Supporting Information

Lawesson's Reagent Promoted Deoxygenation of Azlactones for the Syntheses of 2,4-Disubstituted Thiazoles

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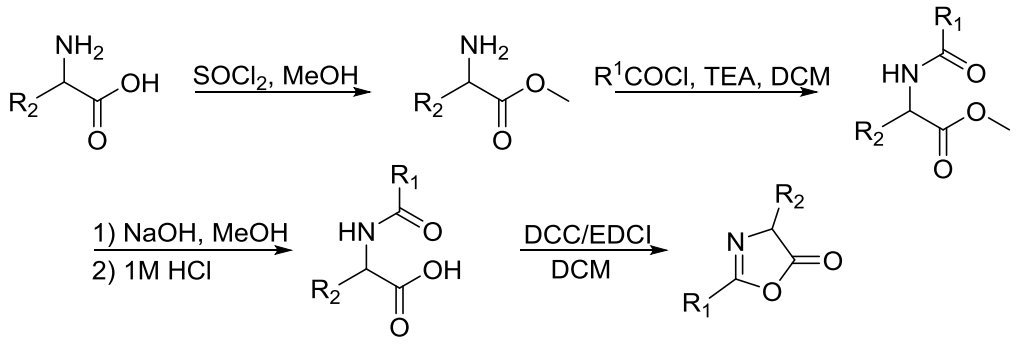
Table of Contents

1. General Information

All reactions were carried out in a dry solvent under an argon atmosphere, and all reagents were obtained from commercial suppliers and used without further purification, unless otherwise noted. All solvents were processed through the reference Purification of Laboratory Chemicals (Seventh Edition). External bath temperatures were used to record all reaction temperatures, and the heating source used was heating mantle. Silica gel (300~400 mesh), and petroleum ether and ethyl acetate were used for product purification by flash column chromatography. NMR spectra were recorded on Bruker 400 MHz or 600 MHz spectrometers. Proton chemical shifts are reported relative to internal standard TMS at δ 0.0 ppm or residual solvent peak ($CDCl_3$ at 7.26 ppm). Carbon chemical shifts are reported relative to a residual solvent peak ($CDCl_3$ at 77.06 ppm). The following abbreviations were used to designate multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet, br = broad. Fourier transform infrared spectra (FT-) were recorded on an Agilent Cary 630 FT-IR instrument. LC-MS spectra were recorded on an Agilent Technologies 1260 Ⅱ-MSD 6125 Quotation with an Agilent HC-C18(2) column (4.6 mm x 250 mm, film: 5 μm). High-resolution mass spectra (HRMS) were measured on a Brucker Daltonics Apex Ⅱ 47e Specification.

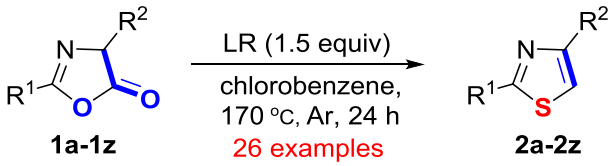
2. Preparation of starting materials



The general synthetic route has been reported in literature. [1-2]

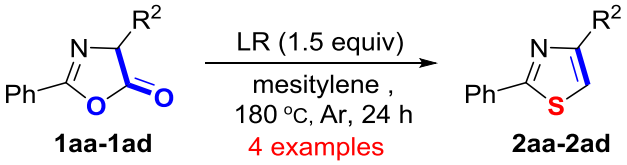
3. General Procedure for LR-Promoted Deoxygenation of Azlactones

3.1 Procedure for the Synthesis of **2a-2z**



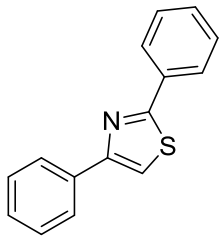
A Schlenk tube was charged with a mixture of azlactone **1** (0.2 mmol) and Lawesson's reagent (1.5 equiv, 0.3 mmol, 121.3 mg) in chlorobenzene (2.0 mL) under Ar. The vial was sealed and stirred vigorously at 170 °C. After 24 hours, the reaction was quenched by rapid cooling. Then the residue was purified by silica gel flash column chromatography to afford the target 2,4-disubstituted thiazoles.

3.1 Procedure for the Synthesis of **2aa-2ad**

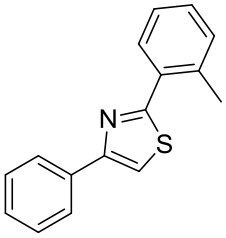


A Schlenk tube was charged with a mixture of azlactone **1** (0.2 mmol) and Lawesson's reagent (1.5 equiv, 0.3 mmol, 121.3 mg) in mesitylene (2.0 mL) under Ar. The vial was sealed and stirred vigorously at 180 °C. After 24 hours, the reaction was quenched by rapid cooling. Then the residue was purified by silica gel flash column chromatography to afford the target 2,4-disubstituted thiazoles.

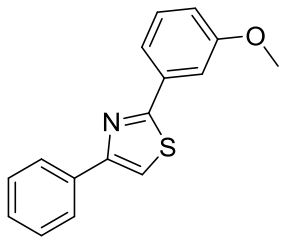
4. Characterization Data of all Products



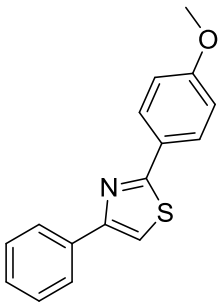
2,4-diphenylthiazole (2a): white solid, mp 91 – 92 °C, 31 mg, 66% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 – 8.05 (m, 2H), 8.04 – 7.99 (m, 2H), 7.51 – 7.42 (m, 6H), 7.40 – 7.35 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 156.3, 134.6, 133.8, 130.1, 129.0, 128.8, 128.2, 126.6, 126.5, 112.6. IR (KBr, *v*/cm^{-1}) 1480, 1443, 760, 731, 690, 673. HRMS (ESI): m/z calcd for $C_{15}H_{12}NS^+$ [M+H$^+$]: 238.0685; Found:238.0681. The spectral data were in accordance with the previously reported data.[1]



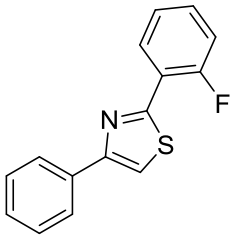
4-Phenyl-2-(o-tolyl)thiazole (2b): white solid, mp 62.1 − 63.5 °C, 32 mg, 64% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 – 8.01 (m, 2H), 7.90 – 7.78 (m, 1H), 7.55 (s, 1H), 7.53 – 7.45 (m, 2H), 7.43 – 7.32 (m, 4H), 2.76 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 154.6, 135.7, 133.6, 131.9, 130.6, 128.8, 128.4, 127.7, 127.1, 125.4, 125.1, 112.1, 20.8. IR (KBr, *v*/cm^{-1}) 3066, 2961, 1482, 1446, 973, 762, 734, 691. HRMS (ESI): m/z calcd for $C_{16}H_{14}NS^+$ [M+H$^+$]: 252.0841; Found:252.0846. The spectral data were in accordance with the previously reported data.[1]



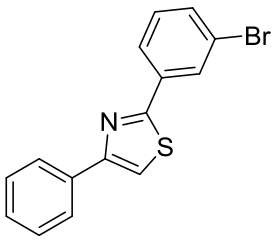
2-(3-methoxyphenyl)-4-phenylthiazole (2c): colorless oil, 35 mg, 66% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 – 7.99 (m, 2H), 7.70 – 7.65 (m, 1H), 7.65 – 7.57 (m, 1H), 7.51 – 7.44 (m, 3H), 7.42 – 7.36 (m, 2H), 7.03 – 6.99 (m, 1H), 3.91 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.7, 160.0, 156.2, 135.1, 134.5, 130.0, 128.8, 128.2, 126.5, 119.3, 116.2, 112.8, 111.5, 55.5. IR (KBr, *v*/cm^{-1}) 3112, 2939, 2835, 1482, 1277, 1049, 777, 734. HRMS (ESI): m/z calcd for $C_{16}H_{14}NOS^+$ [M+H$^+$]: 268.0791; Found:268.0794. The spectral data were in accordance with the previously reported data.[2]



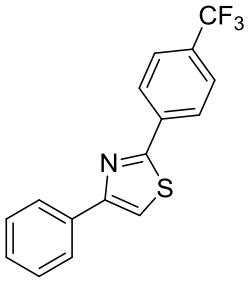
2-(4-methoxyphenyl)-4-phenylthiazole (2d): white solid, mp 101 °C, 37 mg, 69% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 – 7.97 (m, 4H), 7.51 – 7.44 (m, 2H), 7.40 (s, 1H), 7.39 – 7.35 (m, 1H), 7.02 – 6.94 (m, 2H), 3.86 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8, 161.2, 156.0, 134.7, 128.8, 128.1(2C), 126.8, 126.5, 114.3, 111.8, 55.4. IR (KBr, *v*/cm^{-1}) 1521, 1482, 1258, 833, 740. HRMS (ESI): m/z calcd for $C_{16}H_{14}NOS^+$ [M+H$^+$]: 268.0791; Found: 268.0797. The spectral data were in accordance with the previously reported data.[1]



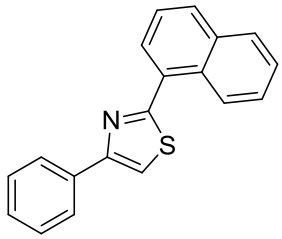
2-(2-fluorophenyl)-4-phenylthiazole (2e): white powder, 29 mg, 56% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 – 8.39 (m, 1H), 8.04 – 7.89 (m, 2H), 7.56 (s, 1H), 7.46 – 7.41 (m, 2H), 7.40 – 7.31 (m, 2H), 7.28 – 7.23 (m, 1H), 7.22 – 7.14 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.2 (d, *J* = 5.0 Hz), 160.1 (d, *J* = 251.9 Hz), 155.1, 134.4, 131.0 (d, *J* = 8.5 Hz), 129.0 (d, *J* = 2.6 Hz), 128.8, 128.2, 126.5, 124.6 (d, *J* = 3.3 Hz), 121.5 (d, *J* = 11.5 Hz), 116.1 (d, *J* = 21.8 Hz), 114.2 (d, *J* = 9.0 Hz). IR (KBr, *v*/cm^{-1}) 1500, 1286, 1209, 982, 764, 740, 695. HRMS (ESI): m/z calcd for $C_{15}H_{11}FNS^+$ [M+H$^+$]: 256.0591; Found:256.0602.



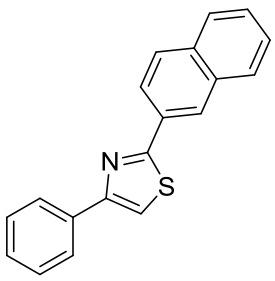
2-(3-bromophenyl)-4-phenylthiazole (2f): white solid, mp 80 – 81 °C, 39 mg, 62% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 – 8.20 (m, 1H), 8.03 – 7.98 (m, 2H), 7.95 – 7.89 (m, 1H), 7.59 – 7.54 (m, 1H), 7.51 – 7.44 (m, 3H), 7.41 – 7.36 (m, 1H), 7.34 – 7.29 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.9, 156.5, 135.6, 134.2, 132.8, 130.4, 129.4, 128.8, 128.3, 126.5, 125.2, 123.1, 113.1. IR (KBr, *v*/cm^{-1}) 1541, 1491, 1236, 1070, 990, 777, 727, 680. HRMS (ESI): m/z calcd for $C_{15}H_{11}BrNS^+$ [M+H$^+$]: 315.9790; Found: 315.9803.



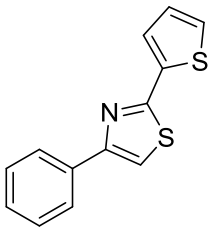
4-phenyl-2-(4-(trifluoromethyl)phenyl)thiazole (2g): white solid, mp 119-120 ºC, 39 mg, 64% yield, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.1 Hz, 2H), 8.05 – 7.96 (m, 2H), 7.72 (d, *J* = 8.2 Hz, 2H), 7.54 (s, 1H), 7.51 – 7.45 (m, 2H), 7.42 – 7.36 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 156.8, 136.8, 134.2, 131.6 (q, *J* = 32.6 Hz), 128.9, 128.5, 126.8, 126.5, 126.0 (q, *J* = 3.8 Hz), 124.0 (q, *J* = 272.3 Hz), 113.6. IR (KBr, *ν*/cm^{-1}) 1480, 1467, 1122, 738, 695. HRMS (ESI): m/z calcd for $C_{16}H_{11}F_3NS^+$ [M+H$^+$]: 306.0559; Found: 306.0553. The spectral data were in accordance with the previously reported data.[1]



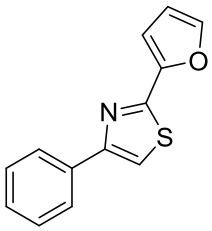
2-(naphthalen-1-yl)-4-phenylthiazole (2h): pale yellow liquid, 31 mg, 54% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.07 – 9.01 (m, 1H), 8.16 – 8.07 (m, 2H), 8.02 – 7.87 (m, 3H), 7.68 – 7.64 (m, 1H), 7.62 – 7.49 (m, 5H), 7.44 – 7.40 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 156.2, 134.6, 134.1, 130.9, 130.6, 130.5, 128.8, 128.5, 128.4, 128.2, 127.4, 126.5, 126.4, 126.0, 125.0, 113.5. IR (KBr, *ν*/cm^{-1}) 1489, 1444, 1100, 1025, 773, 734. HRMS (ESI): m/z calcd for $C_{19}H_{14}NS^+$ [M+H$^+$]: 288.0841; Found: 288.0855.



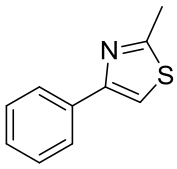
2-(naphthalen-2-yl)-4-phenylthiazole (2i): white powder, 38 mg, 66% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.54 (s, 1H), 8.24 – 8.18 (m, 1H), 8.09 (m, 2H), 7.98 – 7.95 (m, 1H), 7.94 (d, *J* = 8.5 Hz, 1H), 7.90 – 7.87 (m, 1H), 7.57 – 7.55 (m, 2H), 7.54 – 7.51 (m, 2H), 7.48 (s, 1H), 7.45 – 7.41 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.8, 156.3, 134.5, 134.1, 133.2, 131.1, 128.7, 128.64, 128.59, 128.2, 127.8, 126.9, 126.7, 126.5, 125.9, 124.1, 112.8. IR (KBr, *ν*/cm^{-1}) 1467, 1126, 863, 736, 695. HRMS (ESI): m/z calcd for $C_{19}H_{14}NS^+$ [M+H$^+$]: 288.0841; Found: 288.0854.



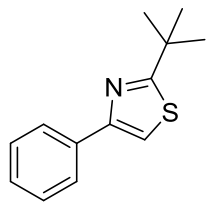
4-phenyl-2-(thiophen-2-yl)thiazole (2j): colorless oil, 35 mg, 72% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 – 7.96 (m, 2H), 7.60 – 7.54 (m, 1H), 7.50 – 7.44 (m, 2H), 7.43 – 7.36 (m, 3H), 7.12 – 7.07 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ161.4, 155.8, 137.5, 134.1, 128.7, 128.2, 127.8, 127.7, 126.6, 126.4, 111.9. IR (KBr, *v*/cm^{-1}) 1478, 1444, 1241, 1057, 926, 831, 775, 703. HRMS (ESI): m/z calcd for $C_{13}H_{10}NS_2^+$ [M+H$^+$]: 244.0249; Found: 244.0243. The spectral data were in accordance with the previously reported data.[3]



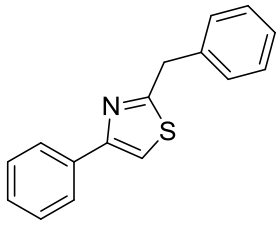
2-(furan-2-yl)-4-phenylthiazole (2k): white solid, mp: 72.3 –72.9 °C, 22 mg, 48% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 – 7.94 (m, 2H), 7.53 (d, J = 1.8 Hz, 1H), 7.48 – 7.42 (m, 3H), 7.39 – 7.33 (m, 1H), 7.09 (d, *J* = 3.5 Hz, 1H), 6.56 (dd, *J* = 3.5, 1.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.9, 156.3, 149.2, 143.6, 134.3, 128.8, 128.3, 126.5, 112.2, 111.9, 109.1. IR (KBr, *v*/cm^{-1}) 1502, 1478, 1021, 880, 732, 691. HRMS (ESI): m/z calcd for $C_{13}H_{10}NOS^+$: 228.0478 [M+H$^+$]; Found: 228.0474. The spectral data were in accordance with the previously reported data.[3]



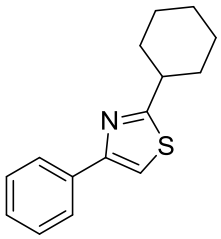
2-Methyl-4-phenylthiazole (2l): red solid, mp:64 − 65 °C, 20 mg, 56% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90 – 7.86 (m, 2H), 7.43 – 7.40 (m, 2H), 7.35 – 7.31 (m, 1H), 7.30 (s, 1H), 2.78 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.9, 155.2, 134.5, 128.7, 128.0, 126.3, 112.3, 19.4. IR (KBr, *v*/cm^{-1}) 2926, 1497, 1170, 742. HRMS (ESI): m/z calcd for $C_{10}H_{10}NS^+$ [M+H$^+$]: 176.0528; Found: 176.0524. The spectral data were in accordance with the previously reported data.[4]



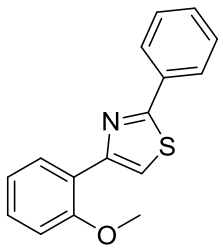
2-(tert-Butyl)-4-phenylthiazole (2m): Yellow oil, 26 mg, 61% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.03 – 7.98 (m, 2H), 7.50 – 7.44 (m, 2H), 7.40 – 7.34 (m, 2H), 1.57 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 180.8, 154.6, 135.0, 128.7, 127.8, 126.4, 111.4, 37.8, 31.0. IR (KBr, *v*/cm^{-1}) 2965, 1497, 1366, 1074, 731, 691. HRMS (ESI): m/z calcd for $C_{13}H_{16}NS^+$ [M+H$^+$]: 218.0998; Found: 218.0994. The spectral data were in accordance with the previously reported data.[4]



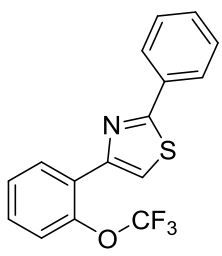
2-benzyl-4-phenylthiazole (2n): pale yellow liquid, 26 mg, 51% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 – 7.90 (m, 2H), 7.47 – 7.44 (m, 2H), 7.42 – 7.36 (m, 5H), 7.35 (s, 1H), 7.34 – 7.31 (m, 1H), 4.42 (s, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.4, 155.2, 137.8, 134.5, 129.1, 128.8, 128.7, 128.0, 127.1, 126.3, 112.9, 39.8. IR (KBr, *v*/cm^{-1}) 2926, 1491, 738, 705. HRMS (ESI): m/z calcd for $C_{16}H_{14}NS^+$ [M+H$^+$]: 252.0841; Found: 252.0854.



2-Cyclohexyl-4-phenylthiazole (2o): red oil, 18 mg, 38% yield, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 – 7.85 (m, 2H), 7.44 – 7.38 (m, 2H), 7.33 (s, 1H), 7.32 – 7.29 (m, 1H), 3.13 – 2.98 (m, 1H), 2.27 – 2.12 (m, 2H), 1.94 – 1.81 (m, 2H), 1.82 – 1.70 (m, 1H), 1.63 – 1.51 (m, 2H), 1.51 – 1.37 (m, 2H), 1.36 – 1.25 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.0, 154.7, 134.9, 128.7, 127.9, 126.4, 111.3, 42.8, 33.9, 26.1, 25.9. IR (KBr, *v*/cm^{-1}) 2930, 2853, 1492, 1446, 728, 691. HRMS (ESI): m/z calcd for $C_{15}H_{18}NS^+$ [M+H$^+$]: 244.1154; Found: 244.1152. The spectral data were in accordance with the previously reported data.[4]

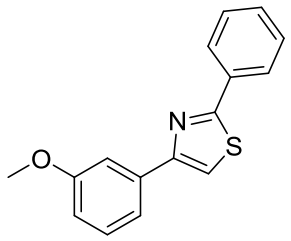


4-(2-methoxyphenyl)-2-phenylthiazole (2p): white solid; mp: 84 – 85 °C, 20 mg, 37% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 – 8.34 (m, 1H), 8.12 – 8.02 (m, 2H), 7.97 (s, 1H), 7.58 – 7.41 (m, 3H), 7.39 – 7.30 (m, 1H), 7.19 – 7.08 (m, 1H), 7.07 – 6.99 (m, 1H), 3.98 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.7, 156.9, 151.9, 133.9, 130.3, 129.8, 128.92, 128.88, 126.7, 123.2, 120.9, 117.2, 111.1, 55.5. IR (KBr, *v*/cm^{-1}) 2927, 1509, 1485, 1243, 1025, 745. HRMS (ESI): m/z calcd for $C_{16}H_{14}NOS^+$ [M+H$^+$]: 268.0791; Found: 268.0795. The spectral data were in accordance with the previously reported data.[5]

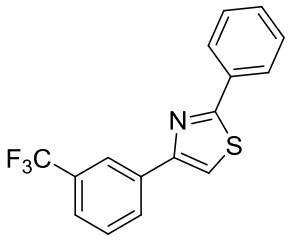


2-phenyl-4-(2-(trifluoromethoxy)phenyl)thiazole (2q): colorless oil, 36 mg, 56% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 – 8.33 (m, 1H), 8.14 – 8.00 (m, 2H), 7.77 (s, 1H), 7.51 – 7.45 (m, 3H), 7.44-7.40 (m, 1H), 7.40 – 7.37 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8, 150.2, 146.3 (q, *J* = 2.0 Hz), 133.5, 131.2, 130.2, 129.04, 128.97, 127.6, 127.1, 126.7, 120.8 (q, *J*=2.0 Hz), 120.7

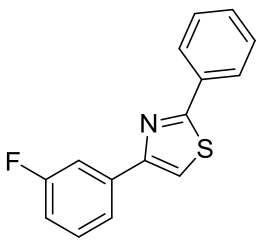
(q, J = 258.5 Hz), 117.7. IR (KBr, v/cm^{-1}) 1509, 1484, 1258, 1200, 1174, 765, 690. HRMS (ESI): m/z calcd for $C_{16}H_{11}F_3NOS^+$ [M+H$^+$]: 322.0508; Found: 322.0521.



· **4-(3-Methoxyphenyl)-2-phenylthiazole (2r):** white solid, mp: 79 – 80 °C, 27 mg, 50% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.09 – 8.02 (m, 2H), 7.66 – 7.60 (m, 1H), 7.59 – 7.55 (m, 1H), 7.51 – 7.42 (m, 4H), 7.37 (t, J = 7.9 Hz, 1H), 6.99 – 6.85 (m, 1H), 3.91 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.8, 160.0, 156.1, 135.9, 133.7, 130.1, 129.8, 128.9, 126.6, 118.9, 113.9, 113.0, 112.0, 55.4. IR (KBr, v/cm^{-1}) 2926, 2852, 1485, 1465, 1280, 1046, 984, 764, 690. HRMS (ESI): m/z calcd for $C_{16}H_{14}NOS^+$ [M+H$^+$]: 268.0791; Found: 268.0793. The spectral data were in accordance with the previously reported data.[2]

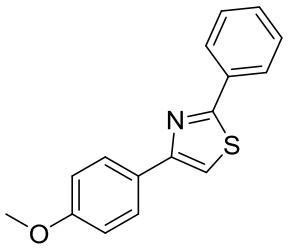


2-Phenyl-4-(3-(trifluoromethyl)phenyl)thiazole (2s): white solid, mp: 112 – 114 °C, 27 mg, 45% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (s, 1H), 8.15 (d, J = 7.7 Hz, 1H), 8.09 – 8.02 (m, 2H), 7.62 (d, J = 7.8 Hz, 1H), 7.56 (d, J = 7.8 Hz, 1H), 7.54 – 7.45 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.4, 154.6, 135.2, 133.4, 131.1 (q, J = 32.3 Hz), 130.3, 129.5, 129.2, 129.0, 126.6, 124.7 (q, J = 3.8 Hz), 124.2 (q, J = 272.4 Hz), 123.3 (q, J = 3.8 Hz), 113.8. IR (KBr, v/cm^{-1}) 1474, 1334, 1265, 1167, 1126, 764, 688. HRMS (ESI): m/z calcd for $C_{16}H_{11}F_3NS^+$ [M+H$^+$]: 306.0559; Found:306.0557. The spectral data were in accordance with the previously reported data.[6]

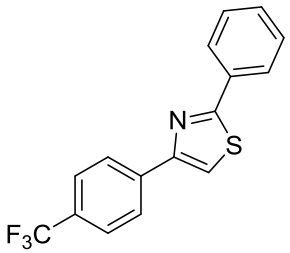


4-(3-Fluorophenyl)-2-phenylthiazole(2t): white solid, mp: 85 – 86 °C, 28 mg, 54% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 – 7.94 (m, 2H), 7.82 – 7.63 (m, 2H), 7.51 – 7.45 (m, 4H), 7.44 – 7.37 (m, 1H), 7.09 – 7.03 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1, 163.2 (d, J = 245.1 Hz), 155.0, 136.7 (d, J = 8.1 Hz), 133.5, 130.22 (d, J = 8.3 Hz), 130.21, 129.0, 126.6, 121.9 (d, J = 2.8 Hz), 115.0 (d, J = 21.3 Hz), 113.51, 113.47(d, J=22.2). IR (KBr, v/cm^{-1}) 1478, 1457, 1264, 1249, 986, 786, 687. HRMS (ESI): m/z calcd for $C_{15}H_{11}FNS^+$ [M+H$^+$]: 256.0591; Found: 256.0596. The spectral data were in accordance with the previously reported

data.[6]

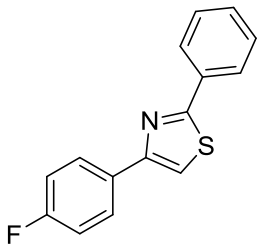


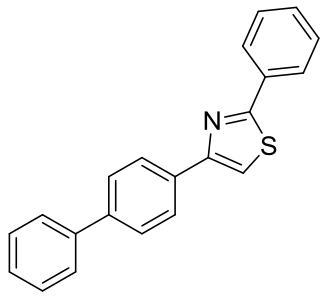
4-(4-Methoxyphenyl)-2-phenylthiazole (2u): pale yellow solid, mp:118 – 120 °C, 28 mg, 52% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.12 – 8.03 (m, 2H), 8.00 – 7.89 (m, 2H), 7.50 – 7.43 (m, 3H), 7.32 (s, 1H), 7.03 – 6.98 (m, 2H), 3.86 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.6, 159.6, 156.0, 133.8, 129.9, 128.9, 127.7, 127.4, 126.5, 114.0, 110.9, 55.2. IR (KBr, *v*/cm^{-1}) 2924, 1483, 1279, 1254, 1056, 977, 836, 783, 690. HRMS (ESI): m/z calcd for $C_{16}H_{14}NOS^+$ [M+H$^+$]: 268.0791; Found: 268.0794. The spectral data were in accordance with the previously reported data.[6]



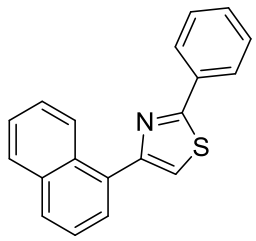
4-(4-Trifluoromethyl-phenyl)-2-phenyl-thiazole (2v): white solid, mp: 136 °C, 31 mg, 51% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.2 Hz, 2H), 8.08 – 7.97 (m, 2H), 7.70 (d, *J* = 8.2 Hz, 2H), 7.56 (s, 1H), 7.51 – 7.45 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.4, 154.7, 137.7(d, *J*=1.0 Hz), 133.5, 130.4, 129.91 (q, *J* = 32.5 Hz), 129.0, 126.7, 126.6, 125.8 (q, *J*=3.8 Hz), 124.3 (q, *J* = 271.9 Hz), 114.4. IR (KBr, *v*/cm^{-1}) 1459, 1338, 1109, 1053, 768, 695. HRMS (ESI): m/z calcd for $C_{16}H_{11}F_3NS^+$ [M+H$^+$]: 306.0559; Found: 306.0554. The spectral data were in accordance with the previously reported data.[7]

4-(4-Fluorophenyl)-2-phenylthiazole(2w): white solid, mp: 104 – 105 °C, 31 mg, 60% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 – 8.04 (m, 2H), 8.04 – 7.93 (m, 2H), 7.57 – 7.40 (m, 3H), 7.36 (s, 1H), 7.19 – 7.12 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 162.67(d, *J* = 247.4 Hz), 155.1, 133.6, 130.7 (d, *J* = 3.2 Hz), 130.1, 128.9, 128.1 (d, *J* = 8.1 Hz), 126.5, 115.6 (d, *J* = 21.6 Hz), 112.2. IR (KBr, *v*/cm^{-1}) 1483, 1226, 1101, 980, 833, 767, 692. HRMS (ESI): m/z calcd for $C_{15}H_{11}FNS^+$ [M+H$^+$]: 256.0591; Found: 256.0594. The spectral data were in accordance with the previously reported data.[6]

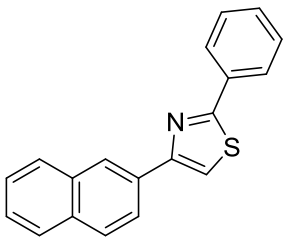




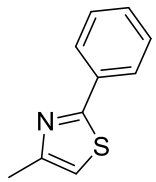
4-([1,1'-Biphenyl]-4-yl)-2-phenylthiazole (2x): white solid, mp: 158 – 160 °C, 58 mg, 92% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 – 8.06 (m, 4H), 7.78 – 7.63 (m, 4H), 7.54 – 7.45 (m, 6H), 7.43 – 7.35 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 155.9, 140.8, 140.7, 133.8, 133.5, 130.1, 129.0, 128.8, 127.4, 127.0, 126.9, 126.6, 112.7. IR (KBr, *v*/cm^{-1}) 1474, 1238, 1057, 978, 762, 746, 690. HRMS (ESI): m/z calcd for $C_{21}H_{16}NS^+$ [M+H$^+$]: 314.0998; Found: 314.0995. The spectral data were in accordance with the previously reported data.[6]



4-(naphthalen-1-yl)-2-phenylthiazole (2y): pale yellow liquid, 13 mg, 23% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.41 – 8.34 (m, 1H), 8.12 – 8.07 (m, 2H), 7.96 – 7.89 (m, 2H), 7.80 – 7.75 (m, 1H), 7.57 – 7.51 (m, 3H), 7.50 – 7.45 (m, 3H), 7.44 (s, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.7, 156.2, 134.0, 133.8, 132.9, 131.6, 130.1, 128.99, 128.96, 128.4, 127.6, 126.7, 126.5, 126.01, 125.96, 125.3, 116.9. IR (KBr, *v*/cm^{-1}) 1507, 1467, 1437, 1010, 967, 775, 688. HRMS (ESI): m/z calcd for $C_{19}H_{14}NS^+$ [M+H$^+$]: 288.0841; Found: 288.0855.

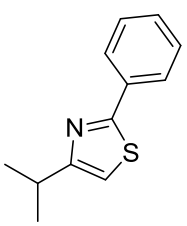


4-(Naphthalen-2-yl)-2-phenylthiazole (2z): white solid, mp: 120 – 122 °C, 31 mg, 54% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 8.17 – 8.05 (m, 3H), 7.99 – 7.85 (m, 3H), 7.57 (s, 1H), 7.54 – 7.47 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.0, 156.2, 133.8, 133.7, 133.2, 131.8, 130.1, 129.0, 128.5, 128.4, 127.7, 126.7, 126.4, 126.1, 125.5, 124.4, 113.1. IR (KBr, *v*/cm^{-1}) 1508, 1472, 1055, 984, 757, 690. HRMS (ESI): m/z calcd for $C_{19}H_{14}NS^+$ [M+H$^+$]: 288.0841; Found: 288.0845. The spectral data were in accordance with the previously reported data.[7]

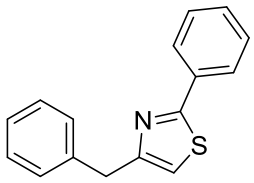


4-Methyl-2-phenylthiazole (2aa): colorless oil, 13 mg, 36% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 – 7.72 (m, 2H), 7.46 – 7.39 (m, 3H), 6.87 (s, 1H), 2.51 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.6, 153.8, 133.8, 129.8, 128.9, 126.5, 113.5, 17.3. IR (KBr, *v*/cm^{-1}) 2922, 2855, 1523, 1459, 1003, 762, 690. HRMS (DART)

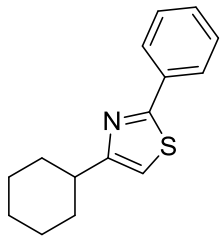
m/z calcd for $C_{10}H_{10}NS^+$ [M+H$^+$]: 176.0528; Found: 176.0536. The spectral data were in accordance with the previously reported data.[3]



4-isopropyl-2-phenylthiazole (2ab): pale yellow oil, 16 mg, 40% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00 – 7.91 (m, 2H), 7.47 – 7.38 (m, 3H), 6.87 (s, 1H), 3.22 – 3.14 (m, 1H), 1.38 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.3, 164.9, 134.0, 129.7, 128.8, 126.5, 110.9, 31.1, 22.4. IR (KBr, *v*/cm^{-1}) 2967, 2931, 2872, 1513, 1459, 1312, 993, 764, 690. HRMS (DART) m/z calcd for $C_{12}H_{14}NS^+$ [M+H$^+$]: 204.0841; Found: 204.0845. The spectral data were in accordance with the previously reported data.[3]



4-benzyl-2-phenylthiazole (2ac): yellow oil, 18 mg, 36% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 – 7.86 (m, 2H), 7.43 – 7.38 (m, 3H), 7.36 – 7.28 (m, 4H), 7.27 – 7.21 (m, 1H), 6.73 (s, 1H), 4.19 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 157.6, 139.1, 133.8, 129.9, 129.2, 128.9, 128.6, 126.6, 126.5, 114.4, 38.1. IR (KBr, *v*/cm^{-1}) 2920, 1507, 1459, 1003, 762, 690. HRMS (ESI): m/z calcd for $C_{16}H_{14}NS^+$ [M+H$^+$]: 252.0841; Found: 252.0844. The spectral data were in accordance with the previously reported data.[8]



4-cyclohexyl-2-phenylthiazole (2ad): colorless oil, 13 mg, 26% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 – 7.90 (m, 2H), 7.52 – 7.35 (m, 3H), 6.85 (s, 1H), 2.88 – 2.78 (m, 1H), 2.19 – 2.10 (m, 2H), 1.88 – 1.82 (m, 2H), 1.79 – 1.69 (m, 1H), 1.53 – 1.40 (m, 4H), 1.34 – 1.24 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2, 164.1, 134.1, 129.7, 128.8, 126.5, 111.1, 40.7, 33.0, 26.4, 26.2. IR (KBr, *v*/cm^{-1}) 2926, 2853, 1511, 1500, 986, 764, 690. HRMS (ESI): m/z calcd for $C_{15}H_{18}NS^+$ [M+H$^+$]: 244.1154; Found: 244.1155. The spectral data were in accordance with the previously reported data.[9]

5. References

[1] X. Huang, H. Chen, Z. Huang, Y. Xu, F. Li, X. Ma, Y. Chen, *J. Org. Chem.* **2019**, *84*, 15283-15293.

[2] A. S. Mayhoub, L. Marler, T. P. Kondratyuk, E. J. Park, J. M. Pezzuto, M. Cushman, *Bioorg. Med. Chem.* **2012**, *20*, 7030-7039

[3] Y. Yu, H. Chen, L. Wang, X. Chen, B. Fu, *Molecules* **2009**, *14*, 4858-4865.

[4] X. Tang, J. Yang, Z. Zhu, M. Zheng, W. Wu, H. Jiang, *J. Org. Chem.* **2016**, *81*, 11461-11466.

[5] T. Yamamoto, H. Togo, *Eur. J. Org. Chem.* **2018**, *2018*, 4187-4196.

[6] P. Ni, J. Tan, R. Li, H. Huang, F. Zhang, G. Deng, *RSC Adv.* **2020**, *10*, 3931-3935.

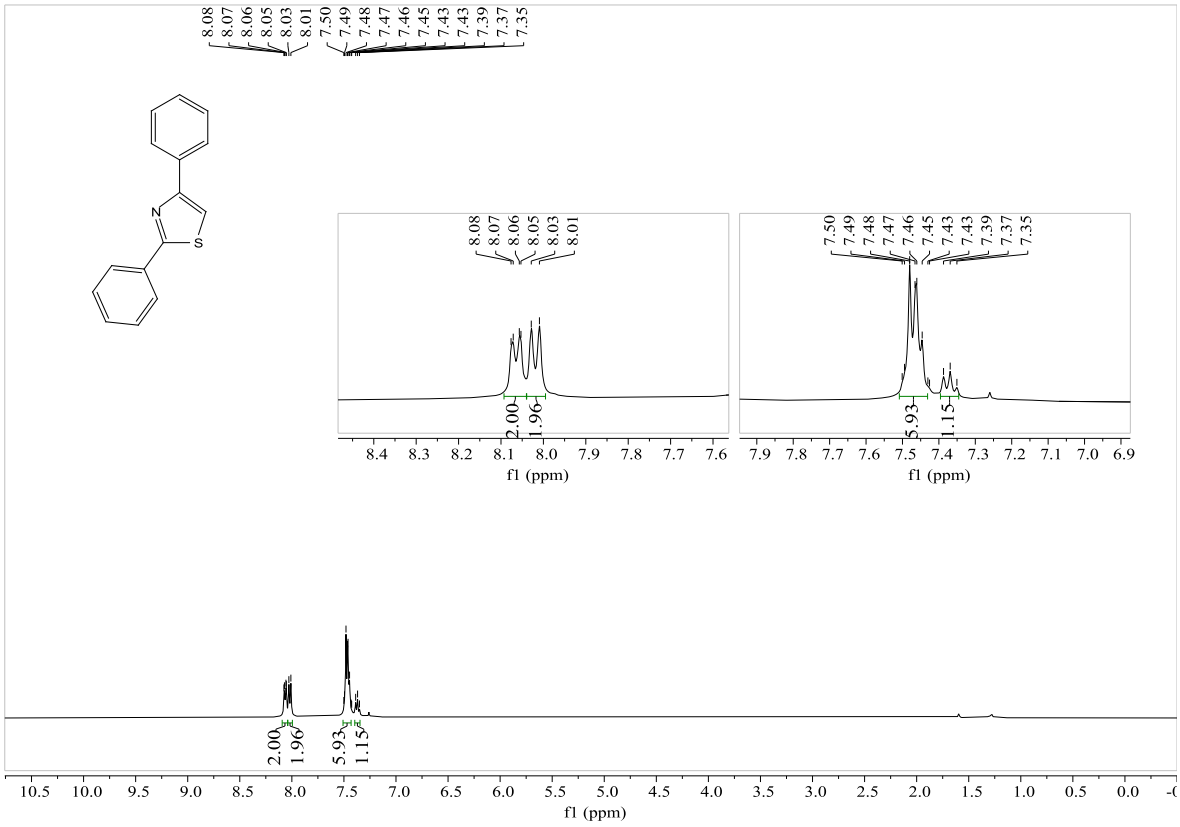
[7] E. Venkateswararao, H. B. Jalani, M. Manoj, S. Jung, *J. Heterocycl. Chem.* **2016**, *53*, 1449-1456

[8] M. Yoshimatsu, T. Yamamoto, A. Sawa, T. Kato, G. Tanabe, O. Muraoka, *Org. Lett.* **2009**, *11*, 2952-2955.

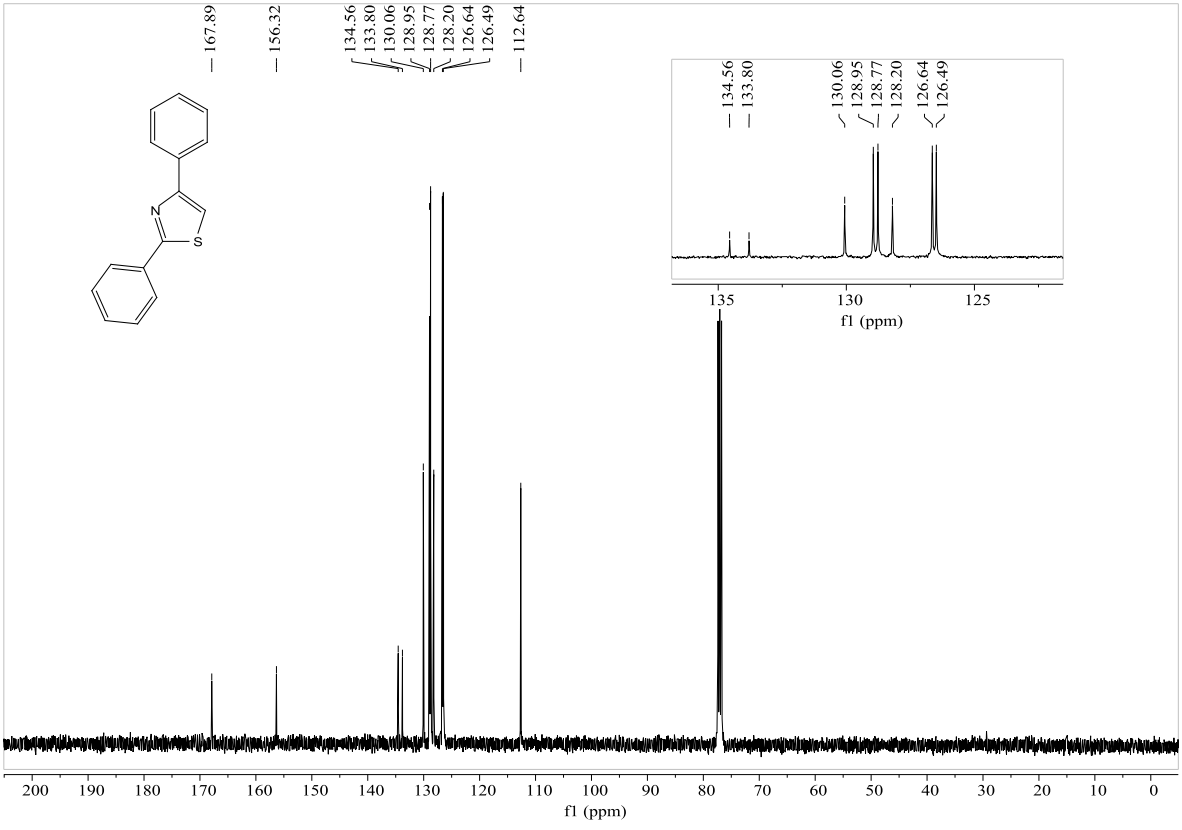
[9] G. Wu, R. Zheng, J. Nelson, L. Zhang, *Adv. Synth. Catal.* **2014**, *356*, 1229-1234.

6. Copies of ^{1}H and ^{13}C NMR Spectra

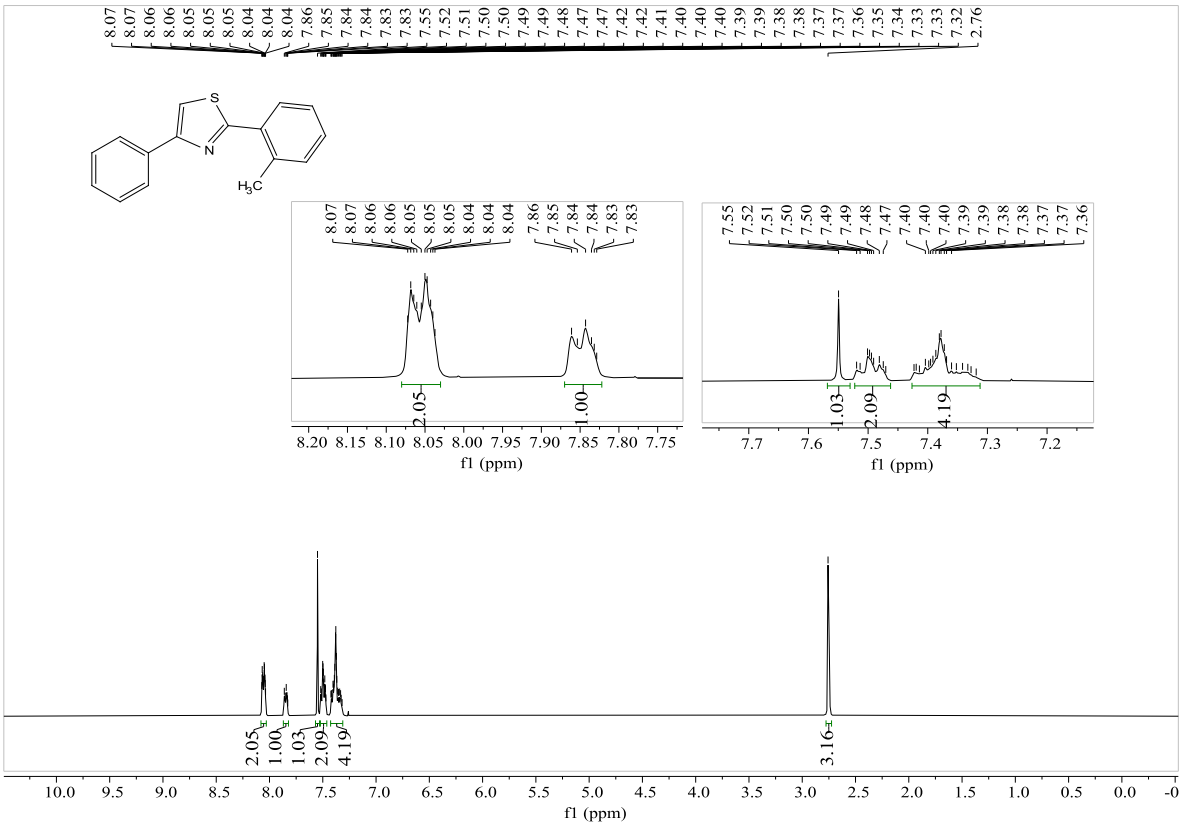
^{1}H NMR spectrum of compound 2a (400 MHz, $CDCl_3$)



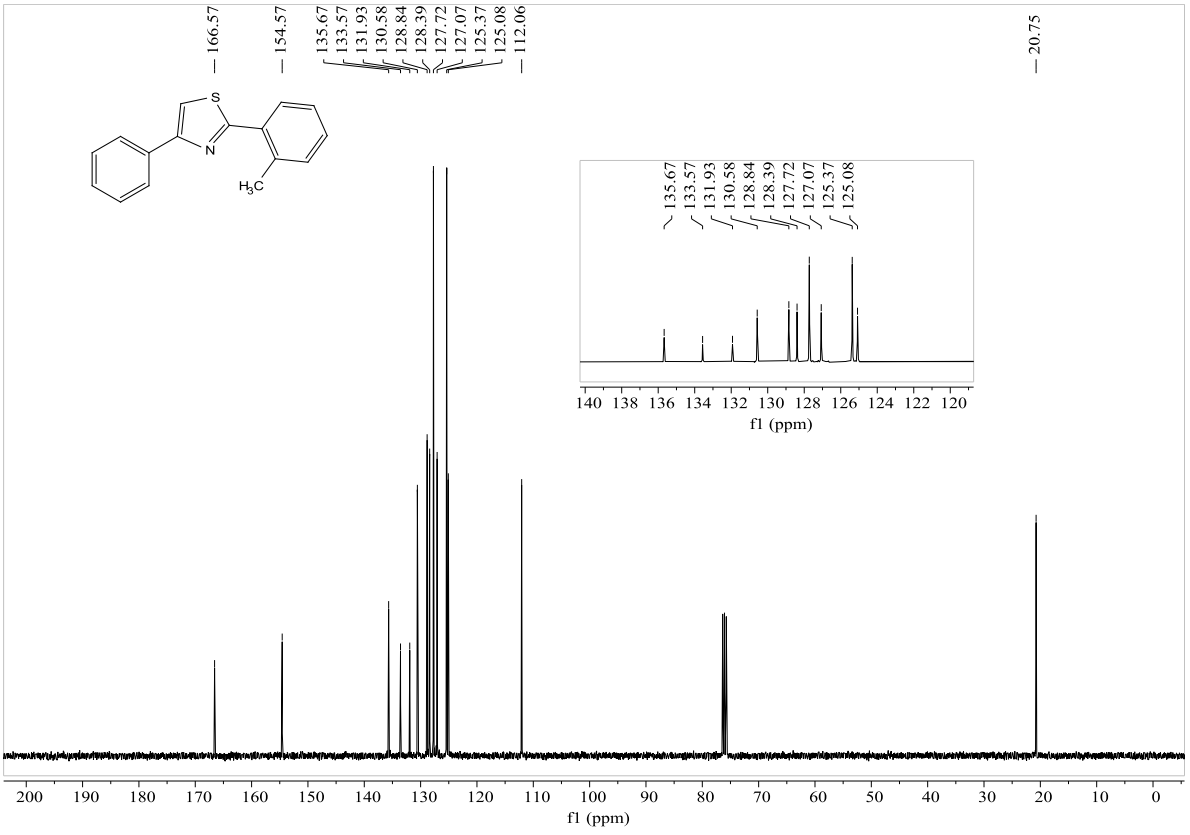
^{13}C NMR spectrum of compound 2a (101 MHz, $CDCl_3$)



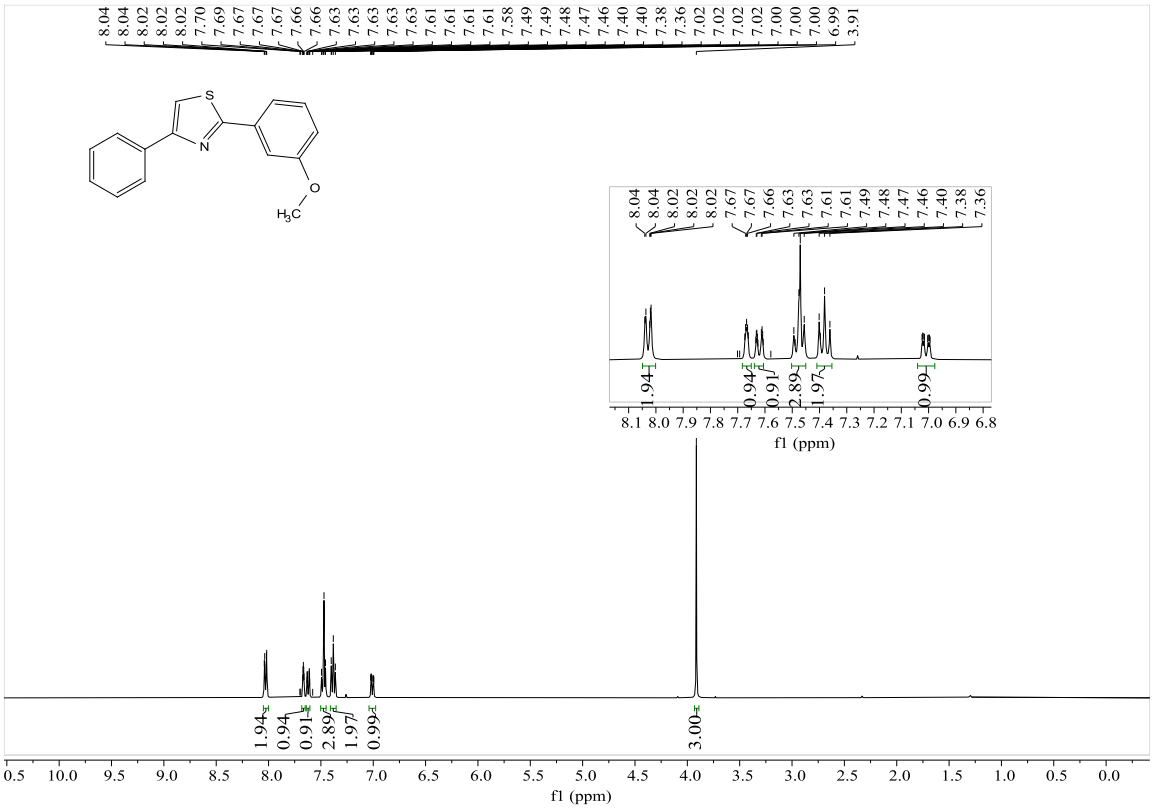
^{1}H NMR spectrum of compound 2b (400 MHz, $CDCl_3$)



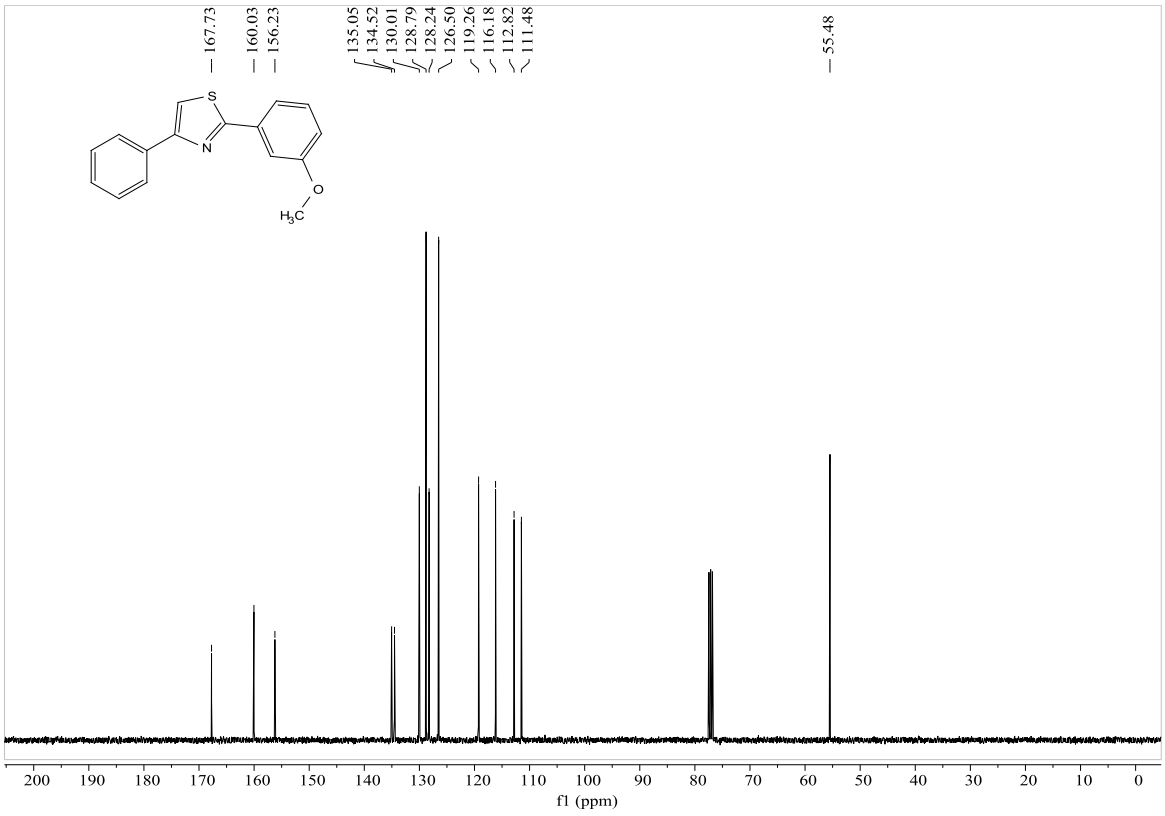
^{13}C NMR spectrum of compound 2b (101 MHz, $CDCl_3$)



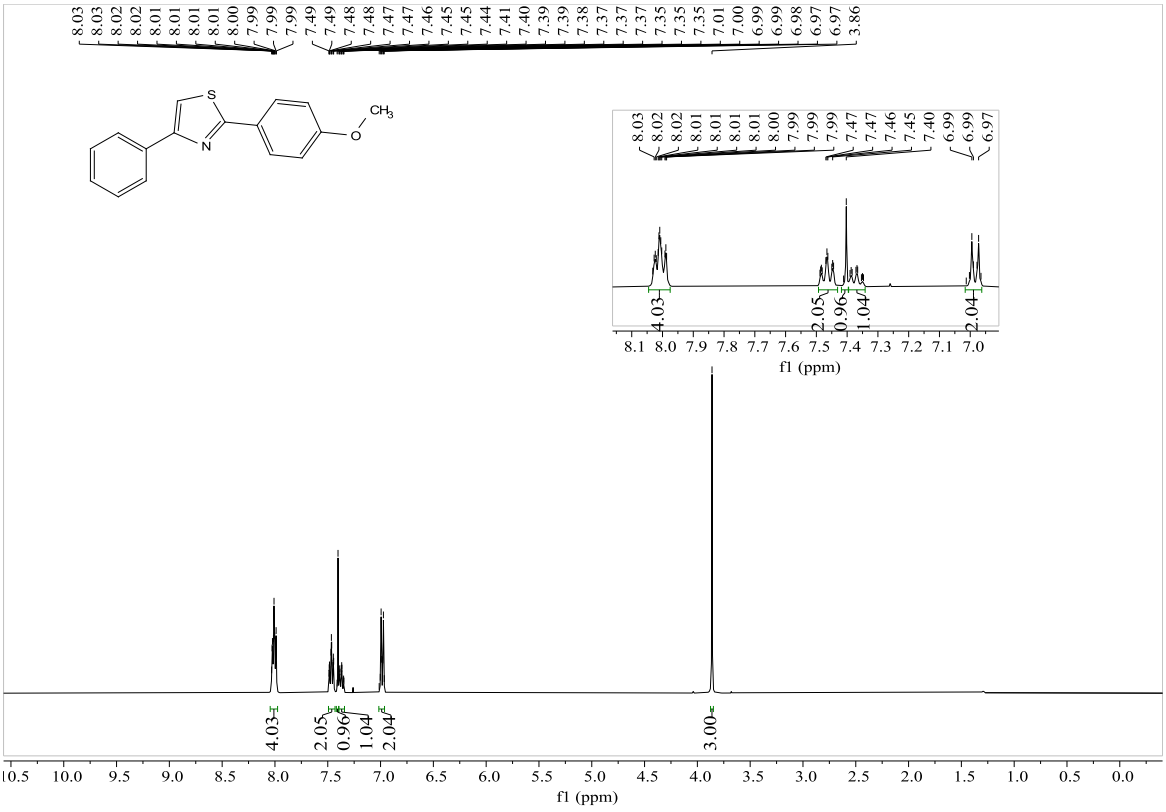
^{1}H NMR spectrum of compound 2c (400 MHz, $CDCl_3$)



^{13}C NMR spectrum of compound 2c (101 MHz, $CDCl_3$)



^{1}H NMR spectrum of compound 2d (400 MHz, $CDCl_3$)



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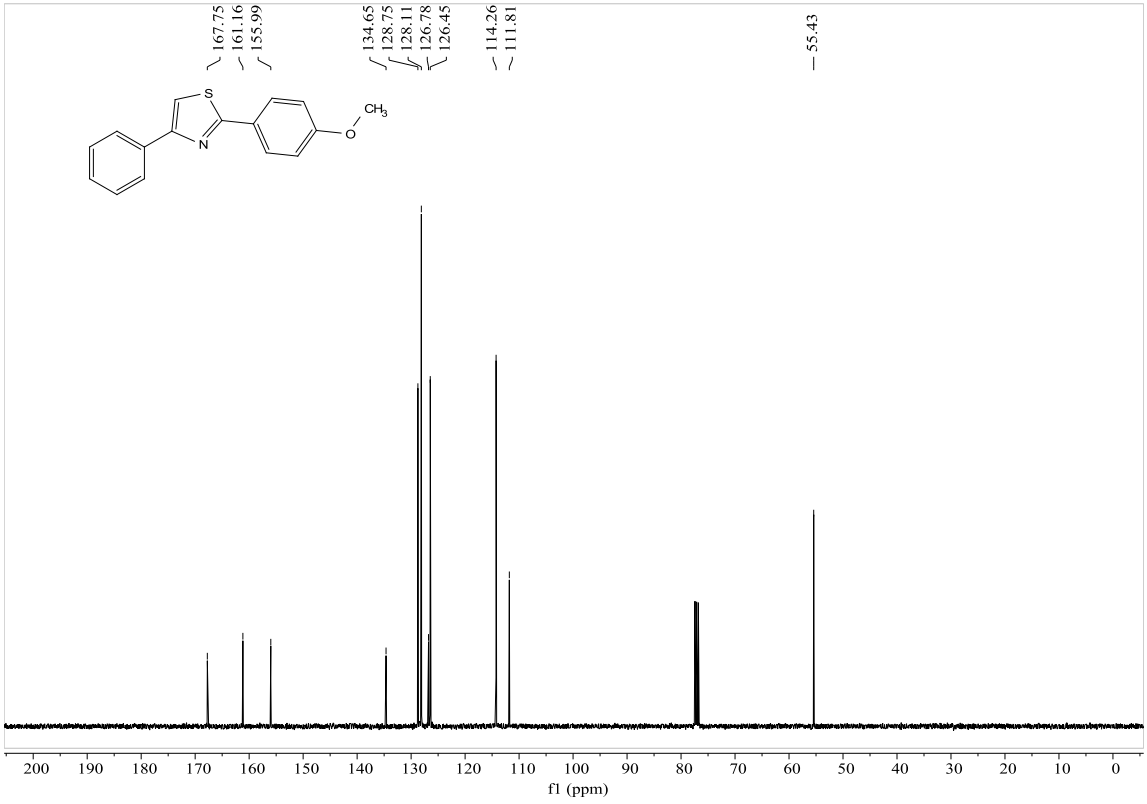
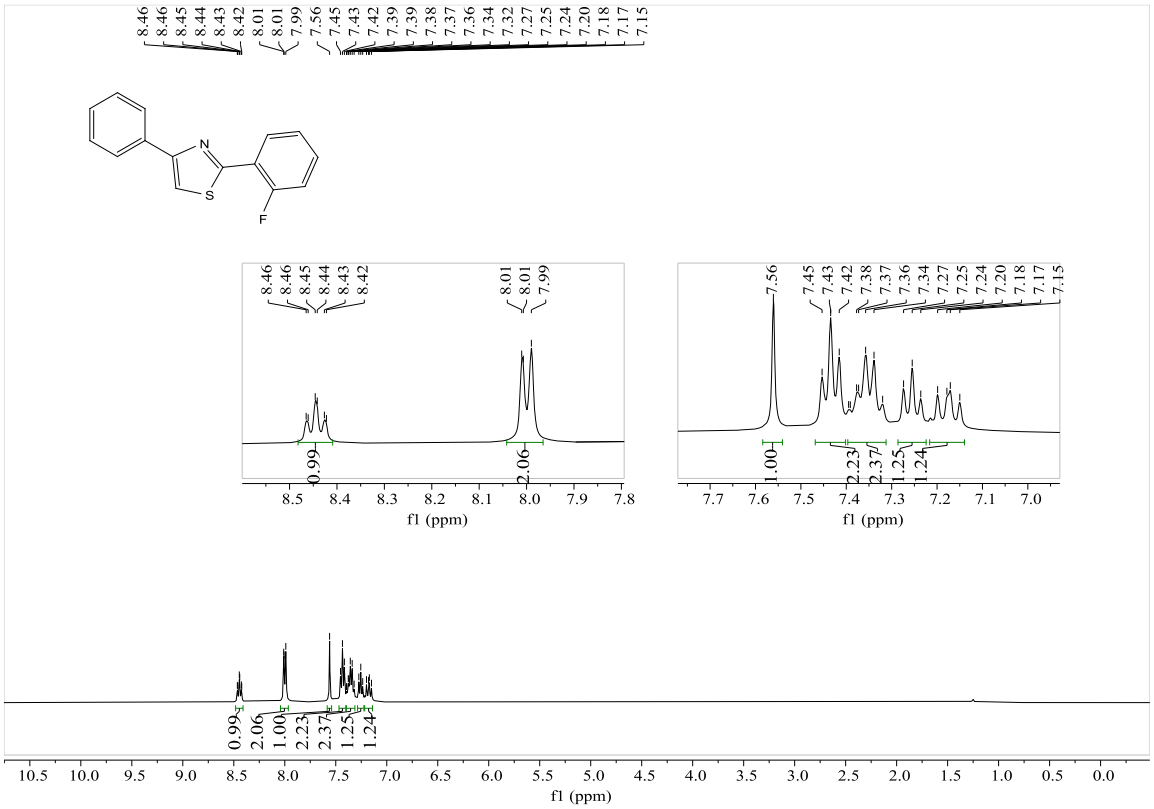
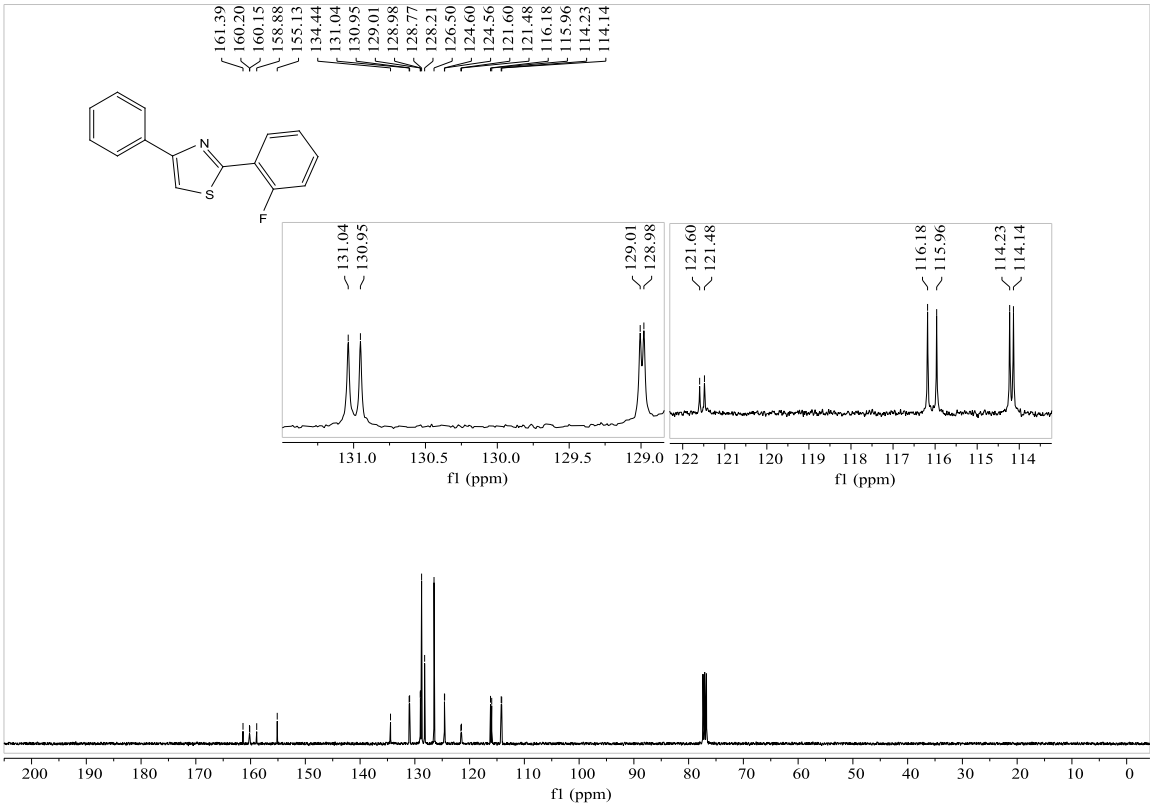


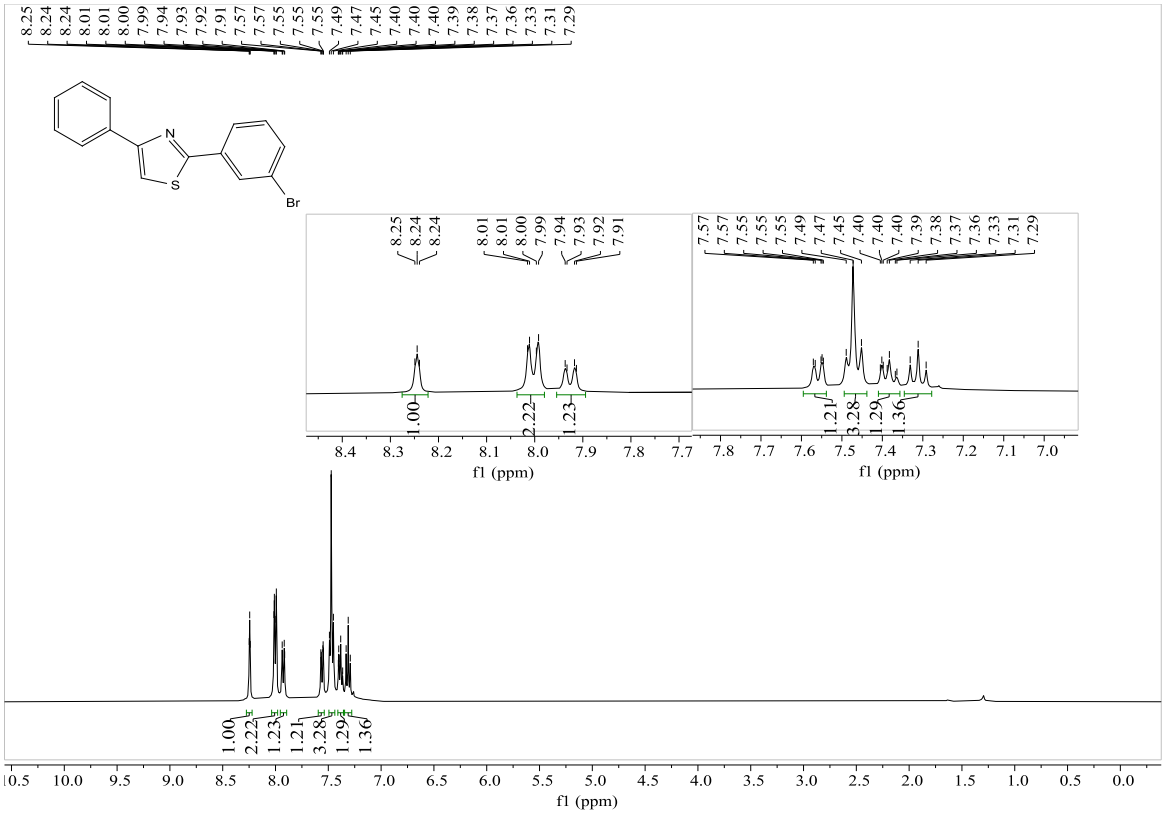
^{1}H NMR spectrum of compound 2e (400 MHz, $CDCl_3$)



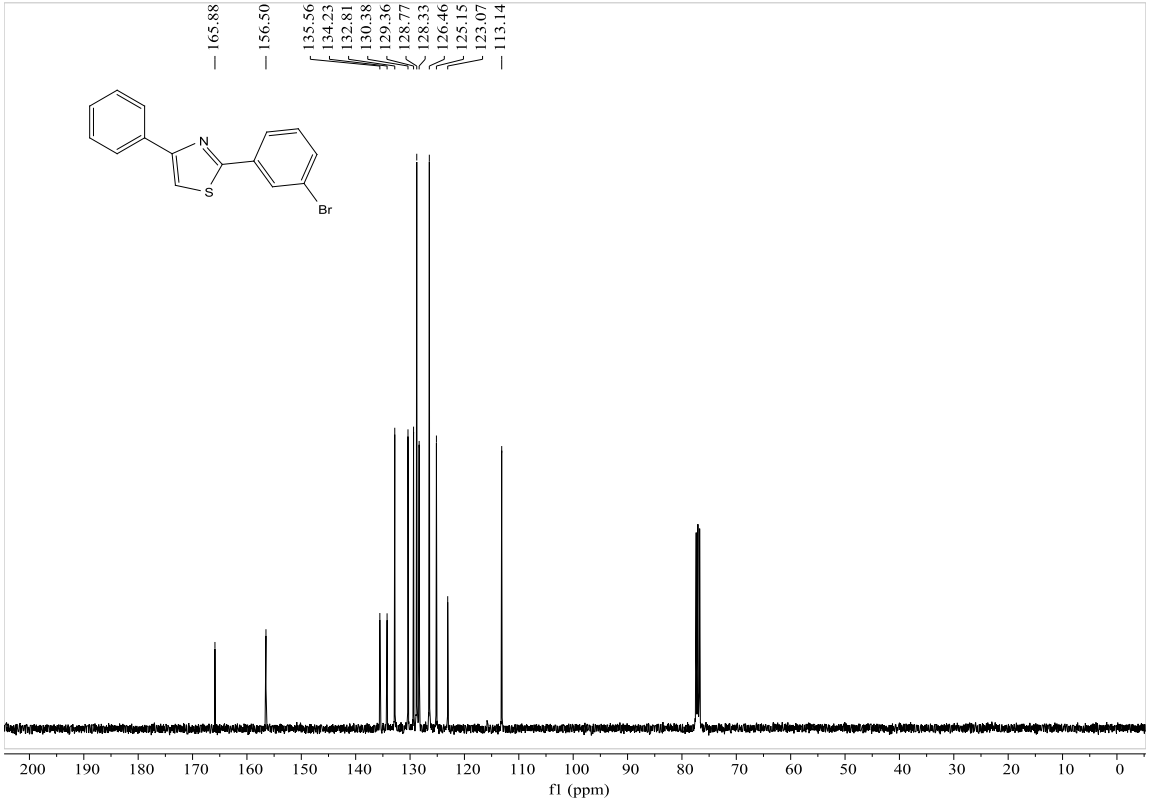
^{13}C NMR spectrum of compound 2e (101 MHz, $CDCl_3$)



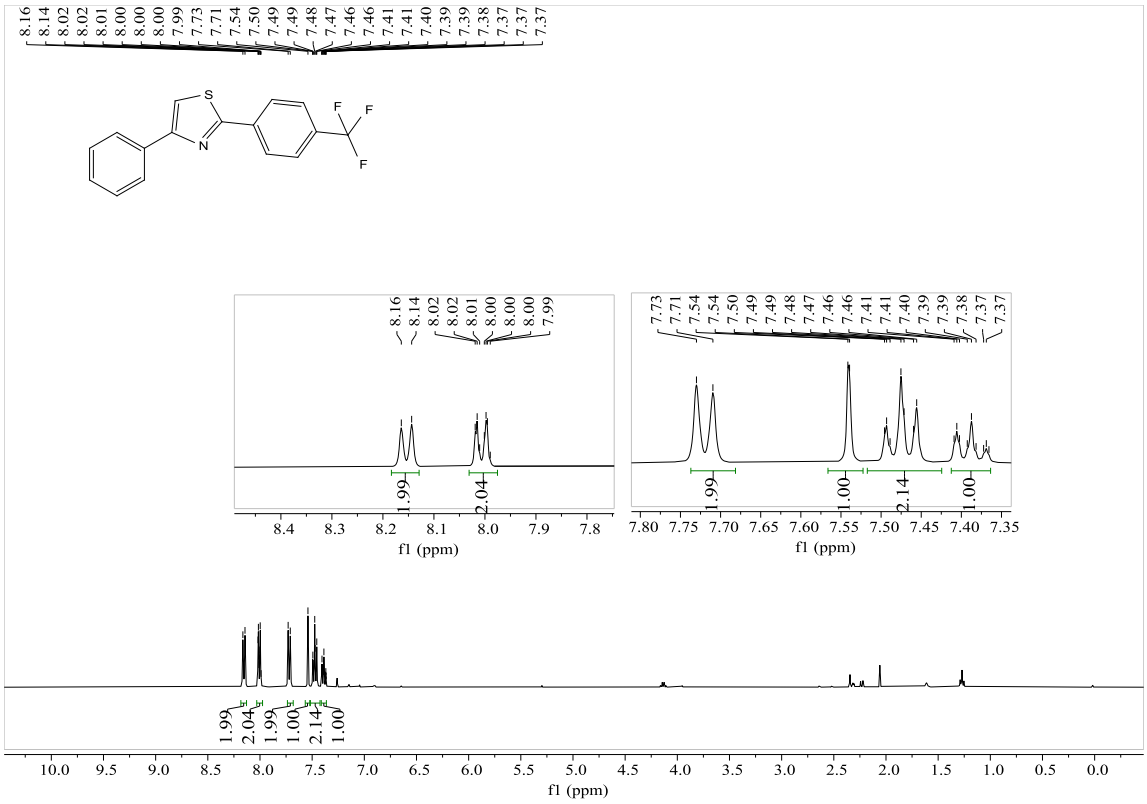
^{1}H NMR spectrum of compound 2f (400 MHz, $CDCl_3$)



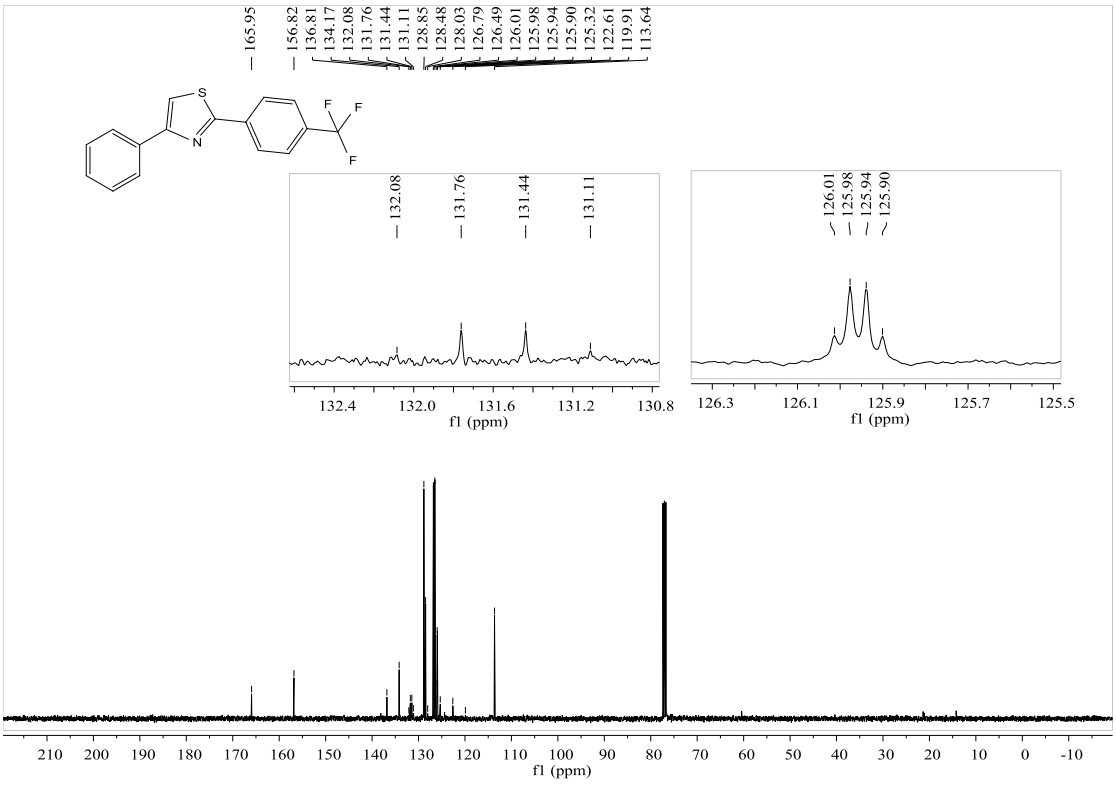
^{13}C NMR spectrum of compound 2f (101 MHz, $CDCl_3$)



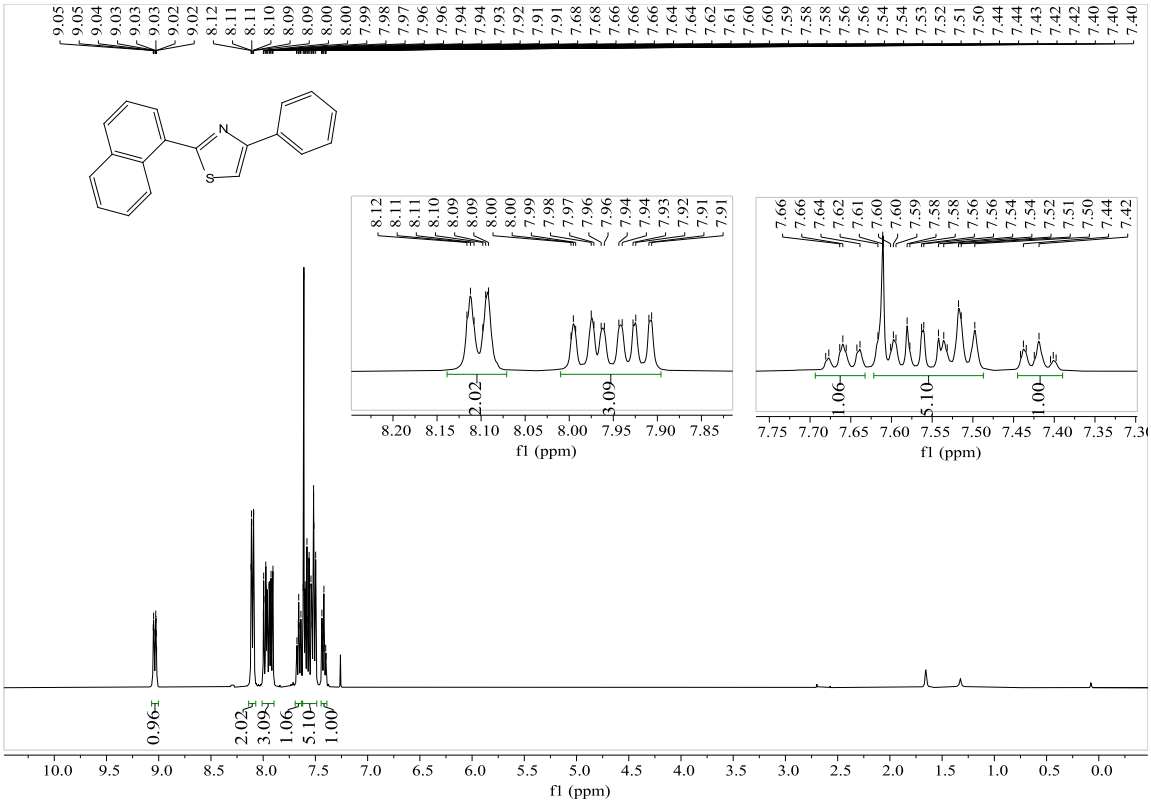
^{1}H NMR spectrum of compound 2g (400 MHz, $CDCl_3$)



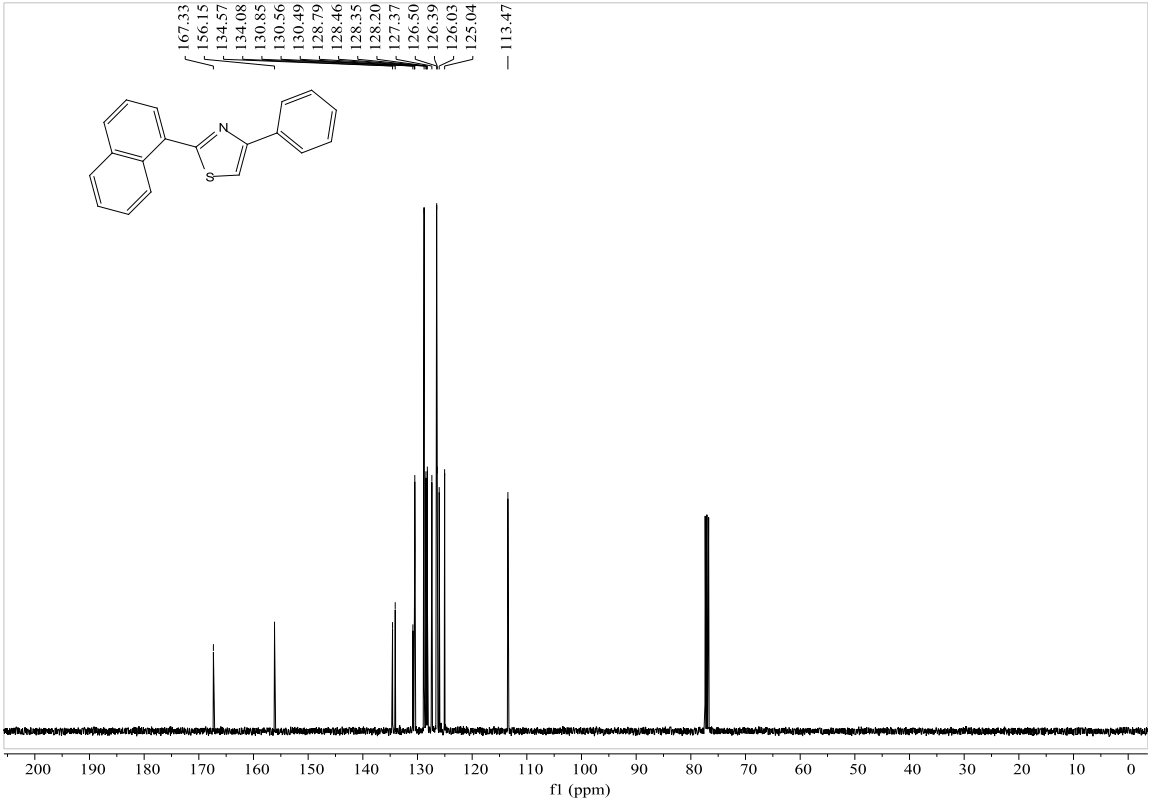
^{13}C NMR spectrum of compound 2g (101 MHz, $CDCl_3$)



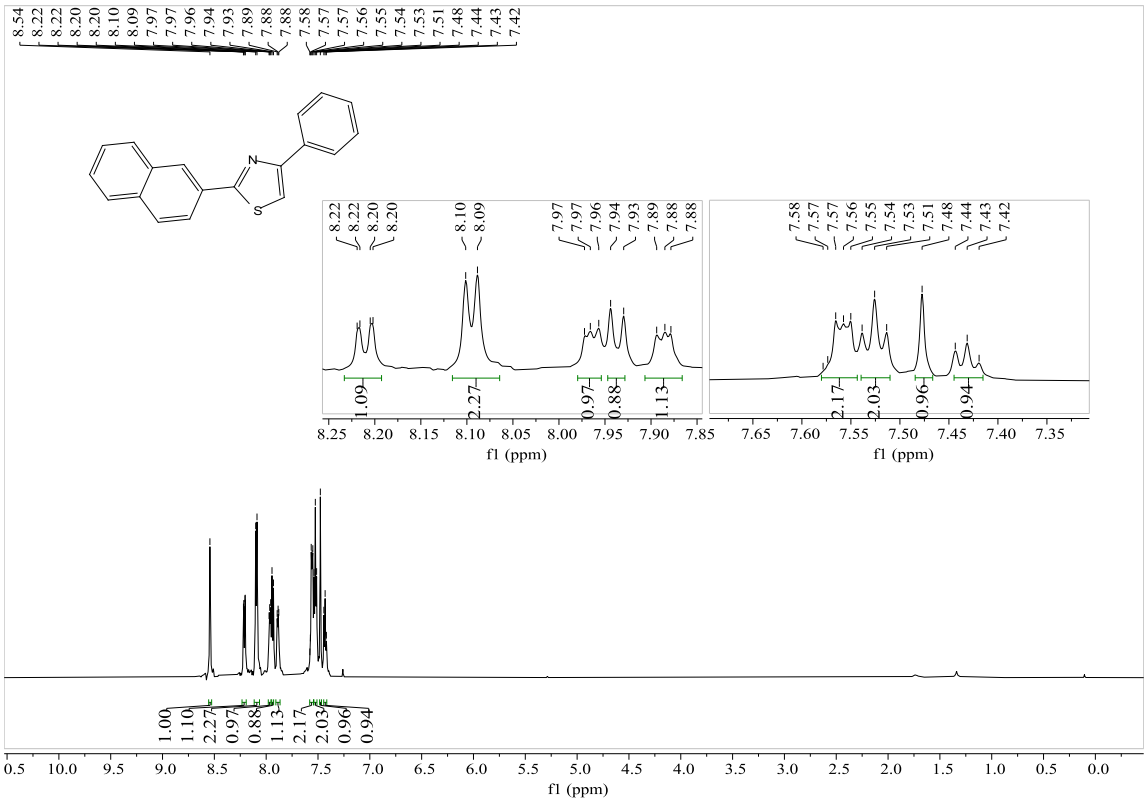
^{1}H NMR spectrum of compound 2h (400 MHz, $CDCl_3$)



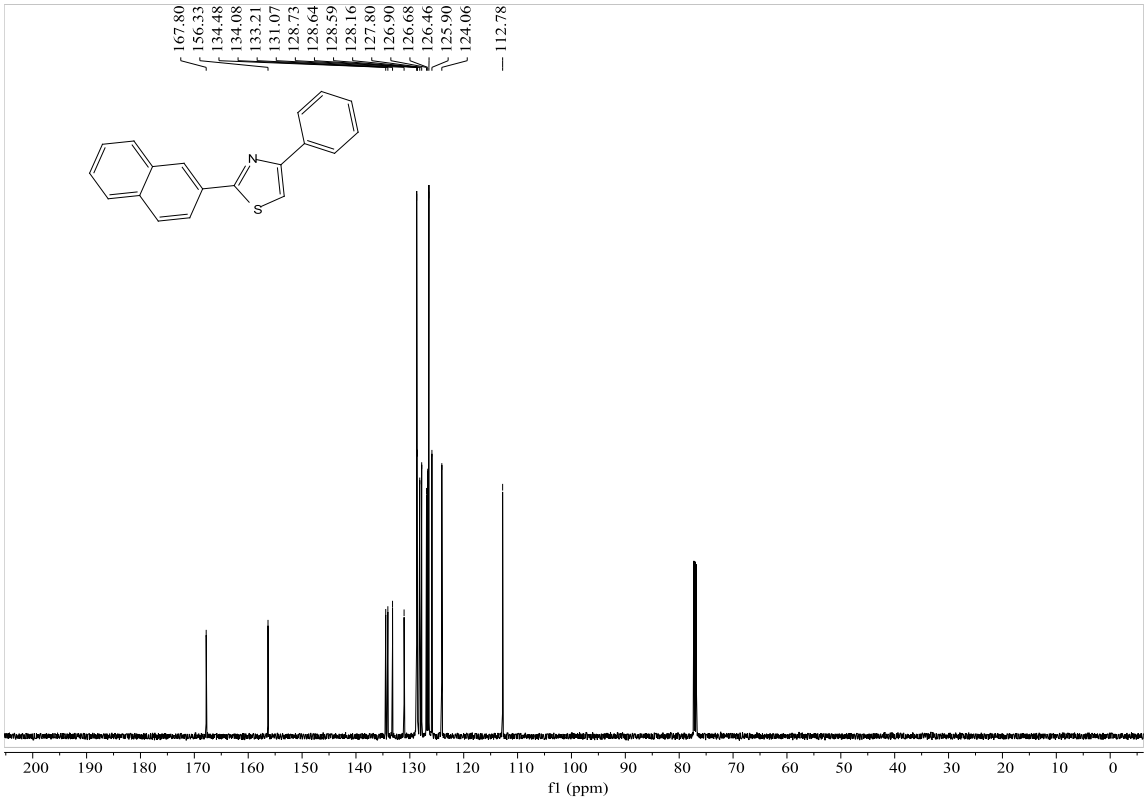
^{13}C NMR spectrum of compound 2h (101 MHz, $CDCl_3$)



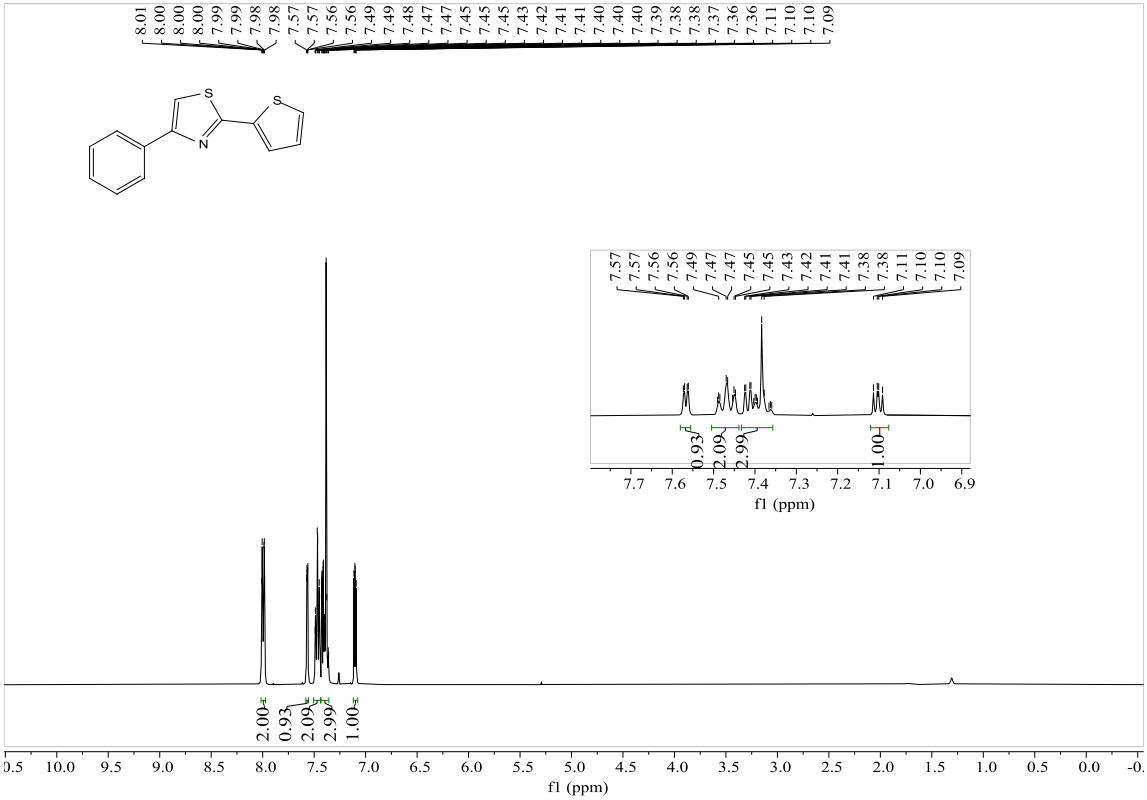
^{1}H NMR spectrum of compound 2i (600 MHz, $CDCl_3$)



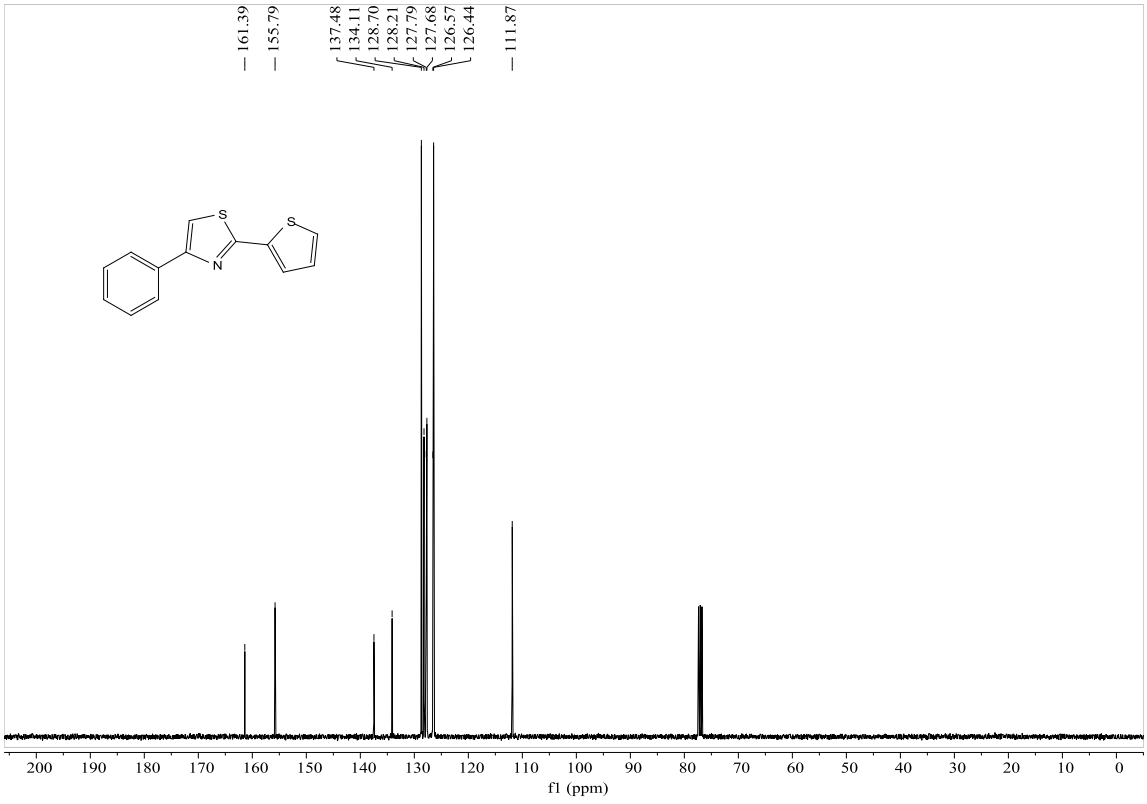
^{13}C NMR spectrum of compound 2i (151 MHz, $CDCl_3$)



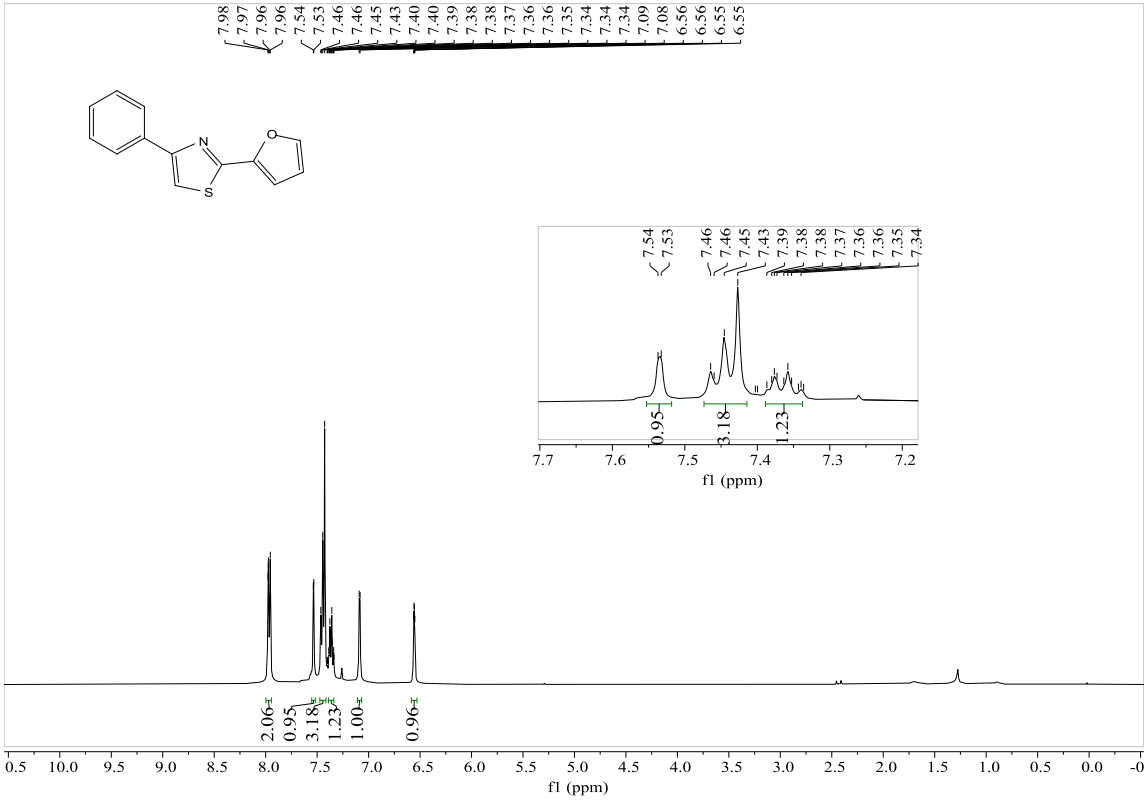
^{1}H NMR spectrum of compound 2j (400 MHz, $CDCl_3$)



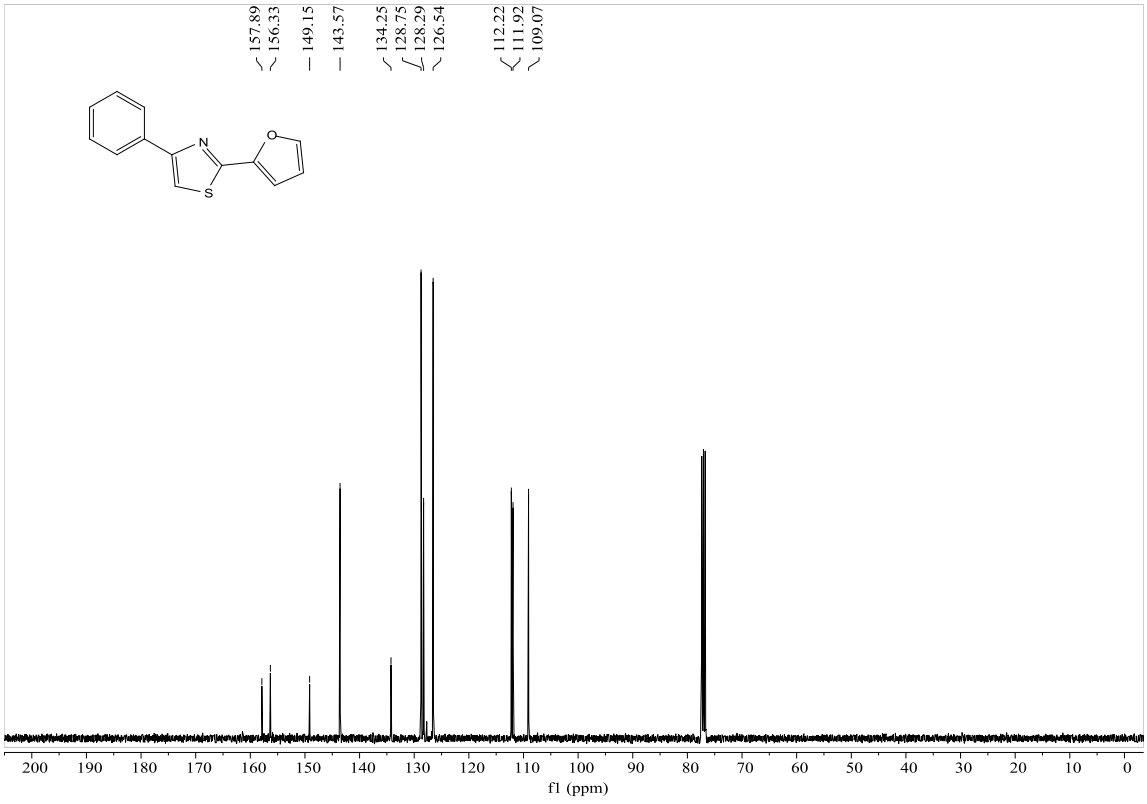
^{13}C NMR spectrum of compound 2j (101 MHz, $CDCl_3$)



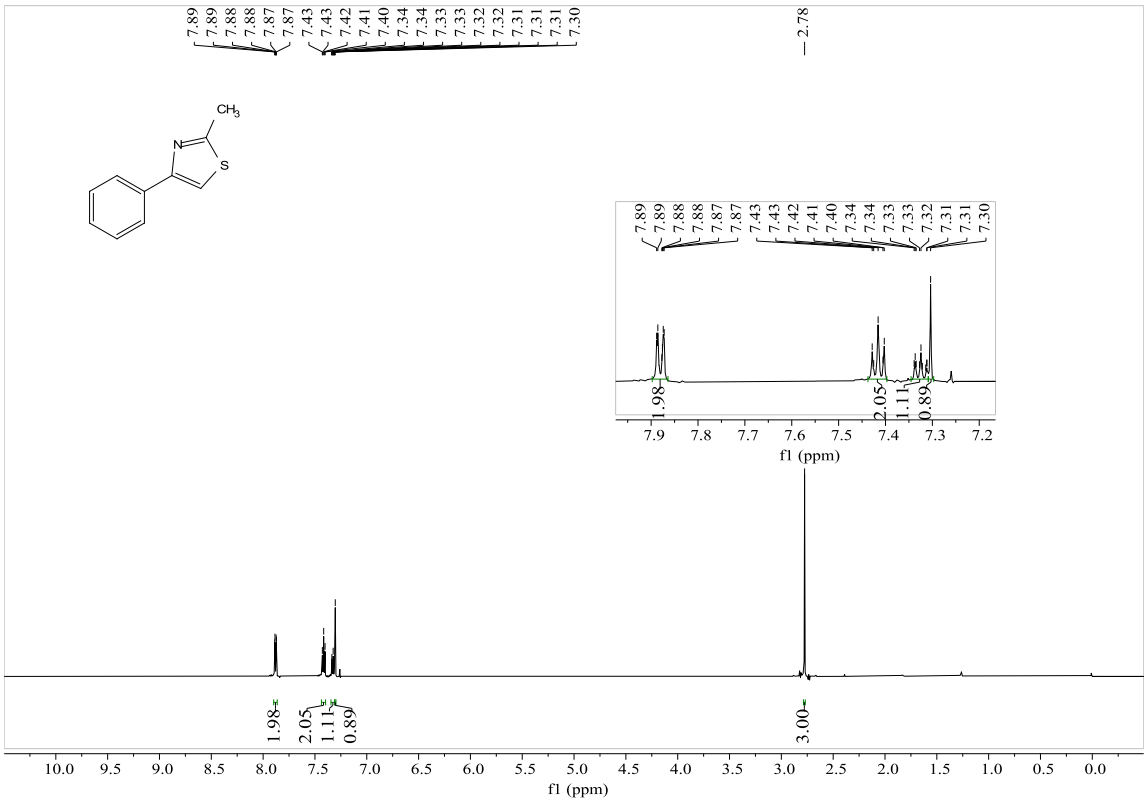
^{1}H NMR spectrum of compound 2k (400 MHz, $CDCl_3$)



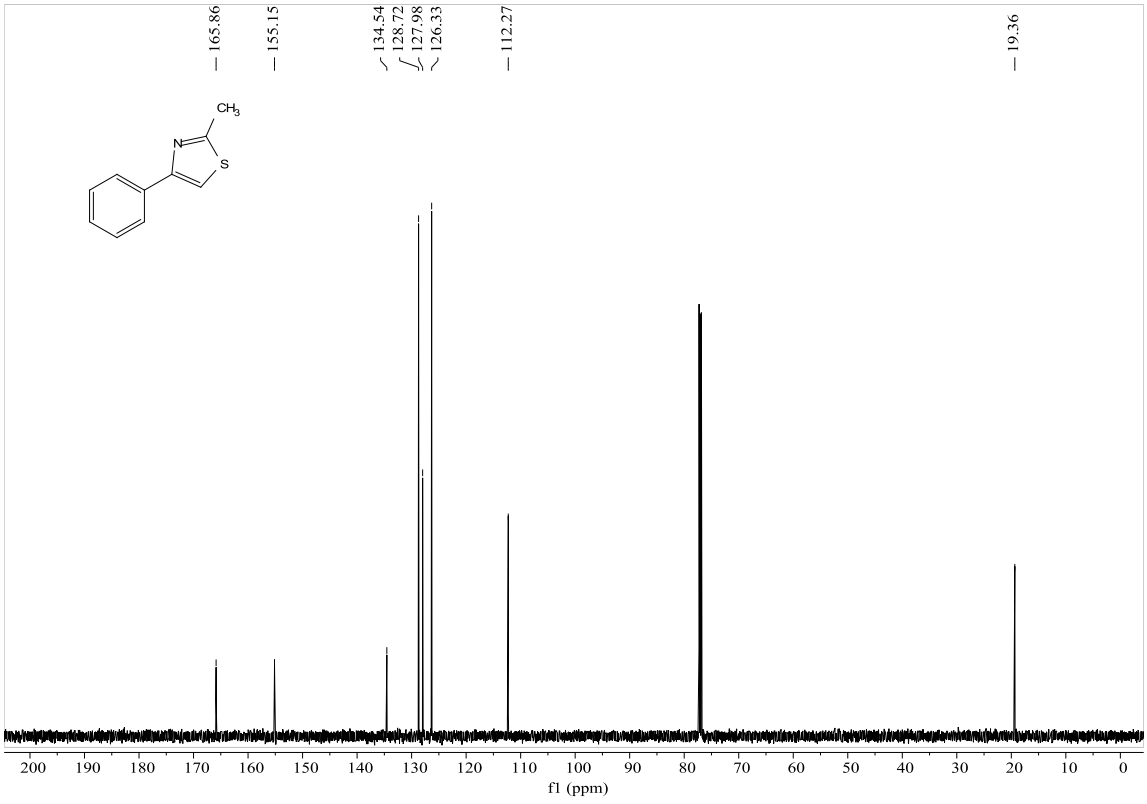
^{13}C NMR spectrum of compound 2k (101 MHz, $CDCl_3$)



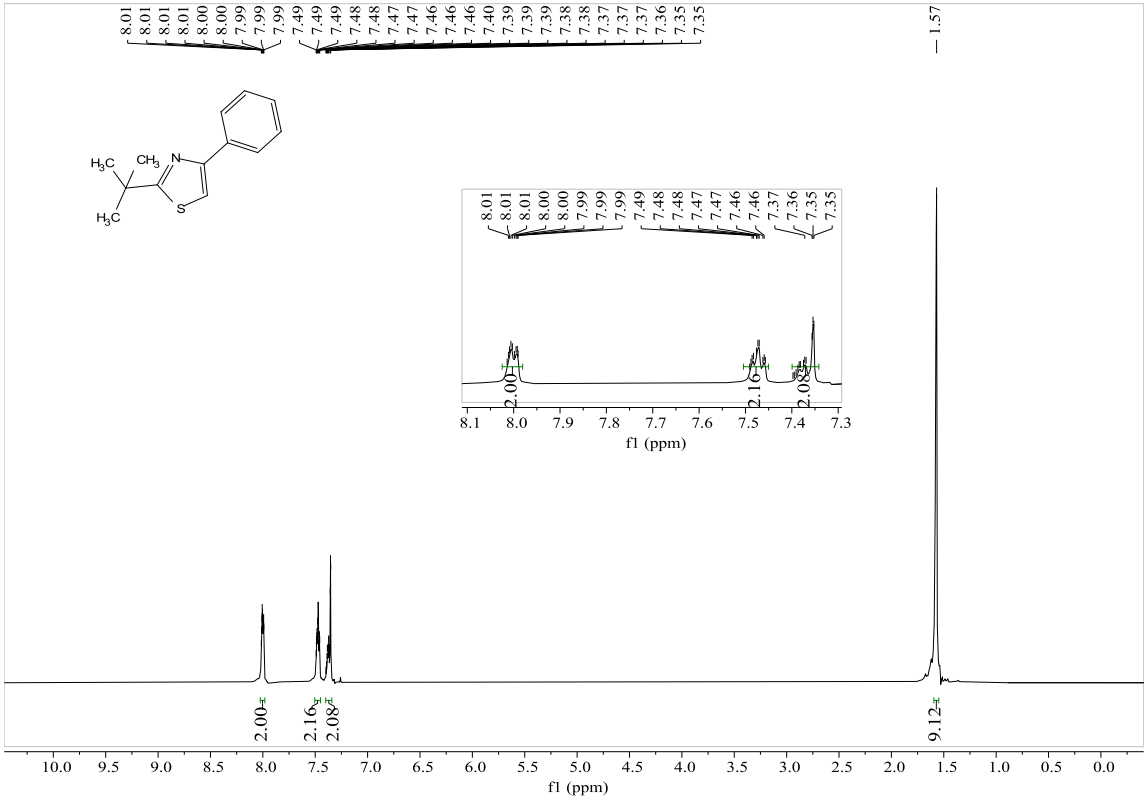
^{1}H NMR spectrum of compound 2l (600 MHz, $CDCl_3$)



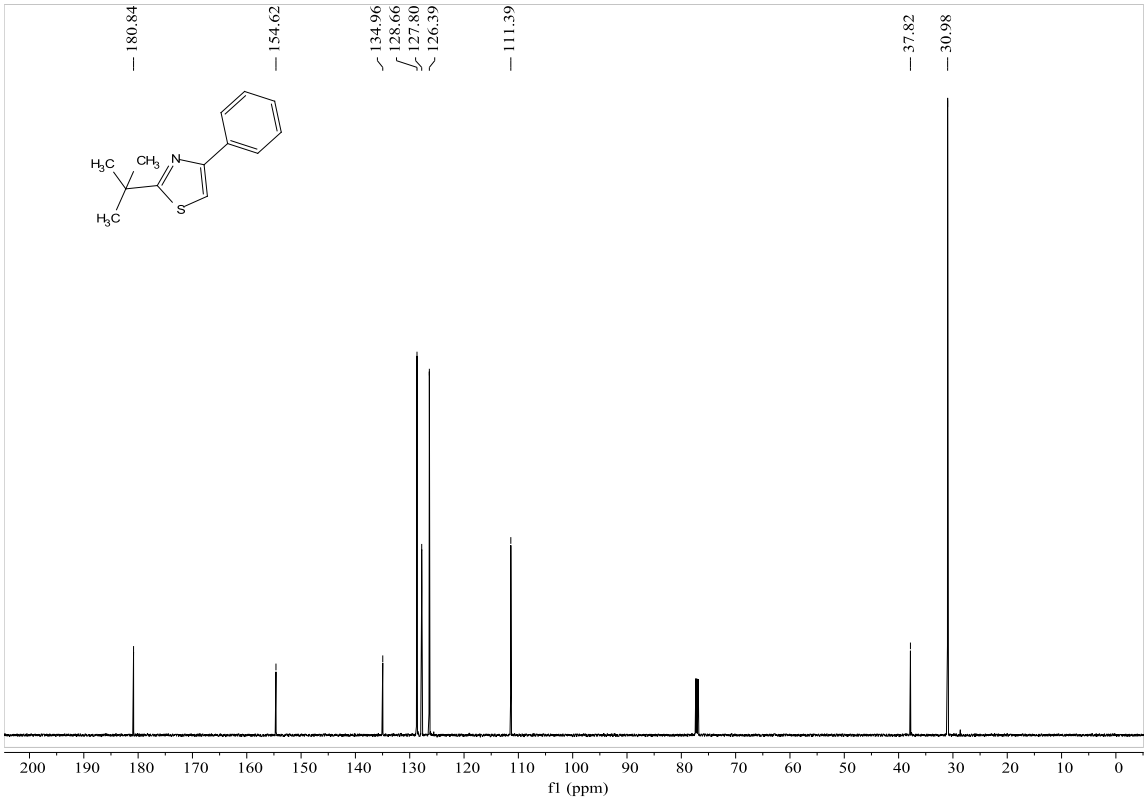
^{13}C NMR spectrum of compound 2l (151 MHz, $CDCl_3$)



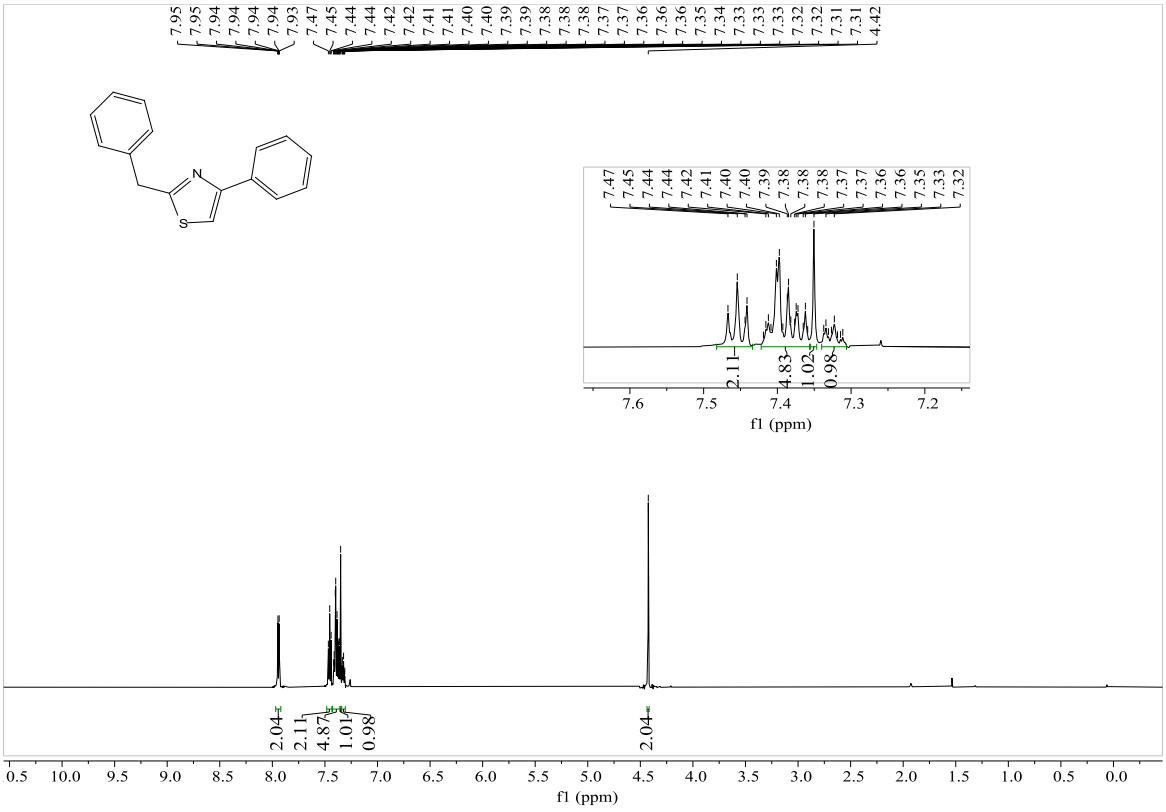
^{1}H NMR spectrum of compound 2m (600 MHz, $CDCl_3$)



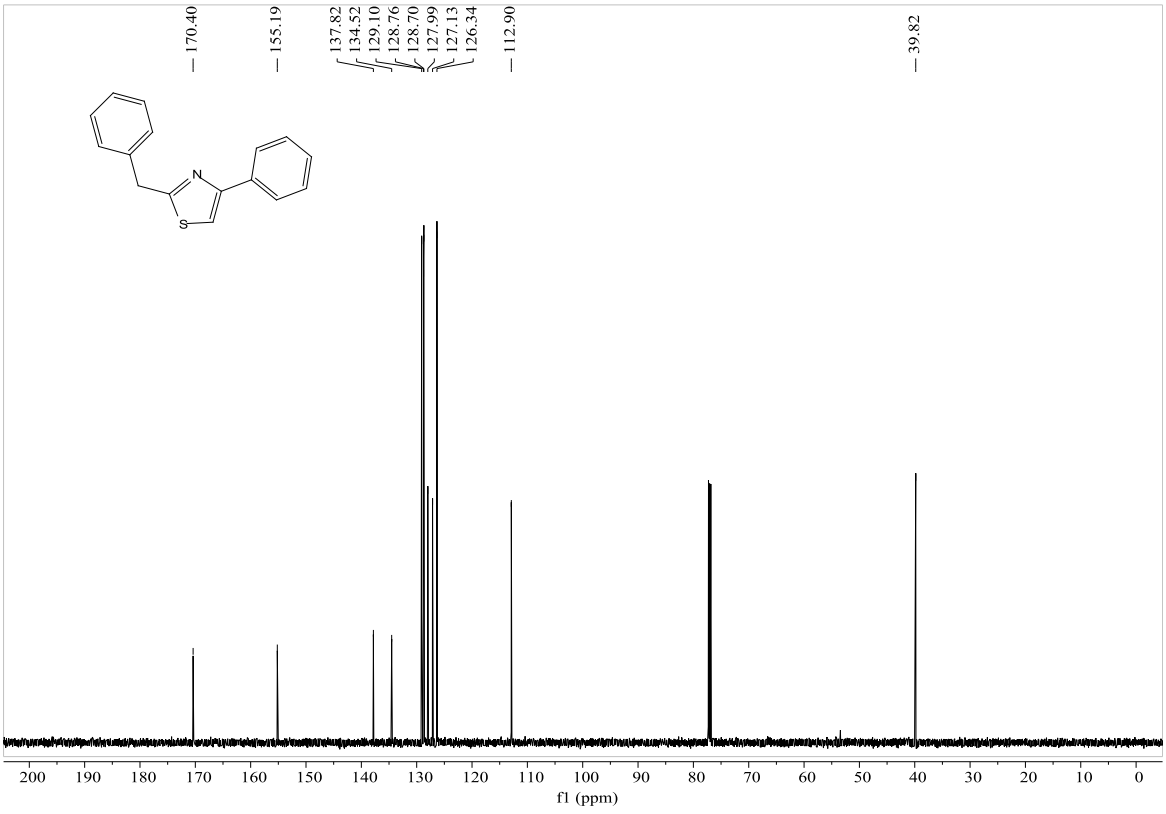
^{13}C NMR spectrum of compound 2m (151 MHz, $CDCl_3$)



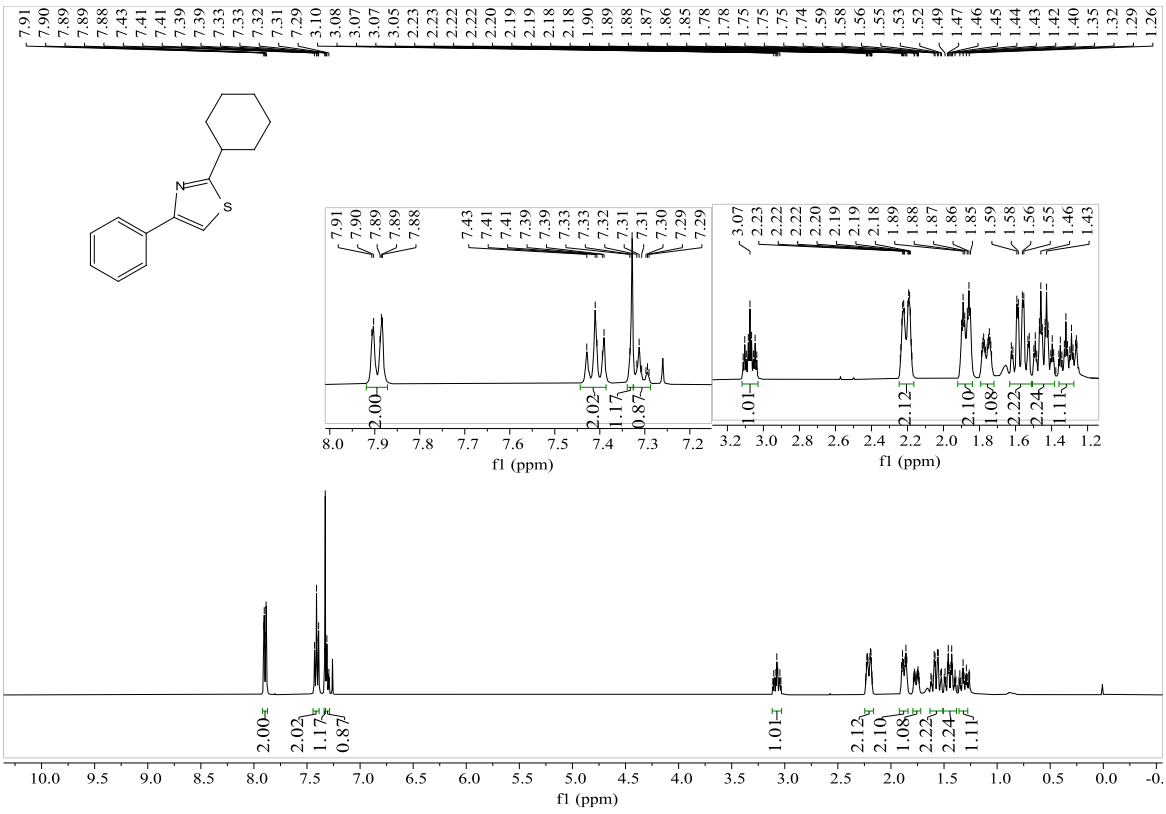
^{1}H NMR spectrum of compound 2n (600 MHz, $CDCl_3$)



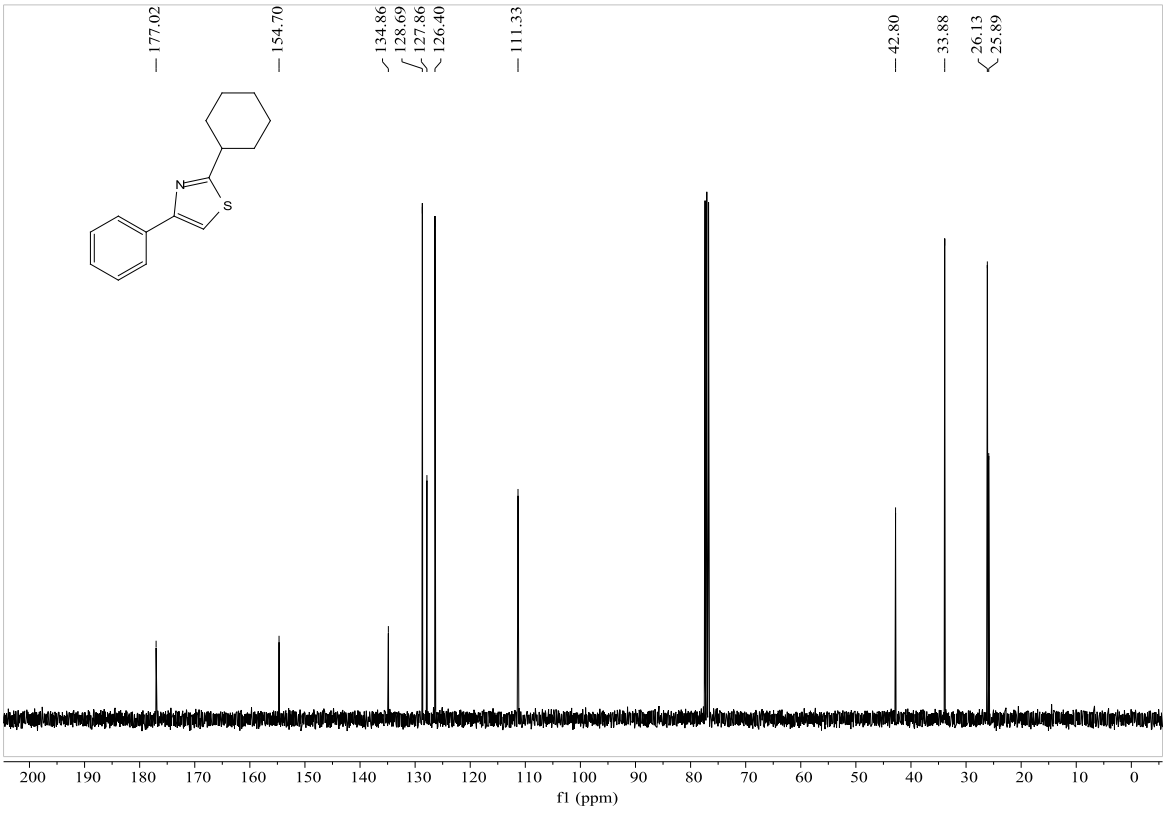
^{13}C NMR spectrum of compound 2n (151 MHz, $CDCl_3$)



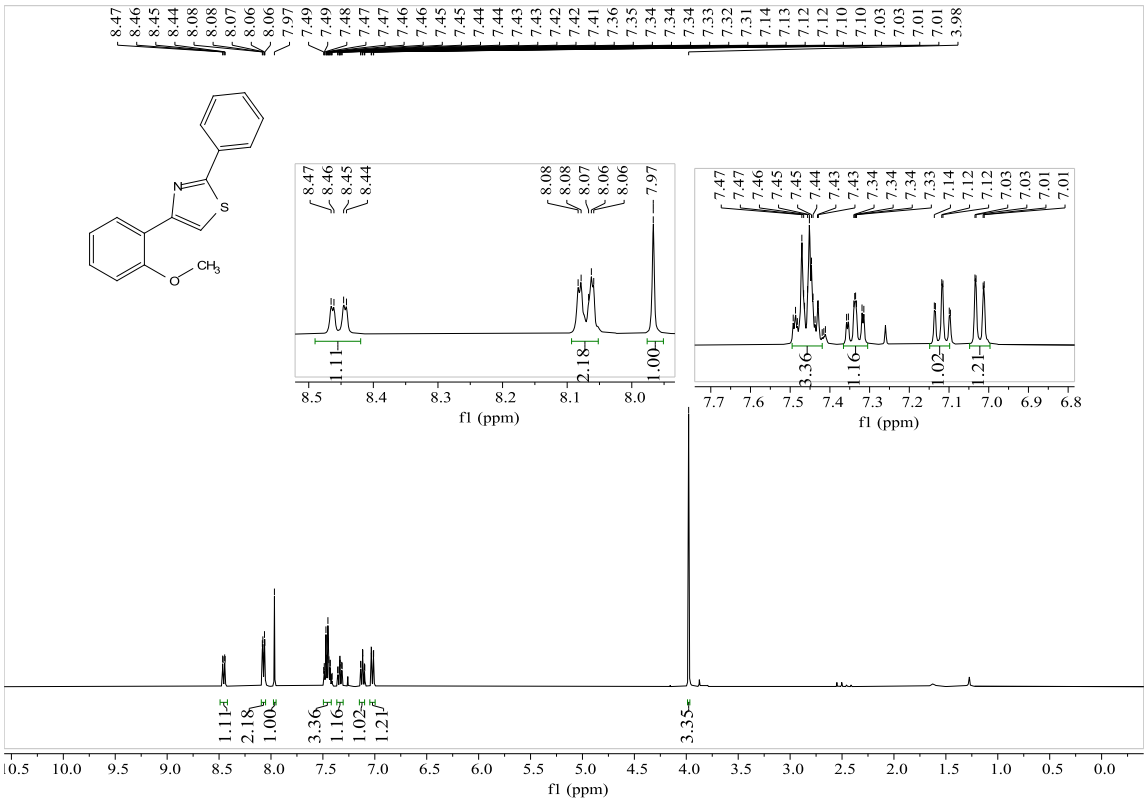
^{1}H NMR spectrum of compound 2o (400 MHz, $CDCl_3$)



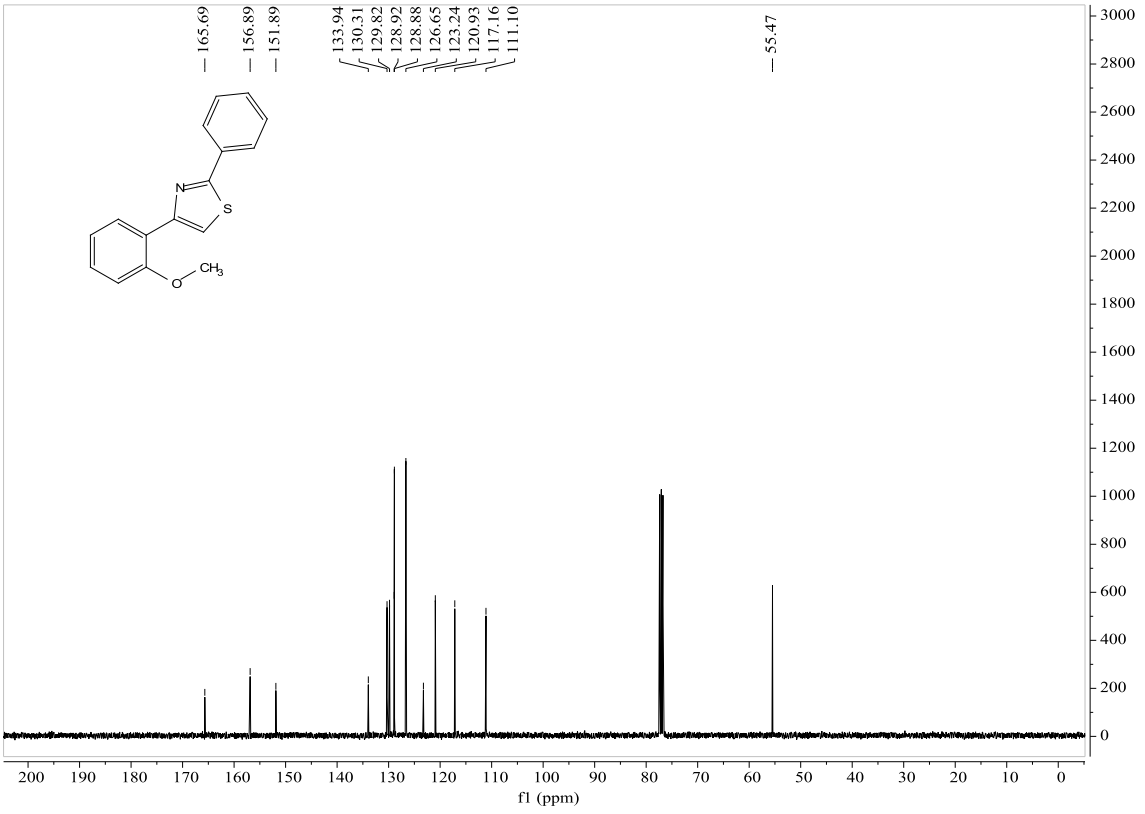
^{13}C NMR spectrum of compound 2o (101 MHz, $CDCl_3$)



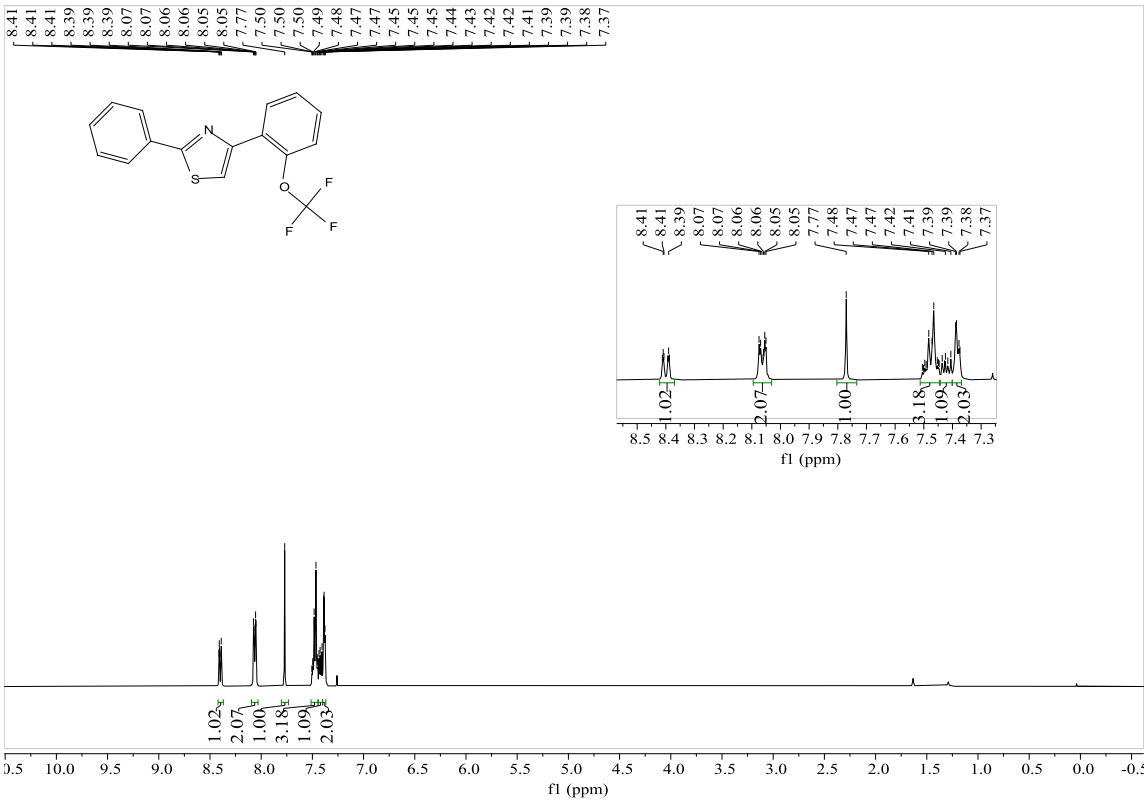
^{1}H NMR spectrum of compound 2p (400 MHz, $CDCl_3$)



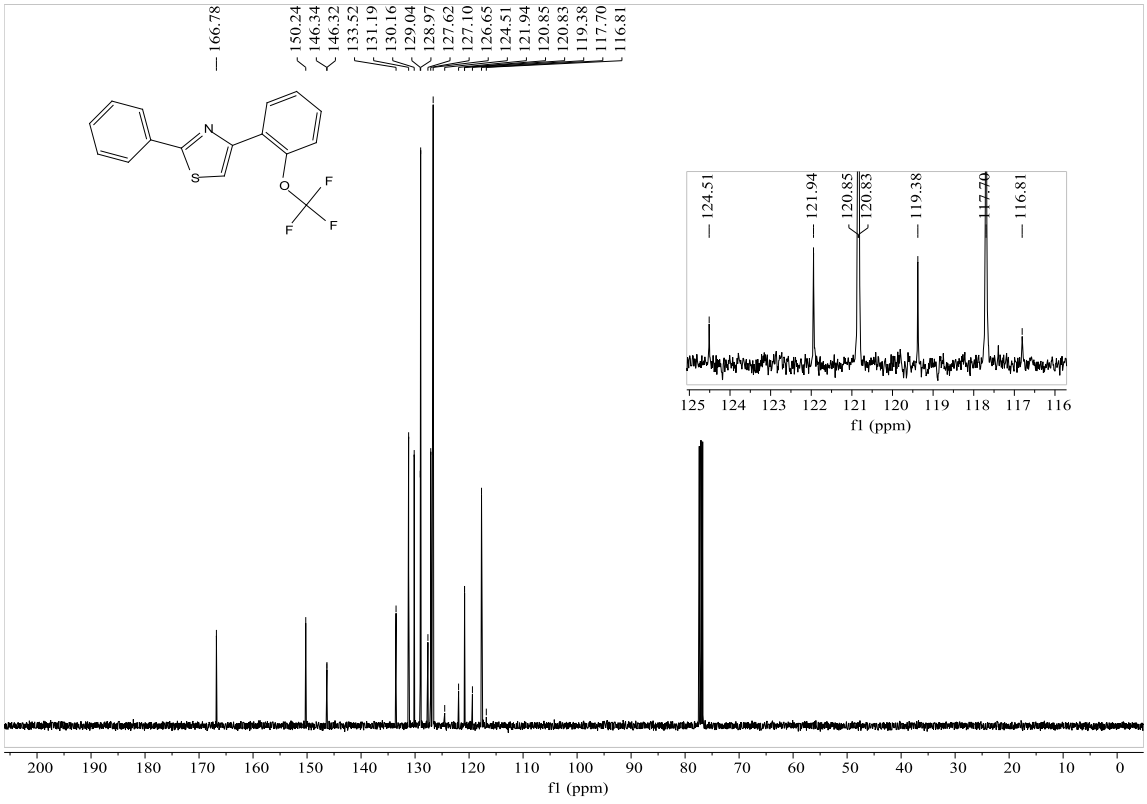
^{13}C NMR spectrum of compound 2p (101 MHz, $CDCl_3$)



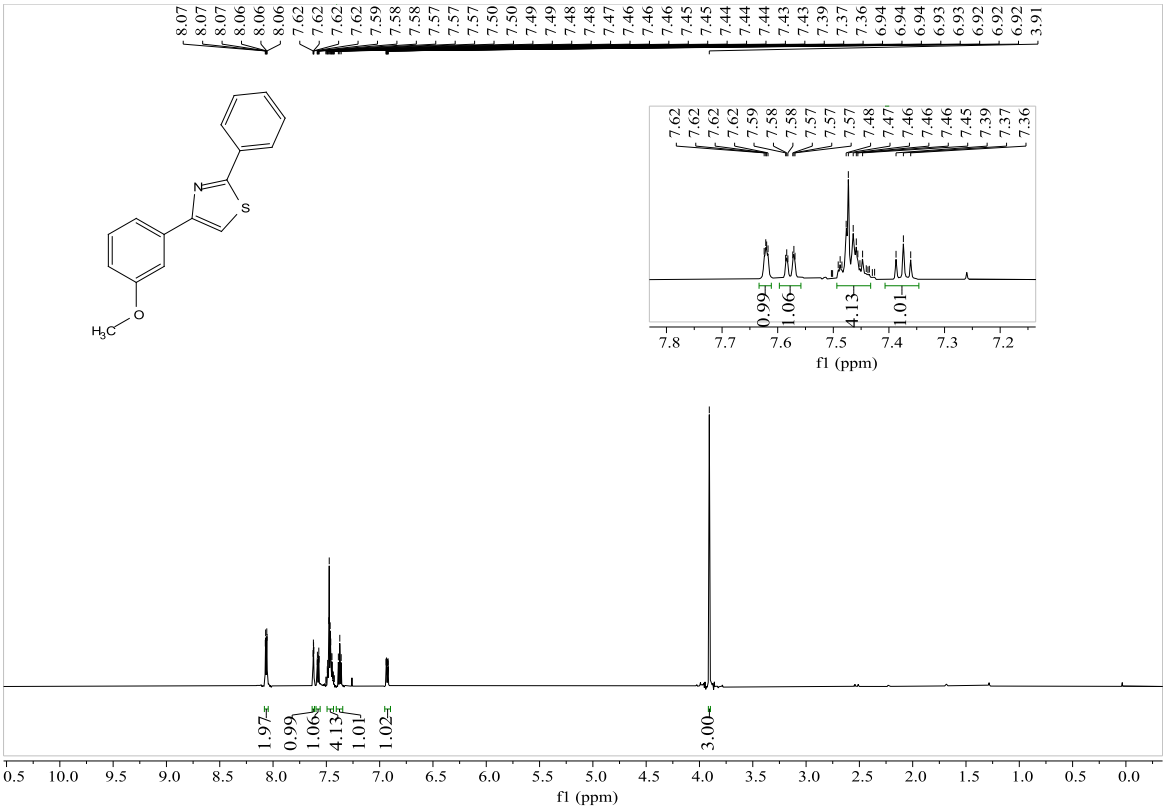
^{1}H NMR spectrum of compound 2q (400 MHz, $CDCl_3$)



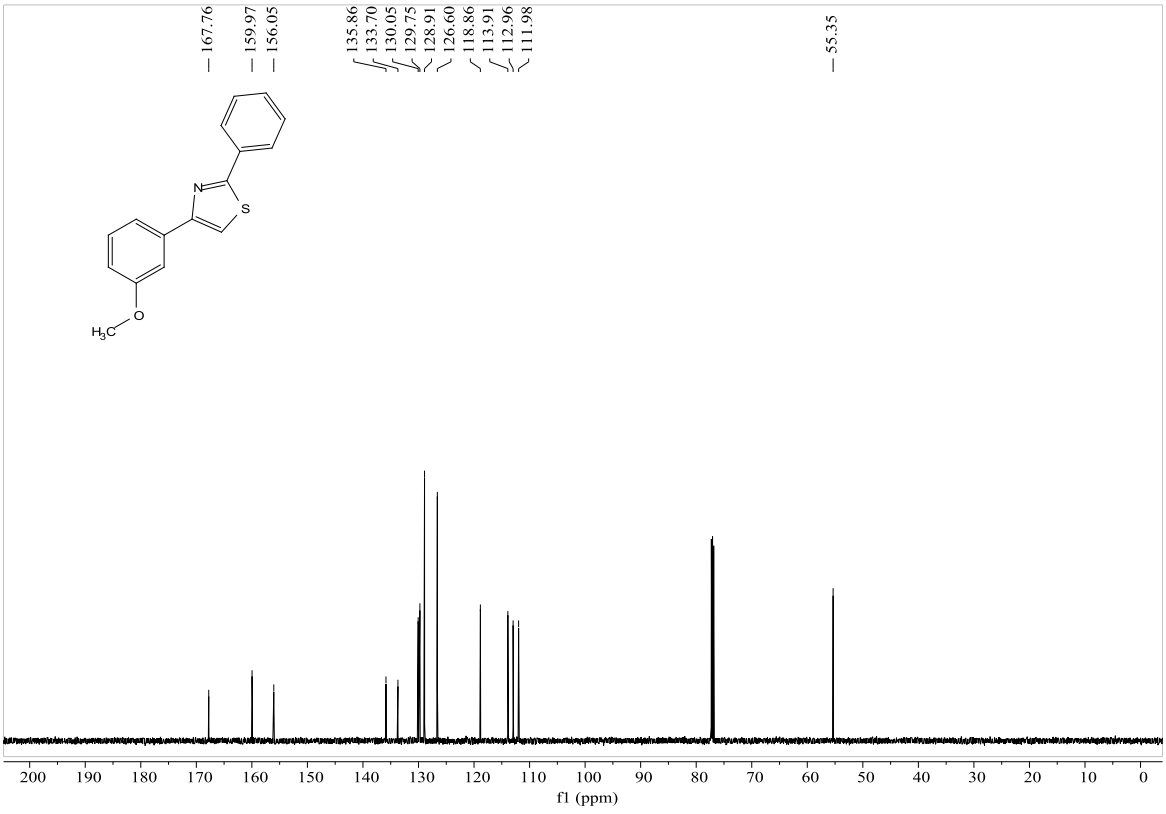
^{13}C NMR spectrum of compound 2q (101 MHz, $CDCl_3$)



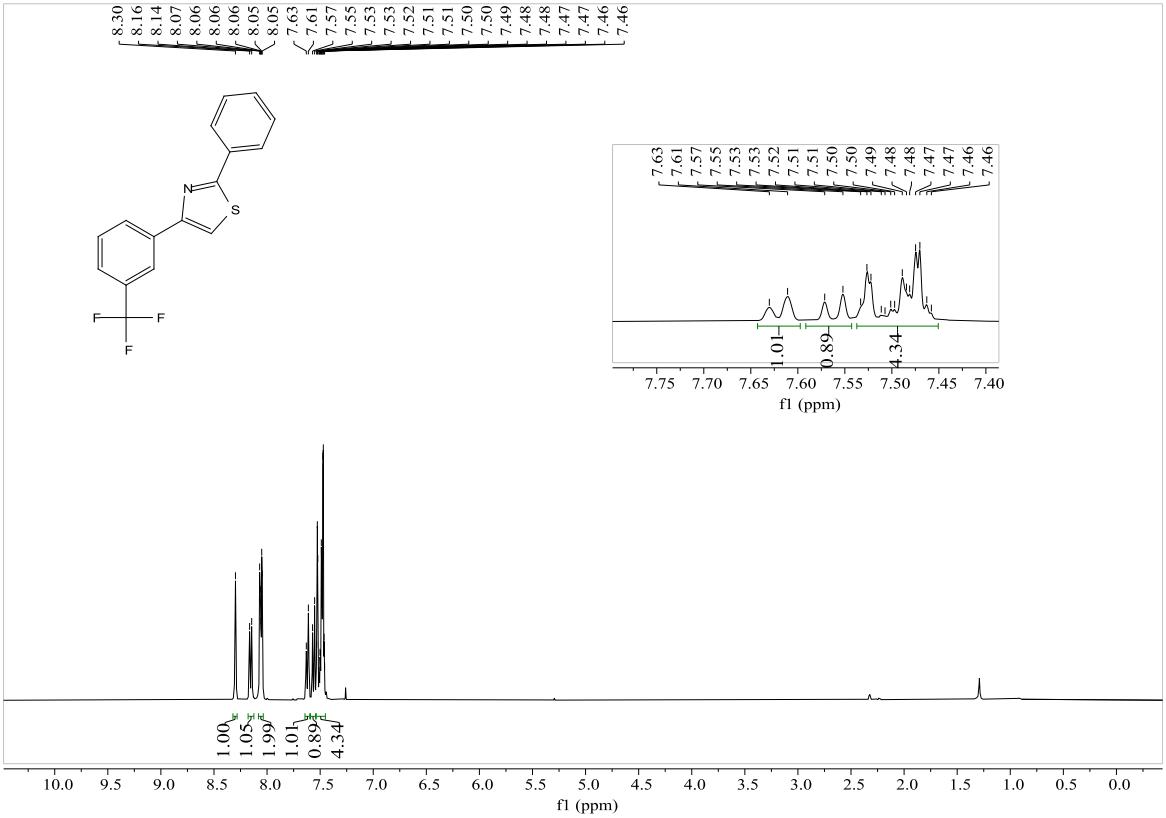
^{1}H NMR spectrum of compound 2r (600 MHz, $CDCl_3$)



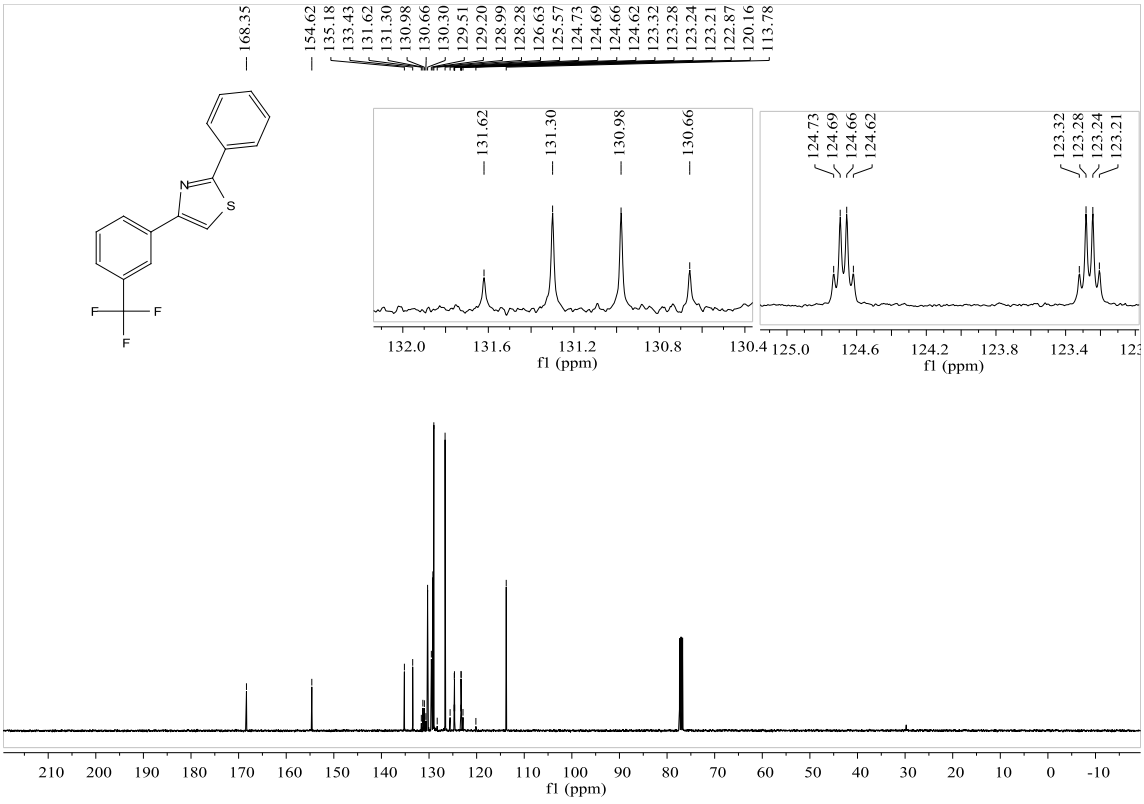
^{13}C NMR spectrum of compound 2r (151 MHz, $CDCl_3$)



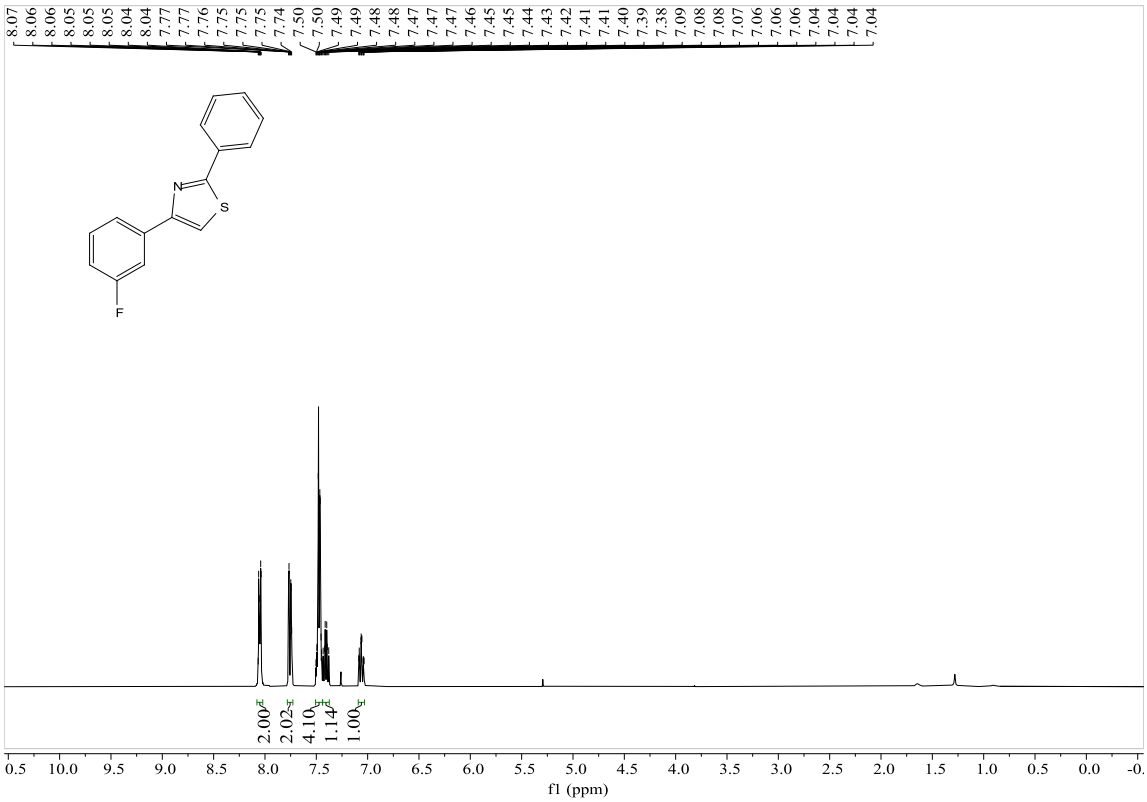
^{1}H NMR spectrum of compound 2s (400 MHz, $CDCl_3$)



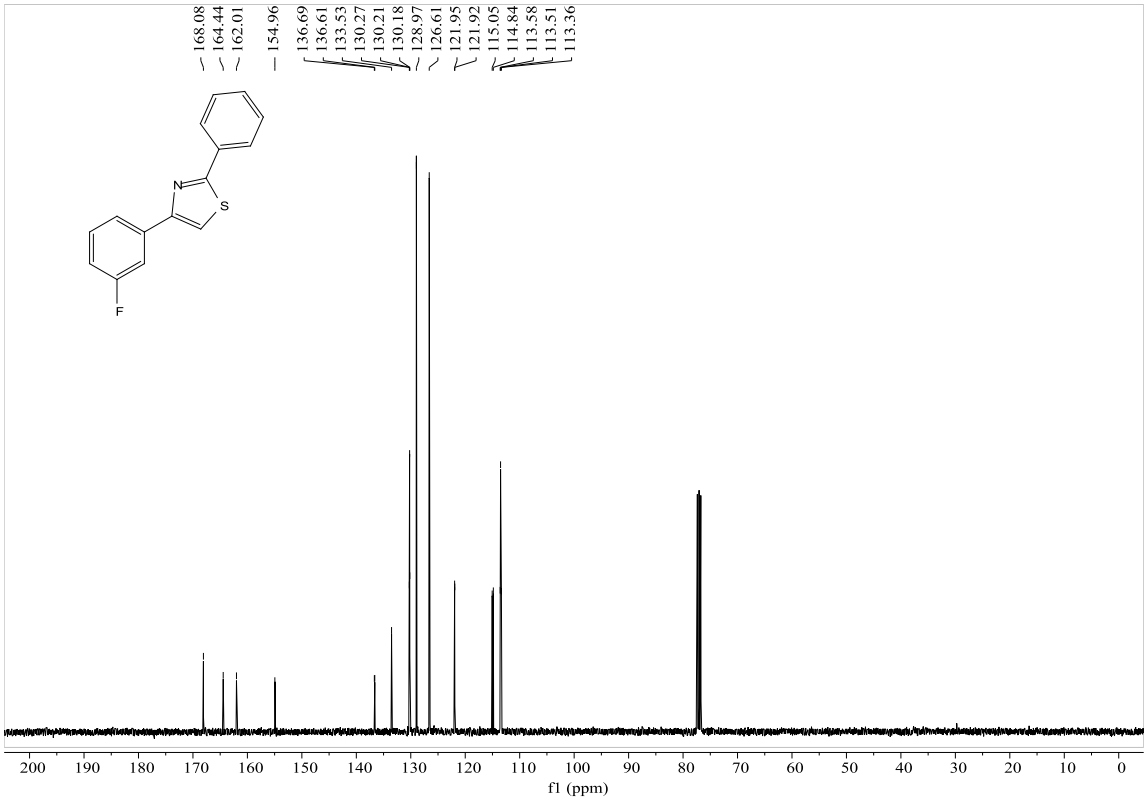
^{13}C NMR spectrum of compound 2s (101 MHz, $CDCl_3$)



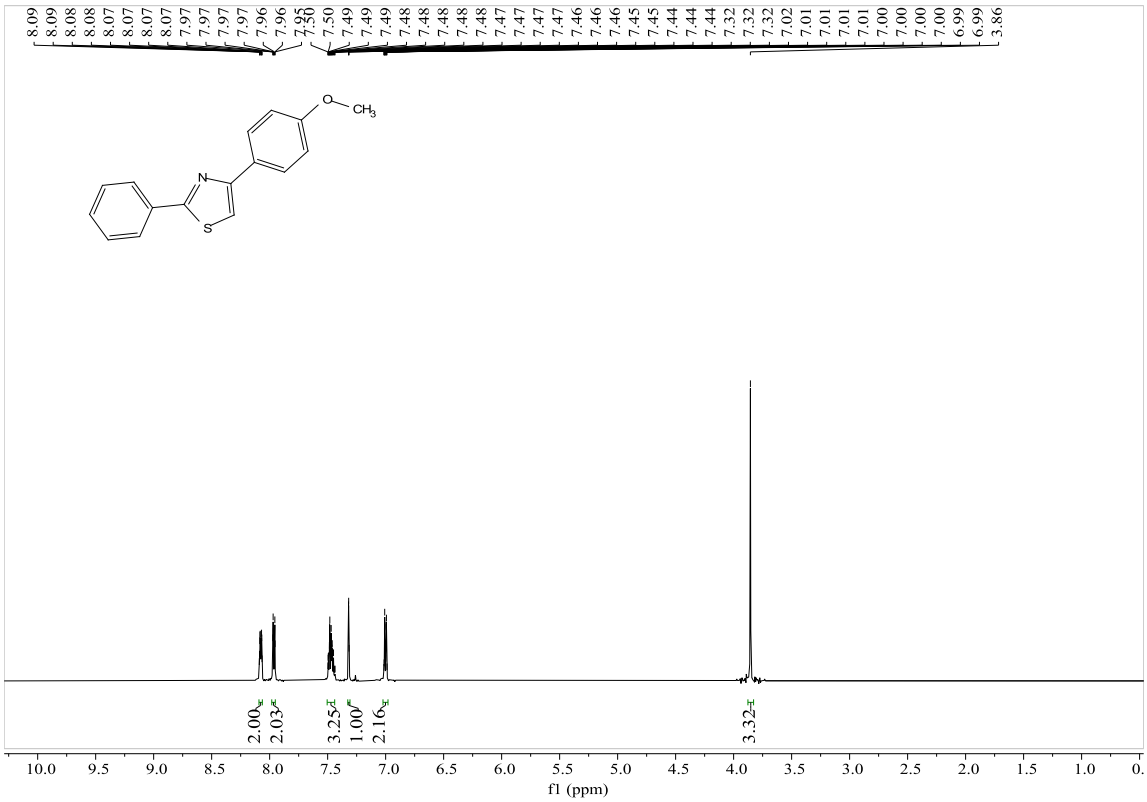
^{1}H NMR spectrum of compound 2t (400 MHz, $CDCl_3$)



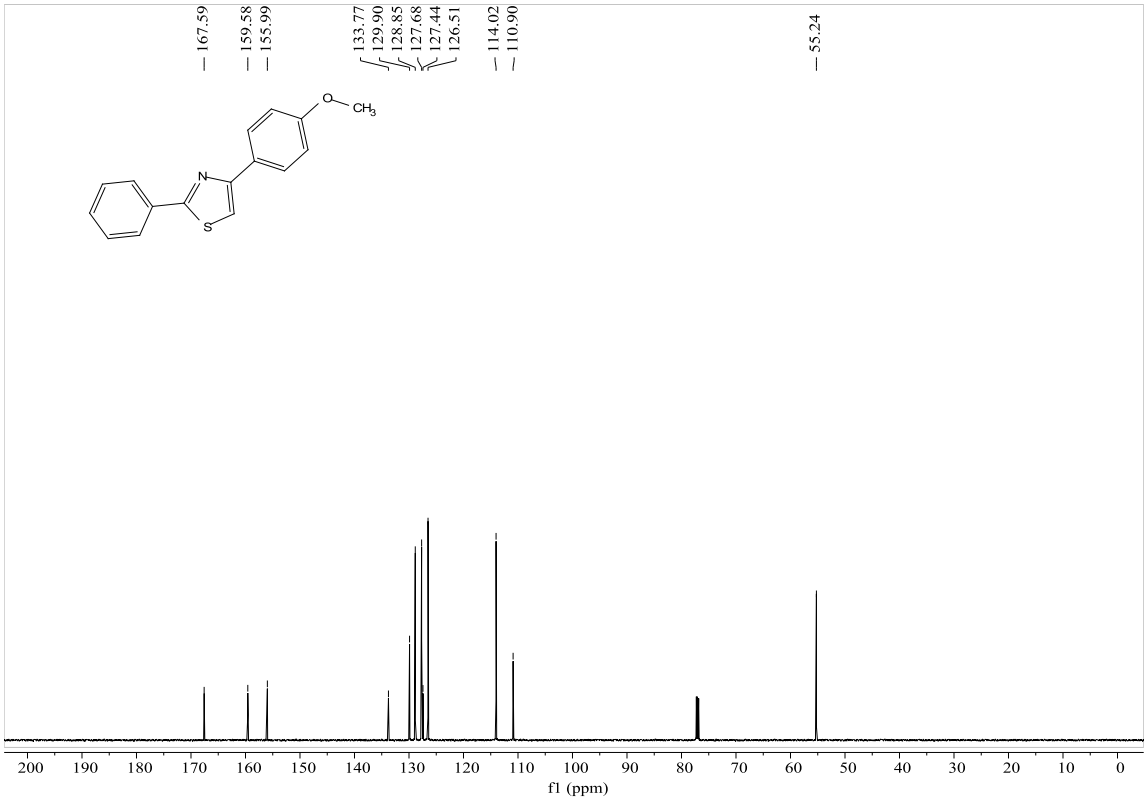
^{13}C NMR spectrum of compound 2t (101 MHz, $CDCl_3$)



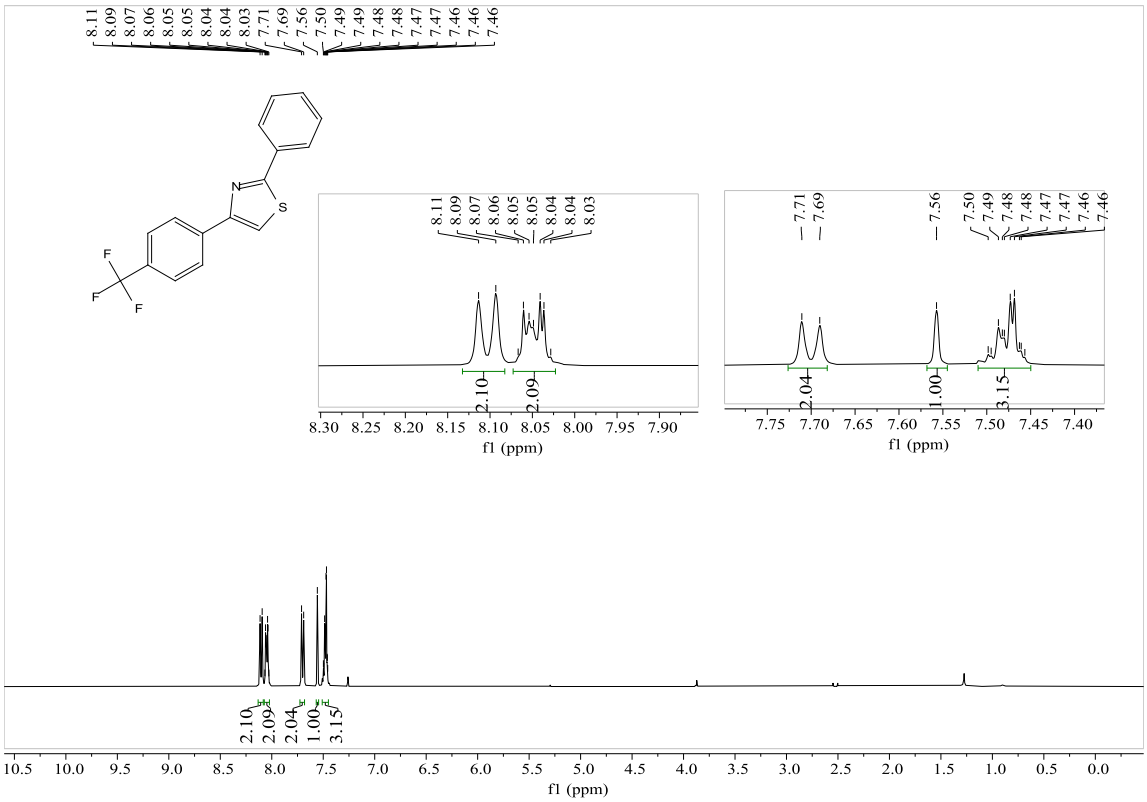
^{1}H NMR spectrum of compound 2u (600 MHz, $CDCl_3$)



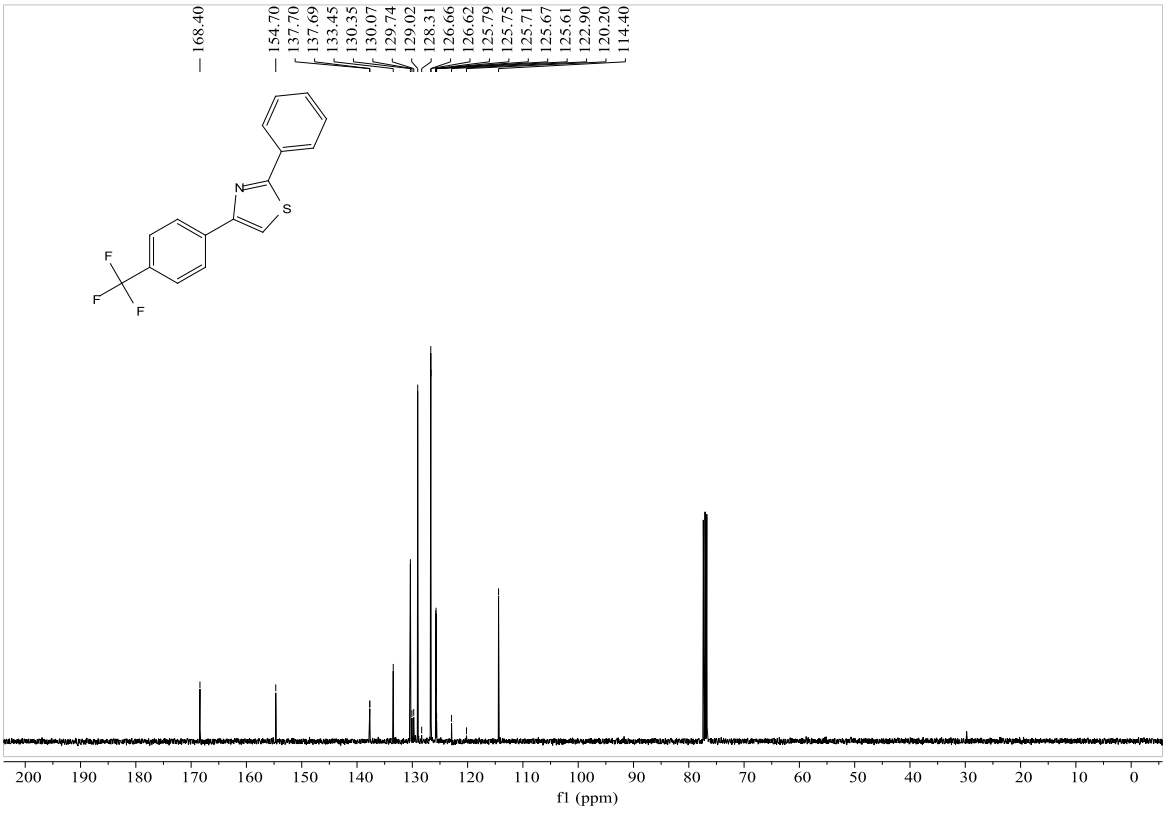
^{13}C NMR spectrum of compound 2u (151 MHz, $CDCl_3$)



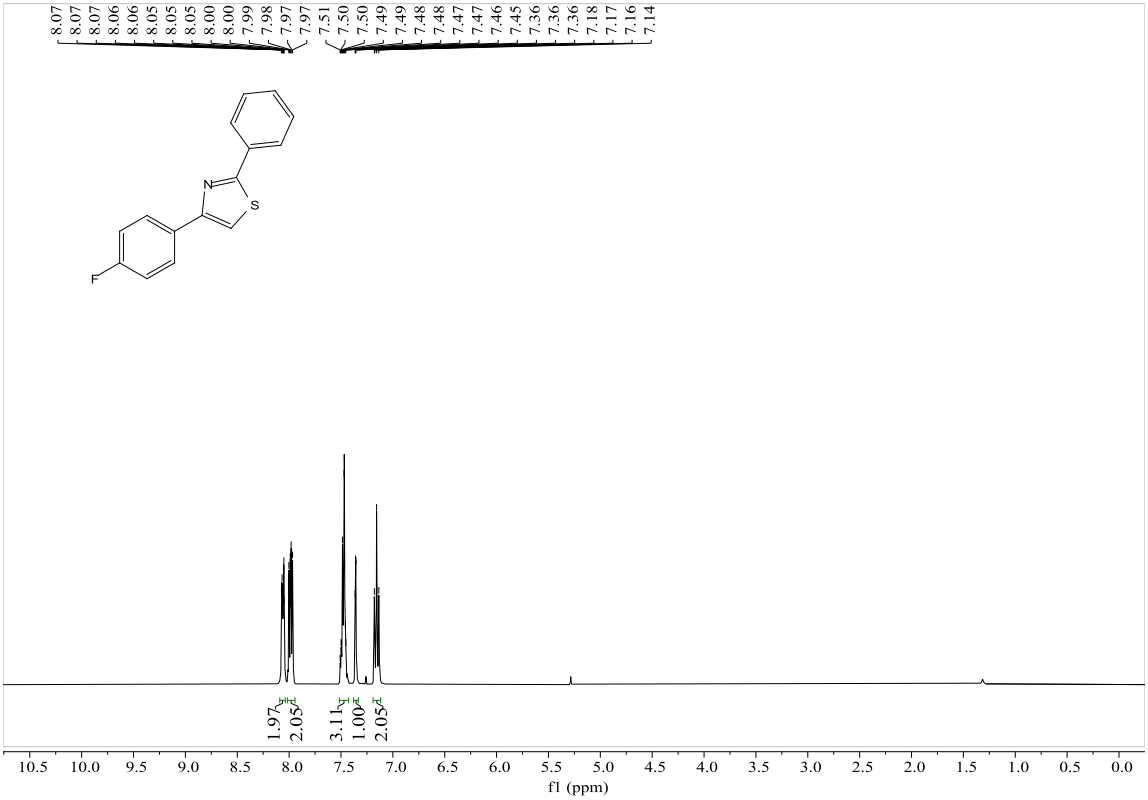
^{1}H NMR spectrum of compound 2v (400 MHz, $CDCl_3$)



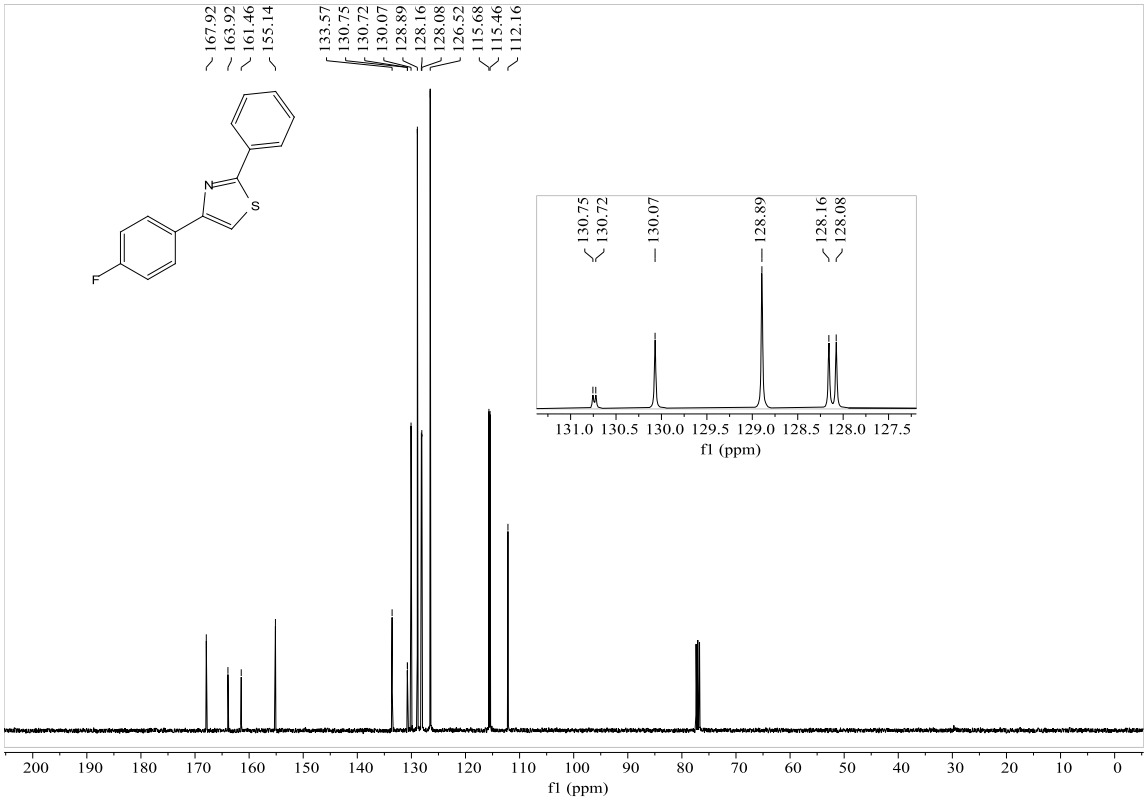
^{13}C NMR spectrum of compound 2v (101 MHz, $CDCl_3$)



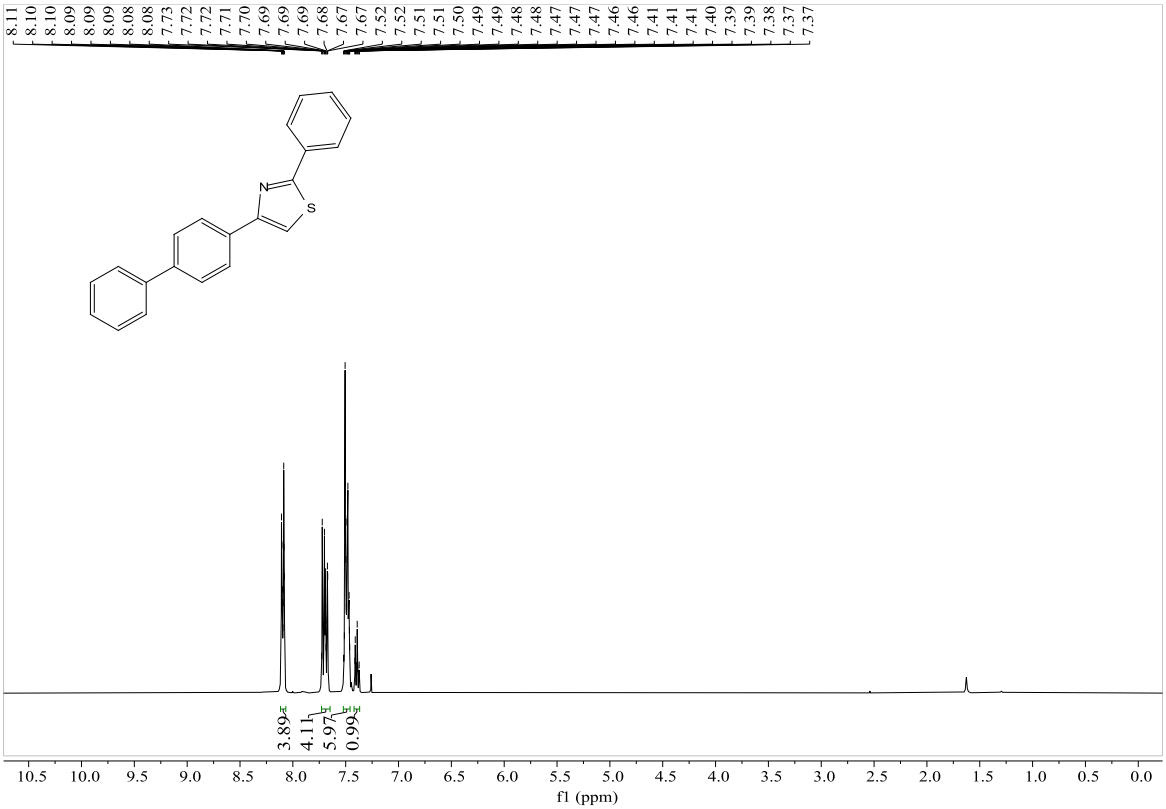
^{1}H NMR spectrum of compound 2w (400 MHz, $CDCl_3$)



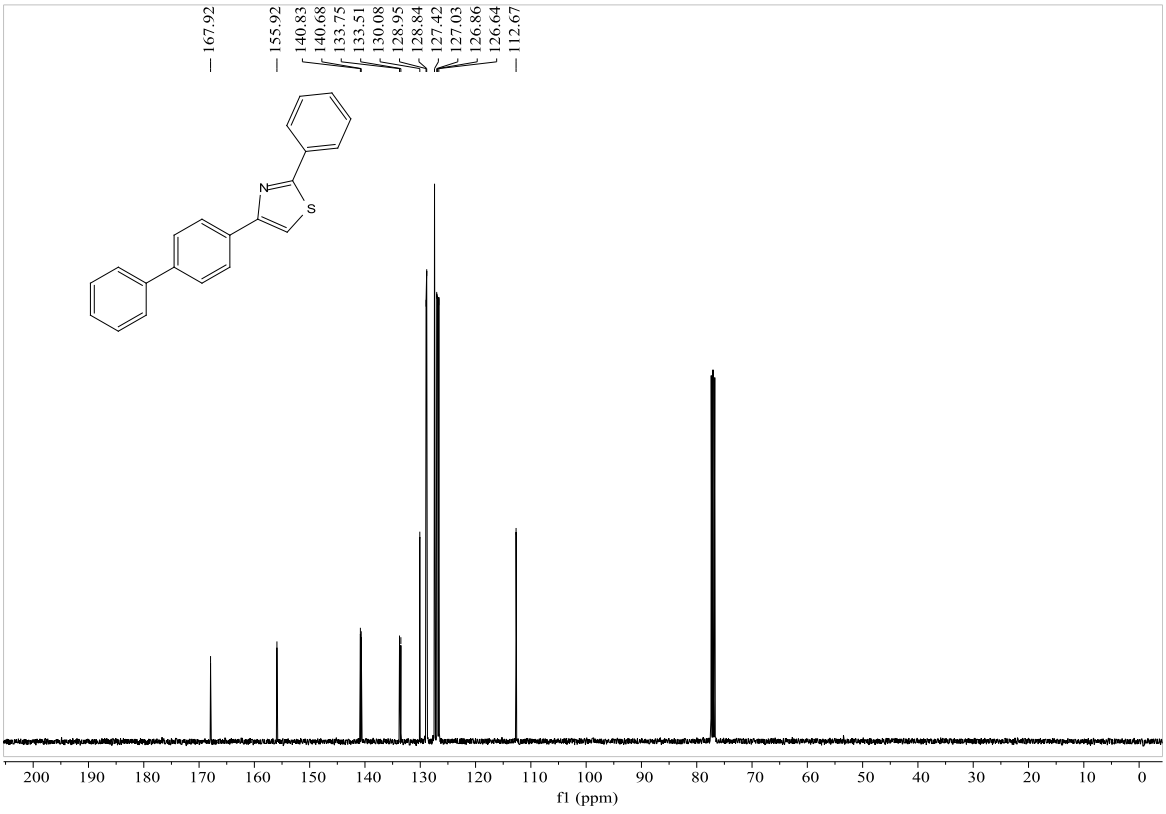
^{13}C NMR spectrum of compound 2w (101 MHz, $CDCl_3$)



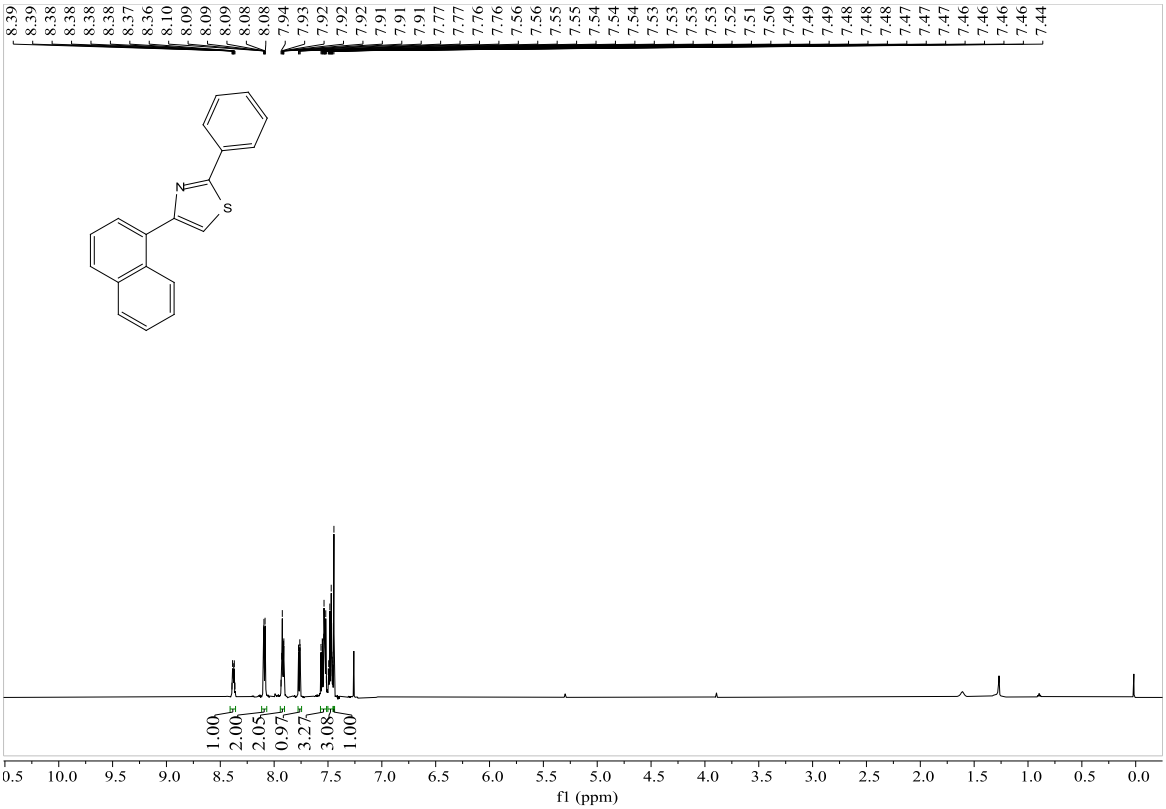
^{1}H NMR spectrum of compound 2x (400 MHz, $CDCl_3$)



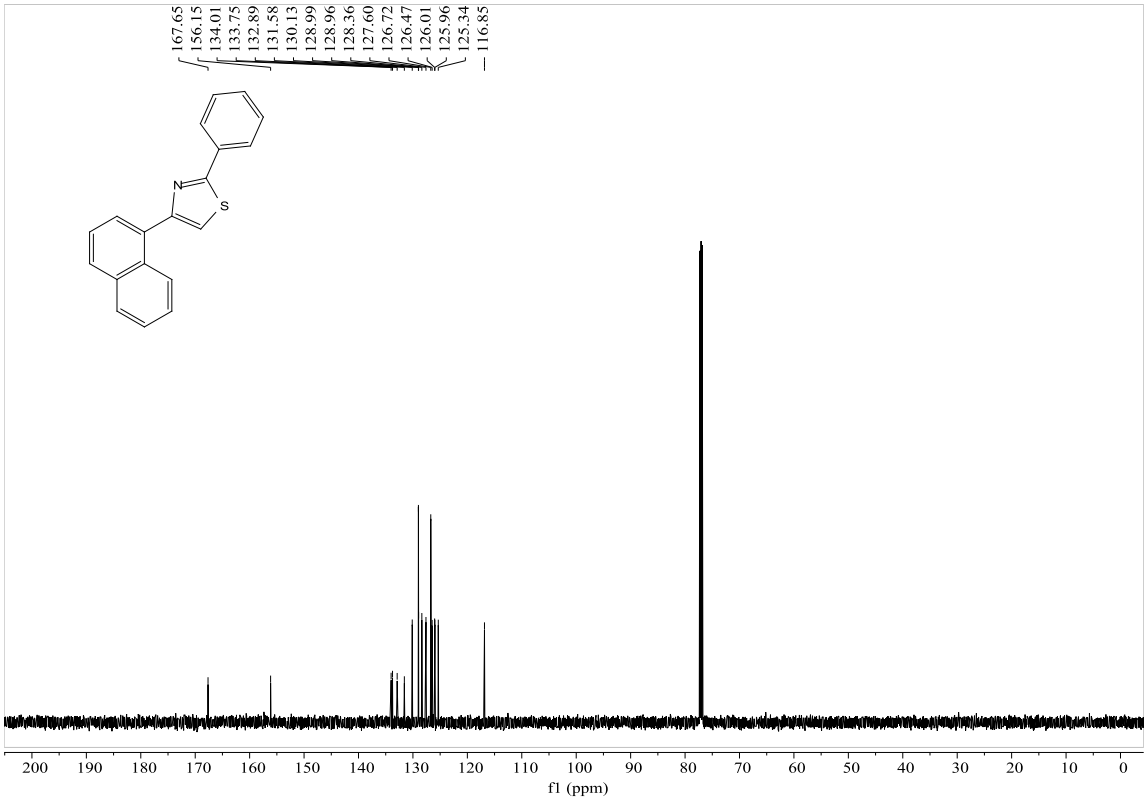
^{13}C NMR spectrum of compound 2x (101 MHz, $CDCl_3$)



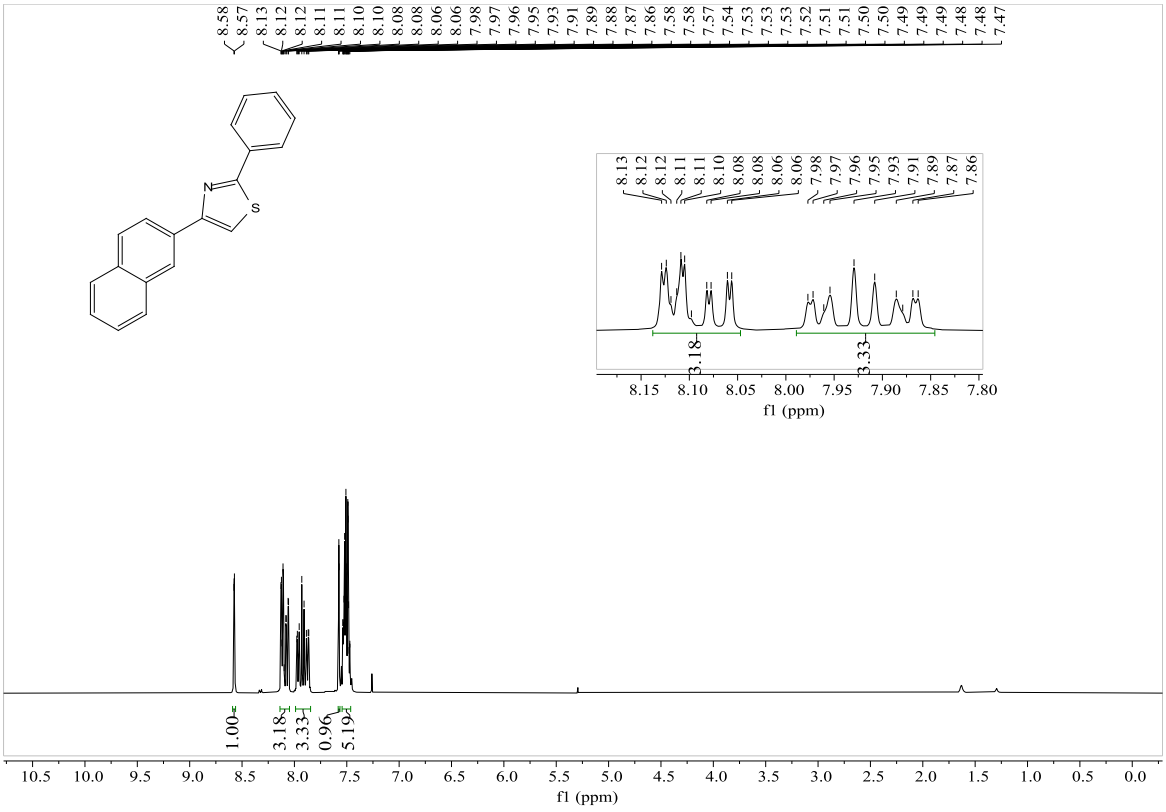
^{1}H NMR spectrum of compound 2y (600 MHz, $CDCl_3$)



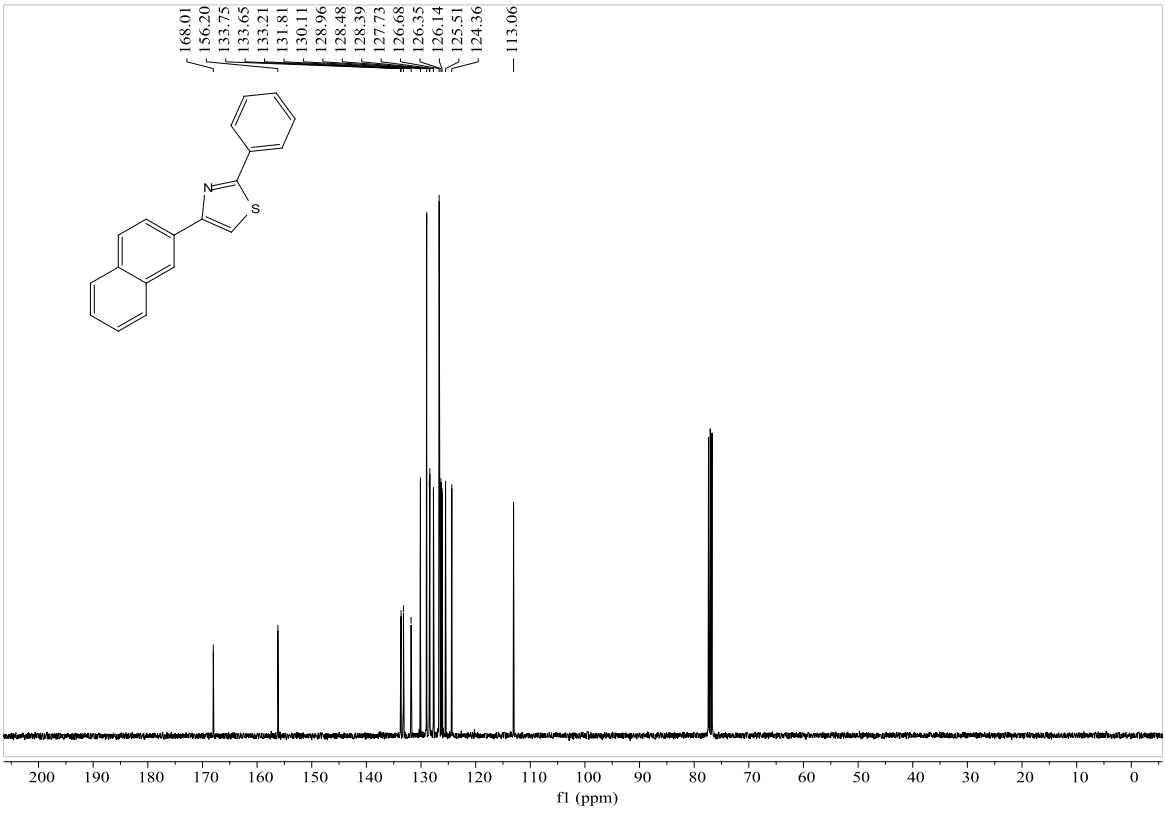
^{13}C NMR spectrum of compound 2y (151 MHz, $CDCl_3$)



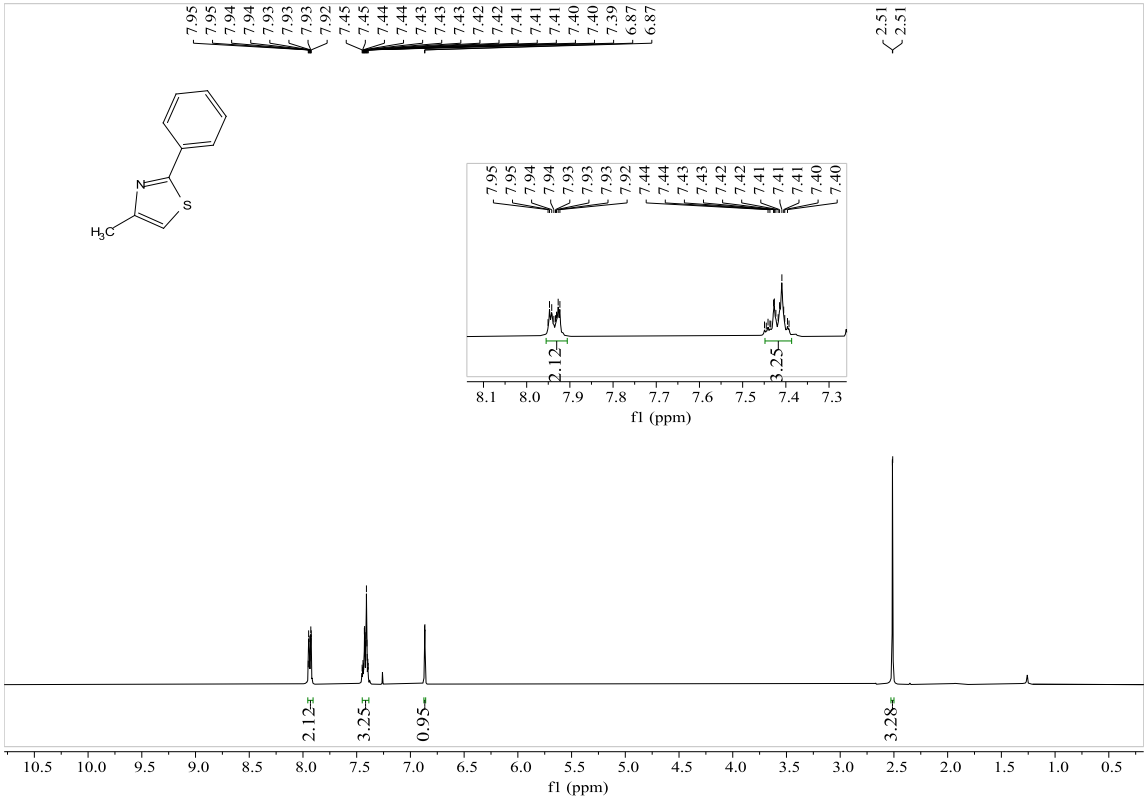
^{1}H NMR spectrum of compound 2z (400 MHz, $CDCl_3$)



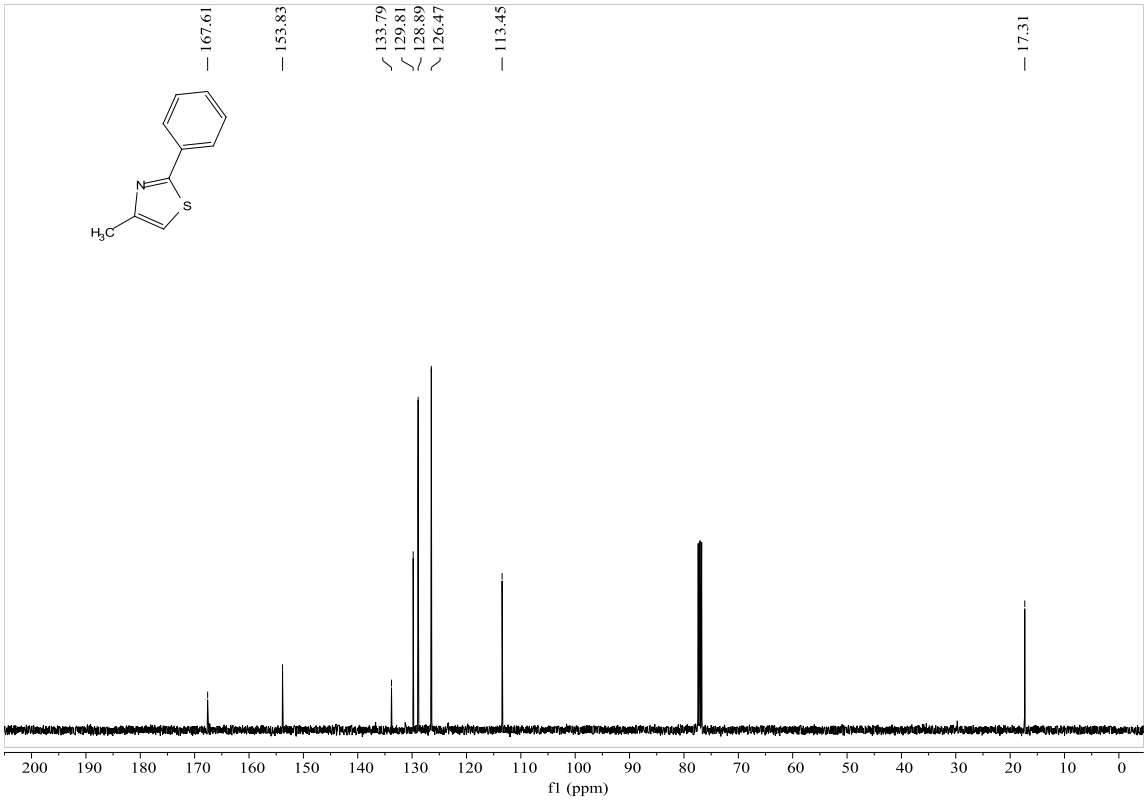
^{13}C NMR spectrum of compound 2z (101 MHz, $CDCl_3$)



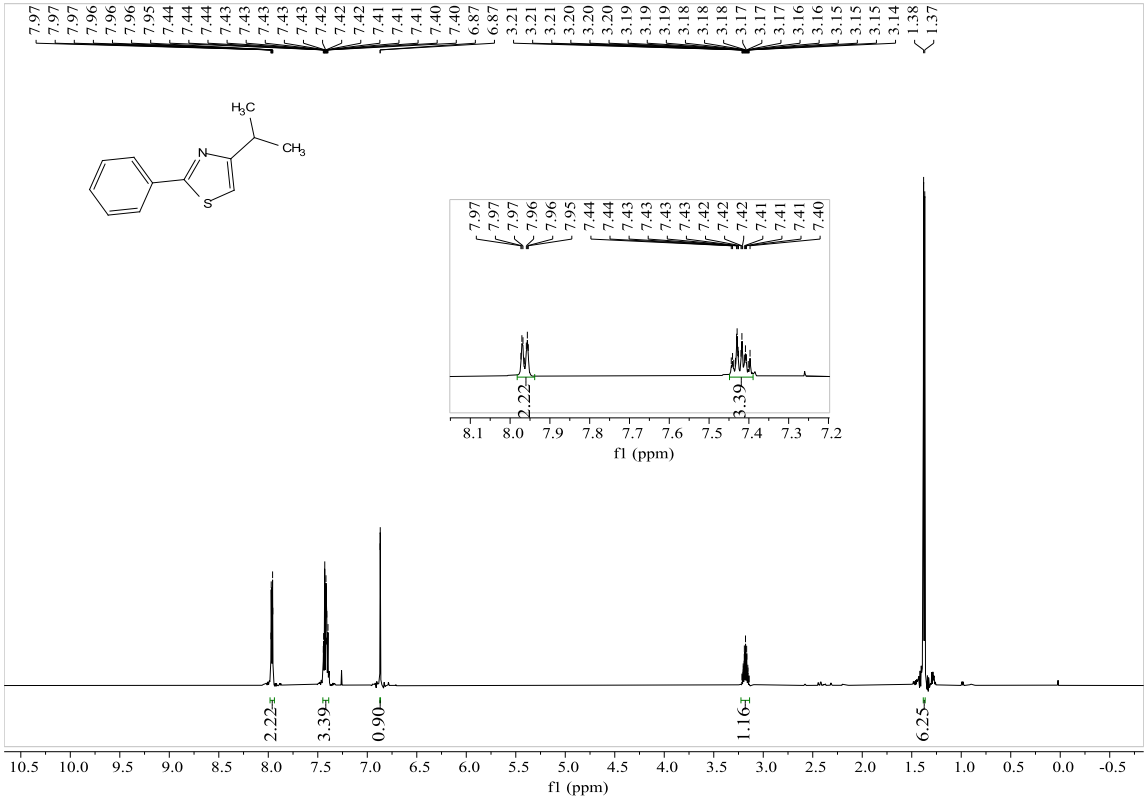
^{1}H NMR spectrum of compound 2aa (400 MHz, $CDCl_3$)



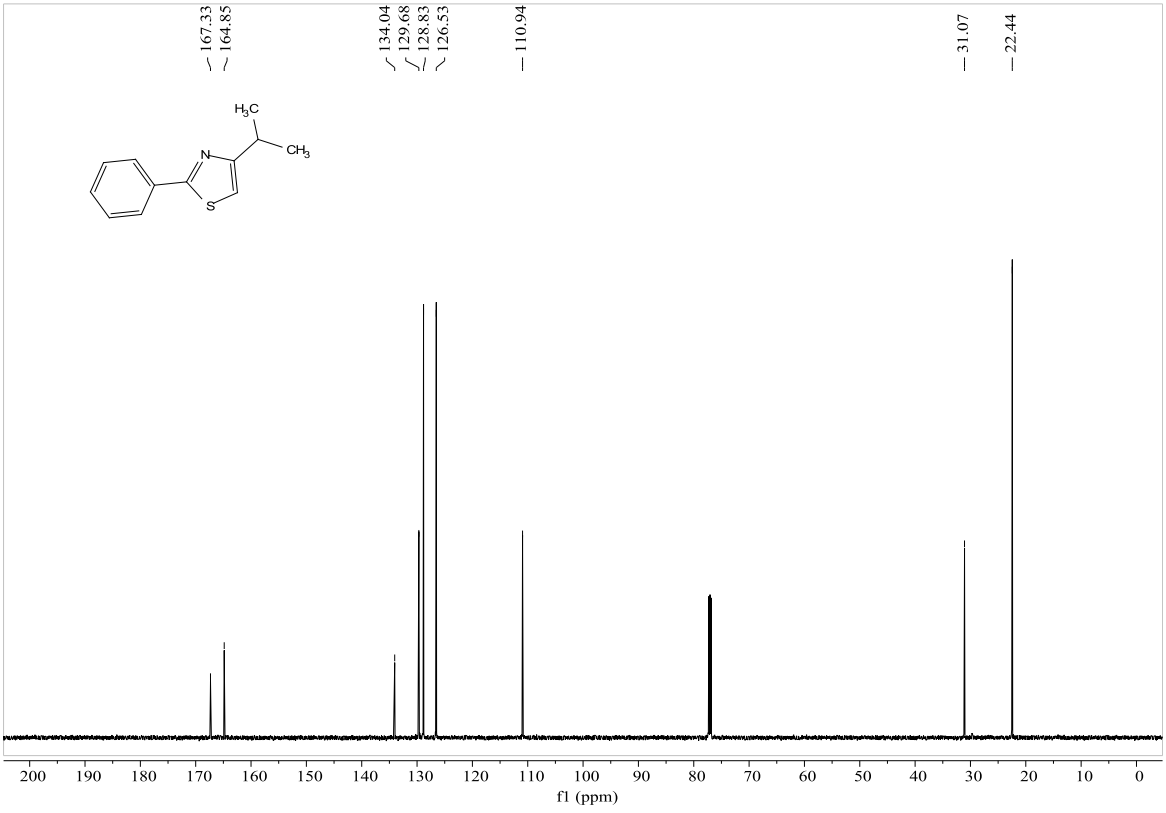
^{13}C NMR spectrum of compound 2aa (101 MHz, $CDCl_3$)



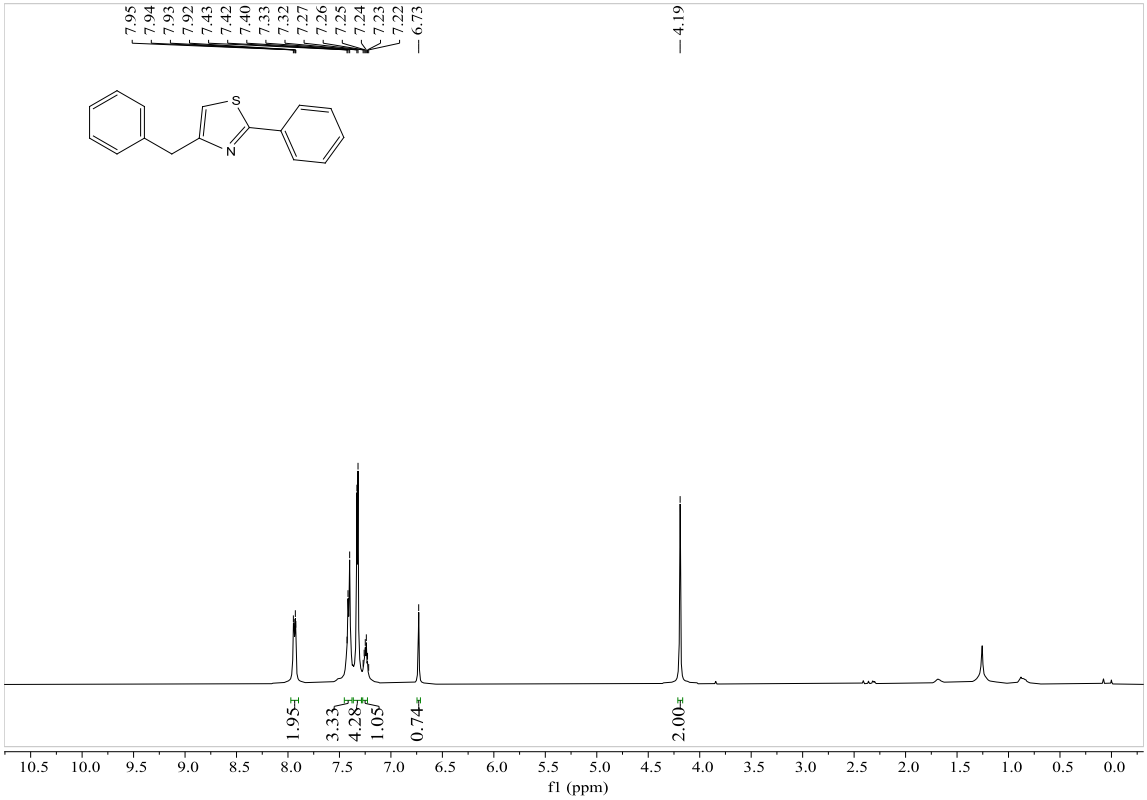
^{1}H NMR spectrum of compound 2ab (600 MHz, $CDCl_3$)



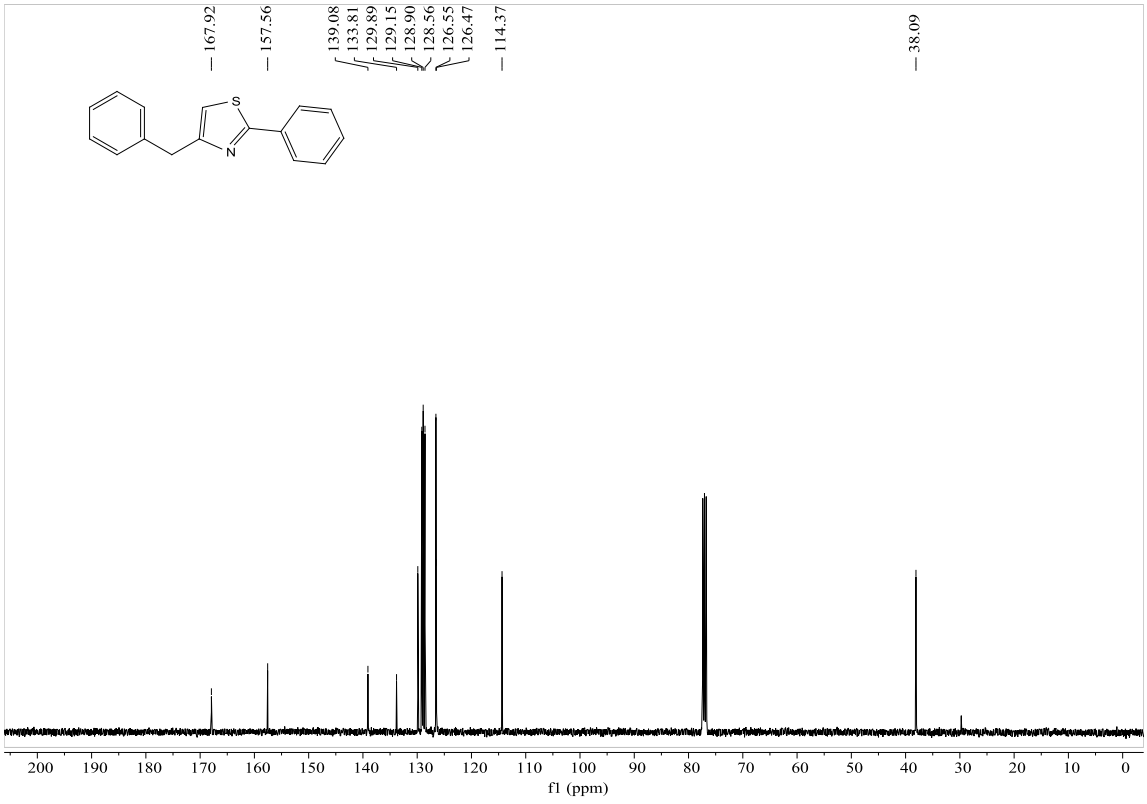
^{13}C NMR spectrum of compound 2ab (151 MHz, $CDCl_3$)



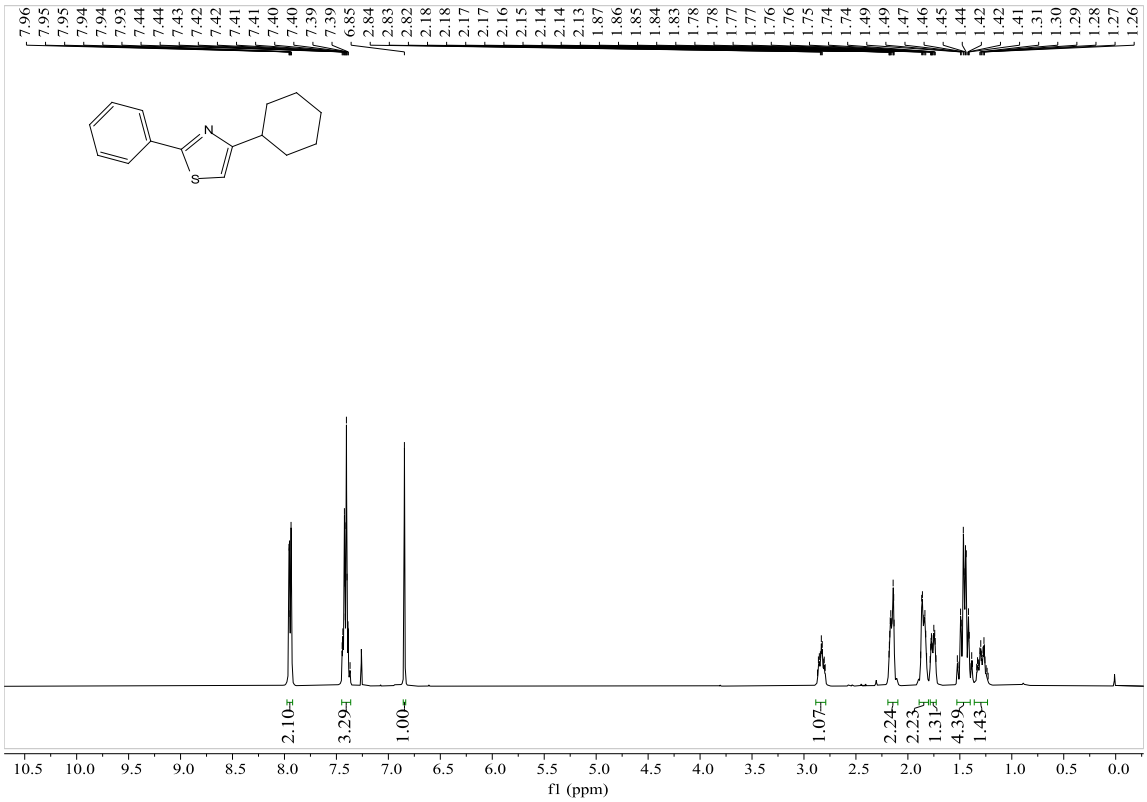
^{1}H NMR spectrum of compound 2ac (400 MHz, $CDCl_3$)



^{13}C NMR spectrum of compound 2ac (101 MHz, $CDCl_3$)



^{1}H NMR spectrum of compound 2ad (400 MHz, $CDCl_3$)



^{13}C NMR spectrum of compound 2ad (101 MHz, $CDCl_3$)