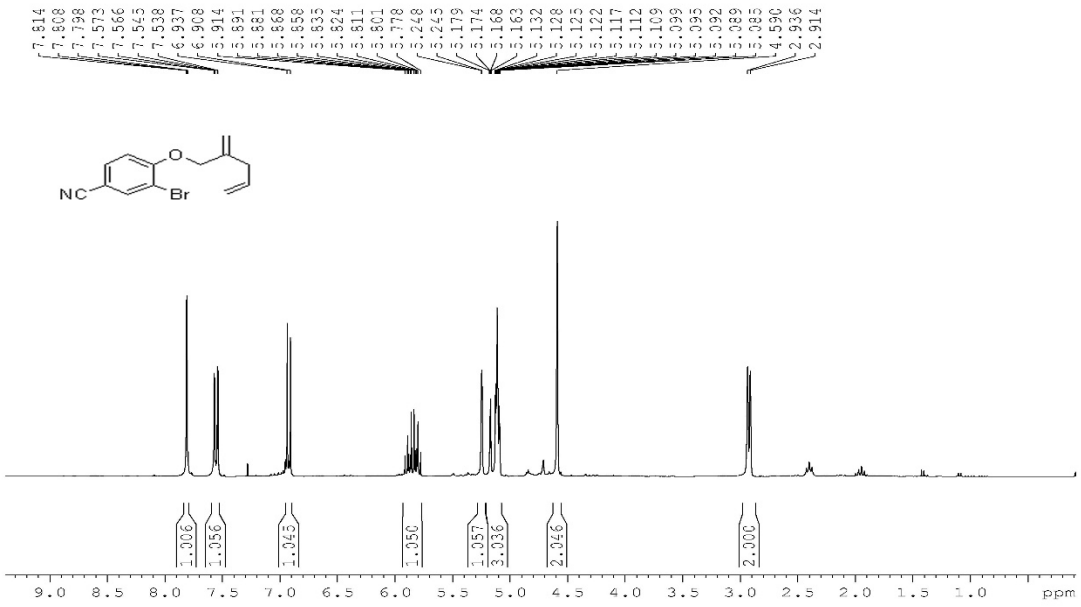
^{1}H NMR spectrum of compound **1e**



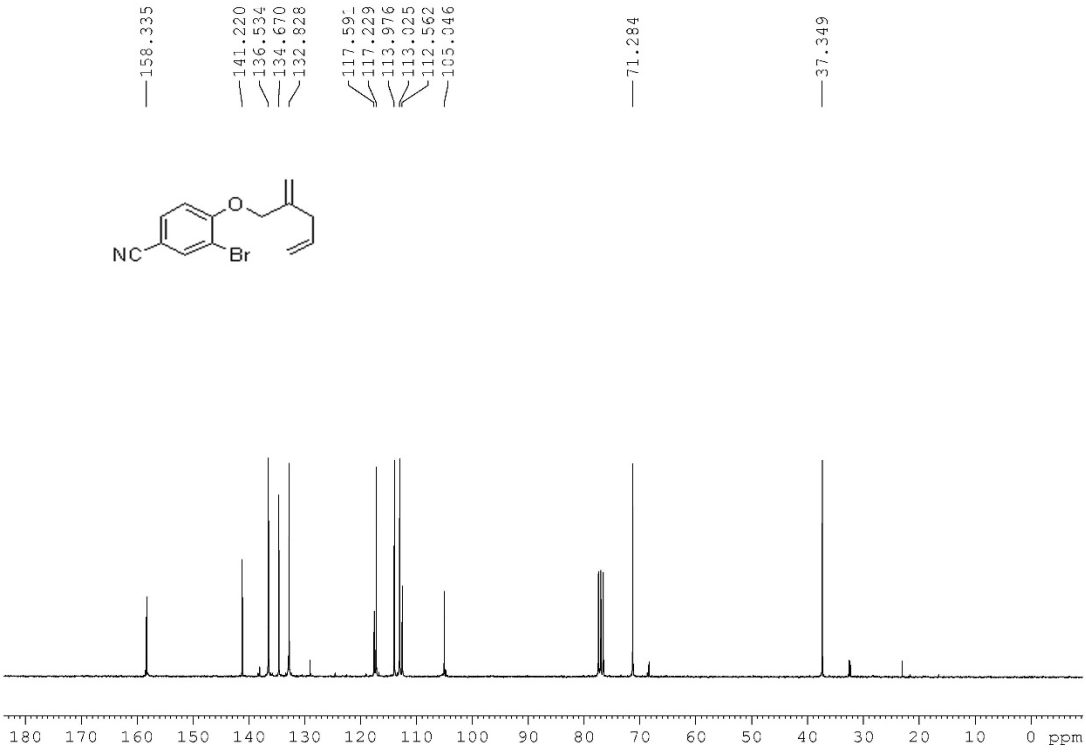
^{13}C NMR spectrum of compound **1e**



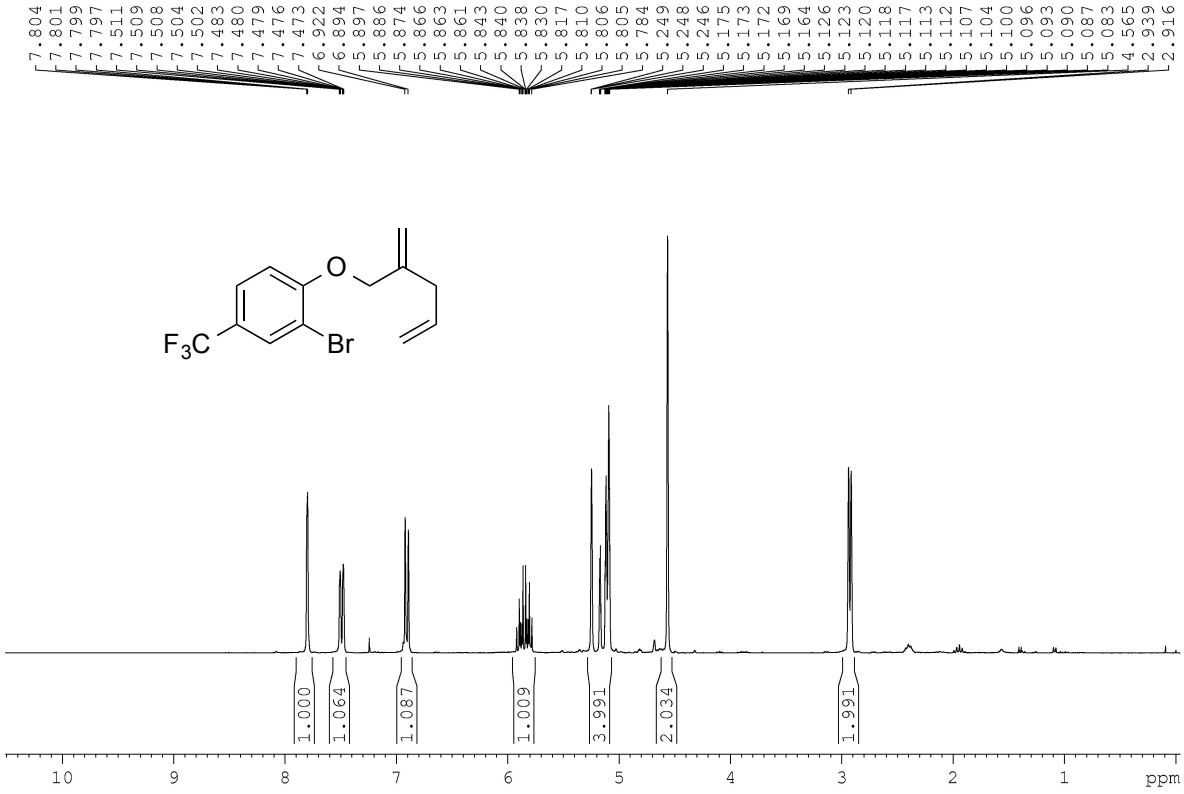
^{1}H NMR spectrum of compound **1f**



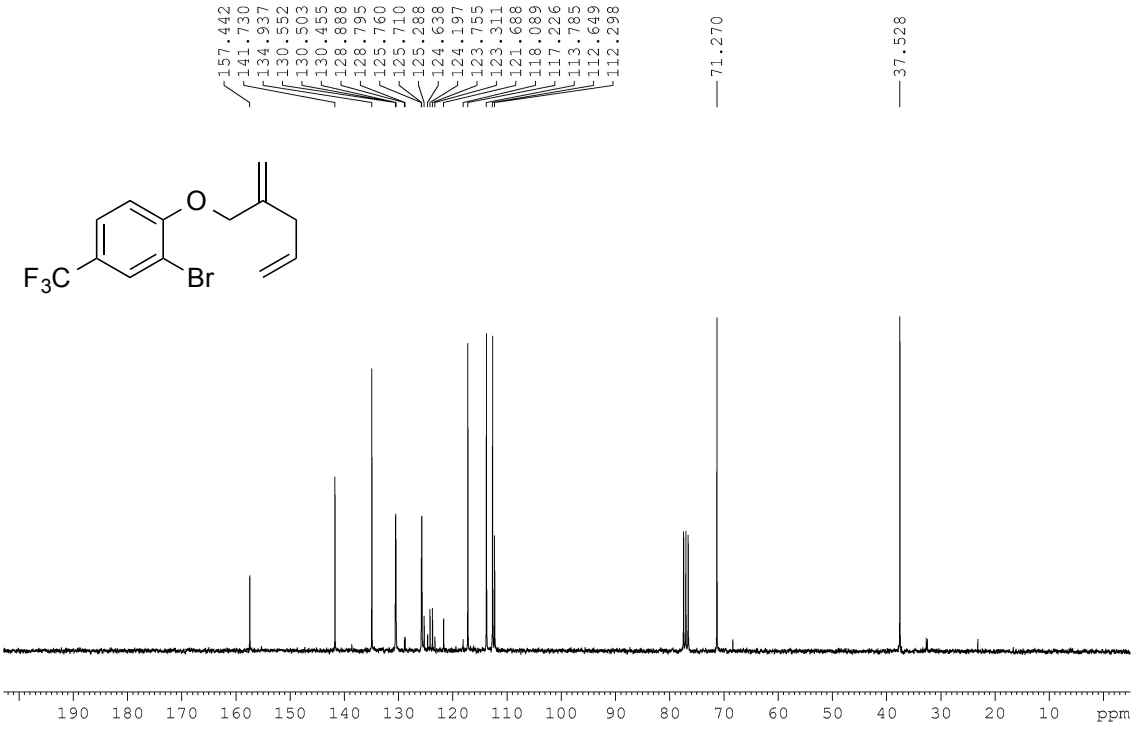
^{13}C NMR spectrum of compound **1f**



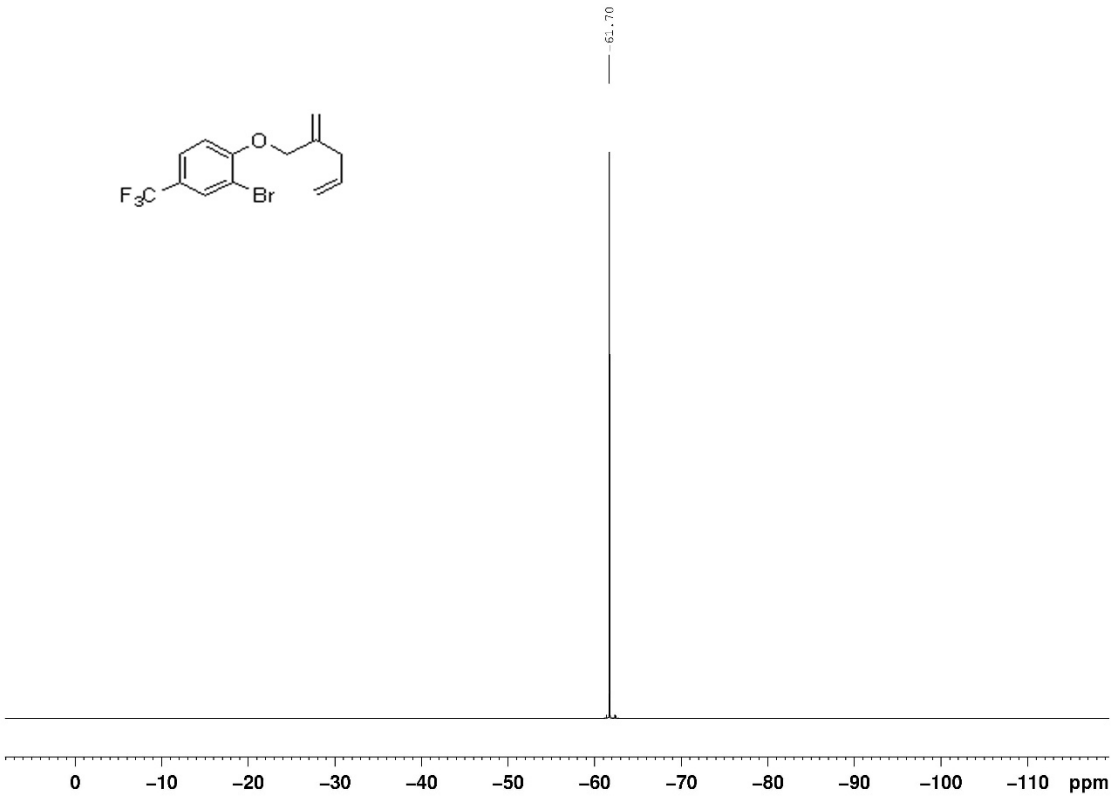
^{1}H NMR spectrum of compound **1g**



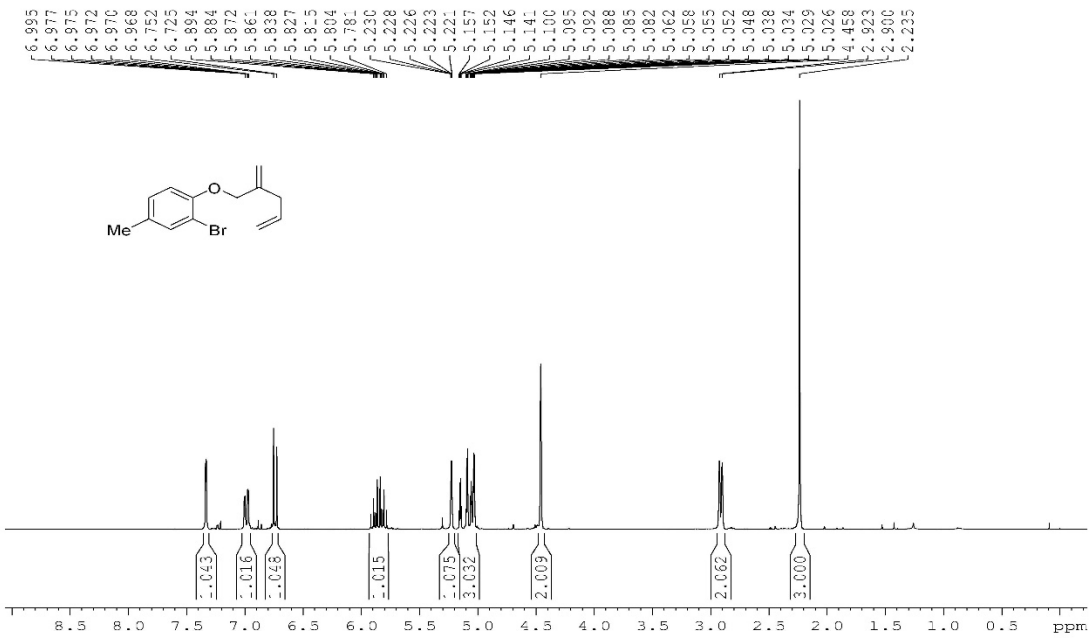
^{13}C NMR spectrum of compound **1g**



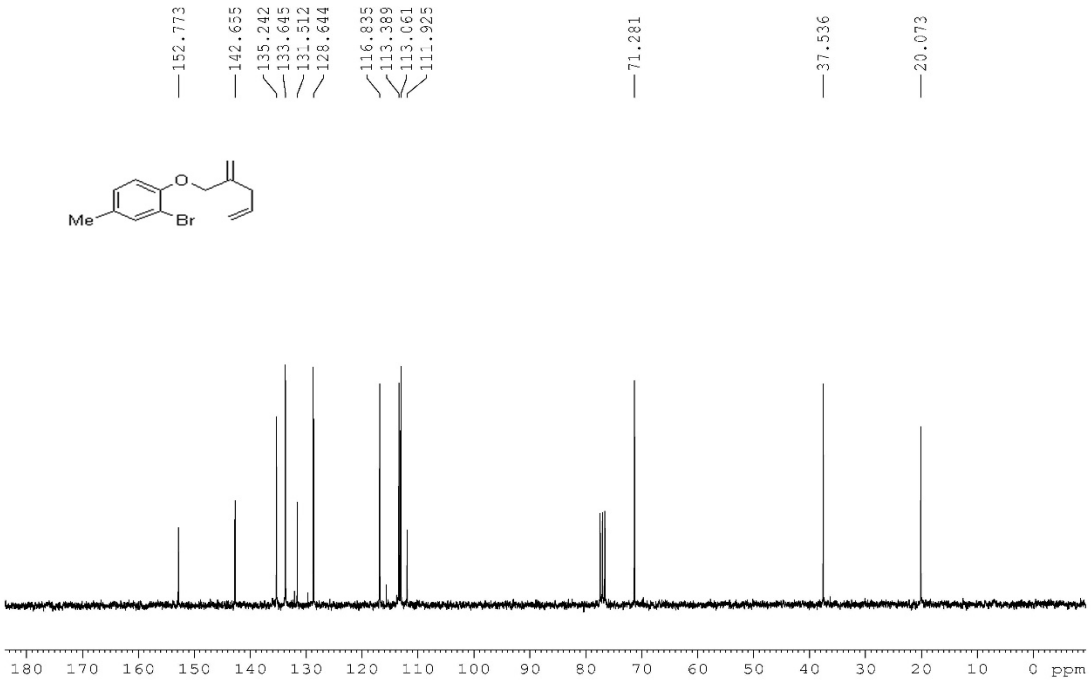
^{19}F NMR spectrum of compound **1g**



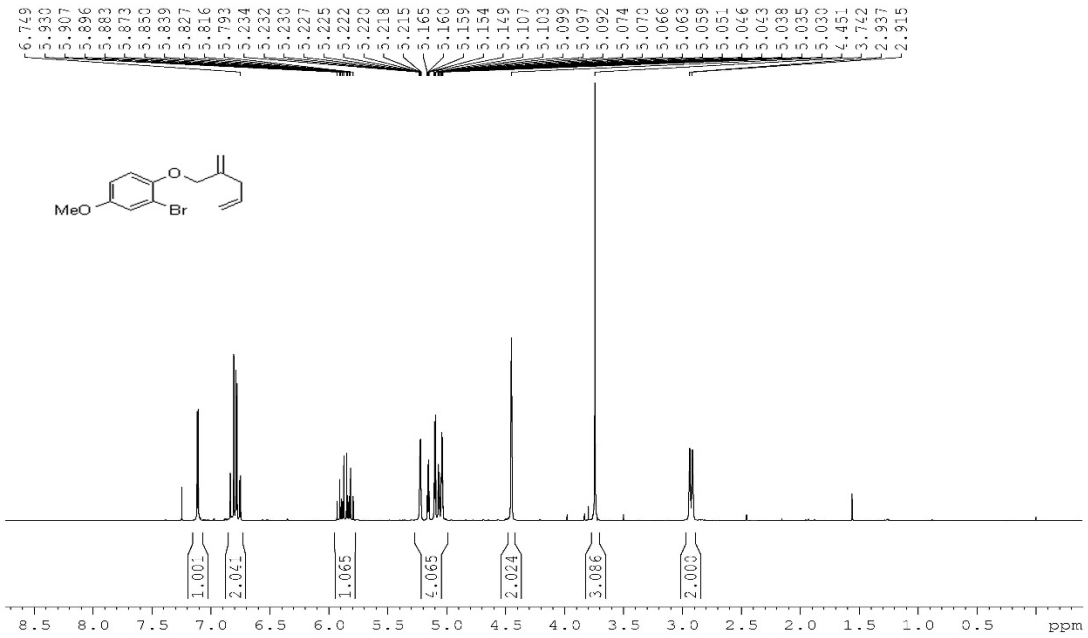
^{1}H NMR spectrum of compound **1h**



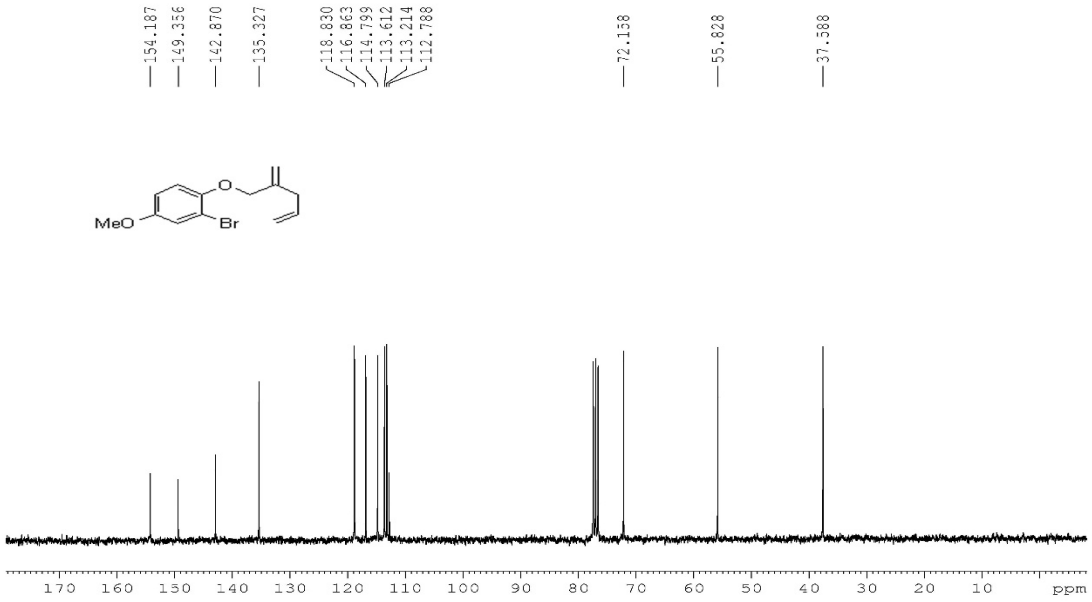
^{13}C NMR spectrum of compound **1h**



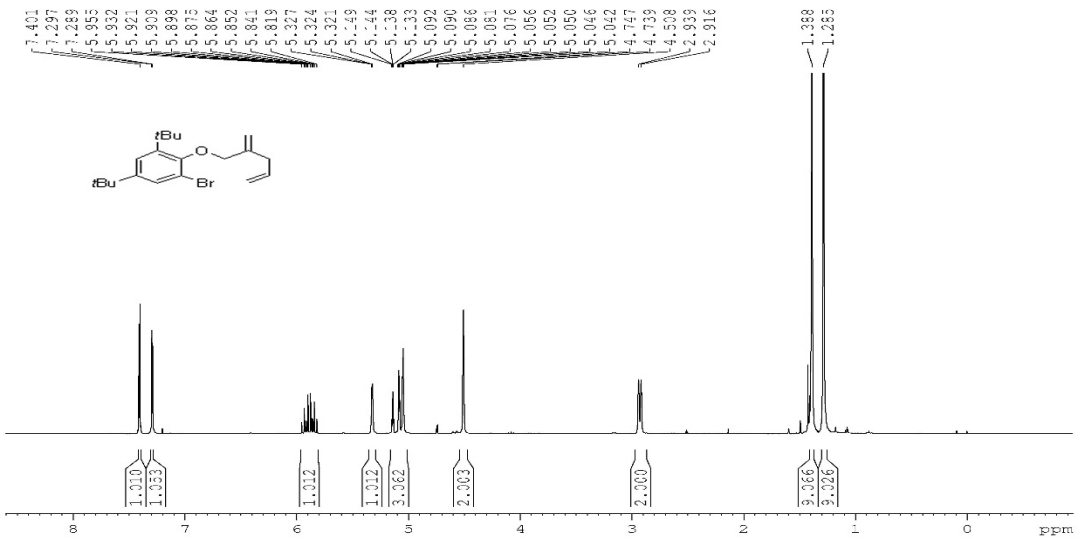
^{1}H NMR spectrum of compound **1i**



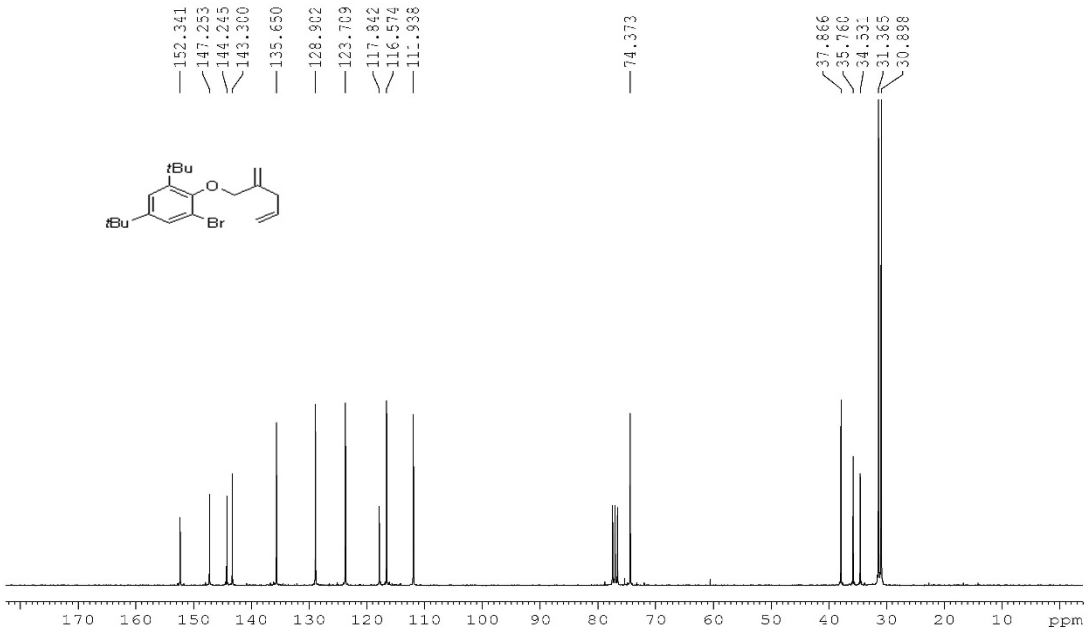
^{13}C NMR spectrum of compound **1i**



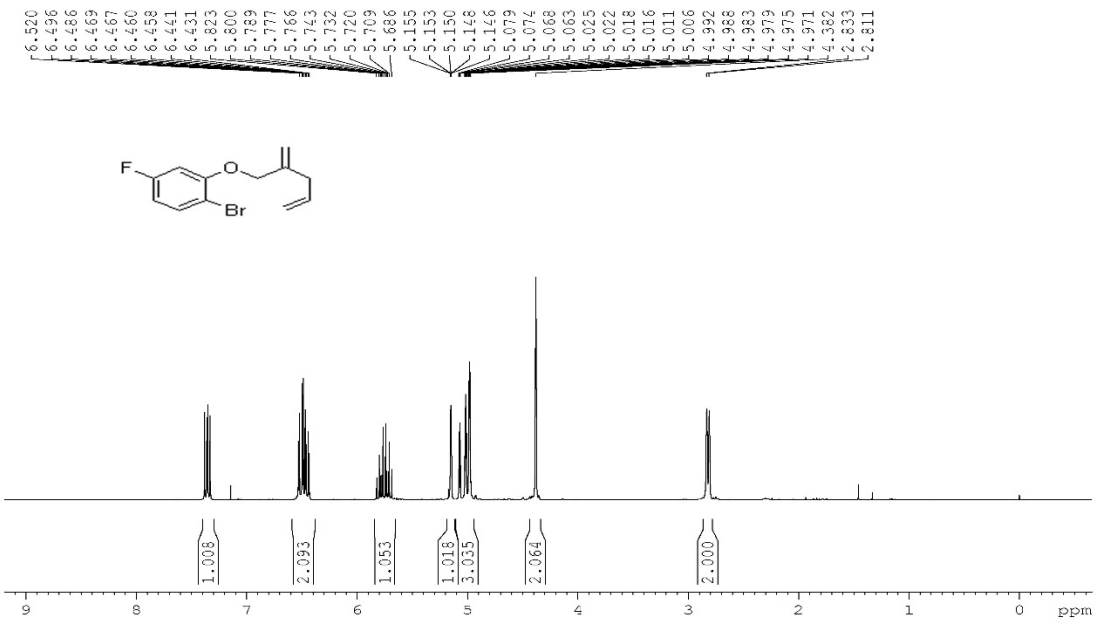
^{1}H NMR spectrum of compound **1j**



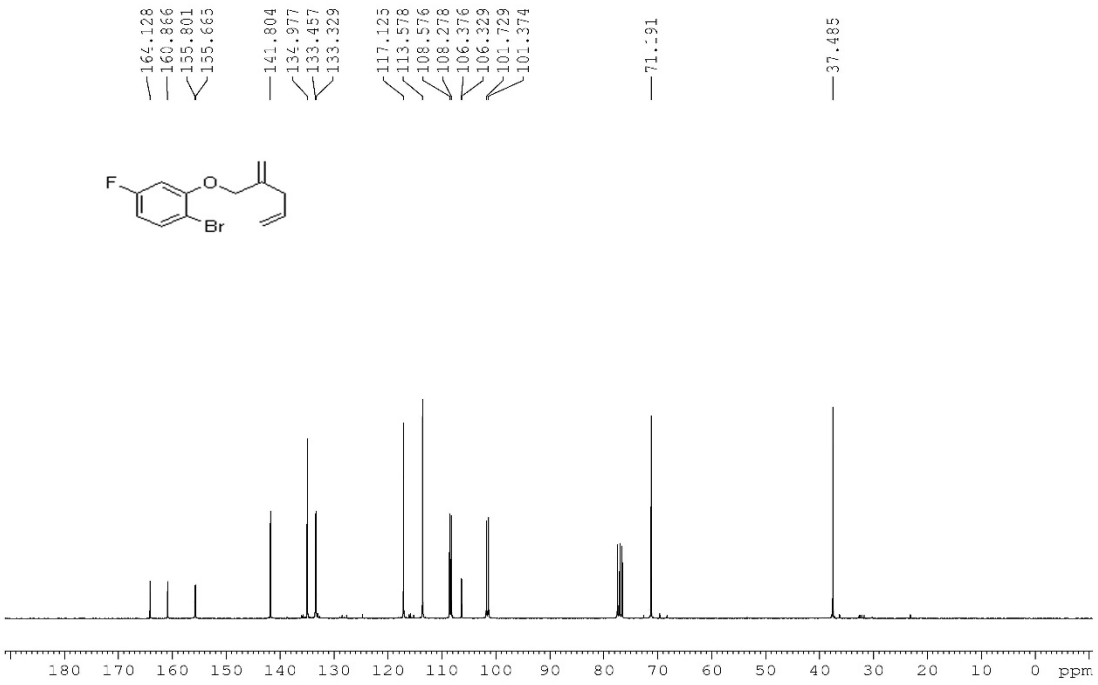
^{13}C NMR spectrum of compound **1j**



^{1}H NMR spectrum of compound **1k**

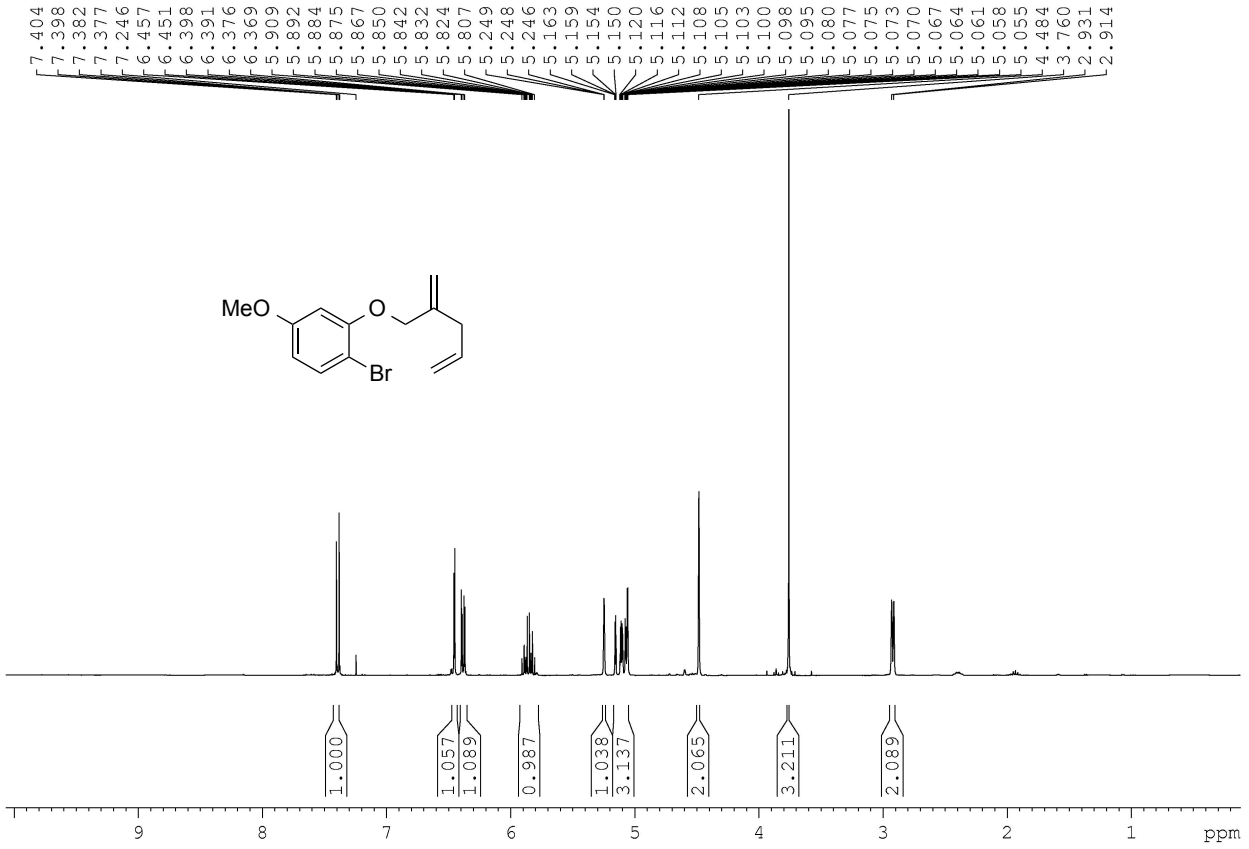


^{13}C NMR spectrum of compound **1k**

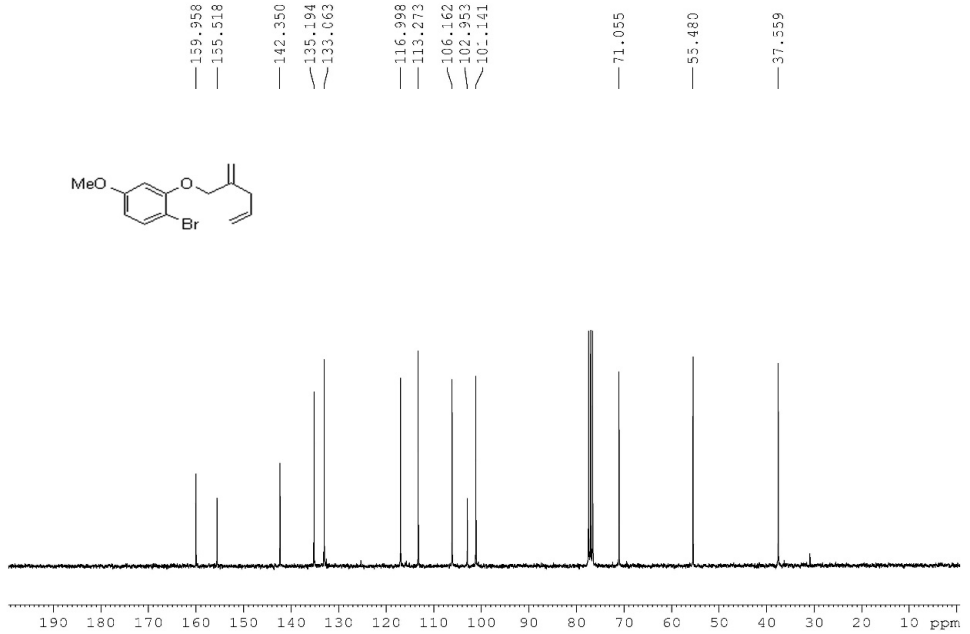


^{19}F NMR spectrum of compound **1k**

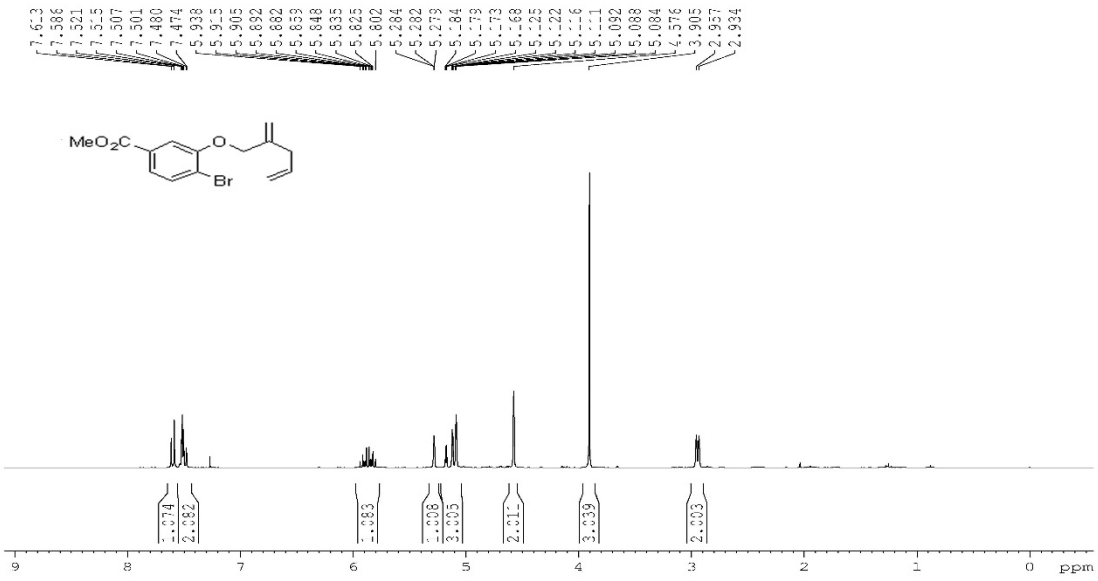
^{1}H NMR spectrum of compound **1l**



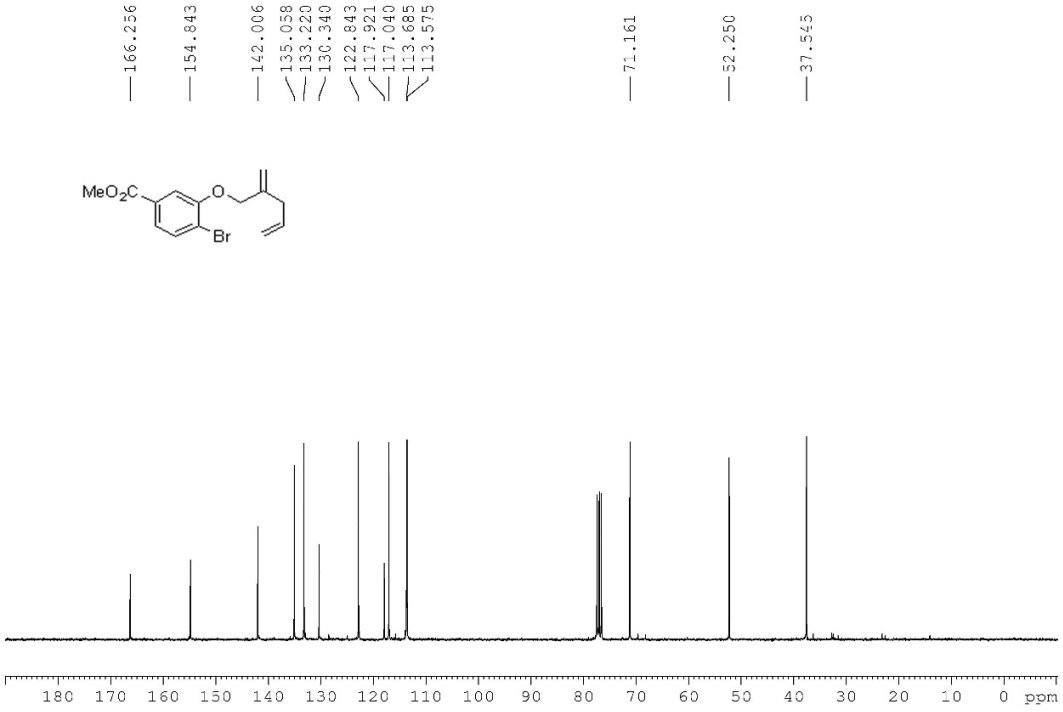
^{13}C NMR spectrum of compound **1l**



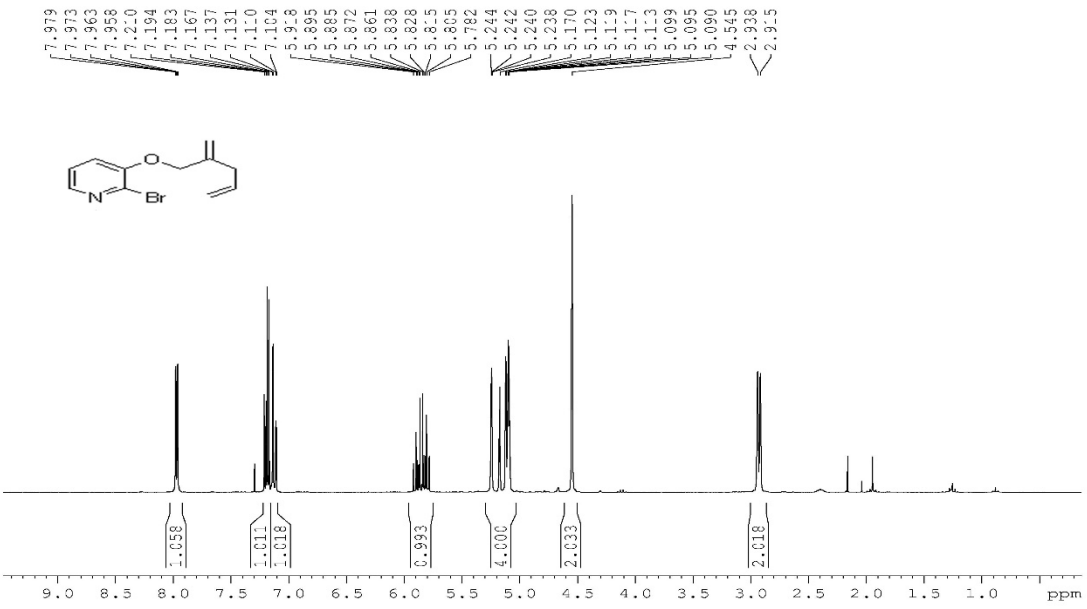
^{1}H NMR spectrum of compound **1m**



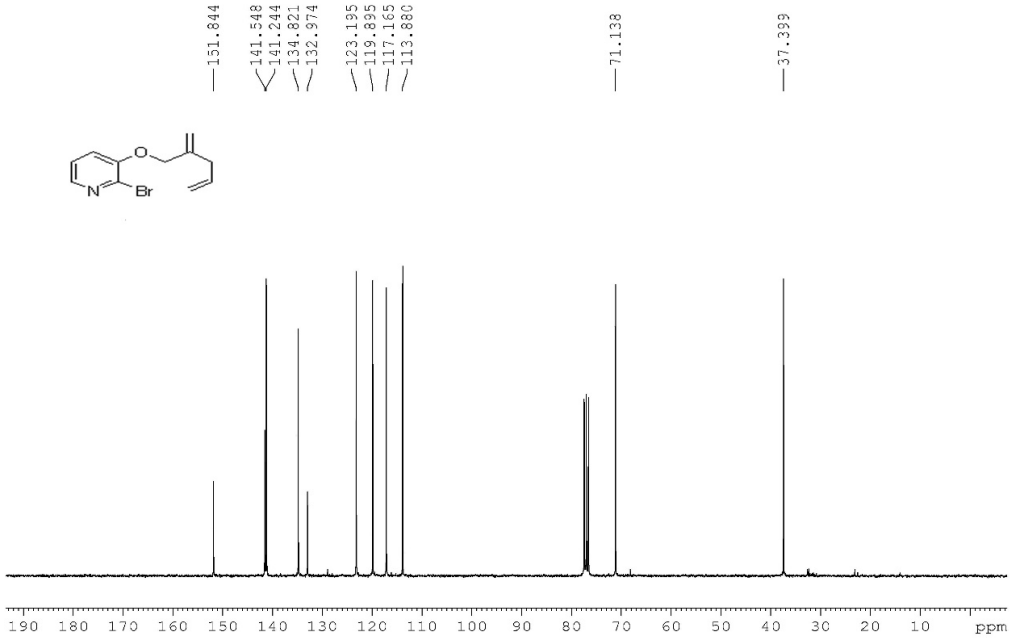
^{13}C NMR spectrum of compound **1m**



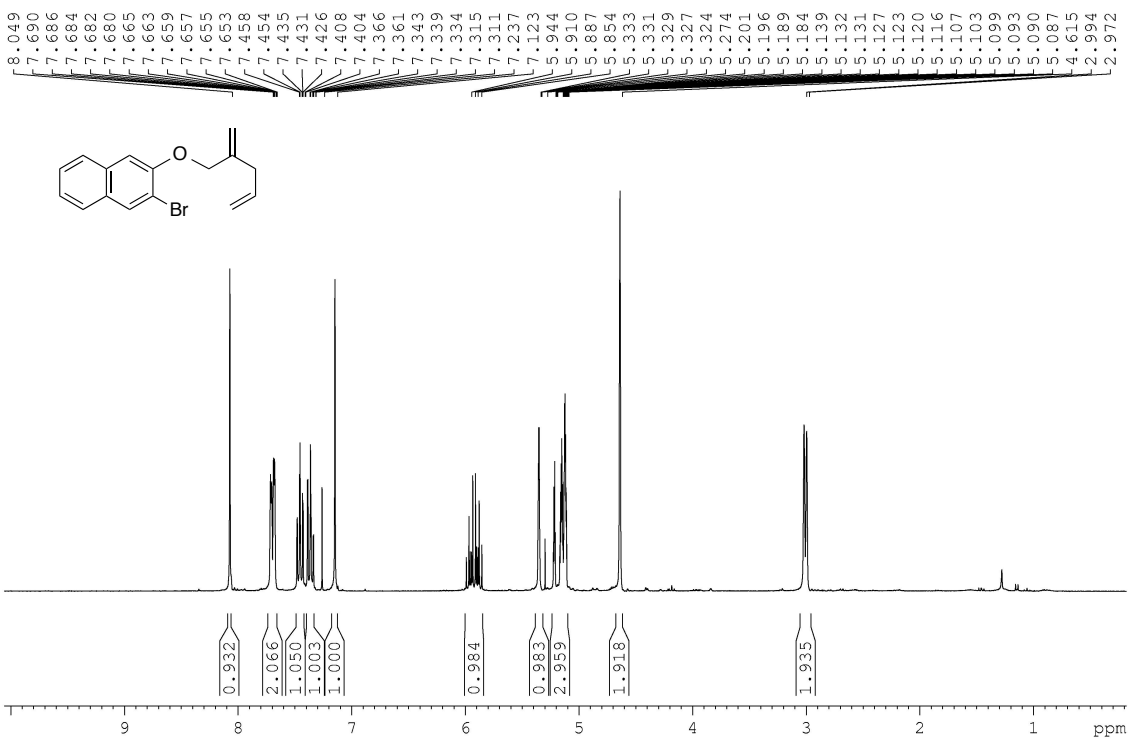
^{1}H NMR spectrum of compound **1n**



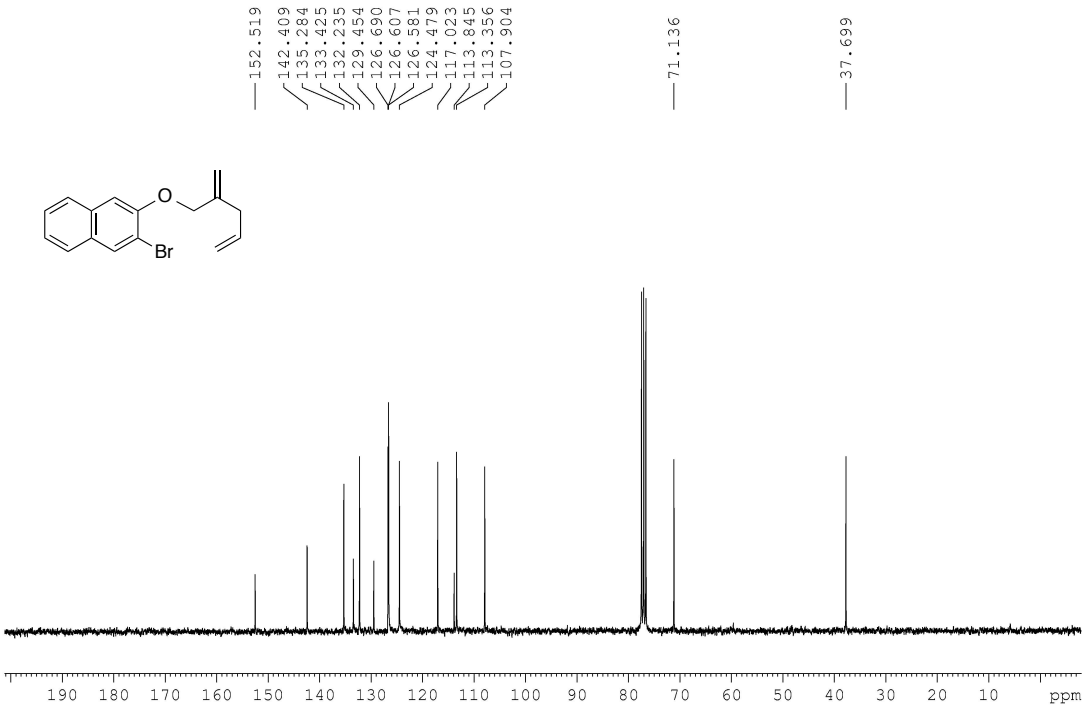
^{13}C NMR spectrum of compound **1n**



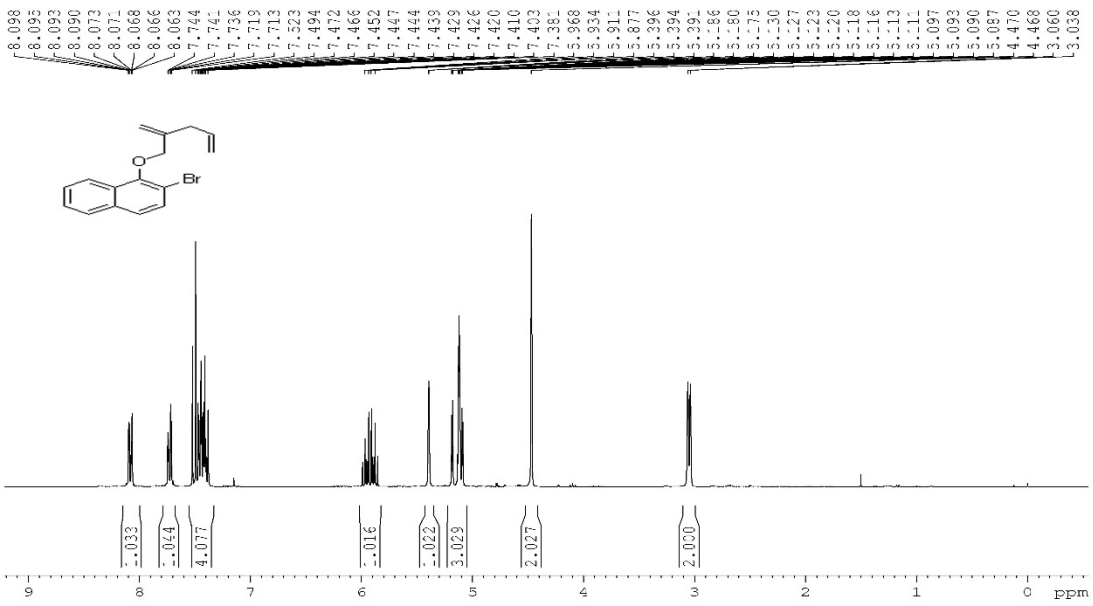
^{1}H NMR spectrum of compound **1o**



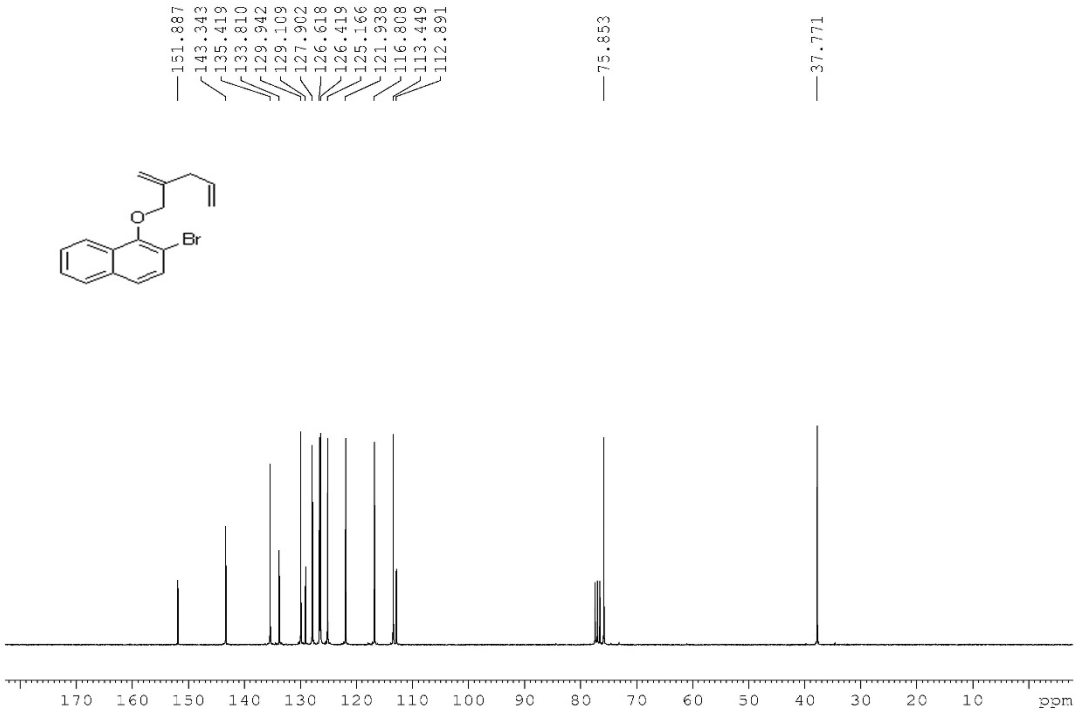
^{13}C NMR spectrum of compound **1o**



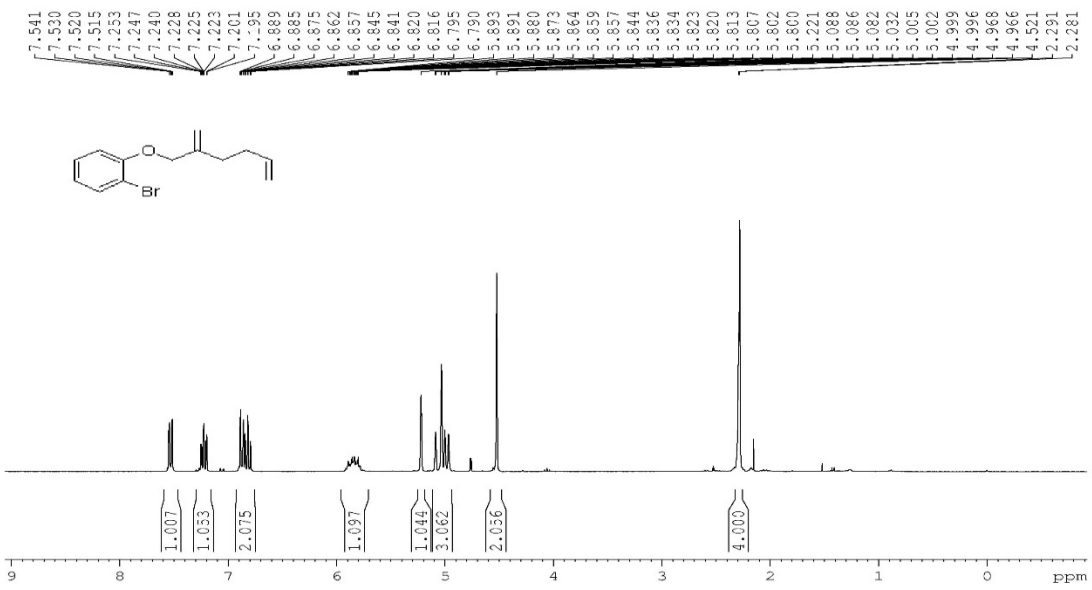
^{1}H NMR spectrum of compound **1p**



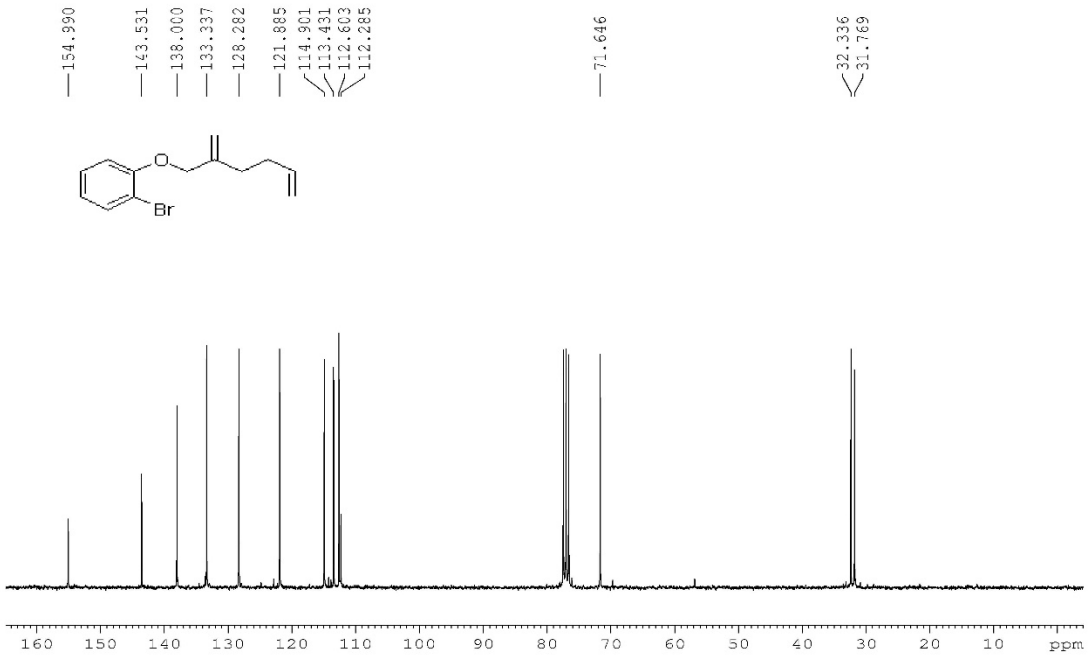
^{13}C NMR spectrum of compound **1p**



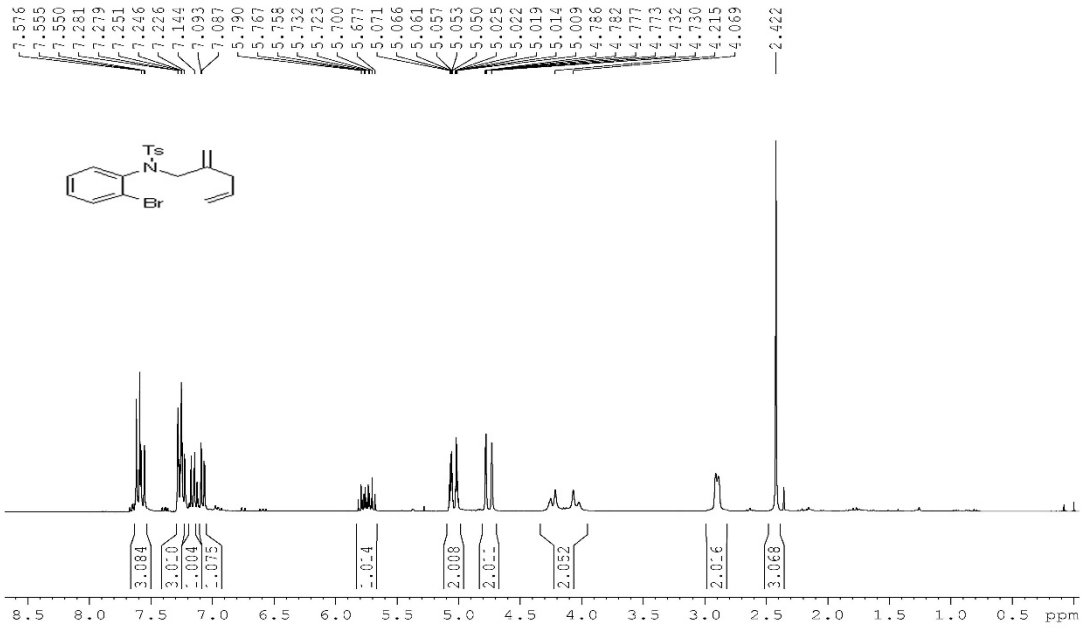
^{1}H NMR spectrum of compound **1q**



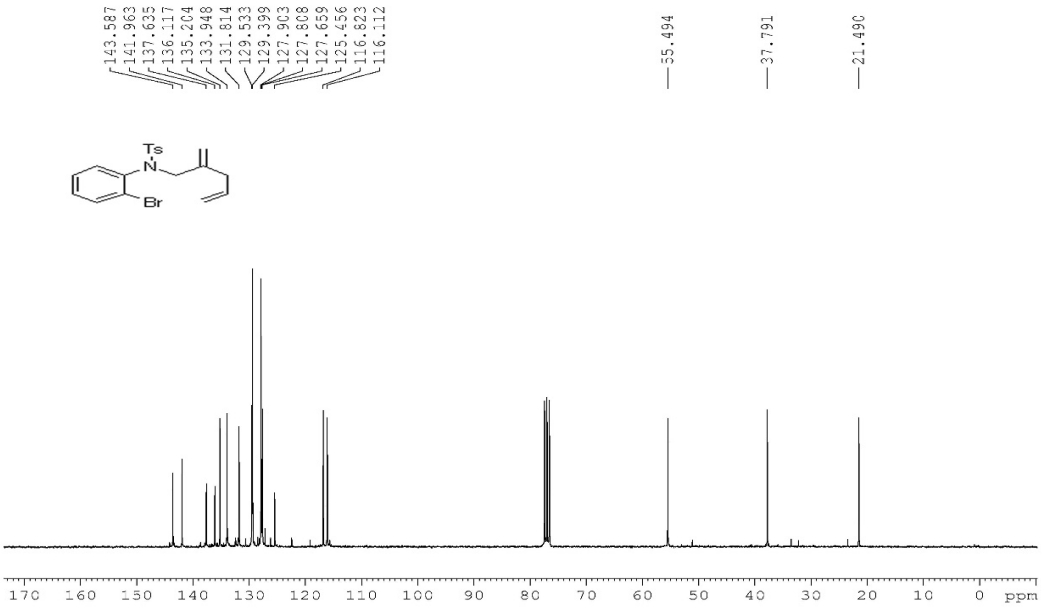
^{13}C NMR spectrum of compound **1q**



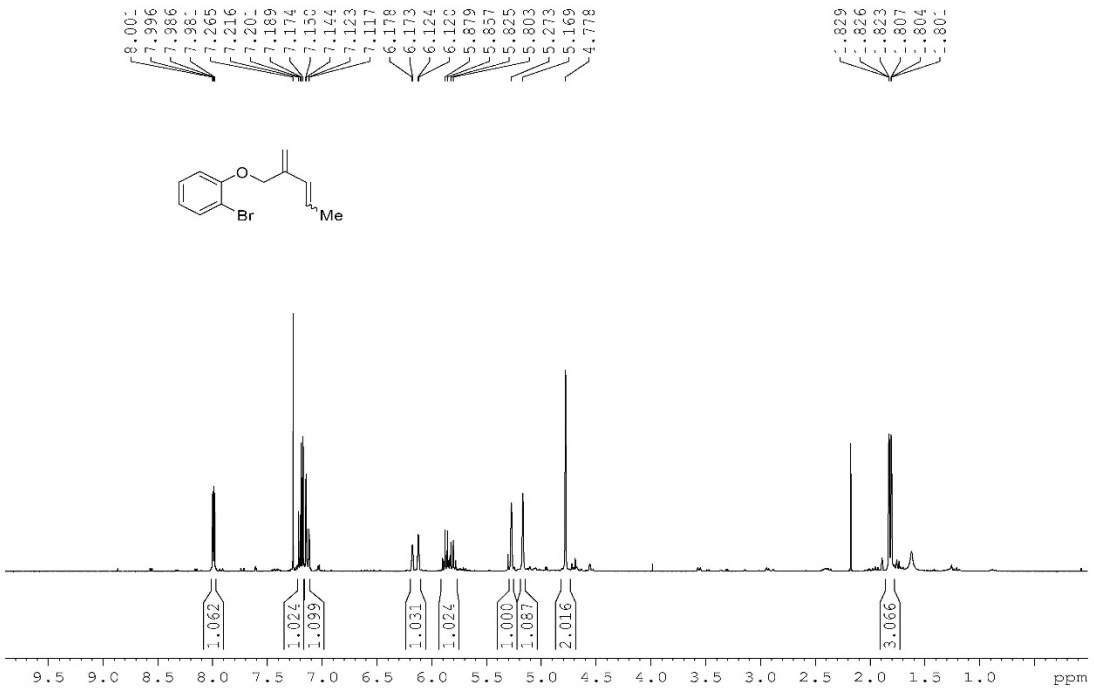
^{1}H NMR spectrum of compound **1r**



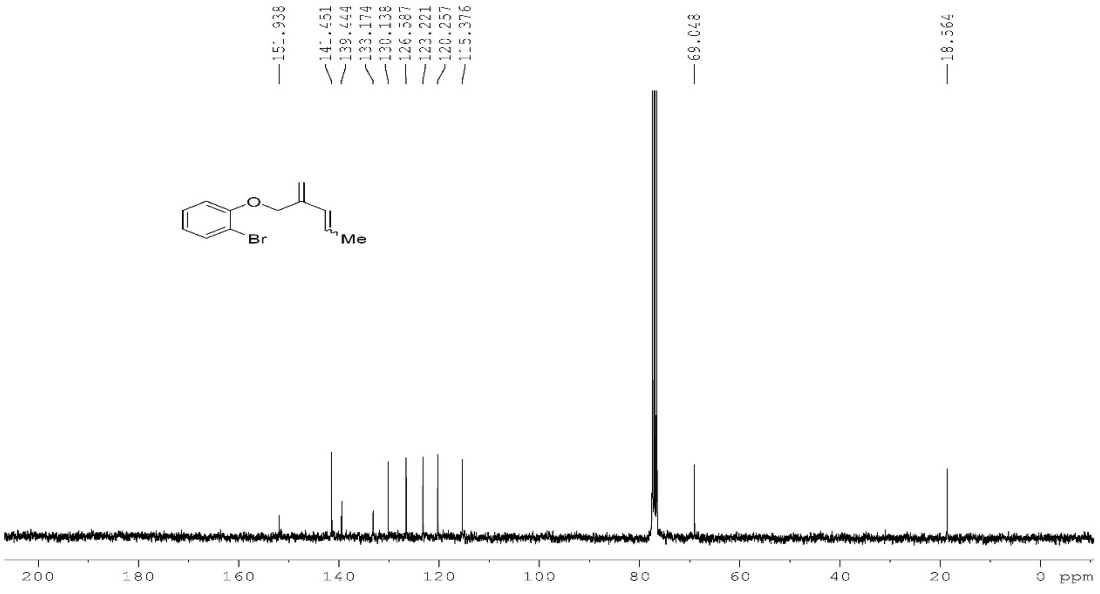
^{13}C NMR spectrum of compound **1r**



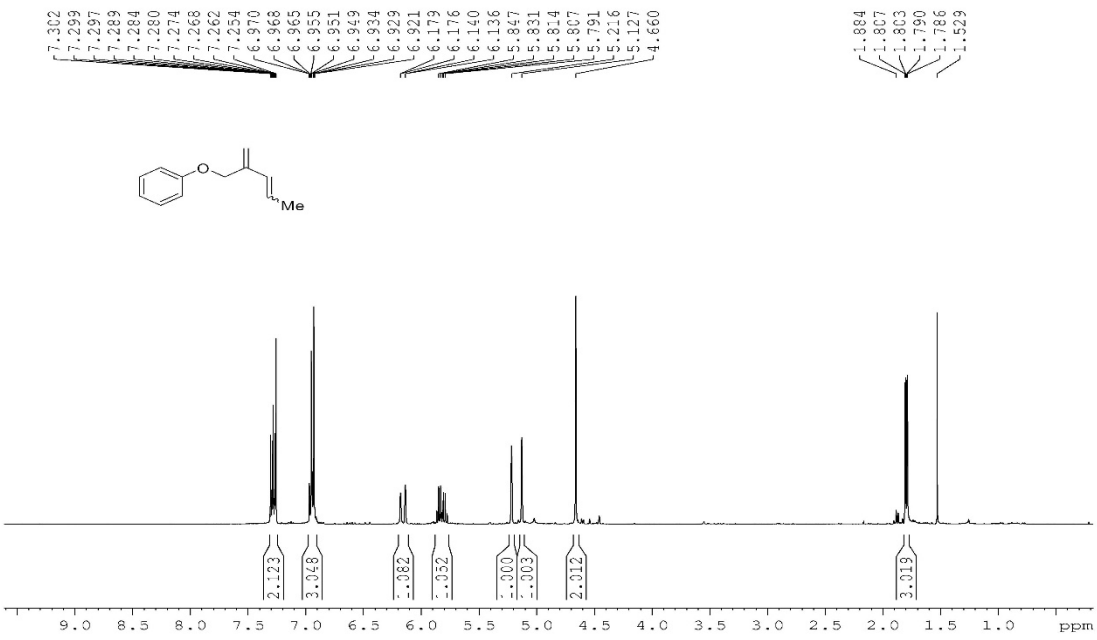
^{1}H NMR spectrum of intermediate **4a**



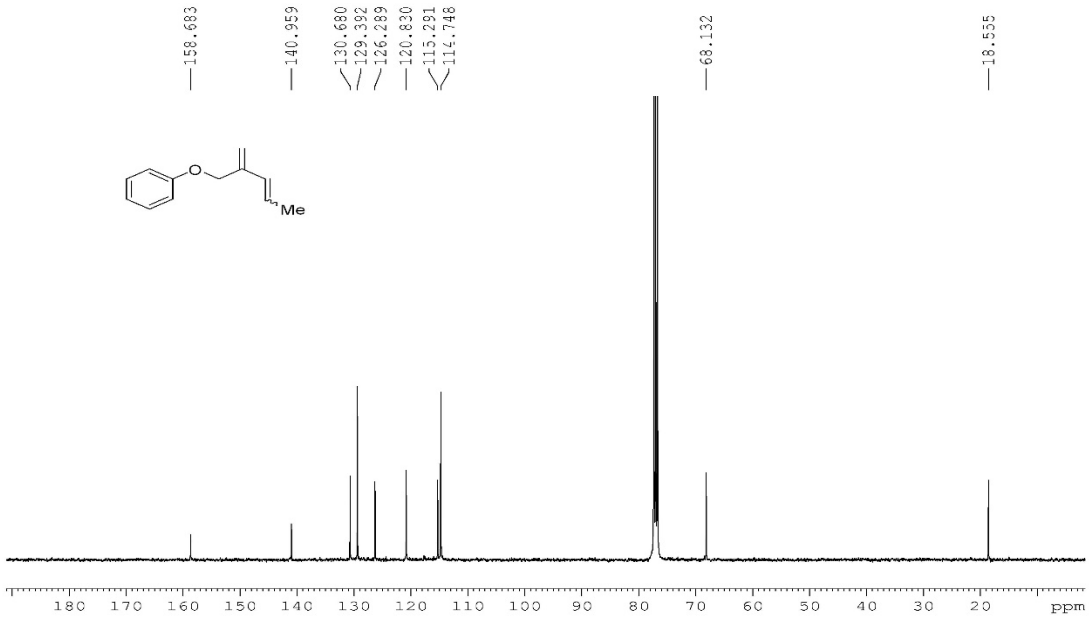
^{13}C NMR spectrum of intermediate **4a**



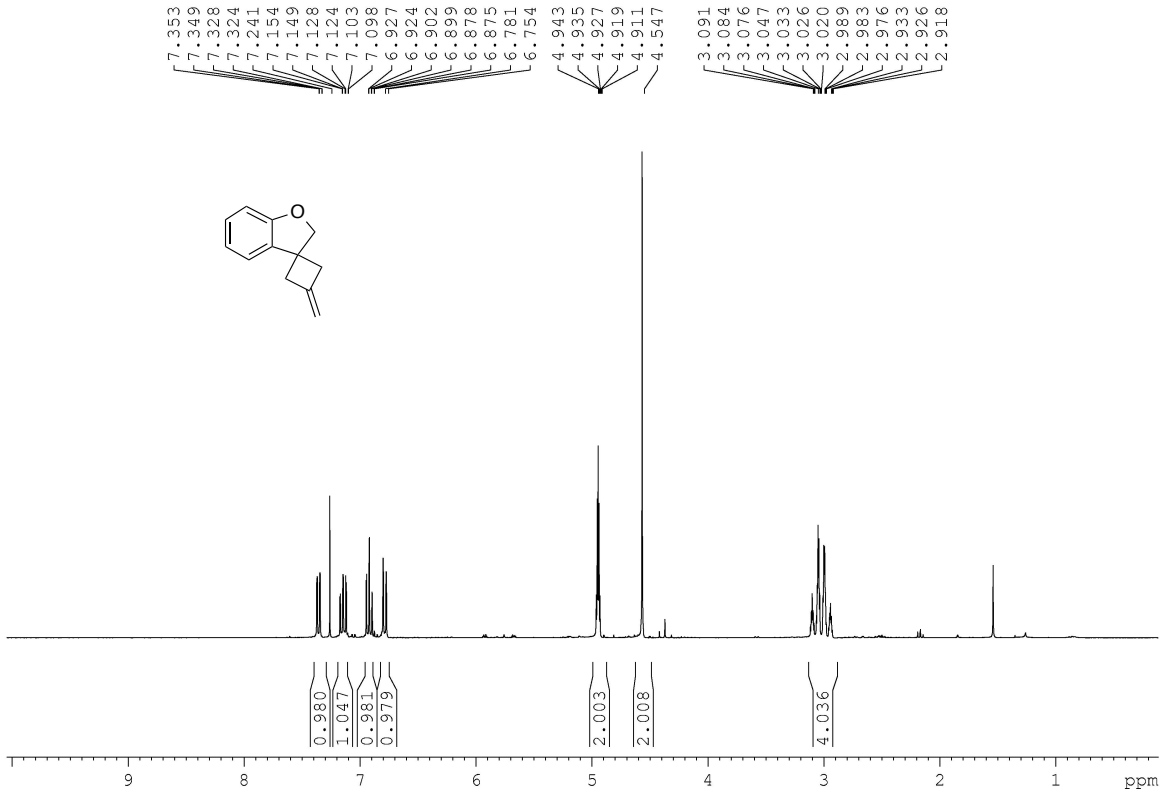
^{1}H NMR spectrum of **4c**



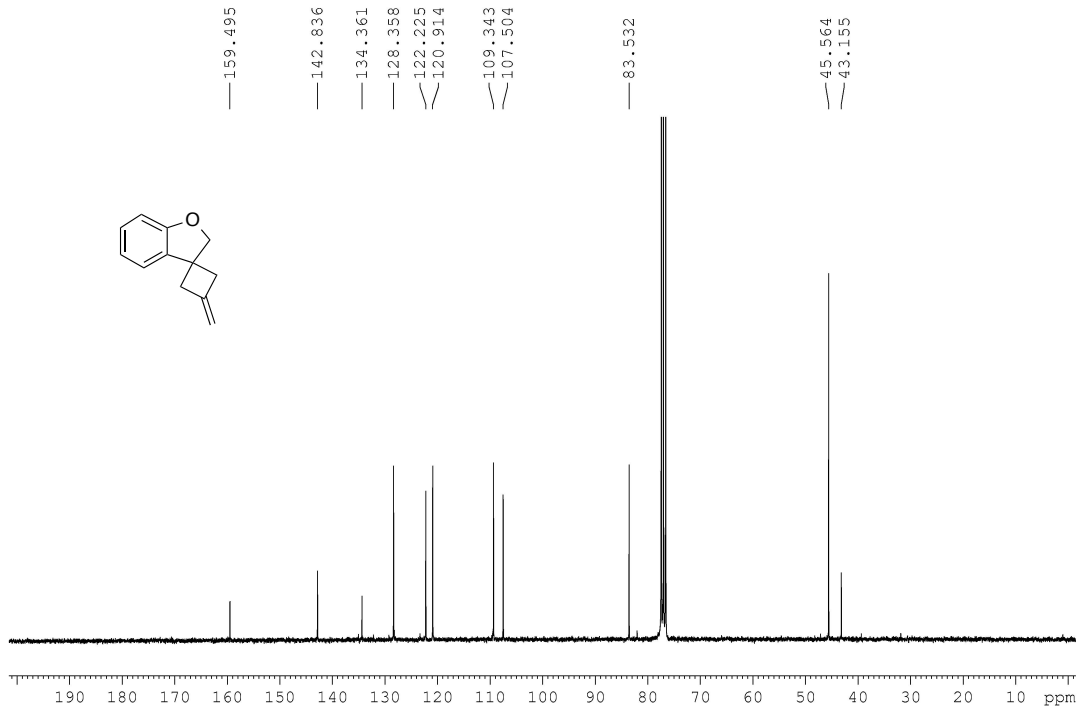
^{13}C NMR spectrum of **4c**



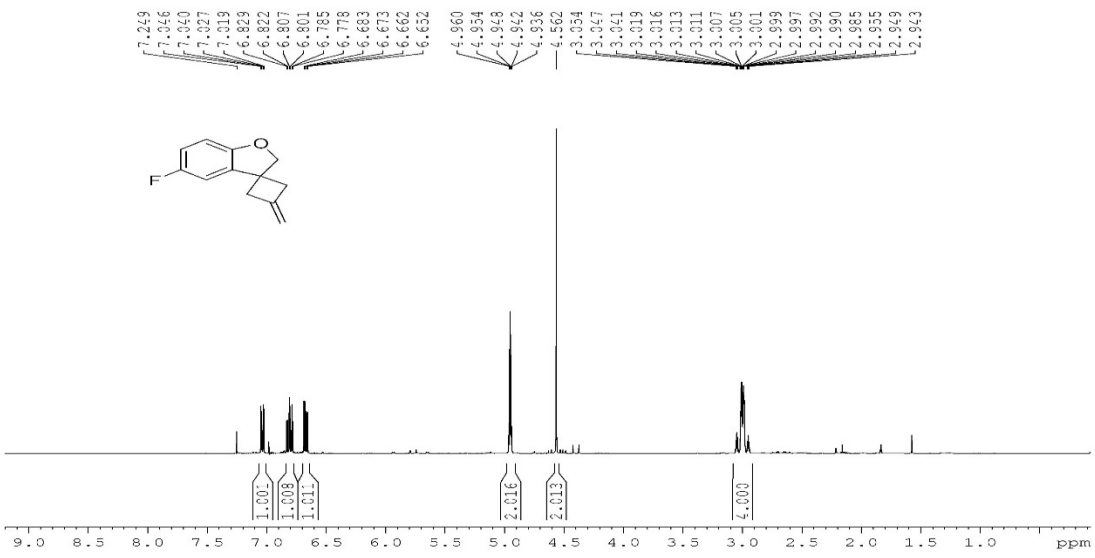
^{1}H NMR spectrum of compound **2a**



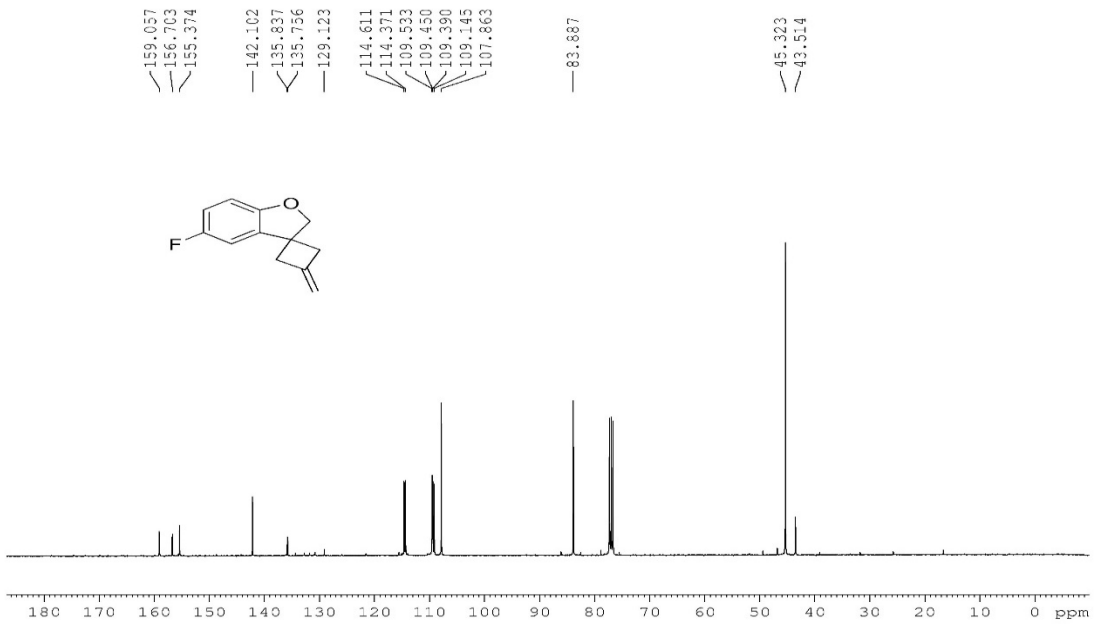
^{13}C NMR spectrum of compound **2a**



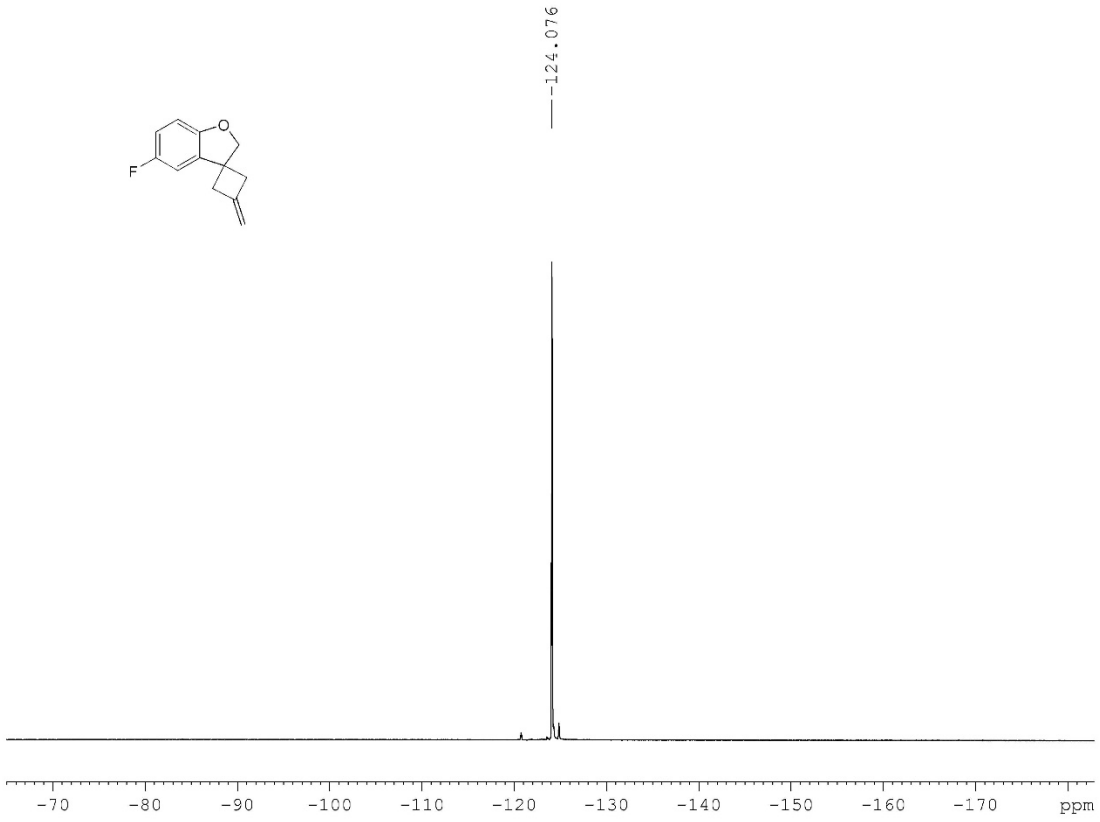
^{1}H NMR spectrum of compound **2b**



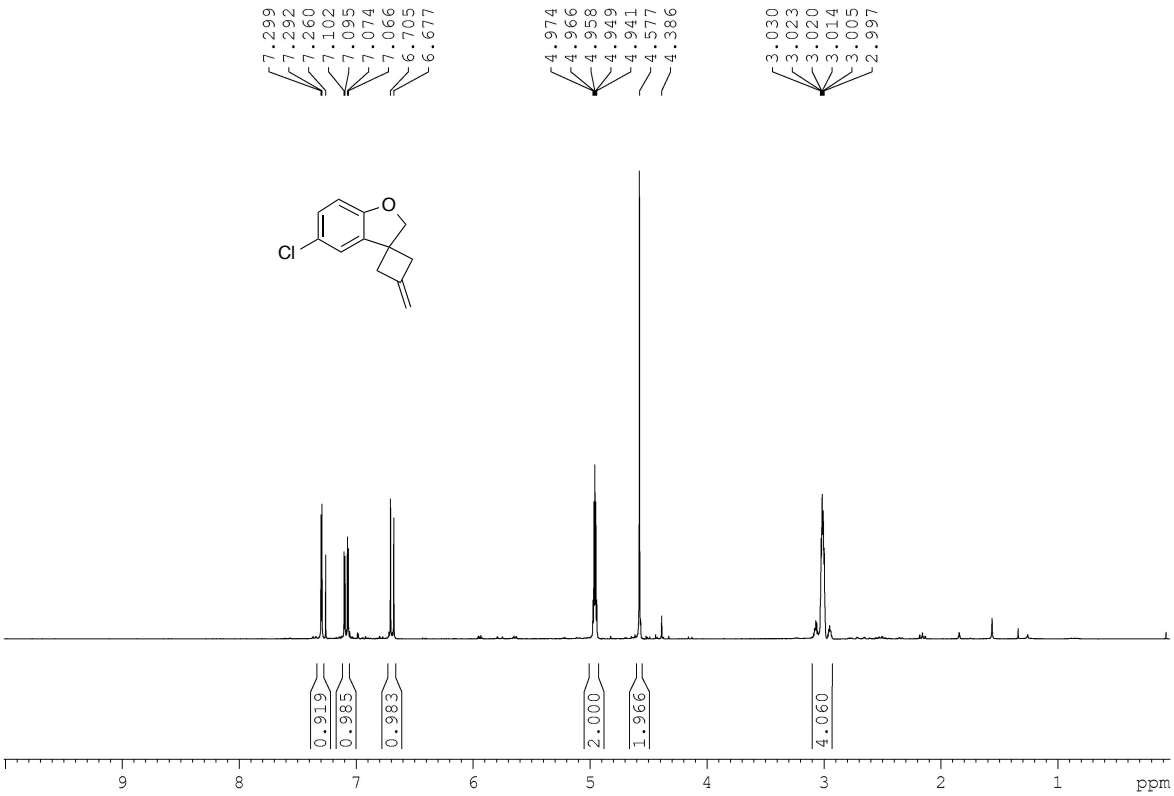
^{13}C NMR spectrum of compound **2b**



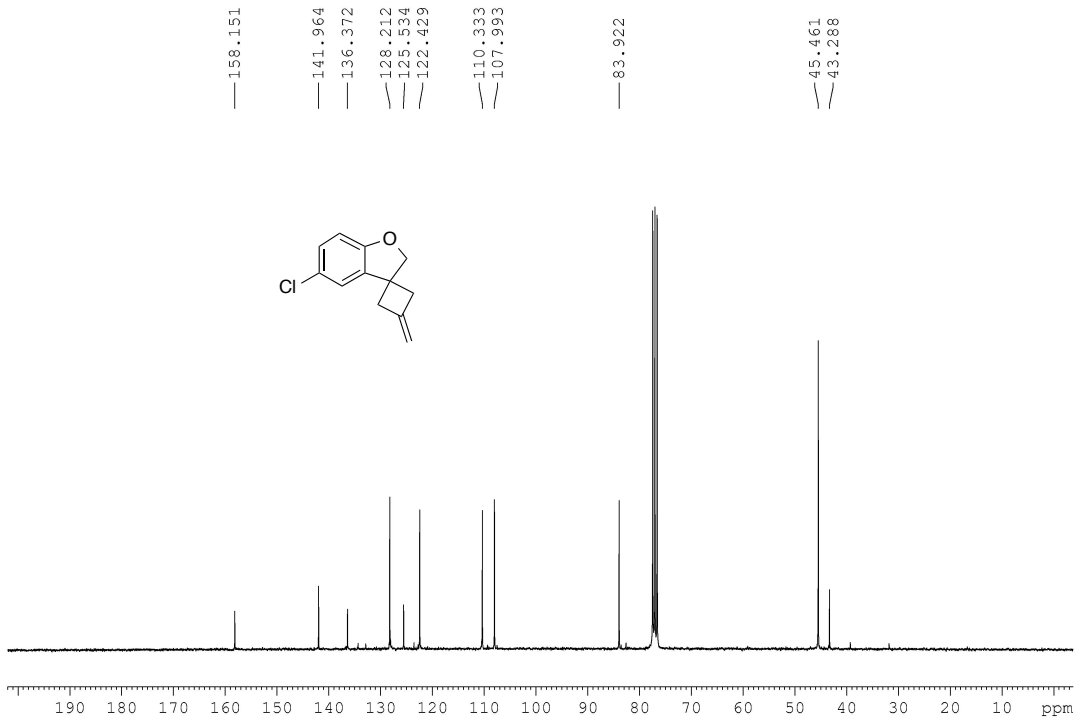
^{19}F NMR spectrum of compound **2b**



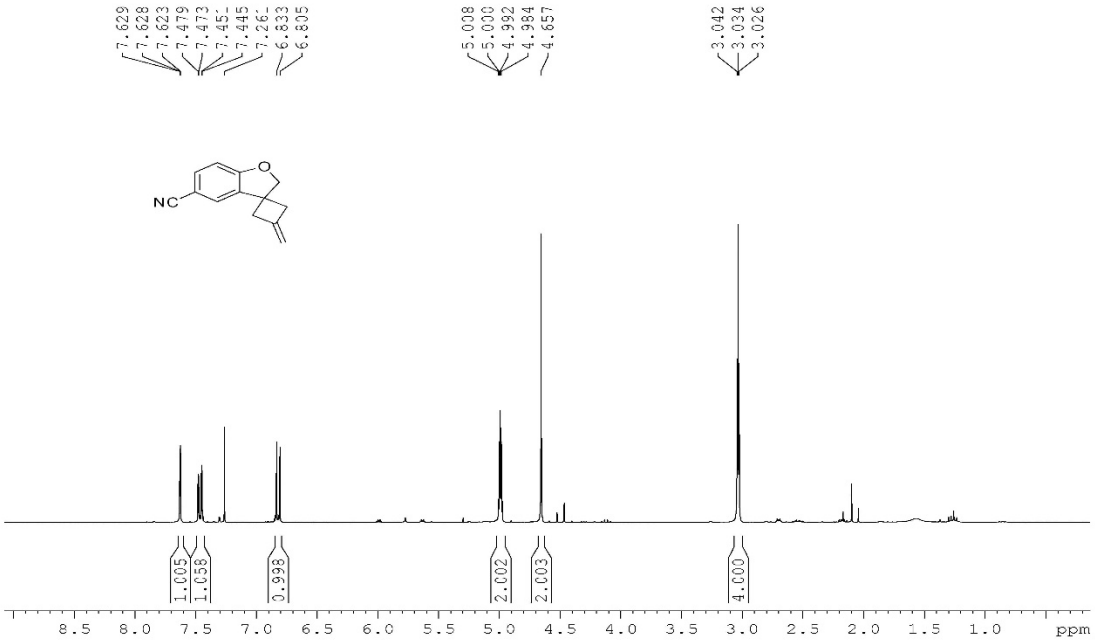
^{1}H NMR spectrum of compound **2c**



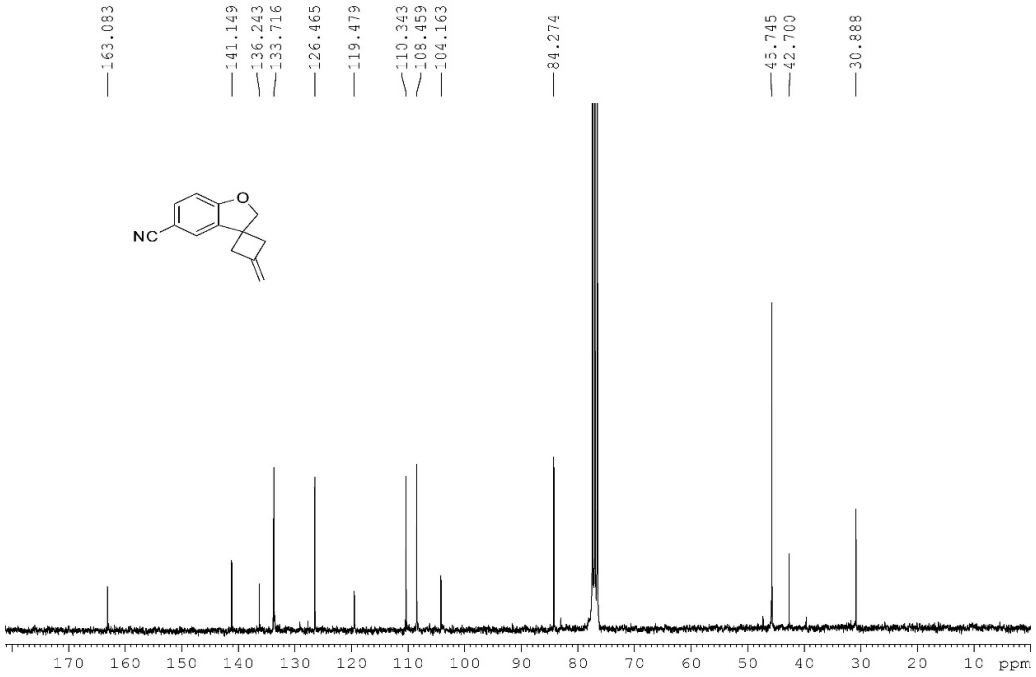
^{13}C NMR spectrum of compound **2c**



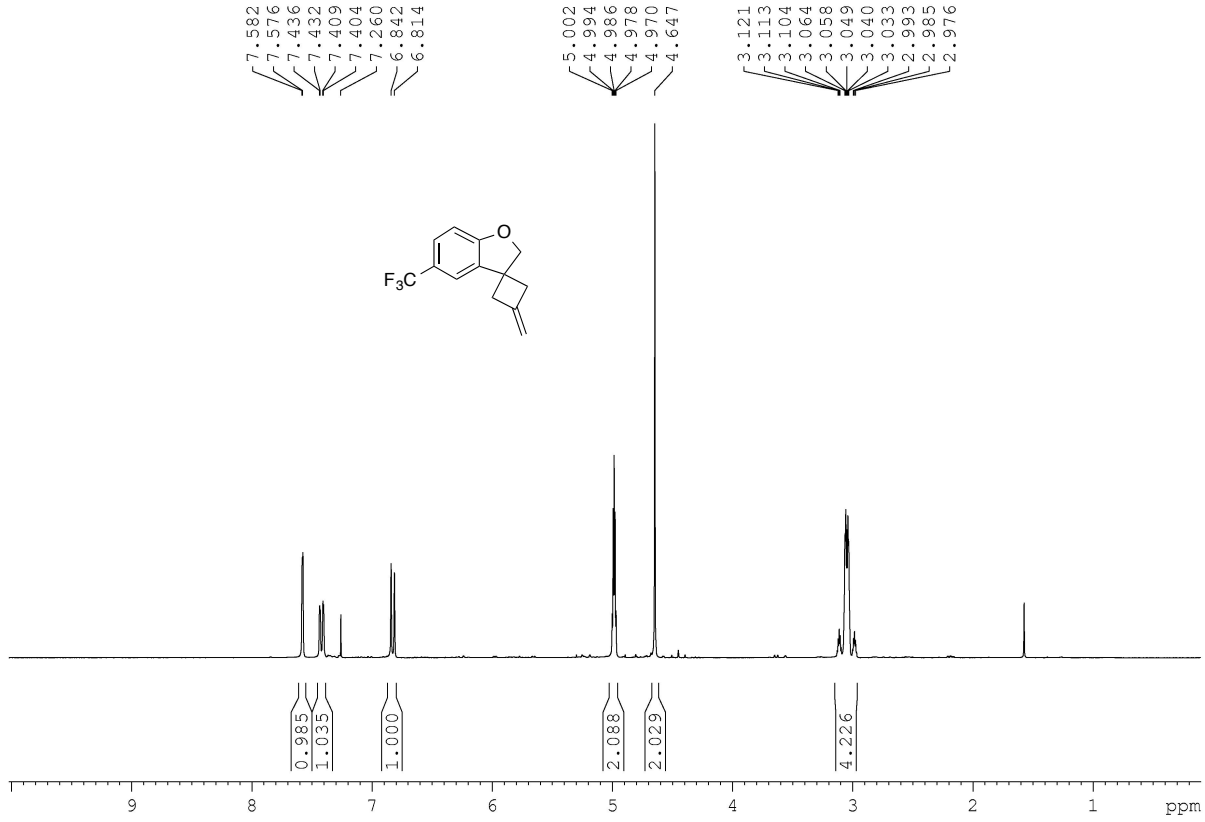
^{1}H NMR spectrum of compound **2d**



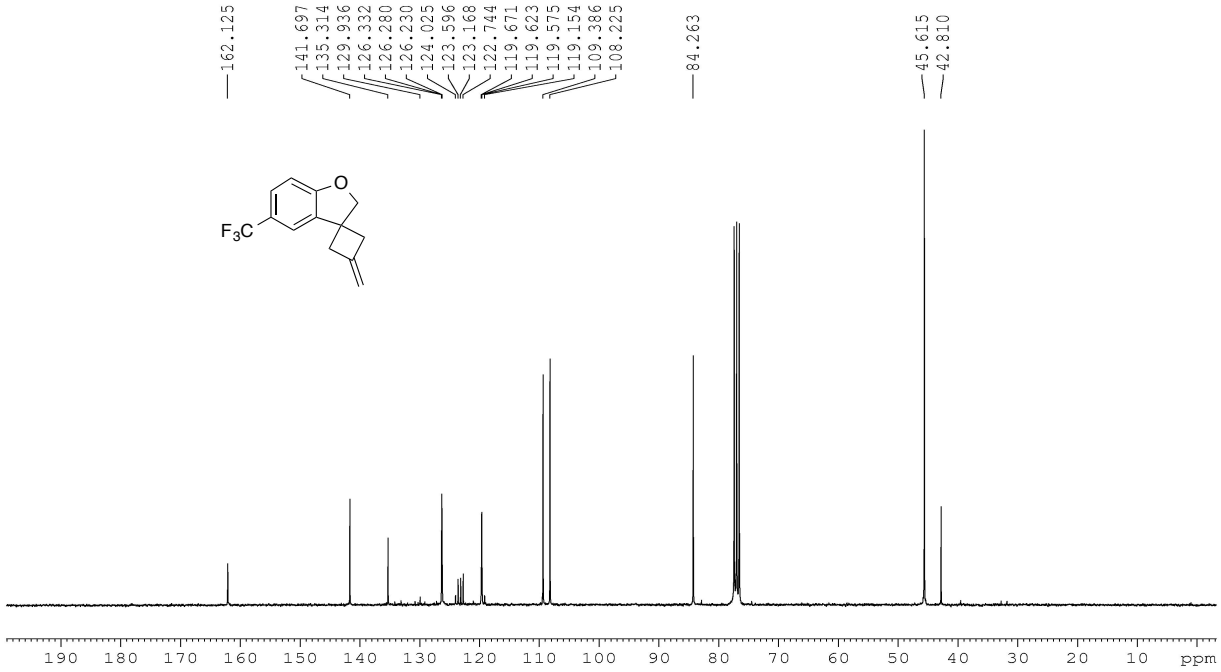
^{13}C NMR spectrum of compound **2d**



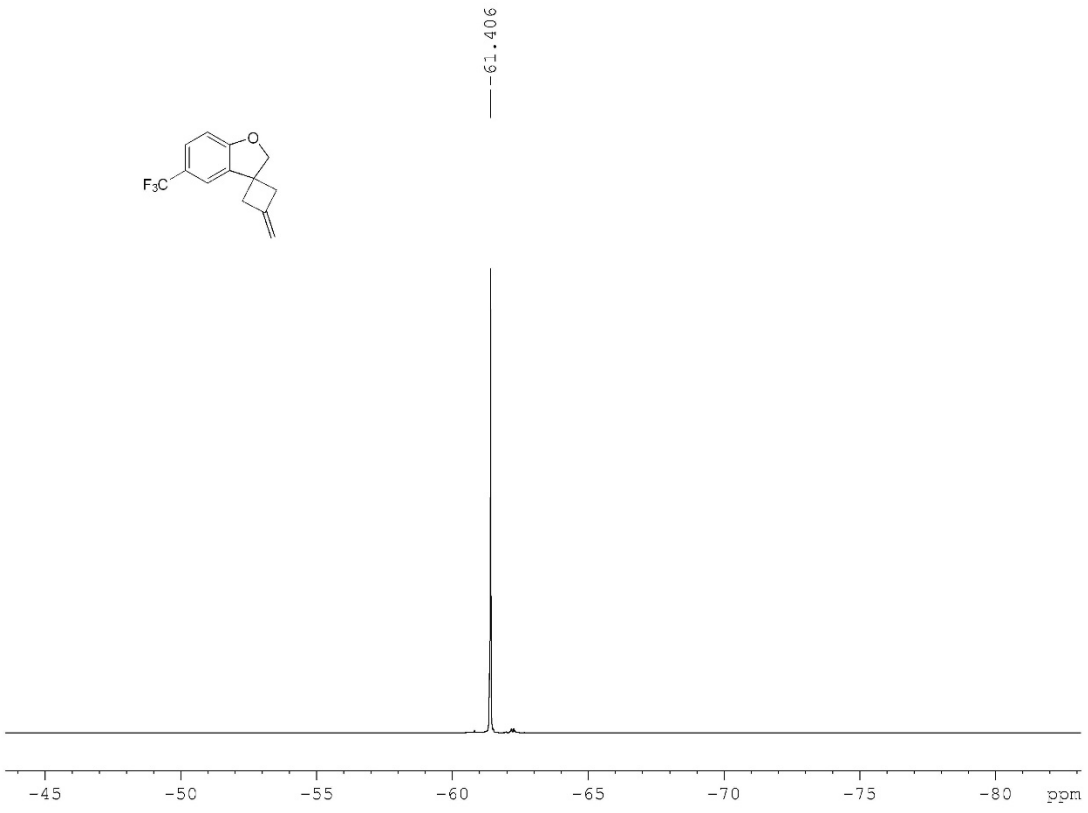
^{1}H NMR spectrum of compound **2e**



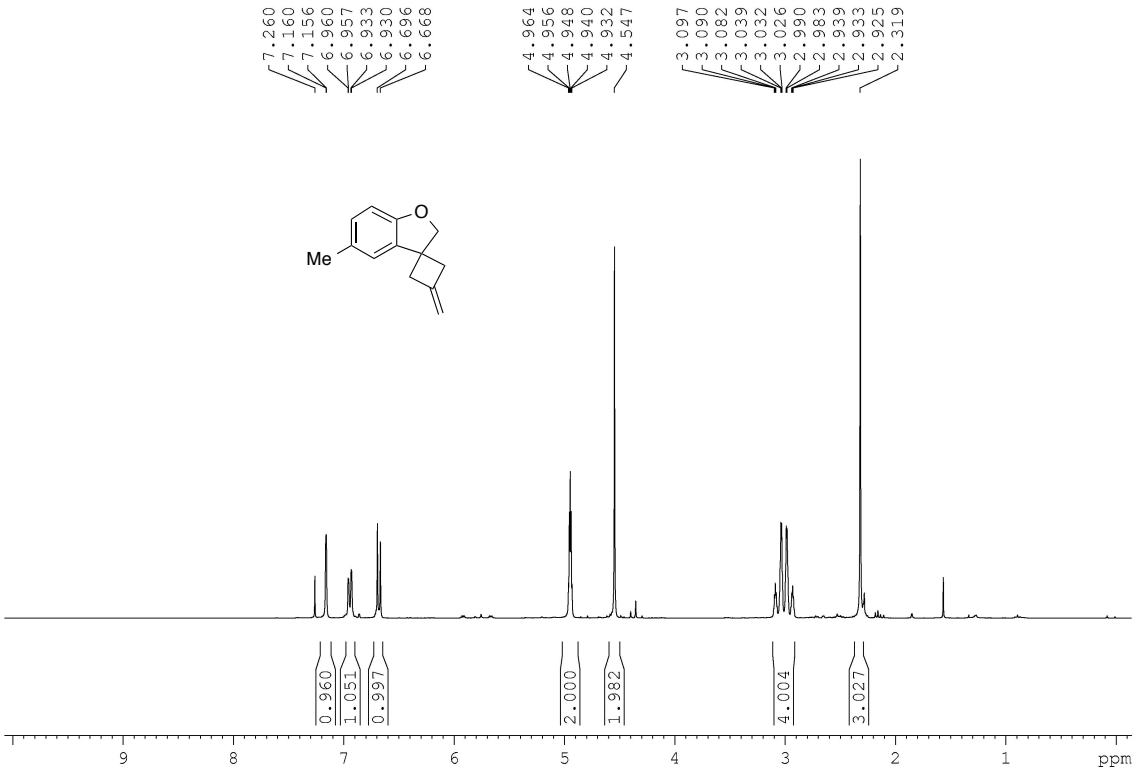
^{13}C NMR spectrum of compound **2e**



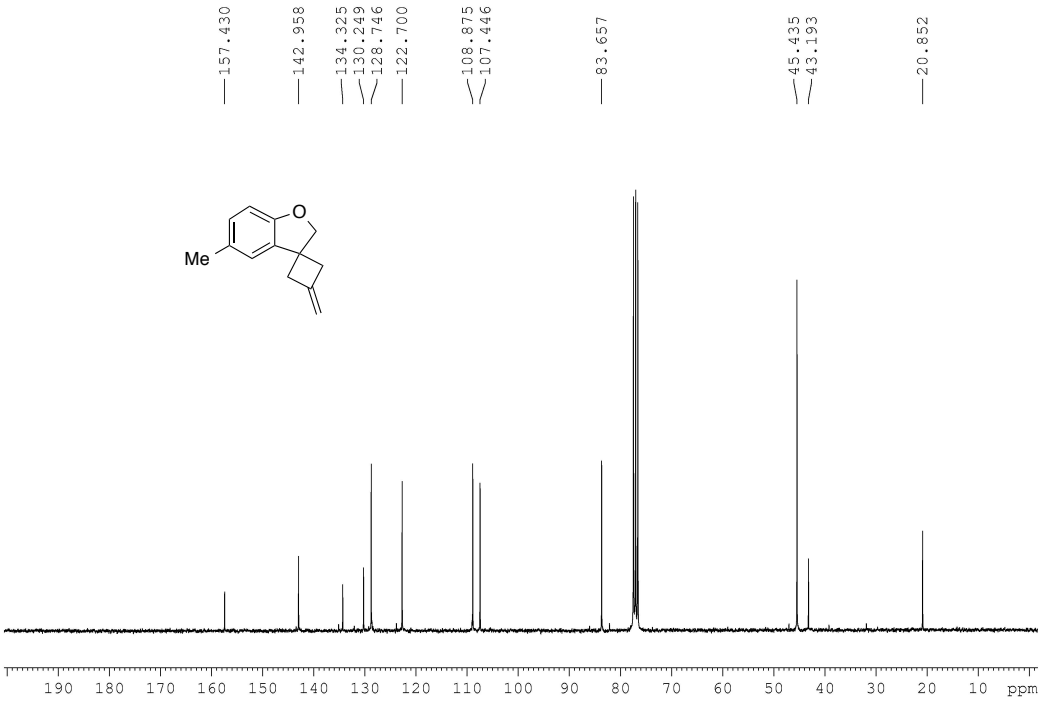
^{19}F NMR spectrum of compound **2e**



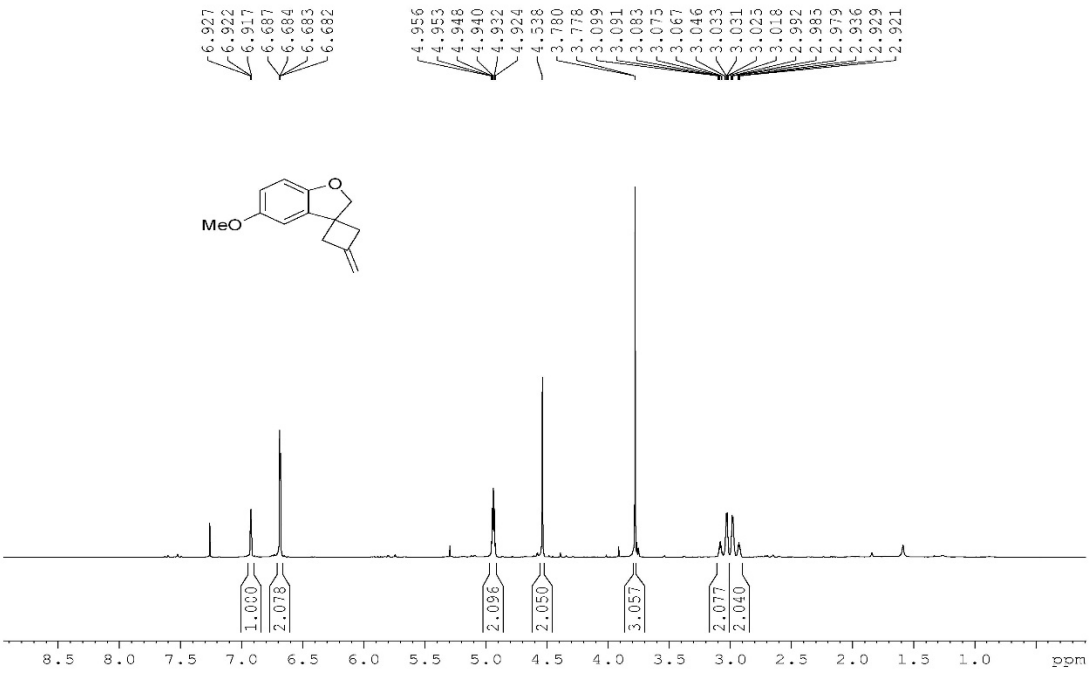
^{1}H NMR spectrum of compound **2f**



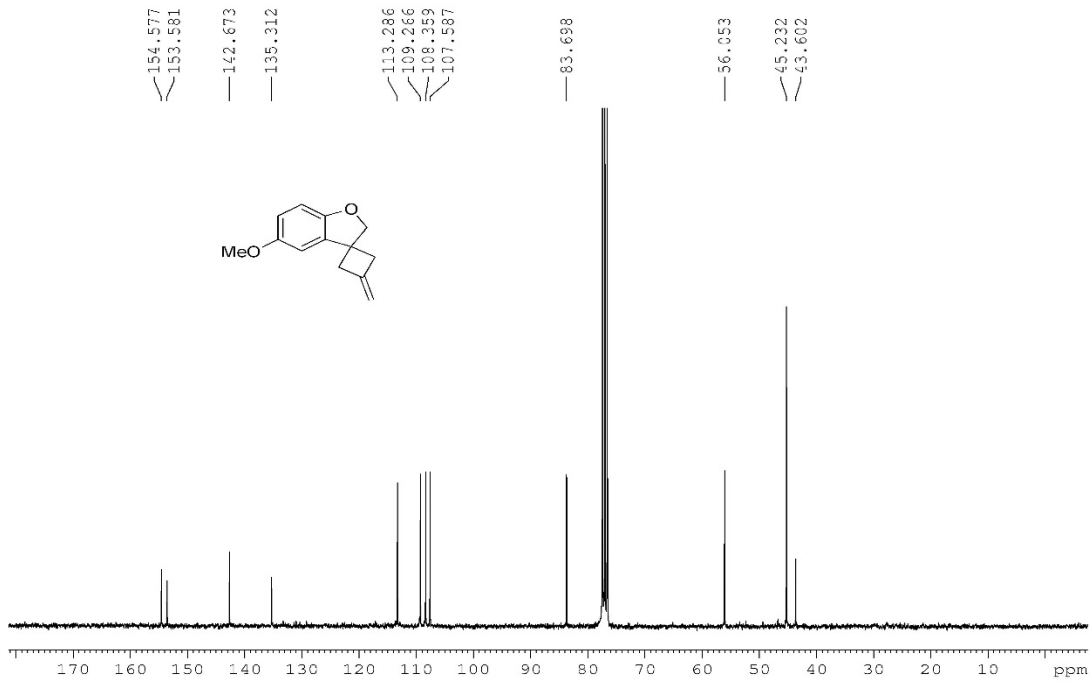
^{13}C NMR spectrum of compound **2f**



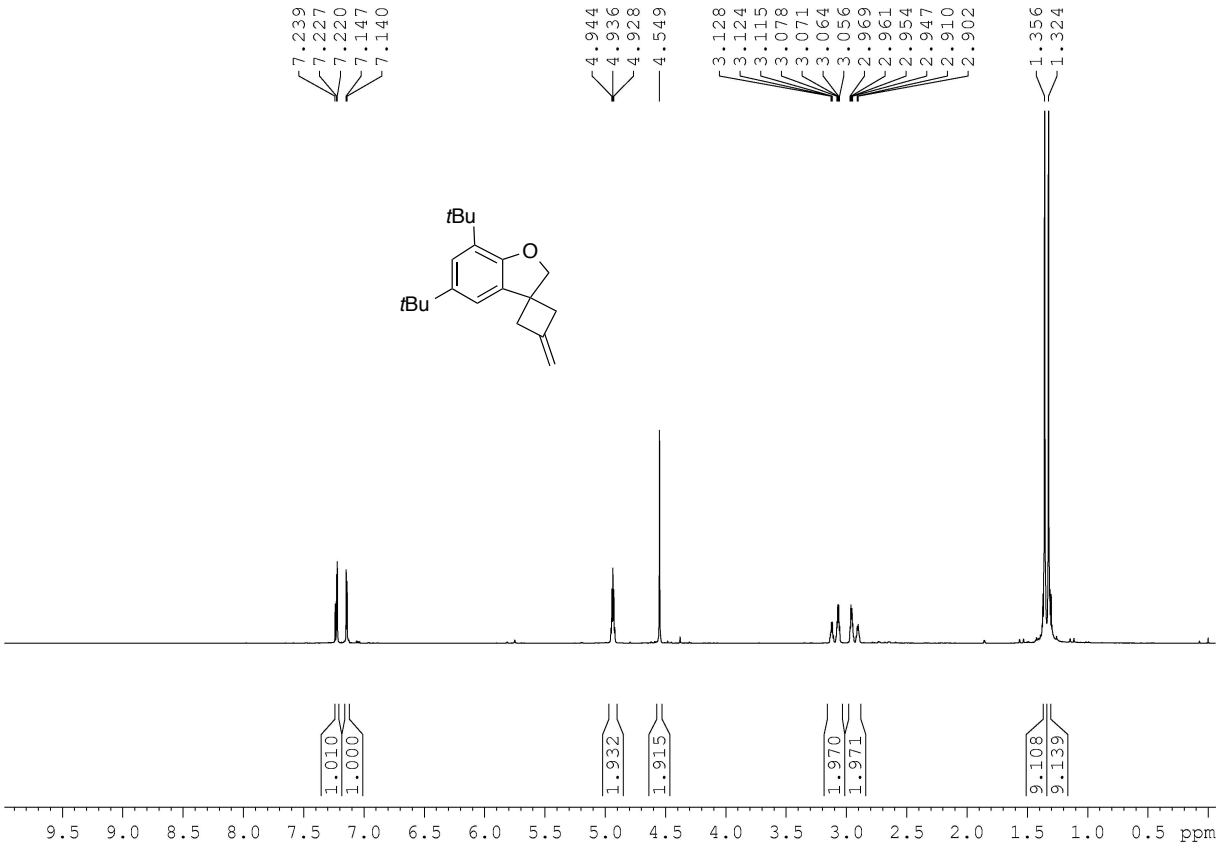
^{1}H NMR spectrum of compound **2g**



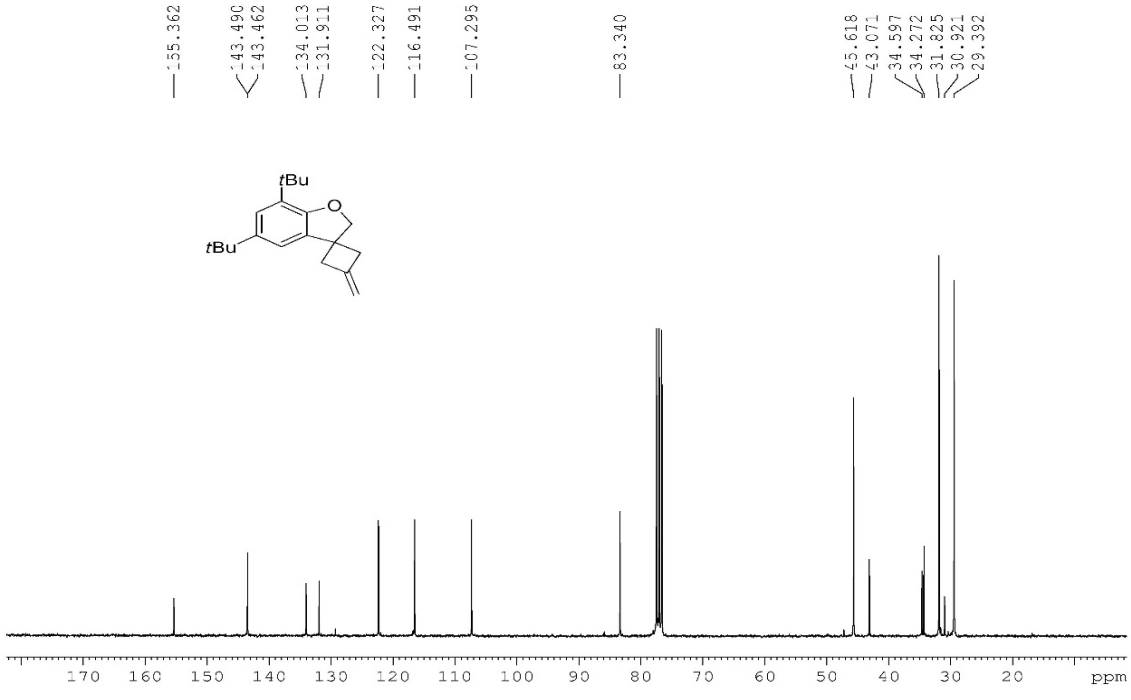
^{13}C NMR spectrum of compound **2g**



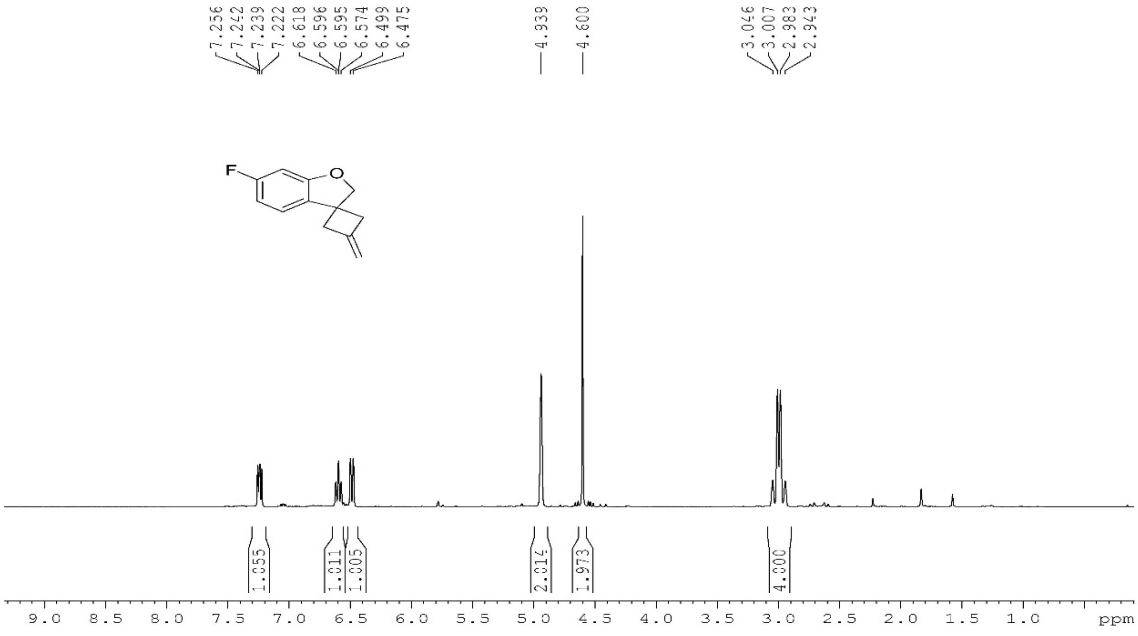
^{1}H NMR spectrum of compound **2h**



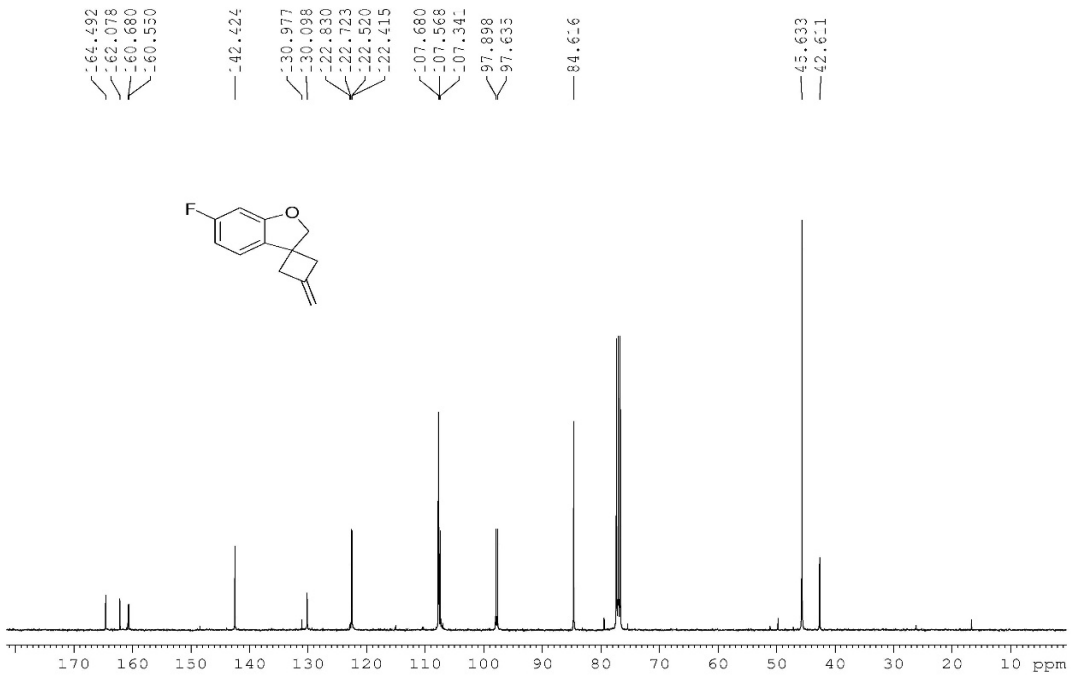
^{13}C NMR spectrum of compound **2h**



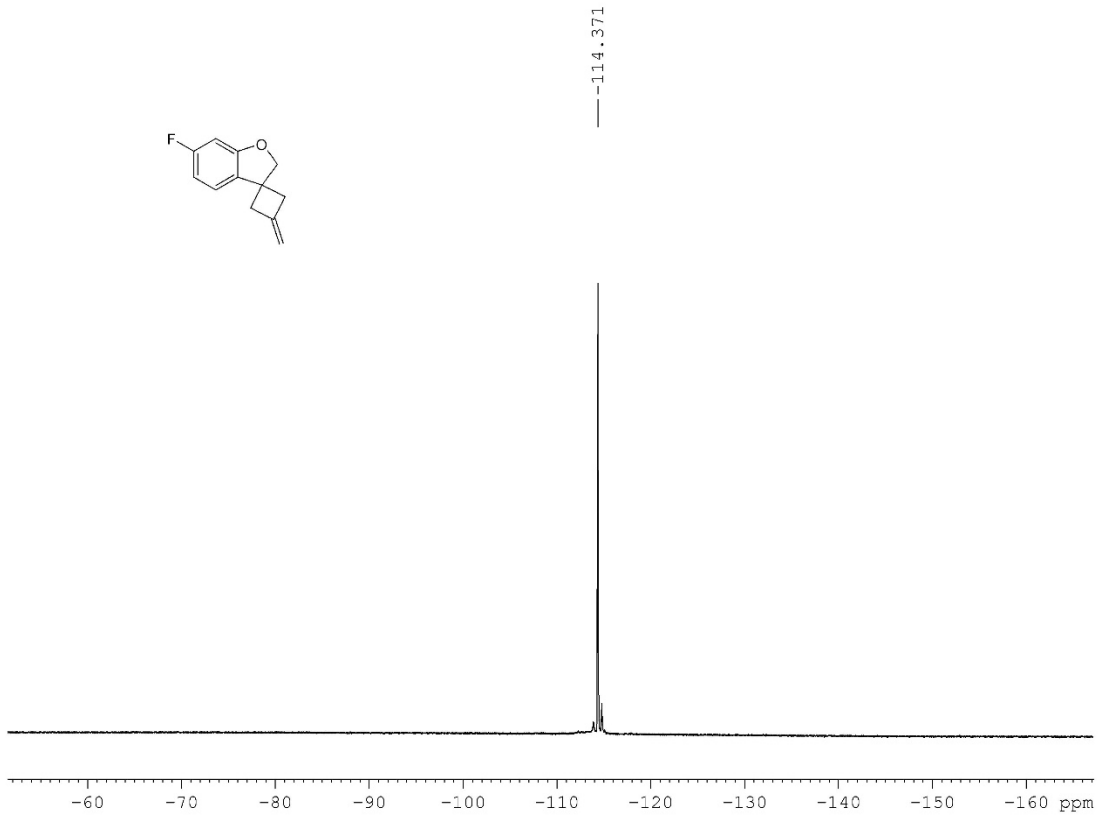
^{1}H NMR spectrum of compound **2i**



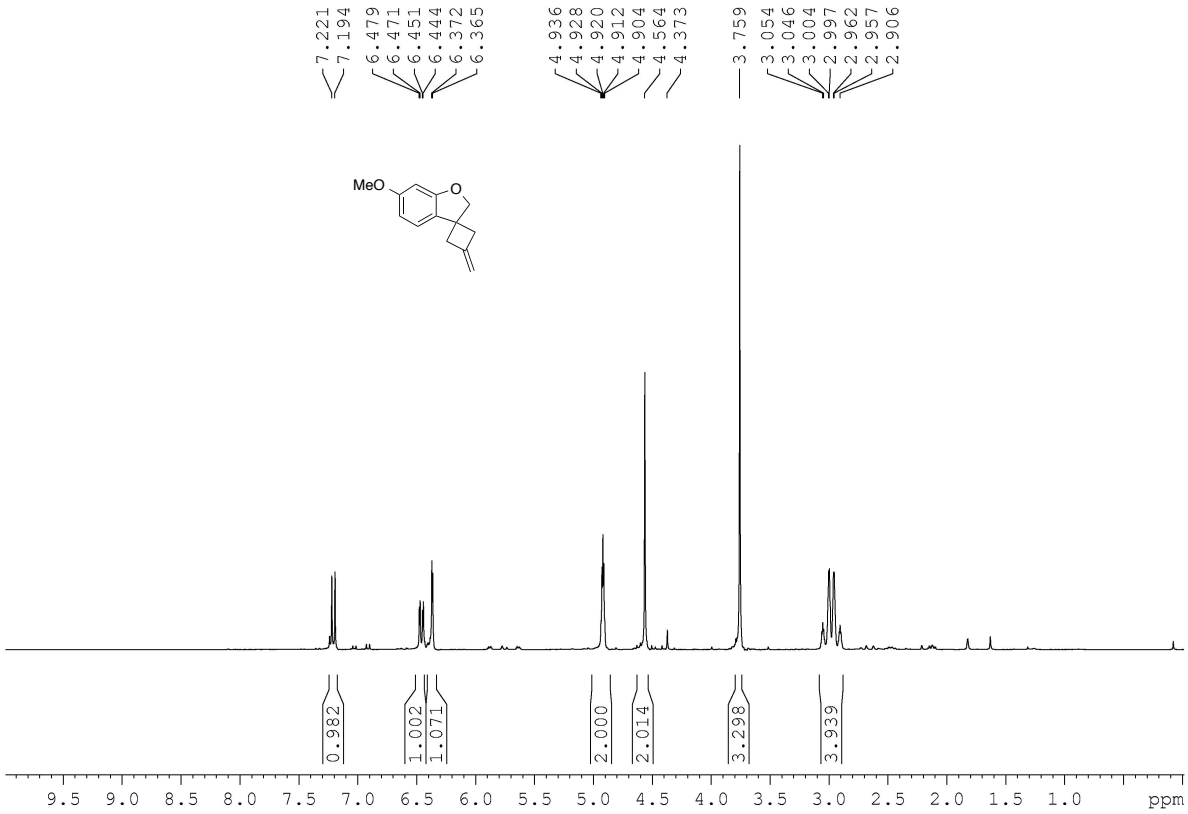
^{13}C NMR spectrum of compound **2i**



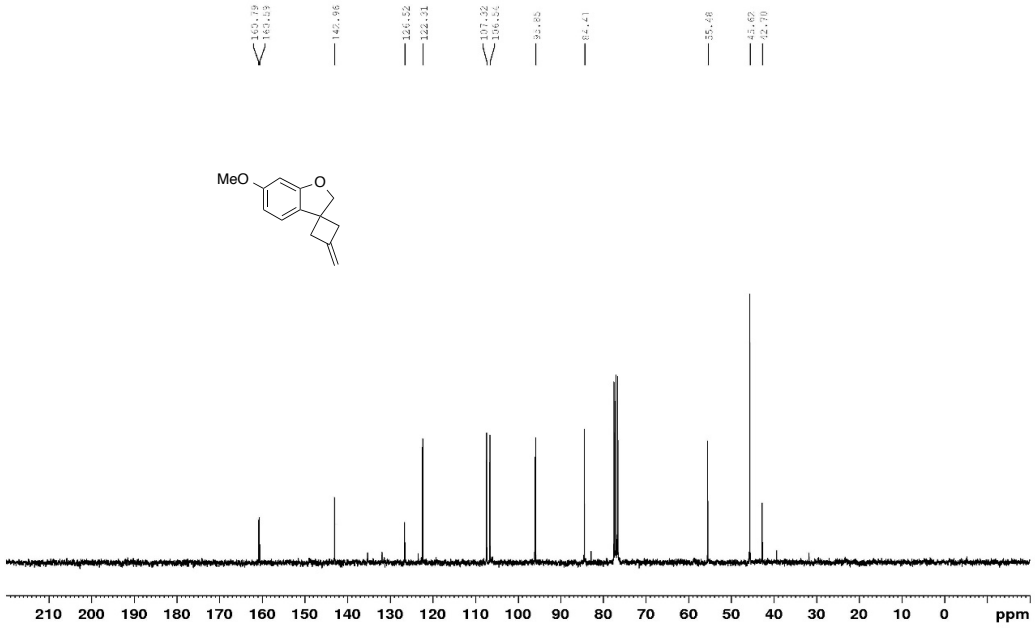
^{19}F NMR spectrum of compound **2i**



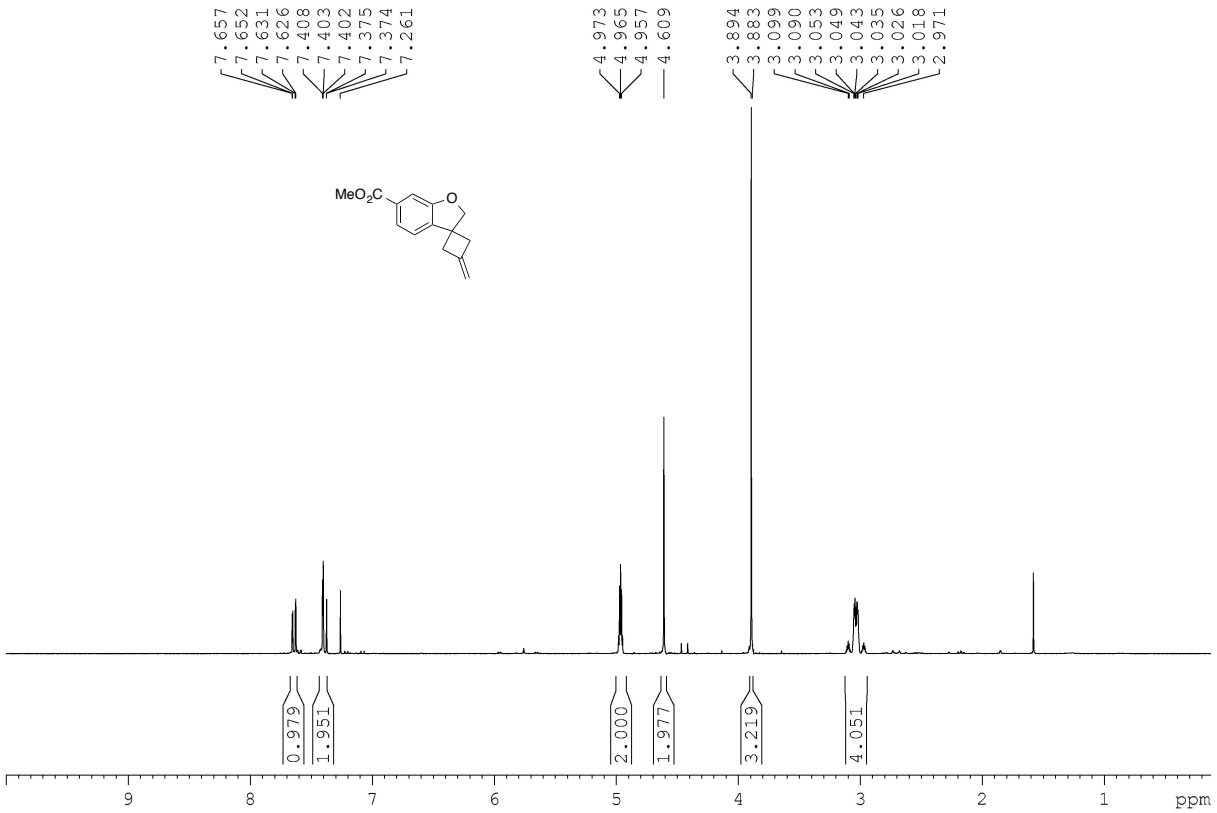
^{1}H NMR spectrum of compound **2j**



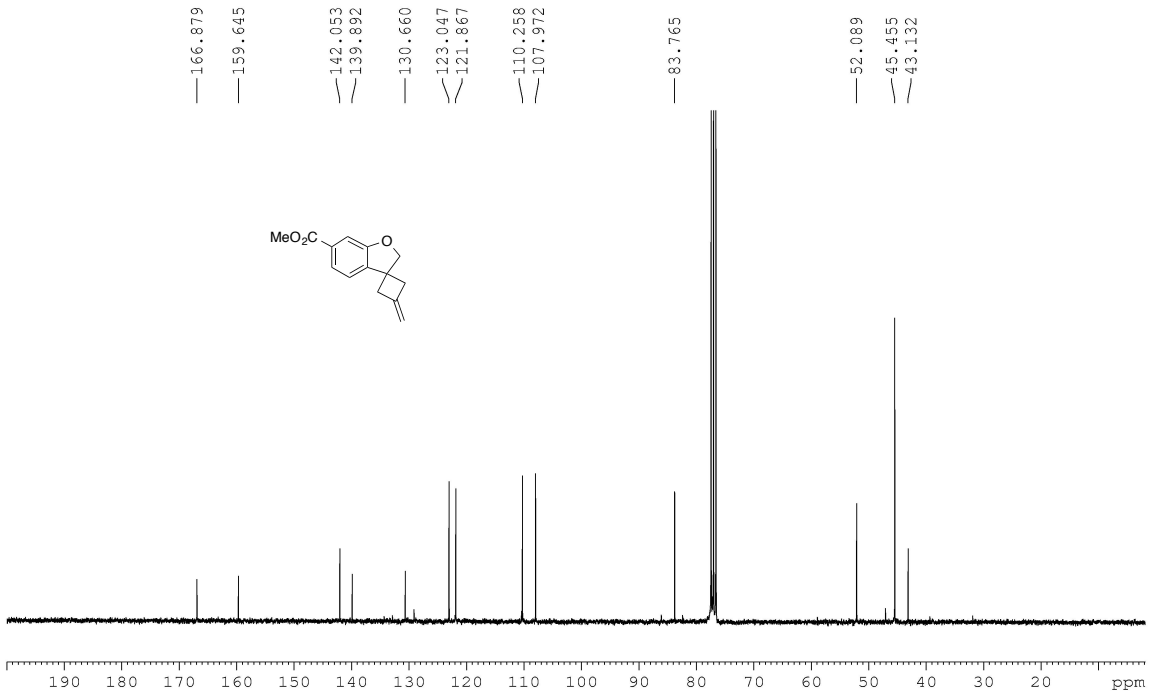
^{13}C NMR spectrum of compound **2j**



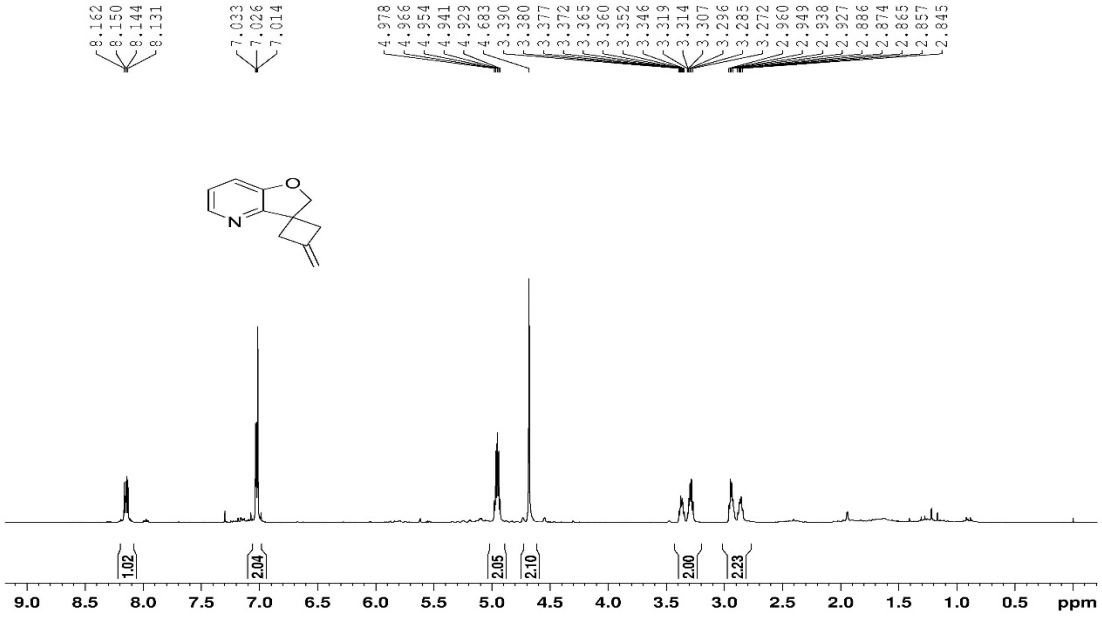
^{1}H NMR spectrum of compound **2k**



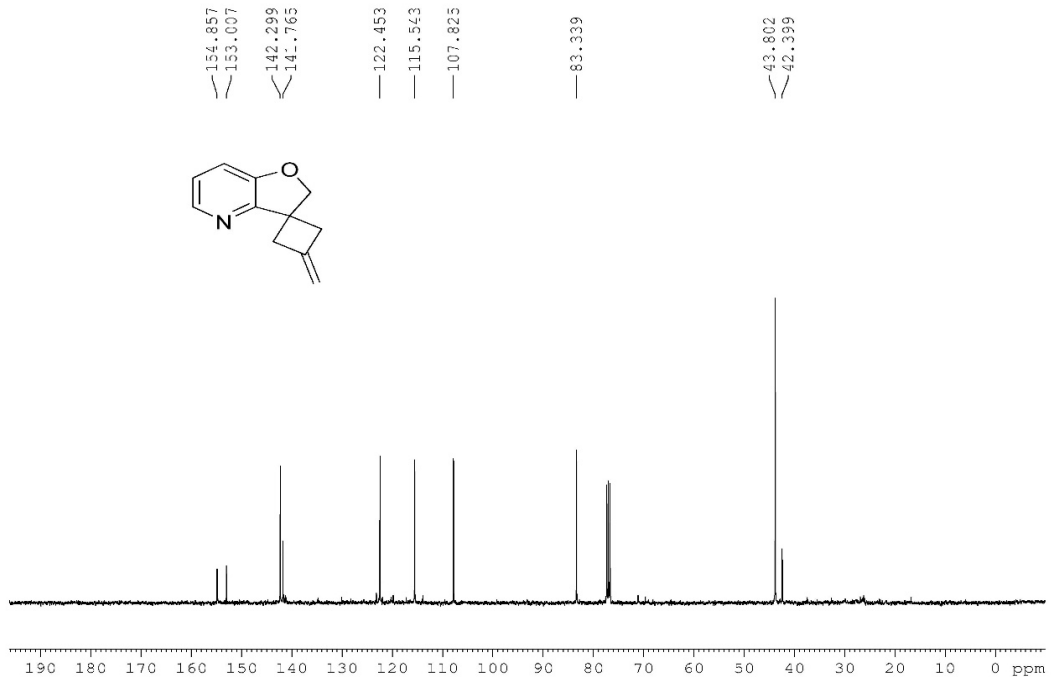
^{13}C NMR spectrum of compound **2k**



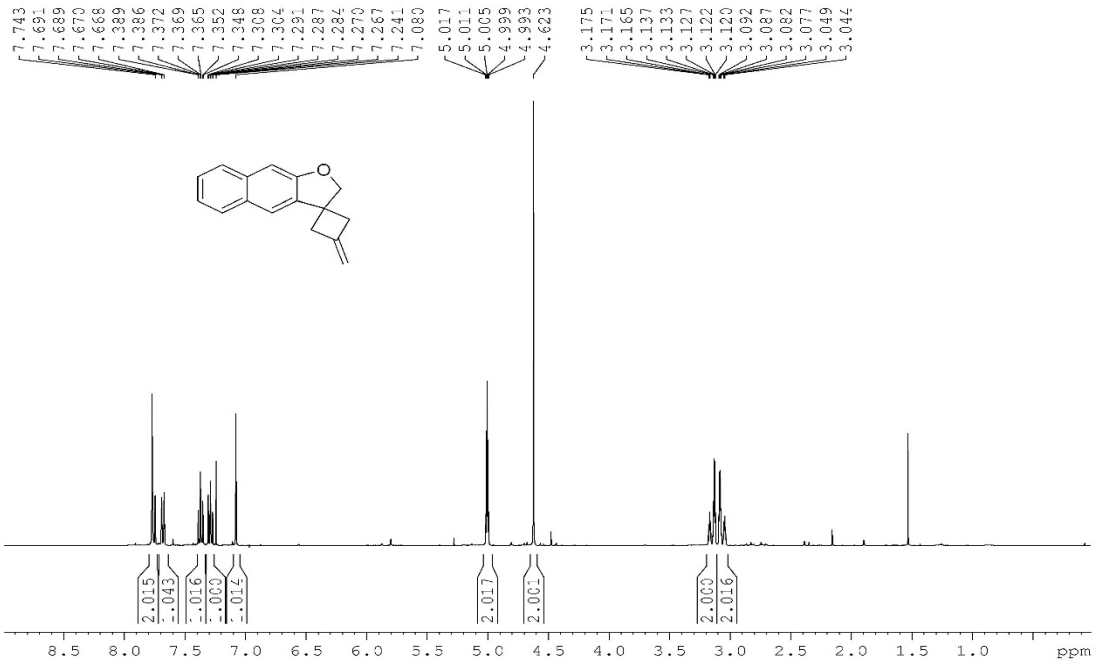
^{1}H NMR spectrum of compound **2l**



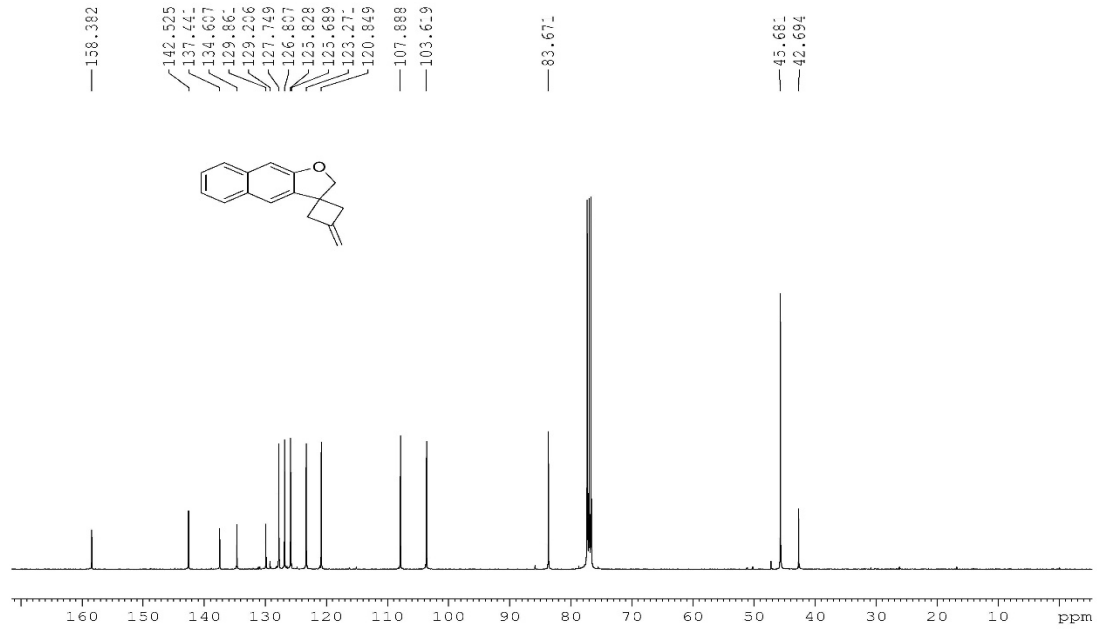
^{13}C NMR spectrum of compound **2l**



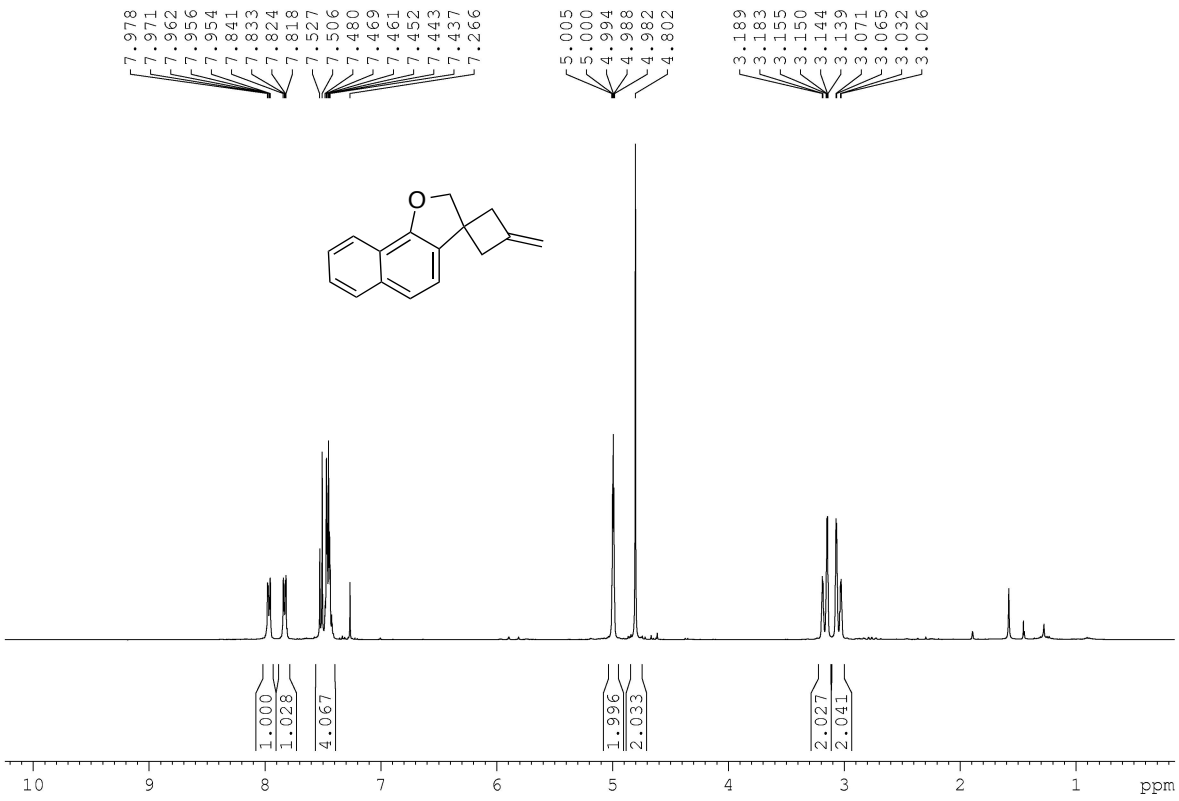
^{1}H NMR spectrum of compound **2m**



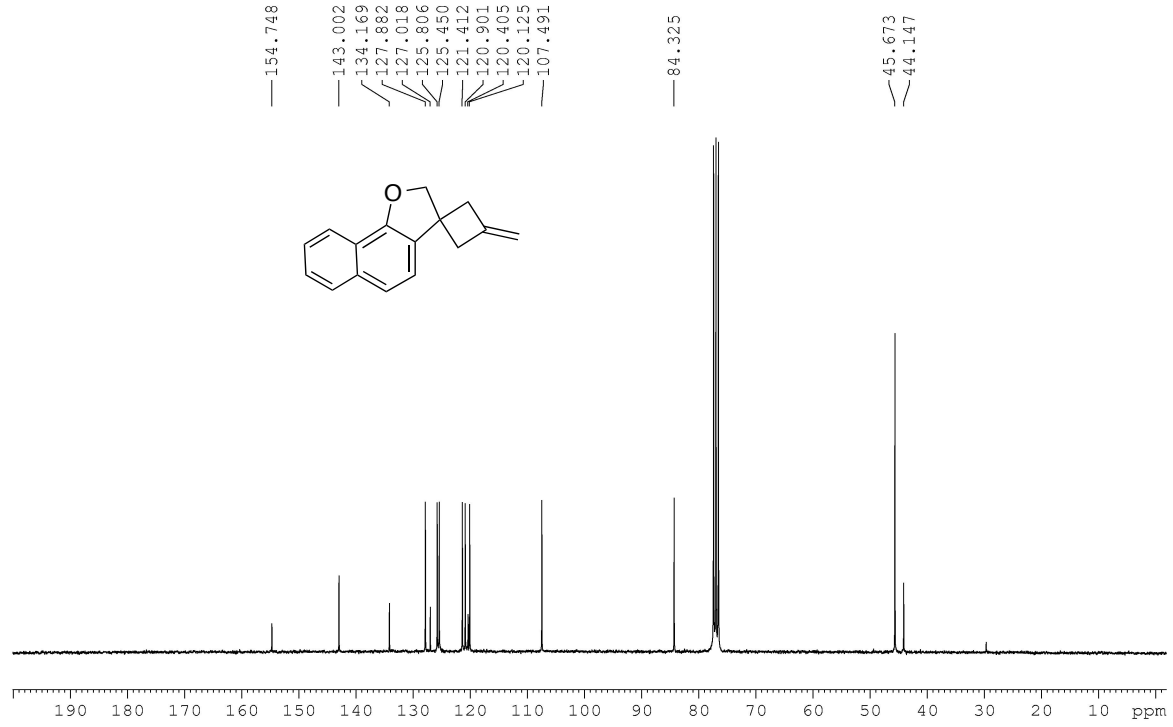
^{13}C NMR spectrum of compound **2m**



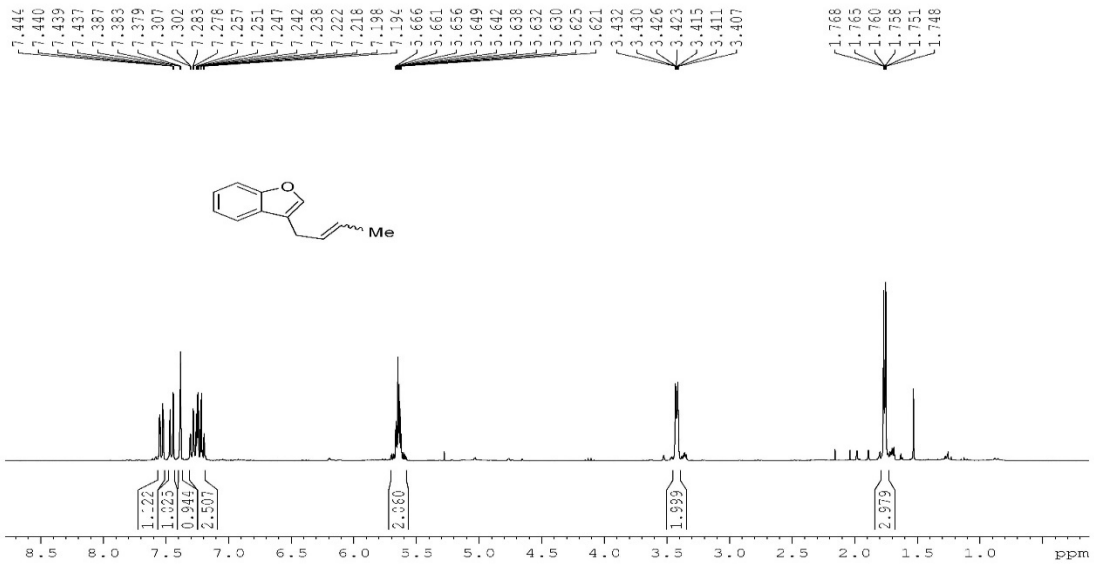
^{1}H NMR spectrum of compound **2n**



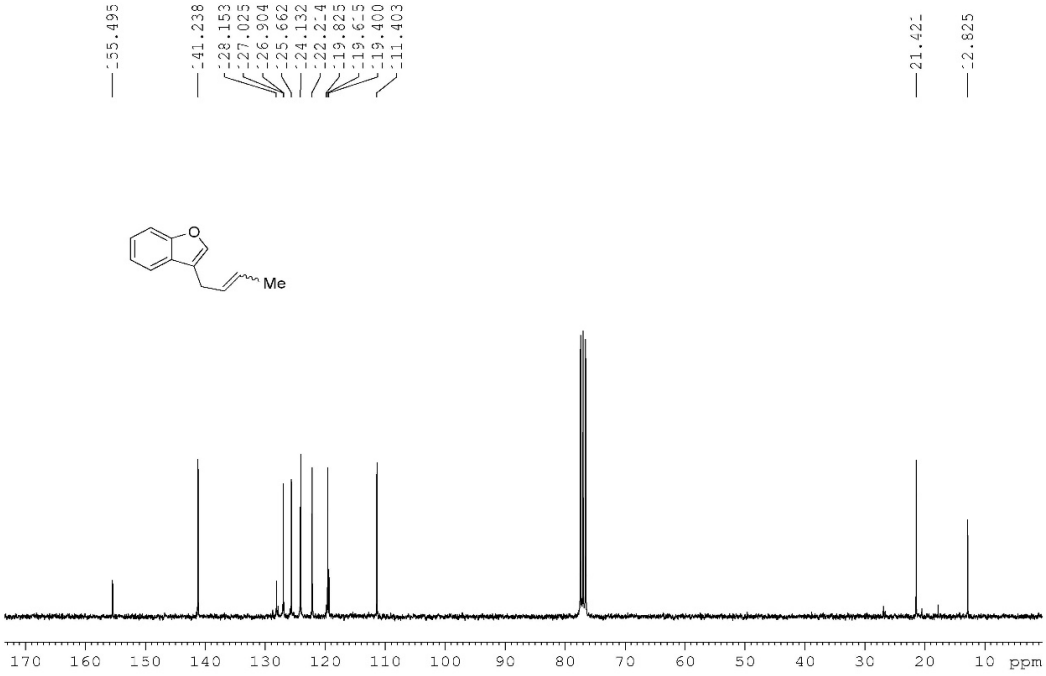
^{13}C NMR spectrum of compound **2n**



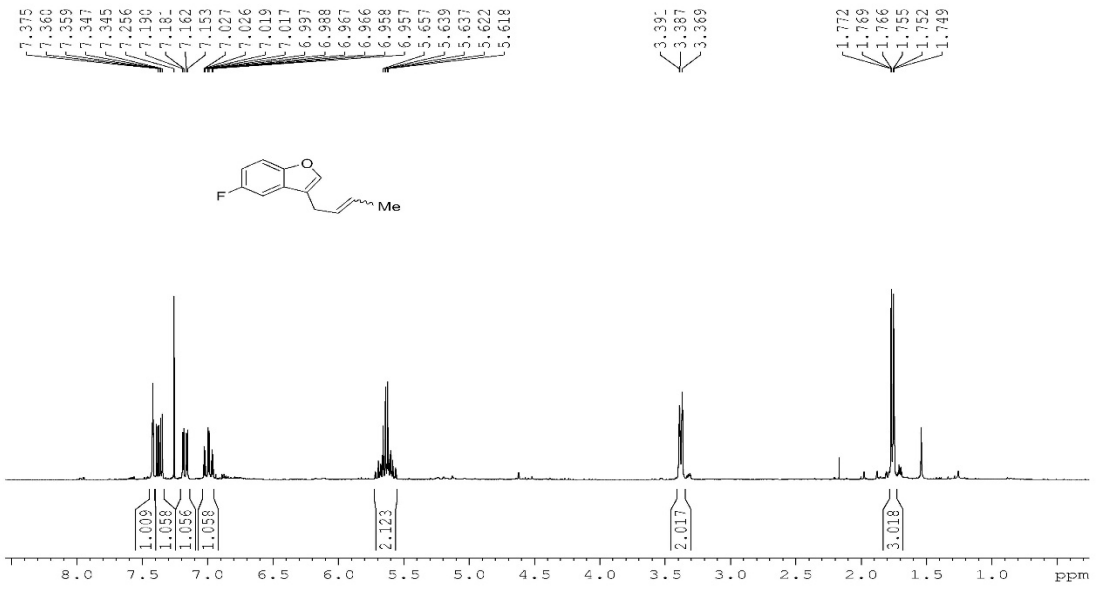
^{1}H NMR spectrum of compound **3a**



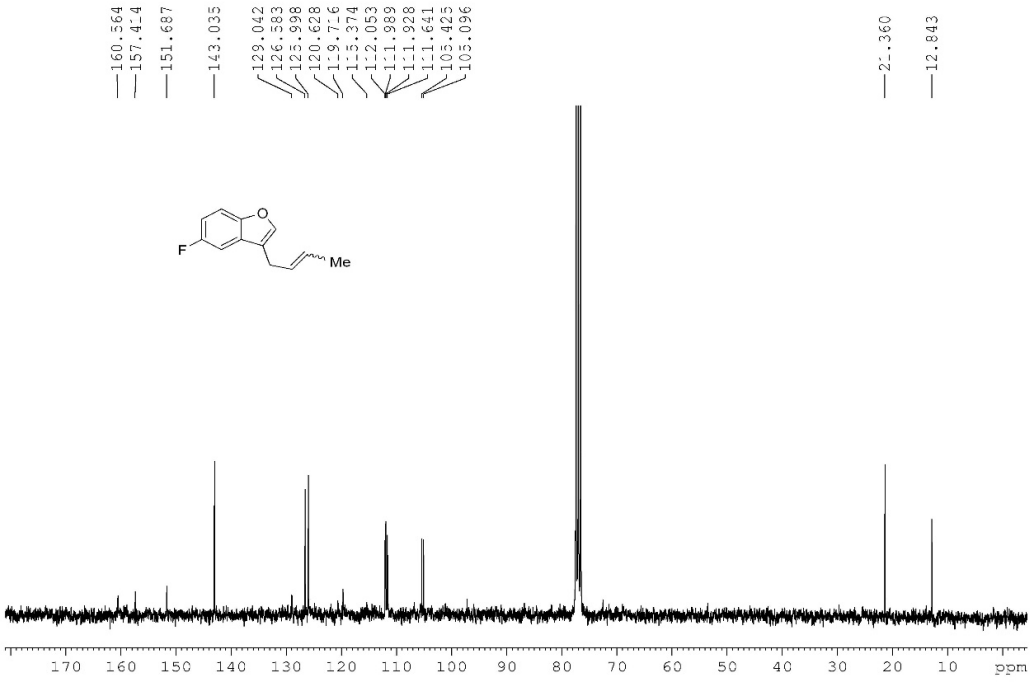
^{13}C NMR spectrum of compound **3a**



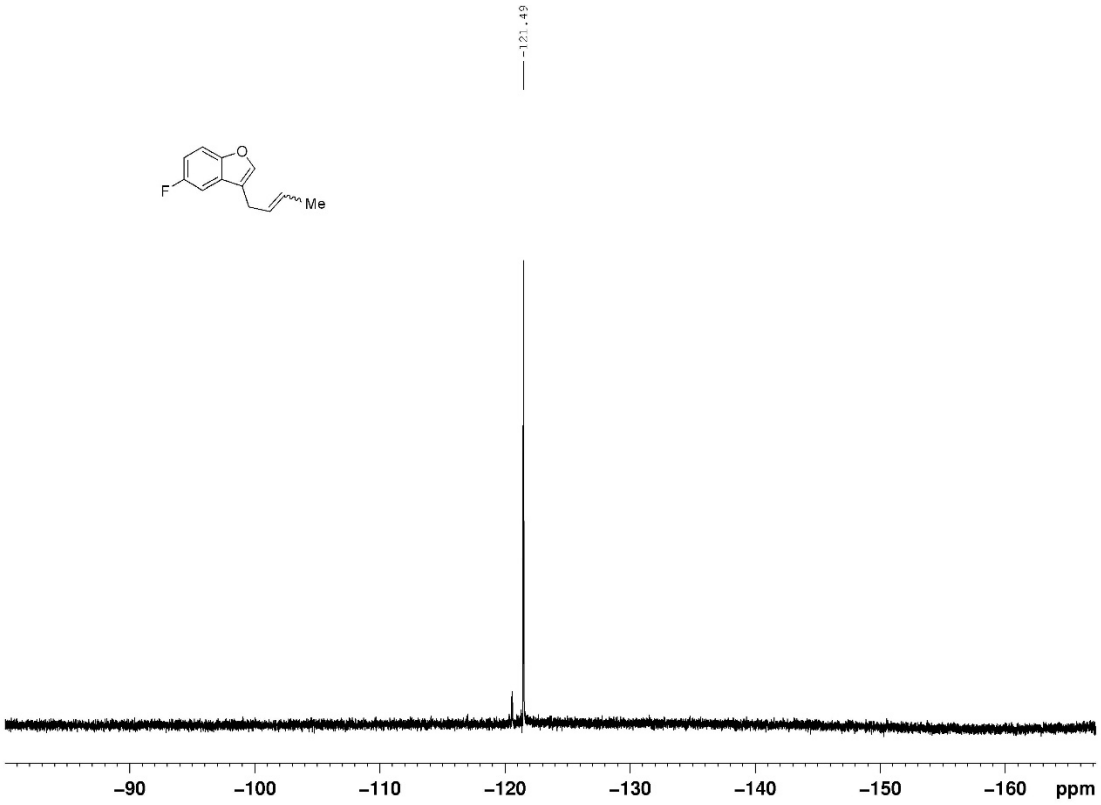
^{1}H NMR spectrum of compound **3b**



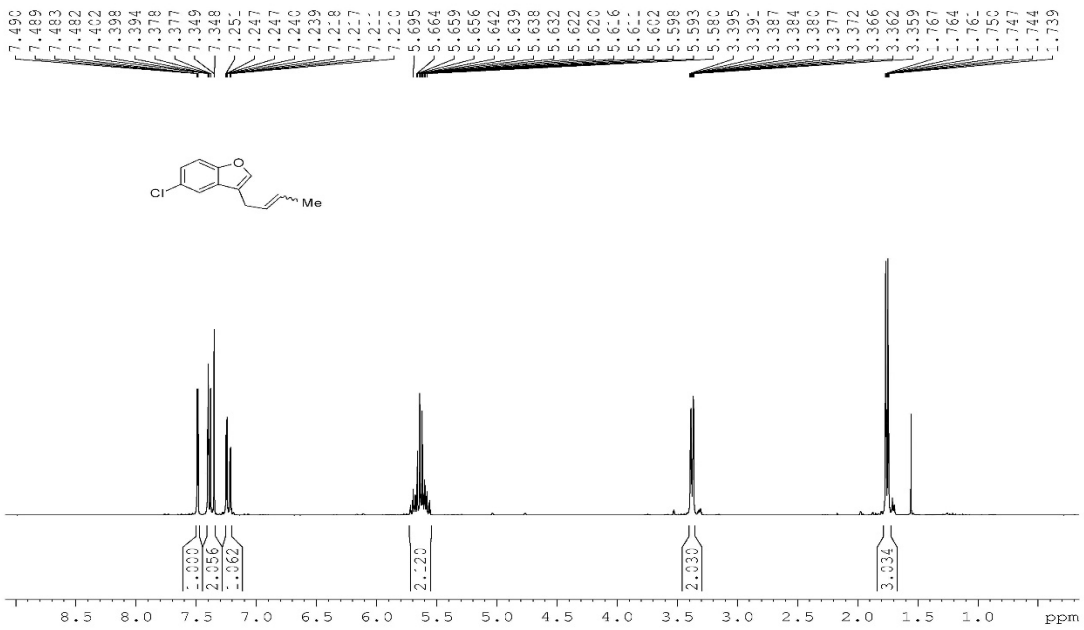
^{13}C NMR spectrum of compound **3b**



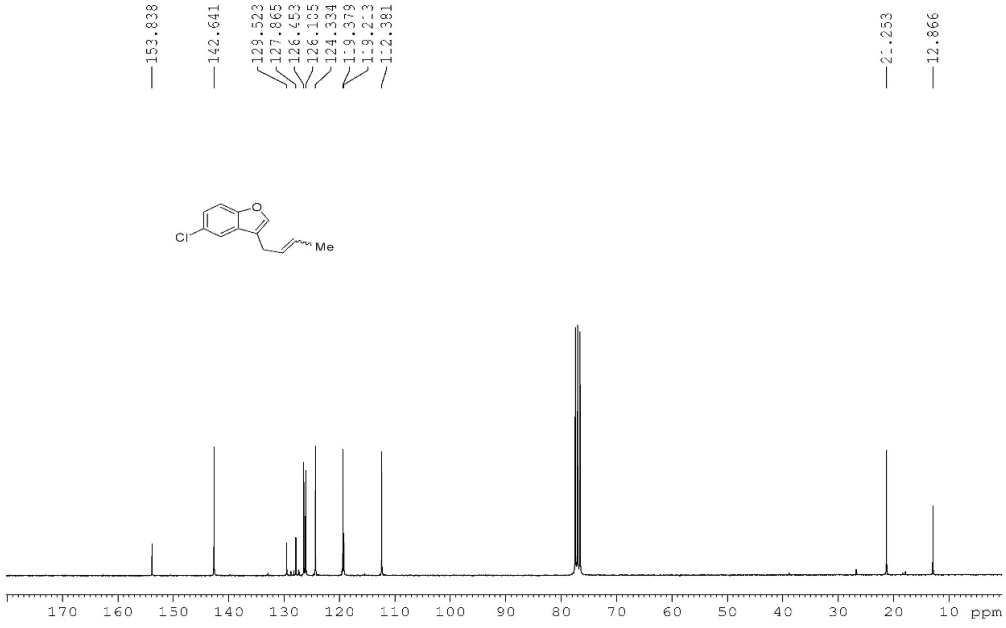
^{19}F NMR spectrum of compound **3b**



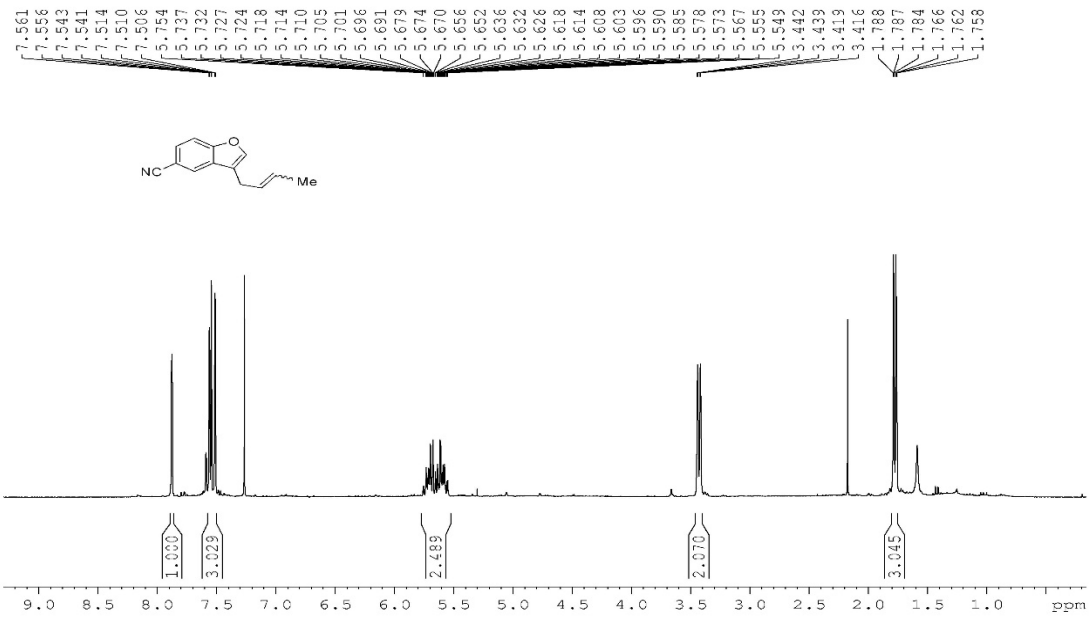
^{1}H NMR spectrum of compound **3c**



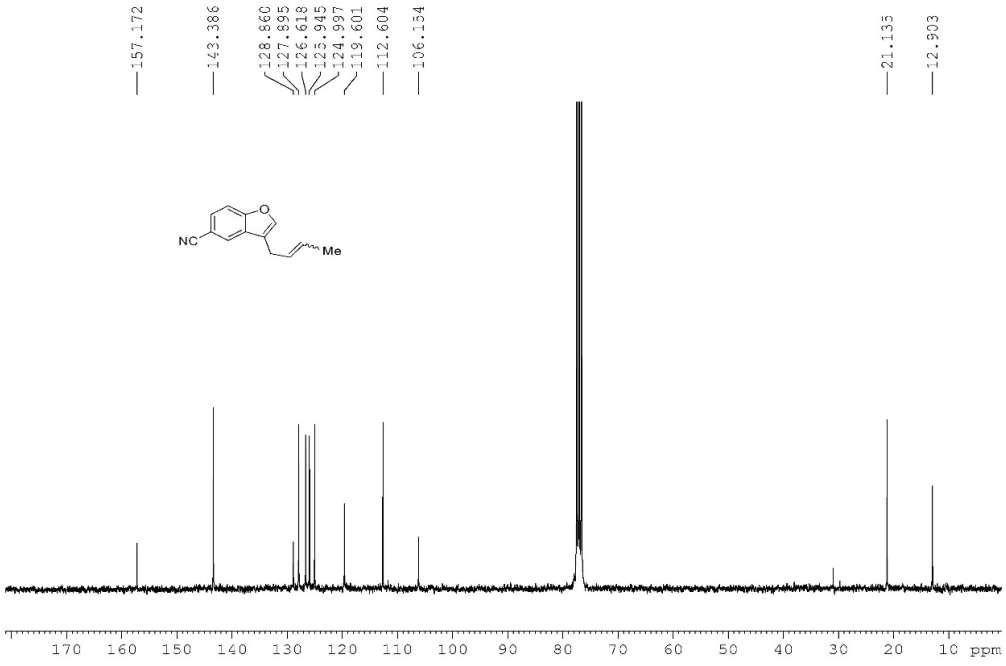
^{13}C NMR spectrum of compound **3c**



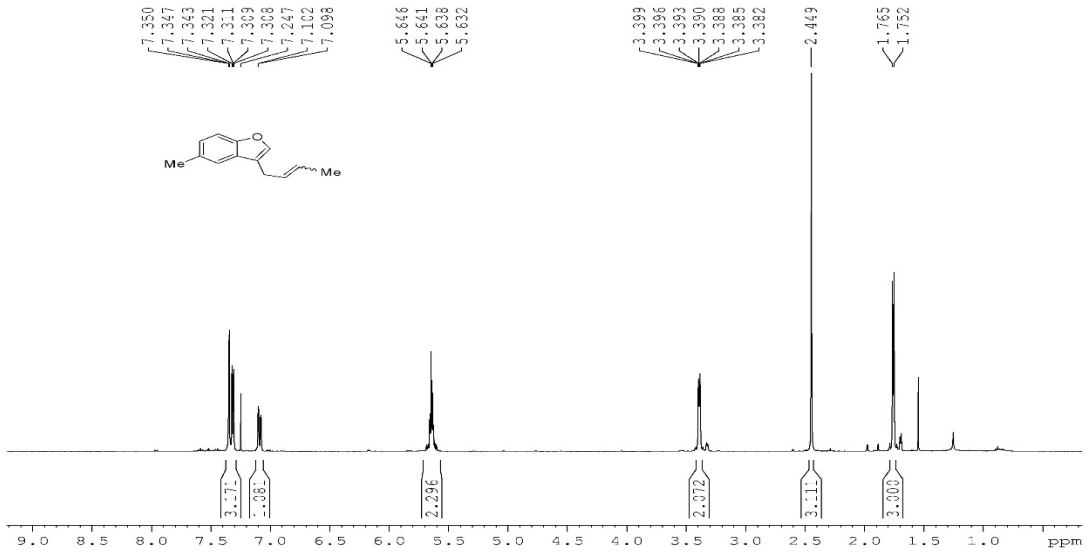
^{1}H NMR spectrum of compound **3d**



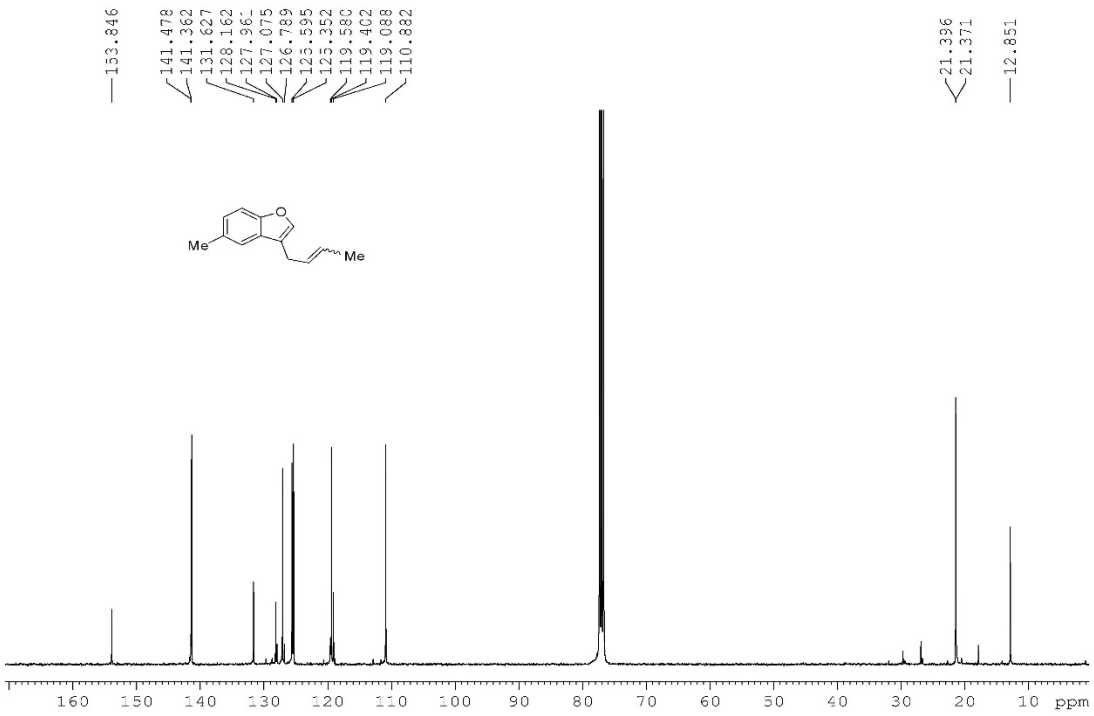
^{13}C NMR spectrum of compound **3d**



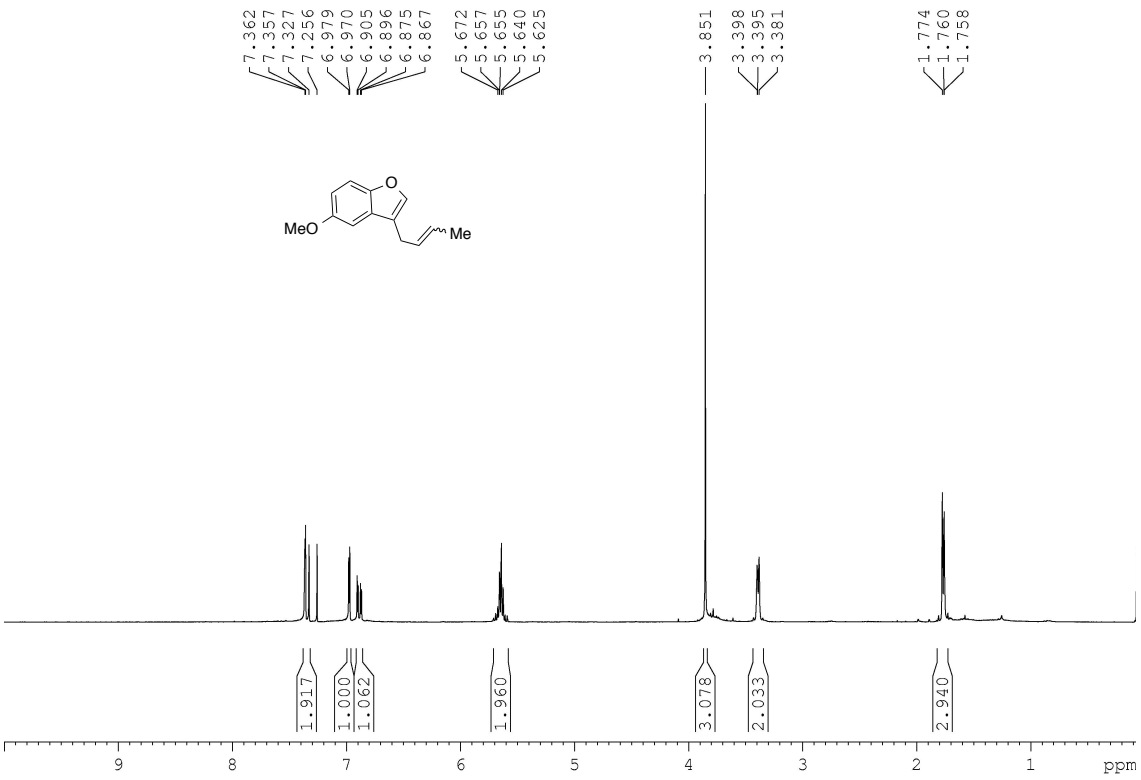
^{1}H NMR spectrum of compound **3e**



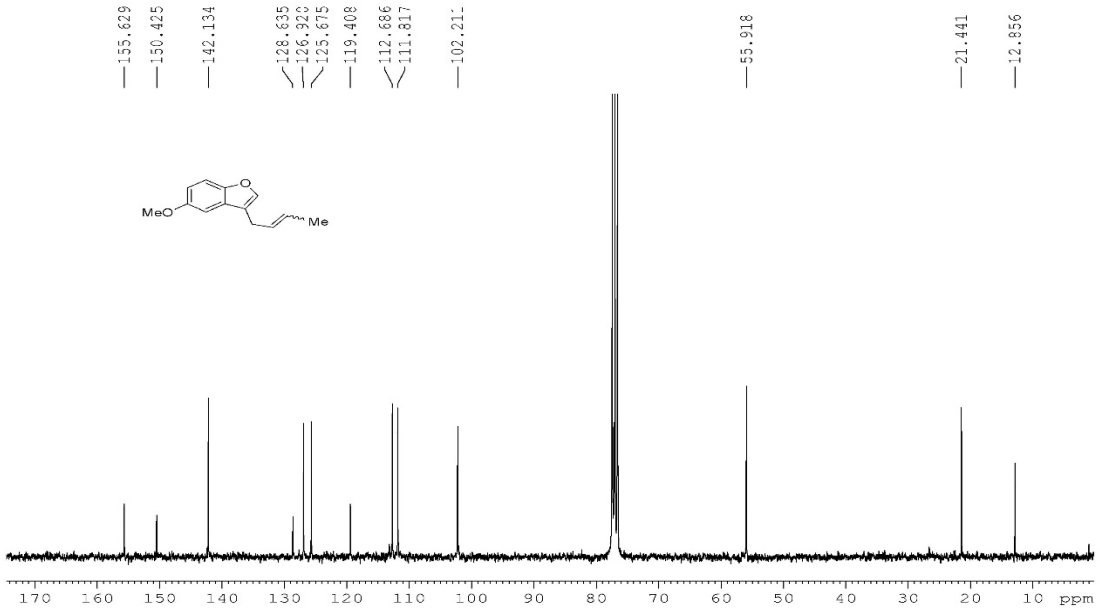
^{13}C NMR spectrum of compound **3e**



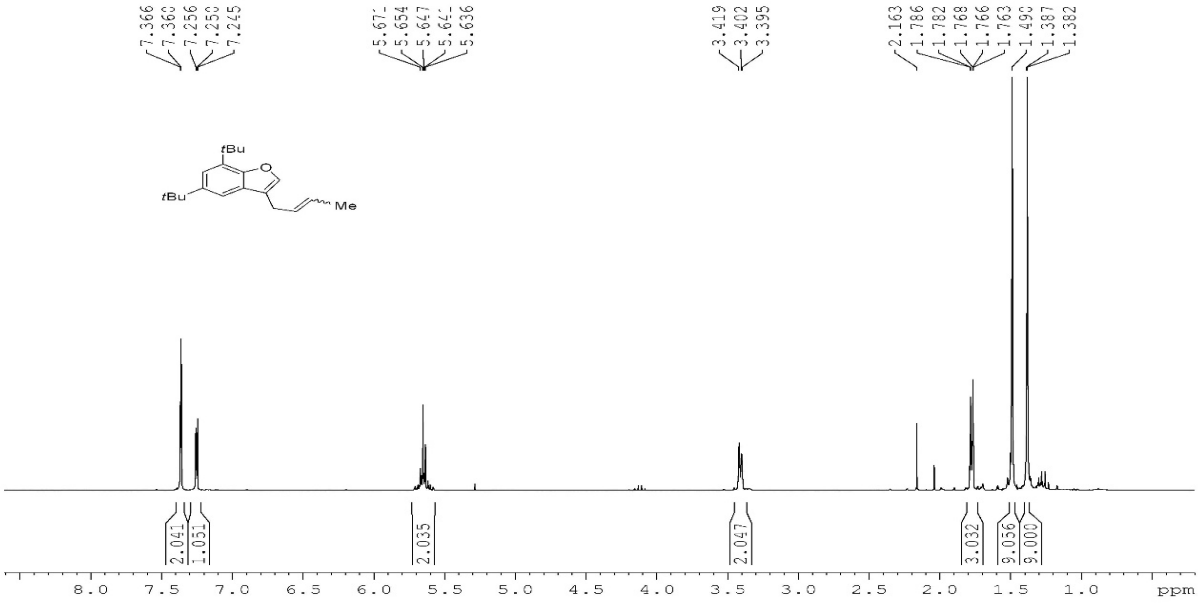
^{1}H NMR spectrum of compound **3f**



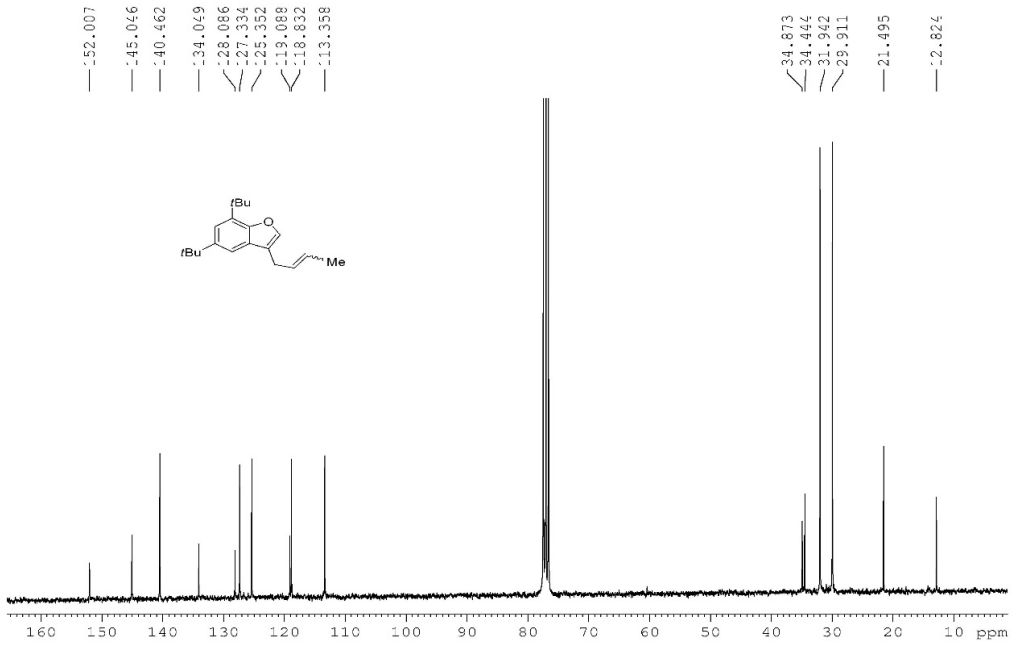
^{13}C NMR spectrum of compound **3f**



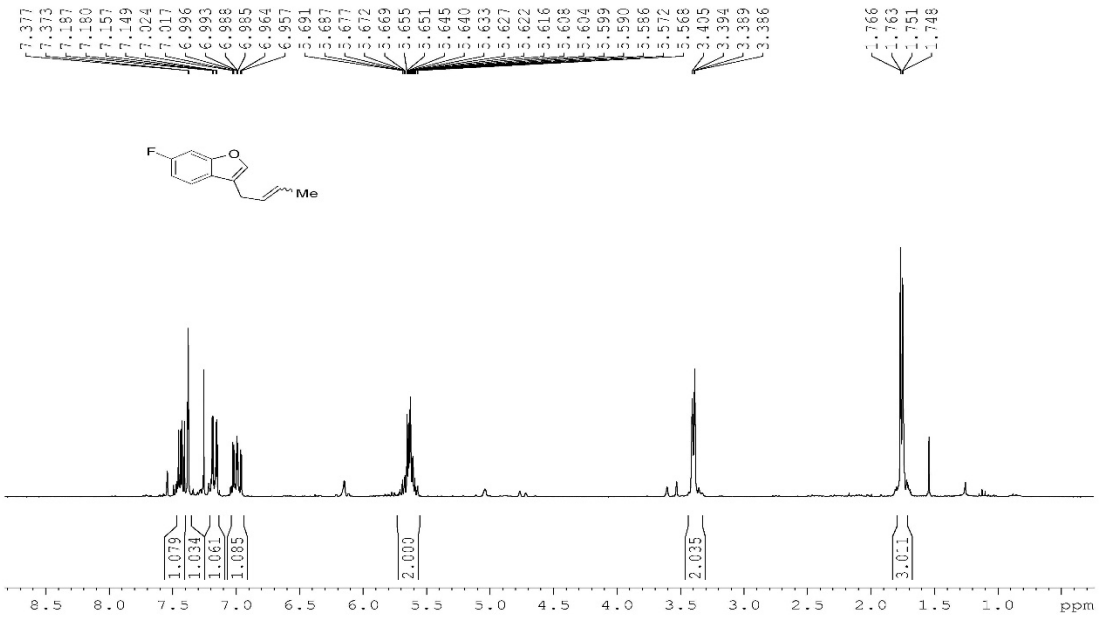
^{1}H NMR spectrum of compound **3g**



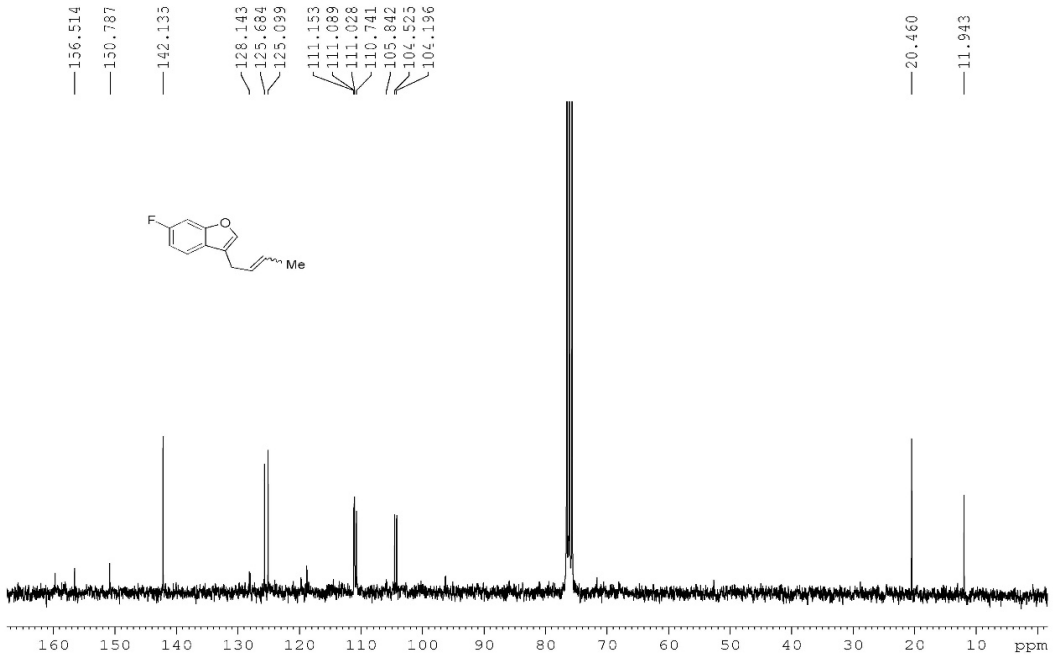
^{13}C NMR spectrum of compound **3g**



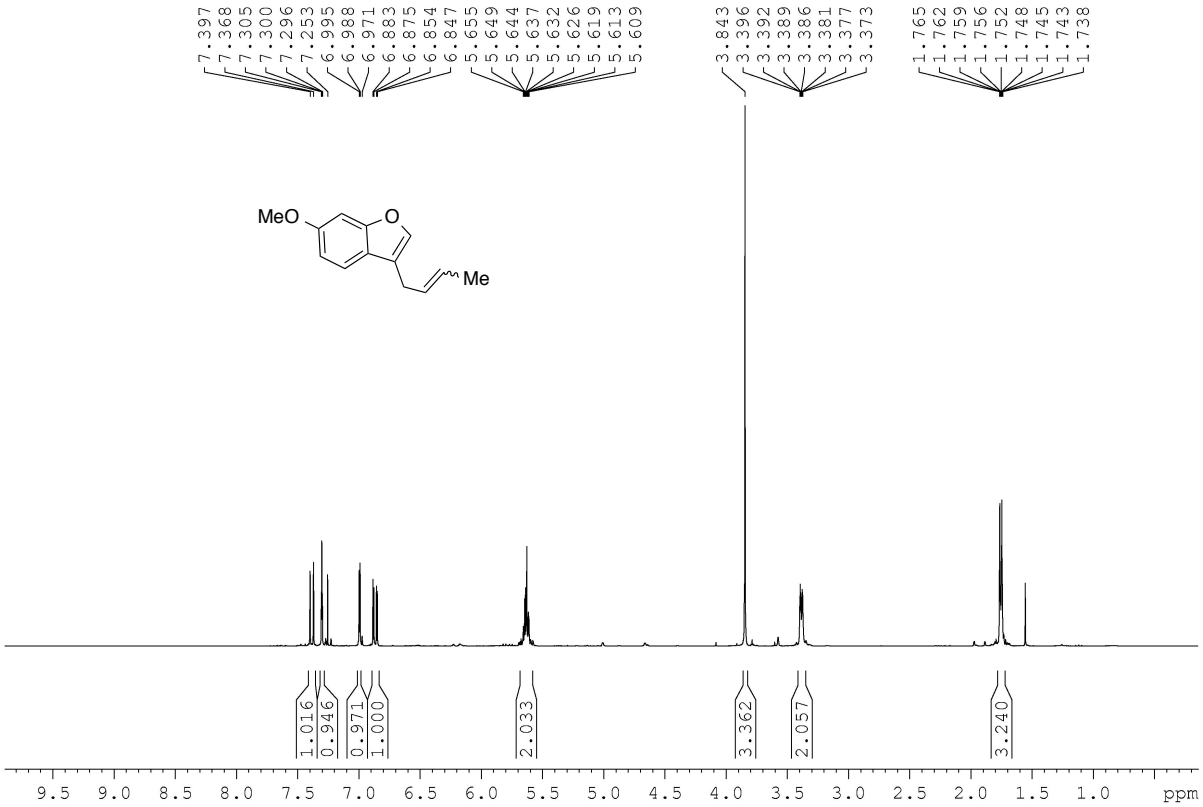
^{1}H NMR spectrum of compound **3h**



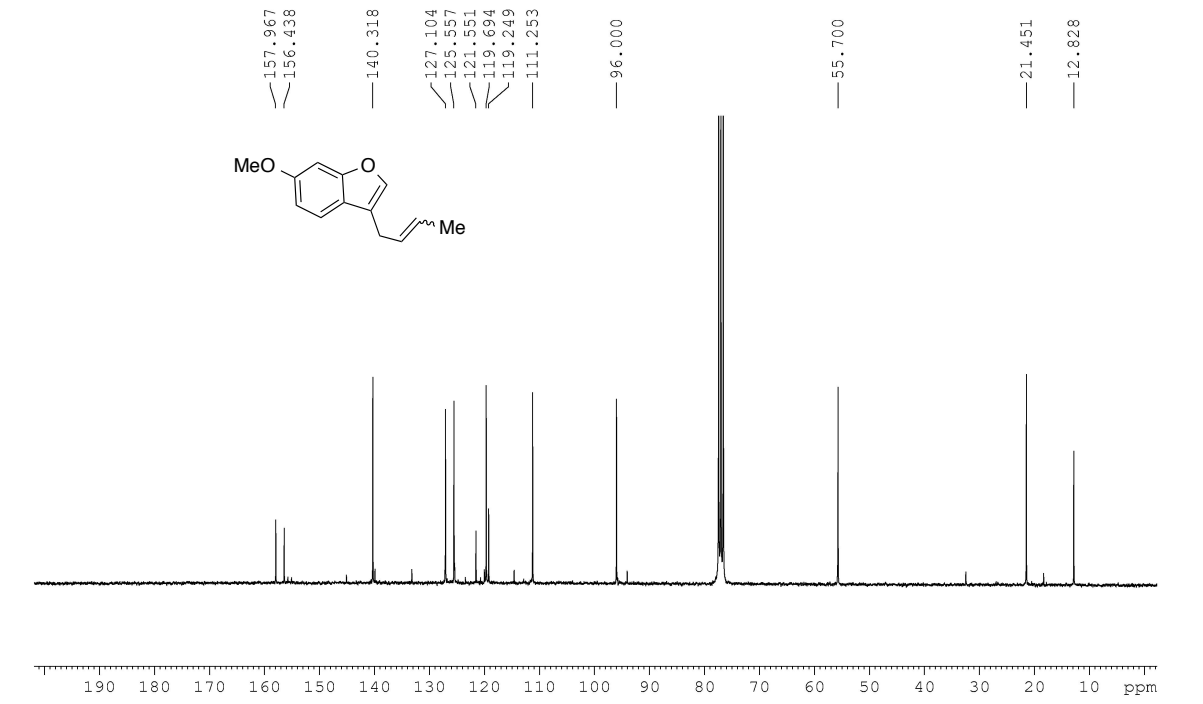
^{13}C NMR spectrum of compound **3h**



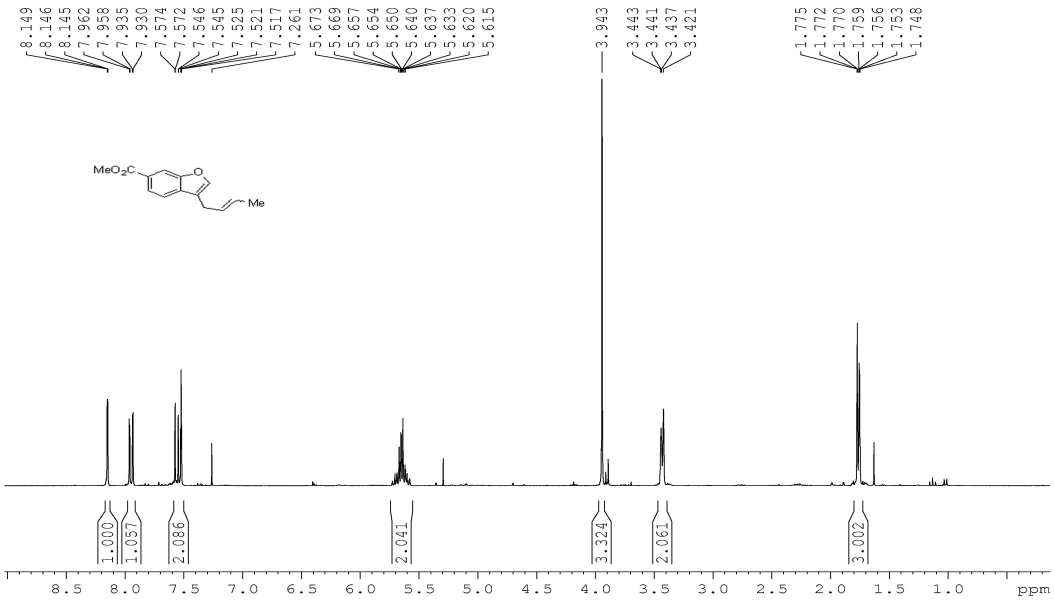
^{1}H NMR spectrum of compound **3i**



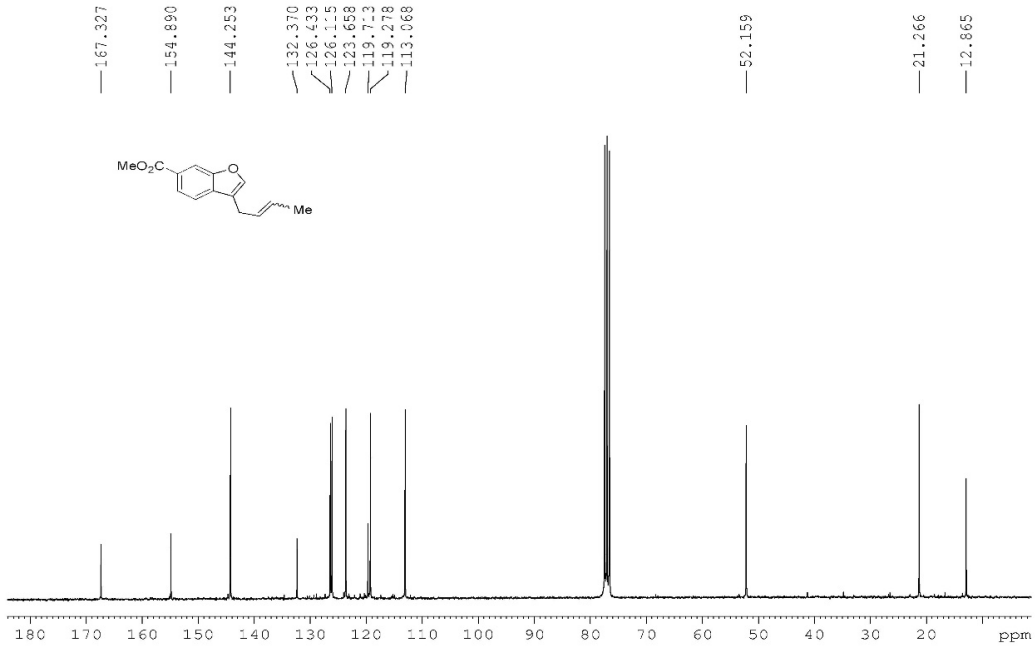
^{13}C NMR spectrum of compound **3i**



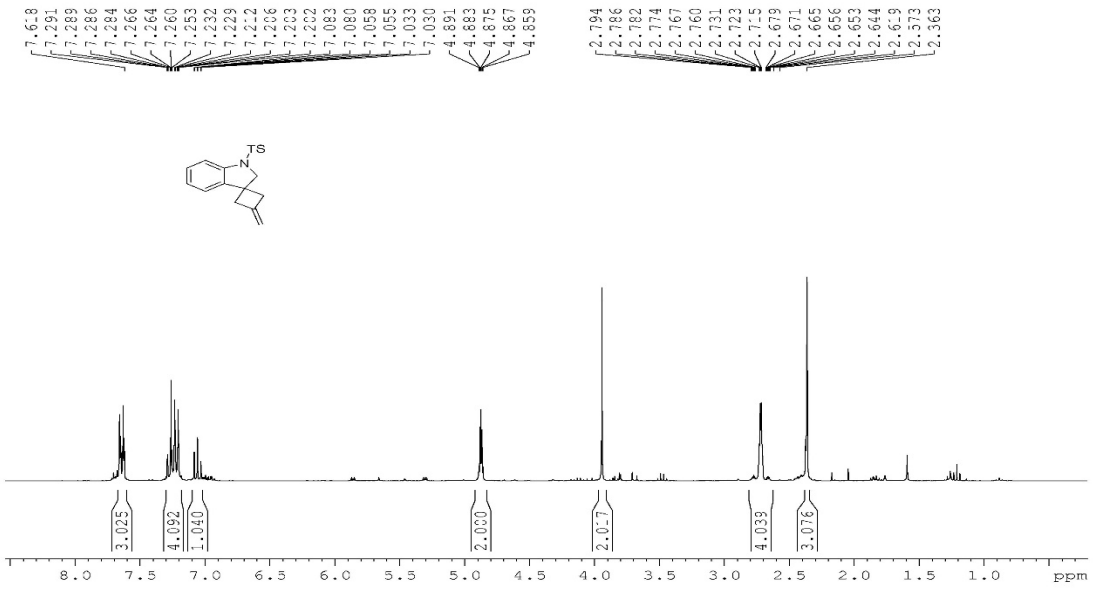
^{1}H NMR spectrum of compound **3j**



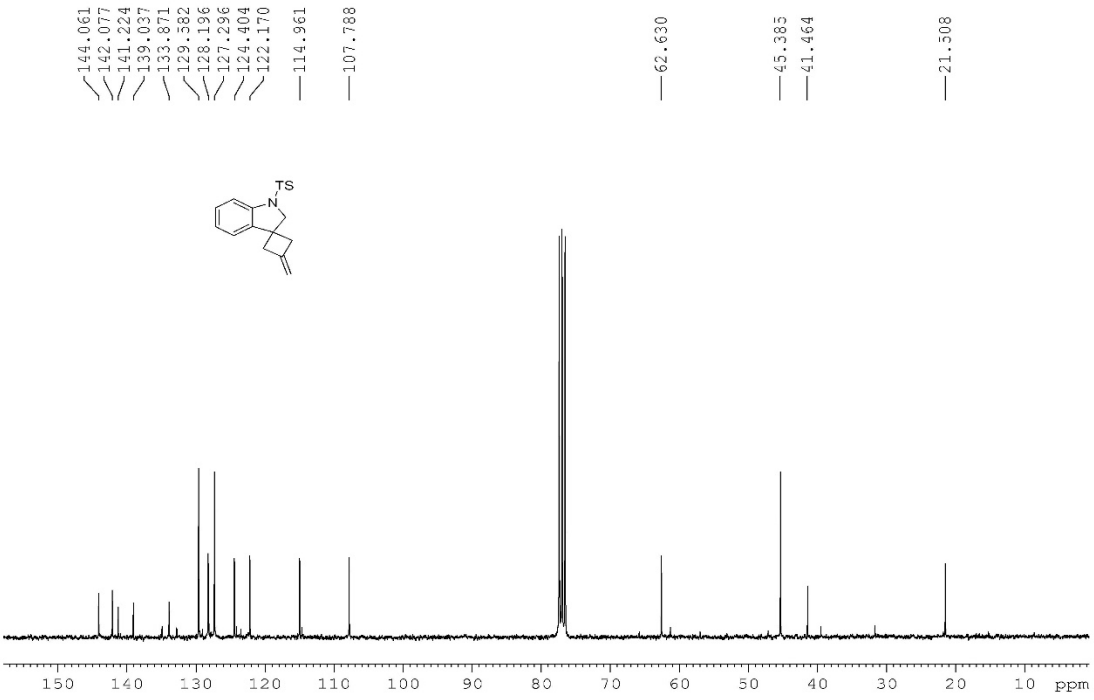
^{13}C NMR spectrum of compound **3j**



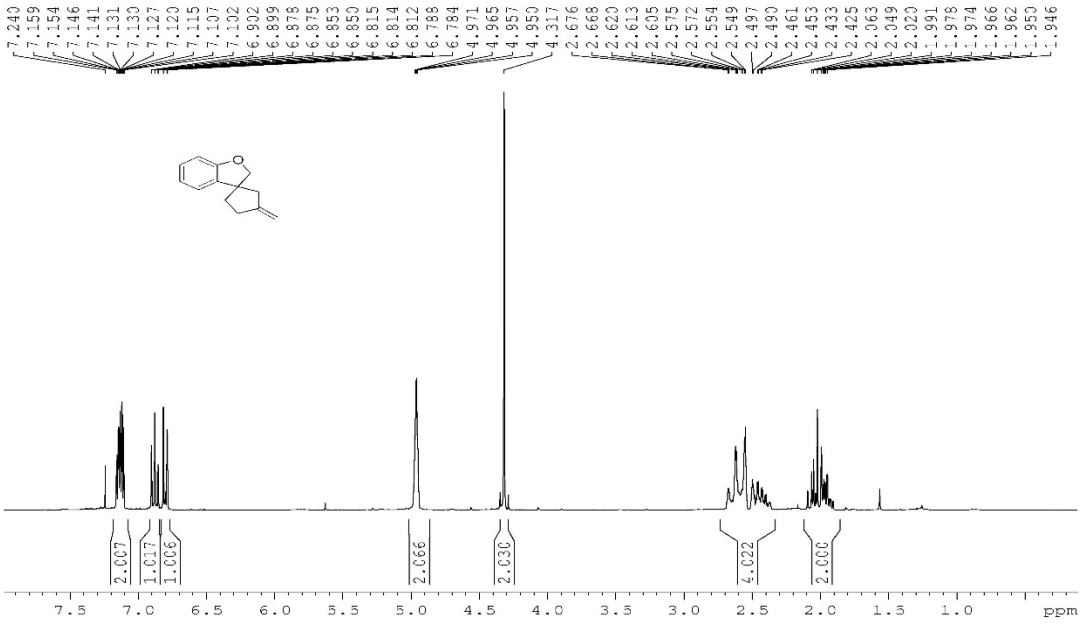
^{1}H NMR spectrum of compound **6**



^{13}C NMR spectrum of compound **6**



^{1}H NMR spectrum of compound **7**



^{13}C NMR spectrum of compound **7**