

Pd-free Sonogashira Coupling: One pot synthesis of Phthalide *via* domino Sonogashira coupling and 5-*exo-dig* cyclization

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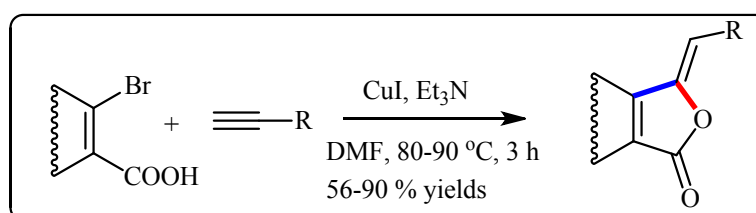
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Supplementary Data11

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General methods: High quality reagents were purchased from Sigma Aldrich. Analytical grade commercial reagents and solvents were purified by standard procedures prior to use. Chromatographic purification was done with 60-120 mesh silica gel (Merck). For reaction monitoring, pre-coated silica gel 60 F254 sheets (Merck) were used. ¹H NMR (200 MHz) spectra were recorded on a BRUCKER-AC 200 MHz spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (deuteriochloroform: 7.26 ppm). Data are reported as follows: chemical shifts, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, dd = double doublet, brs = broad singlet), coupling constant (Hz). ¹³C NMR (50 MHz) spectra were recorded on a BRUKER-AC 200 MHz. Spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (deuteriochloroform: 77.23 ppm). HRMS (ESI) spectra were taken using Waters Xevo G2 QTof mass spectrometer. Melting points of the final compounds were recorded after recrystallization from ethanol.

General Procedure of the preparation of 3-substituted Phthalides:

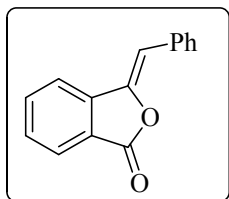


Ortho-bromobenzoic acids (1mmol), terminal alkyne (0.1 mmol), Et₃N (3.0 mmol), CuI (10 mol %), 3mL of DMF were taken in a 25 ml round bottomed flask in argon atmosphere. The mixture was heated to 80 °C temperature for 3 h. The completion of the reaction was monitored by TLC checking. After completion of the reaction mixture was cooled to room temperature and diluted with water. It was then extracted with ethyl acetate (3×50 ml). Combined organic layer was washed with brine and evaporated to dryness under reduced

pressure. The desired phthalide was isolated by usual column chromatography with mixture ethyl acetate and petroleum ether (1:20) as eluents.

Spectral data of Compounds:

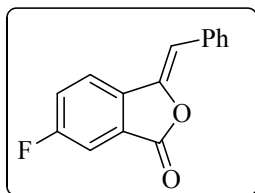
3-benzylideneisobenzofuran-1(3H)-one (3a):



White Solid; mp: 84-86 °C; Yield: 90 %; ¹H NMR (200 MHz, CDCl₃) : 6.40 (1H, s), 7.29-7.44 (3H, m), 7.48-7.56 (1H, m), 7.66-7.76 (2H, m), 7.82-7.92 (3H, m); ¹³C NMR (50 MHz, CDCl₃): 107.2, 120.0, 123.4, 125.6, 128.5, 128.9 (2C), 129.8, 130.2 (2C), 133.2, 134.6, 140.7, 144.7,

167.2; Elemental Analysis: C: 81.07 %; H: 4.54%; Found: C: 81.00%; H: 4.49%; HRMS (ESI) of C₁₅H₁₁O₂⁺ [M+ H⁺]: 223.0754; Observed : 223.0750.

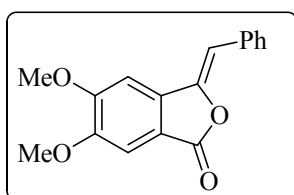
3-benzylidene-6-fluoroisobenzofuran-1(3H)-one (3b):



White Solid; mp: 144-146 °C; Yield: 80 %; ¹H NMR (400 MHz, CDCl₃) : 6.34 (1H, s), 7.29 (1H, q, *J* = 7.2 Hz), 7.37-7.48 (3H, m), 7.53 (1H, d, *J* = 6.8 Hz), 7.72 (1H, q, *J* = 4.0 Hz), 7.78 (2H, t, *J* = 7.6 Hz); ¹³C NMR (100 MHz, CDCl₃): 107.4, 111.9 (d, *J* = 23.9 Hz),

122.0 (d, *J* = 8.7 Hz), 123.1 (d, *J* = 24.5 Hz), 125.3, 128.8, 129.0 (2C), 130.3 (2C), 133.1, 136.8, 144.0, 163.7 (d, *J* = 250.5 Hz), 166.0 ; HRMS (ESI) of C₁₅H₁₀FO₂⁺ [M+H⁺]: 241.0659, Observed: 241.0642; Elemental Analysis: C: 75.00%; H: 3.78%; Found: C: 74.93%; H: 3.72%;

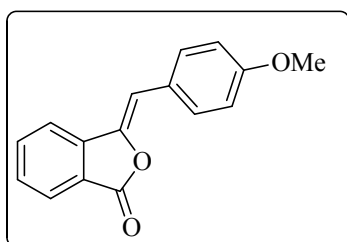
3-benzylidene-5,6-dimethoxyisobenzofuran-1(3H)-one (3c):



White Solid; mp: 84-86 °C; Yield: 64 %; ¹H NMR (200 MHz, CDCl₃) : 4.10 (3H, s), 4.15 (3H, s), 6.38 (1H, s), 7.21 (1H, s), 7.26 (1H, s), 7.38-7.53 (3H, m), 7.92 (2H, d, *J* = 7.6 Hz); ¹³C NMR (50

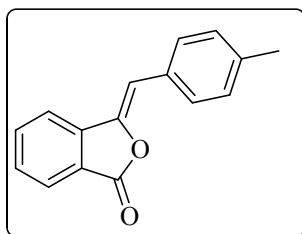
MHz, CDCl₃): 56.6, 56.7, 100.9, 105.7, 105.9, 116.3, 128.3, 128.9 (2C), 130.1 (2C), 133.5, 135.5, 144.9, 151.8, 155.5, 167.5; Elemental Analysis: C: 72.33; H: 5.00%; Found: C: 72.27; H: 4.8%; HRMS (ESI) of C₁₇H₁₅O₄⁺ [M+H⁺]: 283.0965; Observed: 283.0943.

3-(4-methoxybenzylidene)isobenzofuran-1(3H)-one (3d):



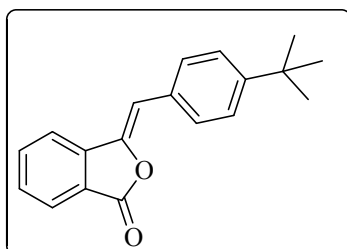
Yellow Solid; mp: 124-126 °C; Yield: 59 %; ¹H NMR (200 MHz, CDCl₃): 3.83 (3H, s), 6.35 (1H, s), 6.92 (2H, d, *J* = 8.8 Hz), 7.45-7.52 (1H, m), 7.64-7.73 (2H, m), 7.80 (2H, d, *J* = 8.8 Hz), 7.89 (1H, d, *J* = 7.6 Hz); ¹³C NMR (50 MHz, CDCl₃): 55.5, 107.1, 114.4 (2C), 119.7, 123.2, 125.6, 126.0, 129.4 (2C), 131.8, 134.5, 140.9, 143.2, 159.9, 167.4; HRMS (ESI) of C₁₆H₁₃O₃⁺ [M+H⁺]: 253.0859; Found: 253.0856 Elemental Analysis: C: 76.18; H: 4.79 %; Found: C: 76.08; H: 4.66%;

3-(4-methylbenzylidene)isobenzofuran-1(3H)-one (3e):



White Solid; mp: 128-130 °C; Yield: 68 %; ¹H NMR (200 MHz, CDCl₃) : 2.42 (3H, s), 6.43 (1H, s), 7.23-7.35 (2H, m), 7.52-7.60 (1H, m), 7.70-7.80 (4H, m), 7.96 (1H, dd, *J* = 7.6 Hz); ¹³C NMR (50 MHz, CDCl₃): 21.6, 107.4, 119.9, 123.4, 125.7, 129.7 (3C), 130.3 (2C), 130.4, 134.6, 138.8, 140.9, 144.1, 167.4; HRMS (ESI) of C₁₆H₁₃O₂⁺[M+H⁺]: 237.0910; Found: 237.0912; Elemental Analysis: C: 81.34; H, 5.12 %; Found : C: 81.26; H, 5.00 %;

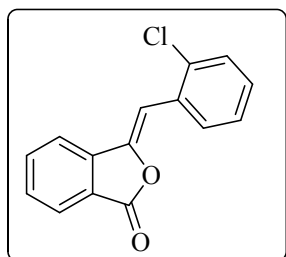
3-(4-(tert-butyl)benzylidene)isobenzofuran-1(3H)-one (3f):



White Solid; mp: 96-98 °C; Yield: 62 %; ¹H NMR (CDCl₃, 200 MHz): 1.36 (9H, s), 6.42 (1H, s), 7.42-7.57 (3H, m), 7.67-7.85 (4H, m), 7.93 (1H, d, *J* = 7.4 Hz); ¹³C NMR (CDCl₃, 50 MHz): 31.4 (3C), 34.9, 107.2, 119.9, 123.5, 125.7, 125.9 (2C),

129.7, 130.1 (2C), 130.5, 134.6, 140.8, 144.3, 151.9, 167.4; HRMS of $C_{19}H_{19}O_2^+$ $[M+H^+]$: 279.1380; Observed: 279.1375; Elemental Analysis: C, 81.99; H, 6.52 %; Found : C, 81.90; H, 6.40%;

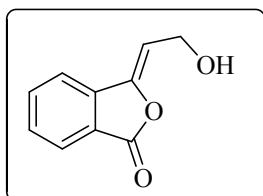
3-(2-chlorobenzylidene)isobenzofuran-1(3H)-one (3g):



White Solid; mp: 142-144 °C; Yield: 55 %; 1H MNR ($CDCl_3$, 200 MHz): 6.35 (1H, s), 7.26-7.39 (2H, m), 7.56-7.63 (1H, m), 7.71-7.83 (4H, m), 7.95 (1H, d, $J = 7.6$ Hz); ^{13}C NMR ($CDCl_3$, 50 MHz): 105.6, 120.1, 123.6, 125.8, 128.3, 128.5, 129.8, 130.1, 130.4, 134.8 (2C), 135.0, 140.4, 145.6, 166.9; Elemental Analysis: C, 70.19; H,

3.53 %; Found: C, 70.10; H, 3.49%;

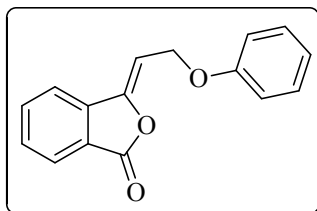
3-(2-hydroxyethylidene)isobenzofuran-1(3H)-one (3h):



Yellow Solid; mp: 75-77 °C; Yield: 65 %; 1H NMR ($CDCl_3$, 200 MHz): 2.76 (1H, br), 4.59 (2H, d, $J = 6.8$ Hz), 5.81 (1H, t, $J = 6.8$ Hz), 7.48-7.59 (1H, m), 7.63-7.72 (2H, m), 7.85 (1H, d, $J = 7.6$ Hz); ^{13}C NMR ($CDCl_3$, 50 MHz): 57.1, 107.2, 120.4, 124.6, 125.5, 130.4,

124.8, 139.2, 146.2, 166.8; HRMS (ESI) of $C_{10}H_9O_3^+$ $[M+H^+]$: 177.0546; Found: 177.0540; Elemental Analysis: C, 68.18; H, 4.58%; Found: C, 68.10; H, 4.52%;

3-(2-phenoxyethylidene)isobenzofuran-1(3H)-one (3i):

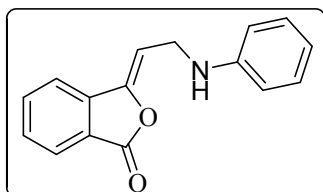


Light yellow Solid; mp: 128-130 °C; Yield: 53 %; 1H NMR ($CDCl_3$, 200 MHz): 5.03 (2H, d, $J = 6.8$ Hz), 5.89 (1H, t, $J = 6.8$ Hz), 6.99-7.03 (3H, m), 7.30-7.38 (2H, m), 7.55-7.63 (1H, m), 7.71-7.74 (2H, m), 7.94 (1H, d, $J = 7.6$ Hz); ^{13}C NMR ($CDCl_3$, 50

Hz): 62.1, 103.5, 114.7 (2C), 120.5, 121.2, 124.7, 125.5, 129.7 (2C), 130.6, 134.7, 138.8,

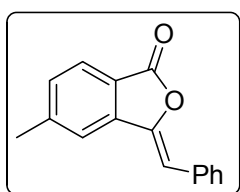
147.1, 158.2, 166.3; HRMS (ESI) of $C_{16}H_{13}O_3^+[M+H^+]$: 253.0859; Found: 253.0848; Elemental Analysis: C, 76.18; H, 4.79 %; Found: C, 76.12; H, 4.70%;

3-(2-(phenylamino)ethylidene)isobenzofuran-1(3H)-one (3j):



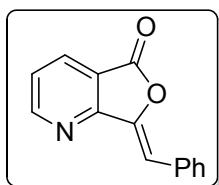
Yellow stikymass; Yield: 56 %; 1H NMR ($CDCl_3$, 200 MHz): 3.74 (1H, br), , 4.25 (2H, d, $J = 6.8$ Hz), 5.74 (1H, t, $J = 6.8$ Hz), 6.69-6.79 (3H, m), 7.18-7.26 (2H, m), 7.51-7.73 (3H, m), 7.92 (1H, q, $J_1 = 7.4$ Hz, $J_2 = 1.0$ Hz); ^{13}C NMR ($CDCl_3$, 50 MHz): 39.6, 106.4, 113.3 (2C), 118.2, 120.3, 124.7, 125.6, 129.6 (2C), 130.3, 134.7, 139.3, 146.7, 147.6, 166.8; HRMS of $C_{16}H_{14}NO_2^+[M+H^+]$: 252.1019; Observed: 252.1016; Elemental Analysis: C, 76.48; H, 5.21; Found: C, 76.42; H, 5.15%.

3-benzylidene-5-methylisobenzofuran-1(3H)-one (3k):



White Solide; mp: 106-108 °C; Yields: 72%; 1H NMR ($CDCl_3$, 200 MHz): 2.53 (3H, s), 6.38 (1H, s), 7.31-7.45 (4H, m), 7.55 (1H, s), 7.76-7.86 (3H, m); ^{13}C NMR ($CDCl_3$, 50 MHz): 22.4, 106.8, 120.1, 121.2, 125.5, 128.5, 128.9 (2C), 130.3 (2C), 131.3, 133.4, 141.3, 144.8, 146.0, 167.2; Elemental Analysis: C, 81.34; H, 5.12; Found: C, 81.25; H, 5.02 %; HRMS (ESI) of $C_{16}H_{13}O_2^+[M+H^+]$: 237.0910; Observed: 237.0908.

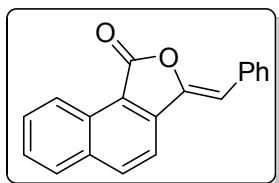
7-benzylidenefuro[3,4-b]pyridin-5(7H)-one (3l):



Lightyellow stikysolid; Yields: 80%; 1H NMR ($CDCl_3$, 200 MHz): 6.98 (1H, s), 7.37-7.51 (4H, m), 7.89-7.93 (2H, m), 8.25 (1H, dd, $J_1 = 1.6$ Hz, $J_2 = 7.8$ Hz), 8.92 (1H, dd, $J_1 = 1.6$ Hz, $J_2 = 6.8$ Hz); ^{13}C NMR ($CDCl_3$, 50 MHz): 109.0, 117.6, 124.3, 129.1 (2C), 129.4, 131.0 (2C), 132.8, 134.0, 143.9, 156.4,

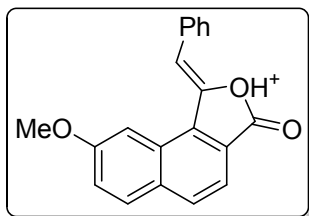
158.8, 165.0; Elemental Analysis: C, 75.33; H, 4.06; N, 6.27%; Found: C, 75.29; H, 3.98; N, 6.16%; HRMS (ESI) of $C_{14}H_{10}NO_2^+$ $[M+H]^+$: 224.0706; Observed: 224.0701.

3-benzylidenenaphtho[1,2-c]furan-1(3H)-one (3m):



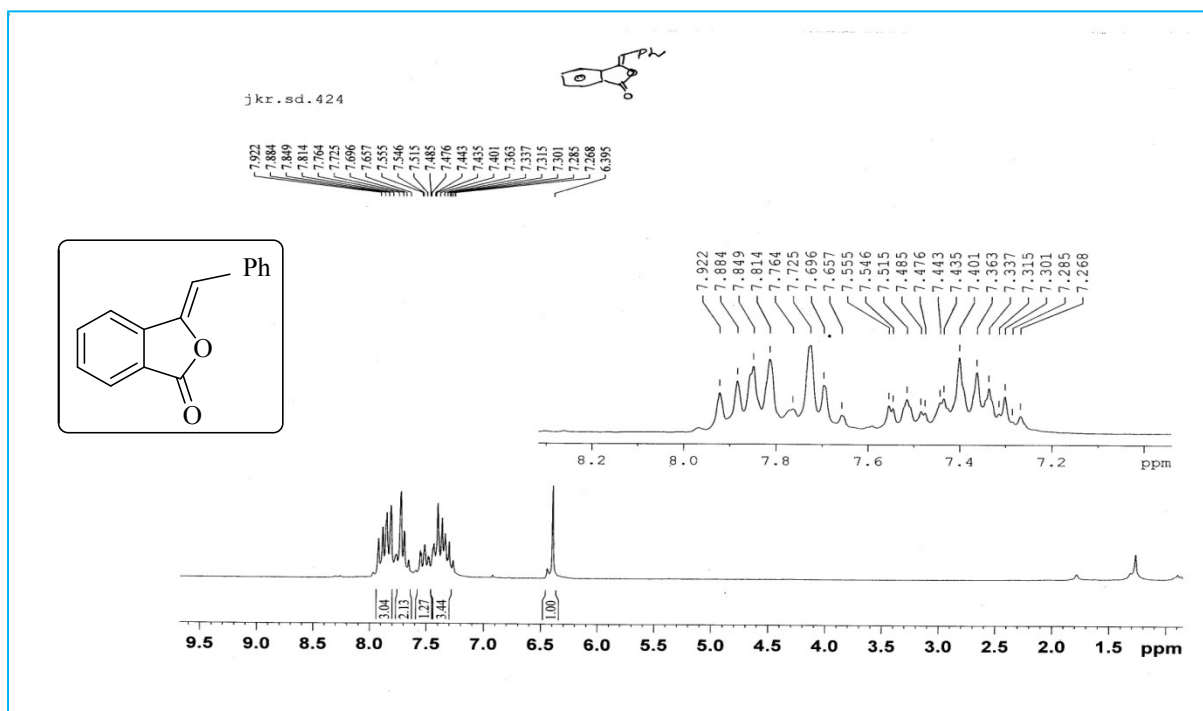
Yellow Solid; mp: 178-180 °C; Yields: 65%; 1H NMR ($CDCl_3$, 200 MHz): 6.55 (1H, s), 7.38-7.52 (5H, m), 7.80 (2H, d, $J = 8.6$ Hz), 7.93-8.01 (2H, m), 8.16 (1H, d, $J = 8.4$ Hz), 8.93 (1H, d, $J = 8.2$ Hz); ^{13}C NMR ($CDCl_3$, 50 MHz): 108.5, 114.3, 116.6, 117.9, 124.1, 127.8, 128.8, 129.0 (2C), 129.2, 129.6, 130.6 (2C), 133.4, 134.0, 135.9, 141.5, 145.1, 167.4; Elemental Analysis: C, 83.81; H, 4.44 %; Found: C, 83.71; H, 4.30 %; HRMS (ESI) of $C_{19}H_{13}O_2^+$ $[M+H]^+$: 273.0910; Observed: 273.0915.

1-benzylidene-8-methoxynaphtho[1,2-c]furan-3(1H)-one (3n):

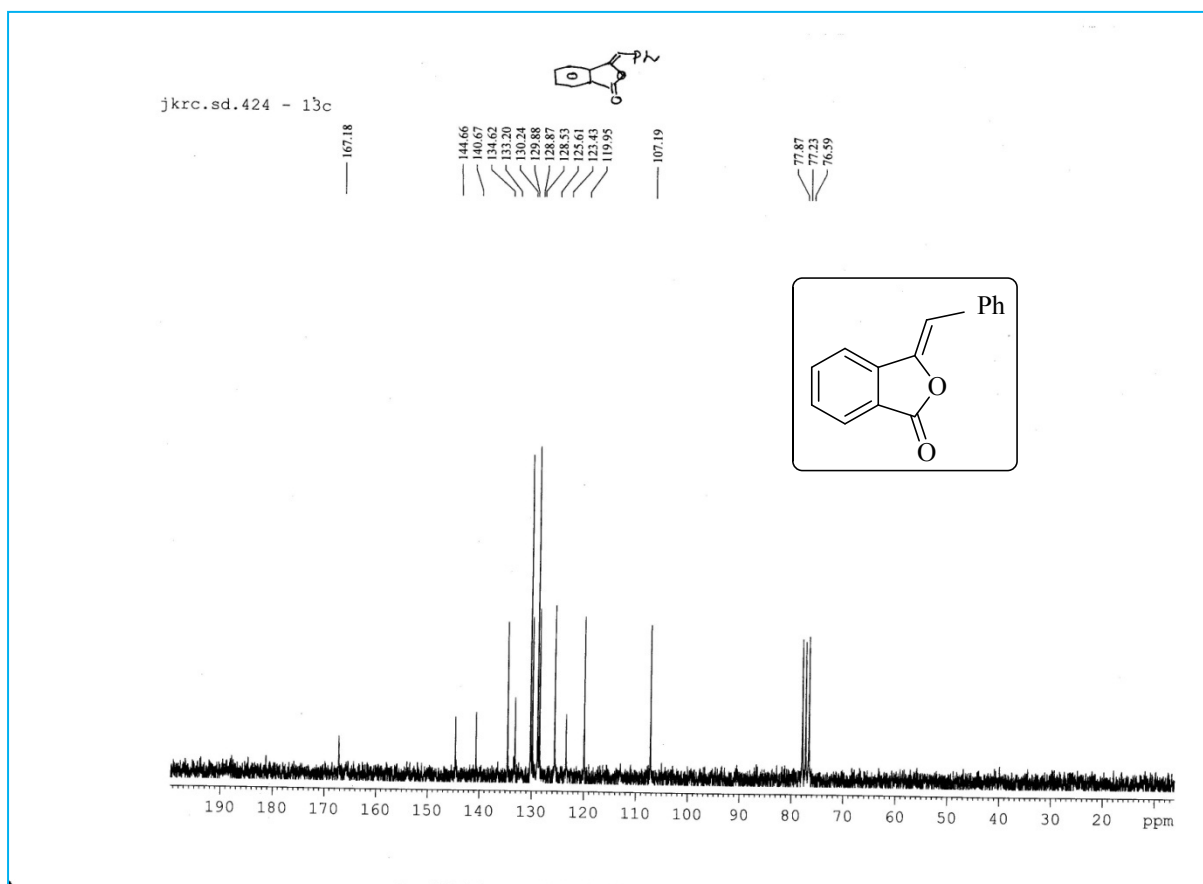


Yellowish solid; Yields: 60%; 1H NMR ($CDCl_3$, 200 MHz): 3.89 (3H, s), 6.78 (1H, s), 7.08-7.47 (6H, m), 7.69 (1H, s), 7.83 (2H, d, $J = 7.4$ Hz), 8.22 (1H, m); ^{13}C NMR ($CDCl_3$, 50 MHz): 55.7, 108.5, 112.6, 120.9, 121.0, 121.2, 125.6, 125.9, 127.6, 128.0, 129.0 (2C), 130.4, 130.9 (2C), 133.9, 139.1, 146.1, 159.8, 167.5; Elemental Analysis: C, 79.46; H, 4.67%; Found: C, 79.36; H, 4.52%; HRMS (ESI) of $C_{20}H_{15}O_3^+$ $[M+H]^+$: 303.1016; Observed: 303.1005.

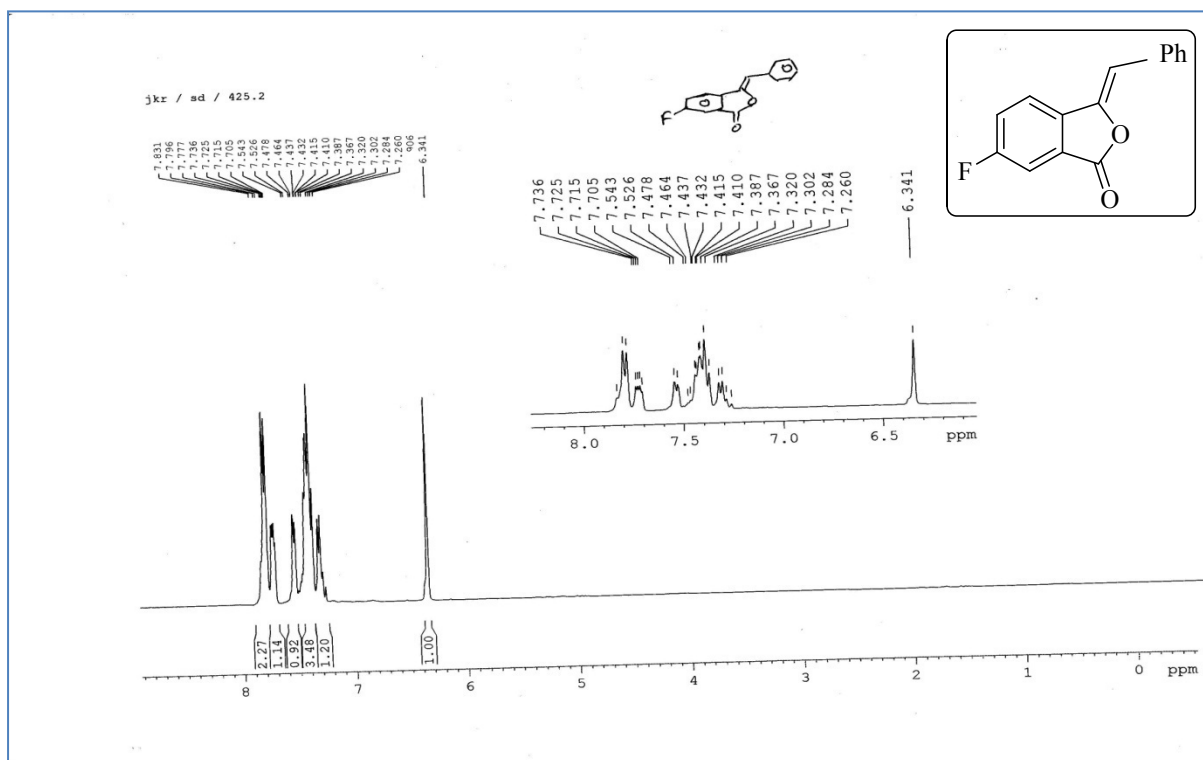
¹H NMR (CDCl₃, 200 MHz) of Compound (3a):



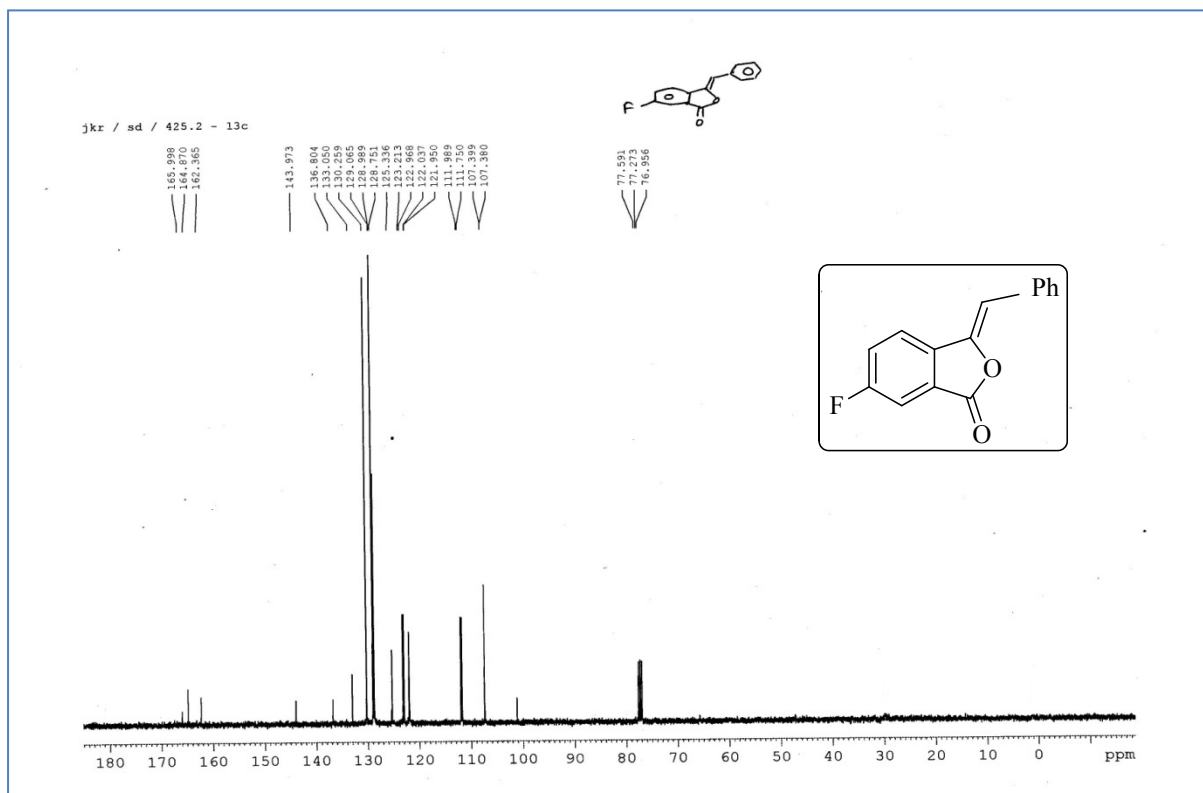
¹³C NMR (CDCl₃, 50 MHz) of Compound (3a):



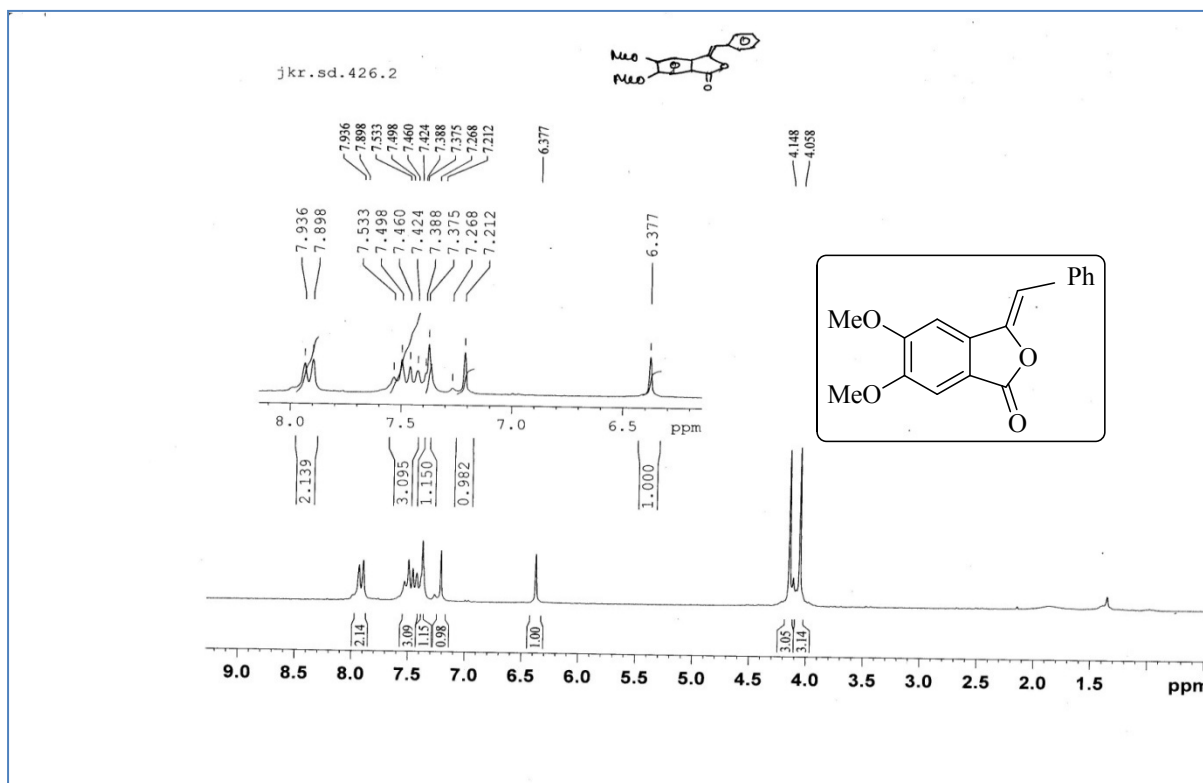
¹H NMR (CDCl₃, 400 MHz) of Compound (3b):



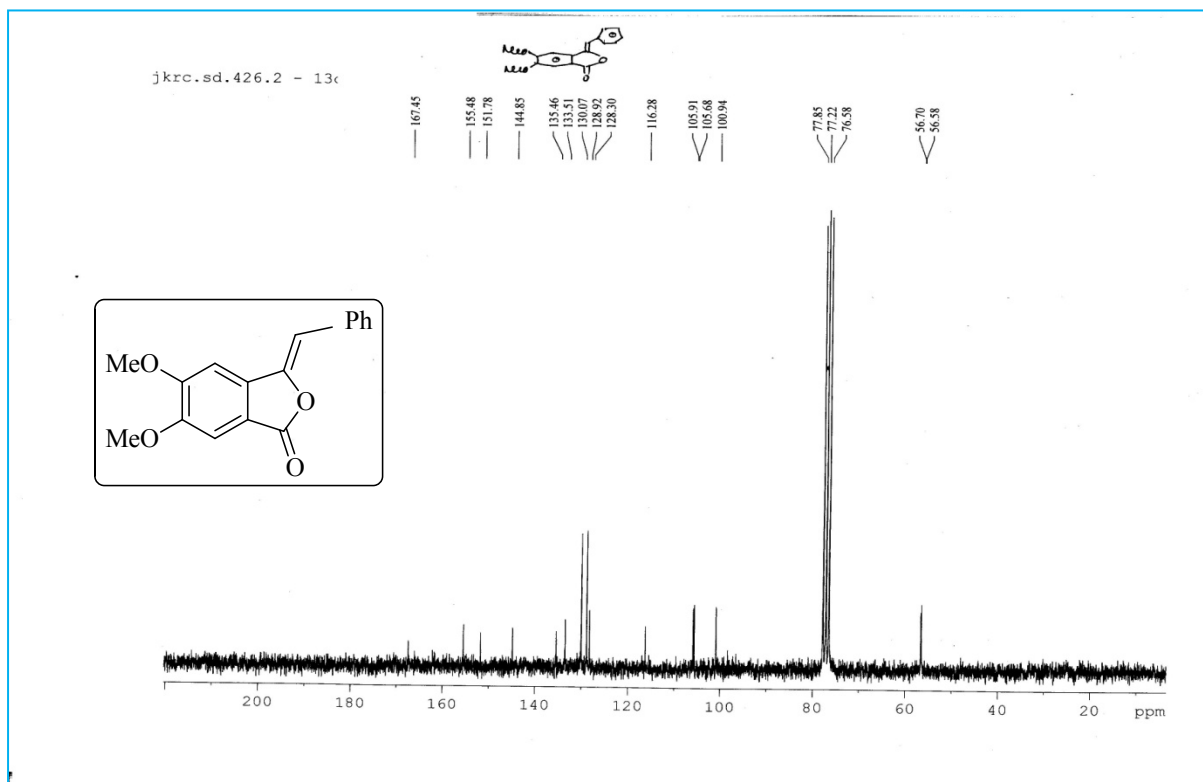
¹³C NMR (CDCl₃, 100 MHz) of Compound (3b):



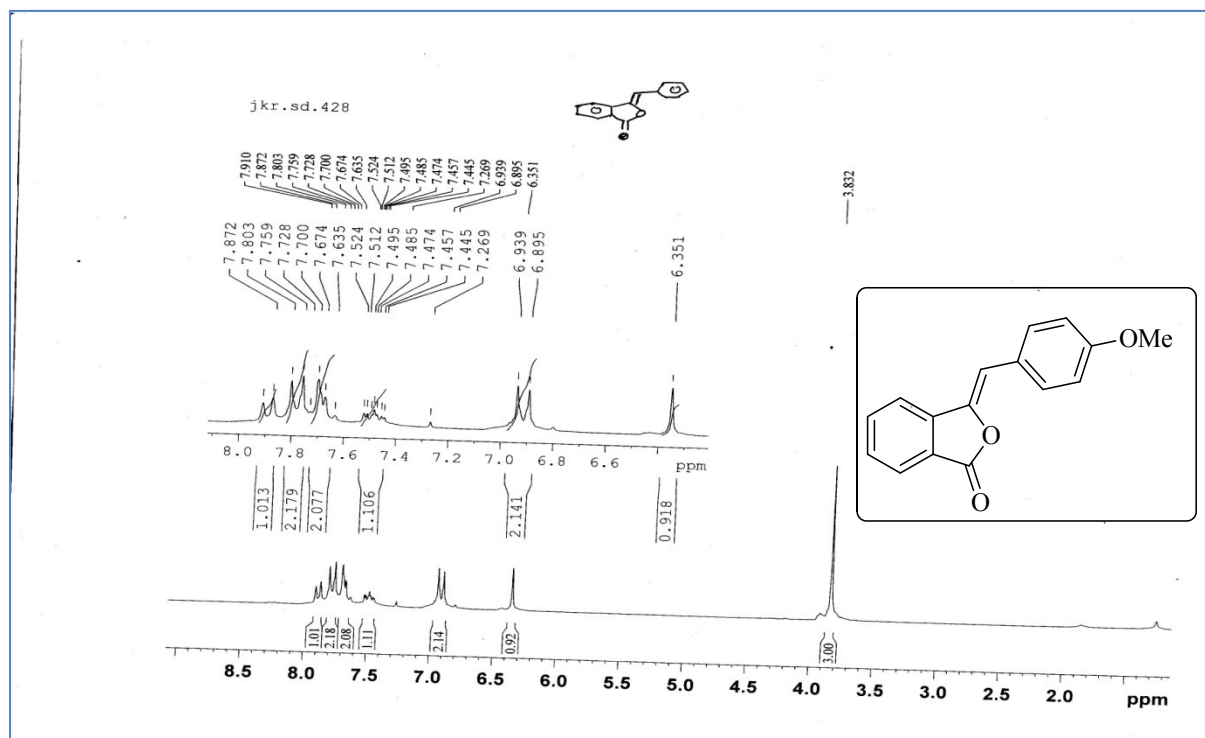
¹H NMR (CDCl₃, 200 MHz) of Compound (3c):



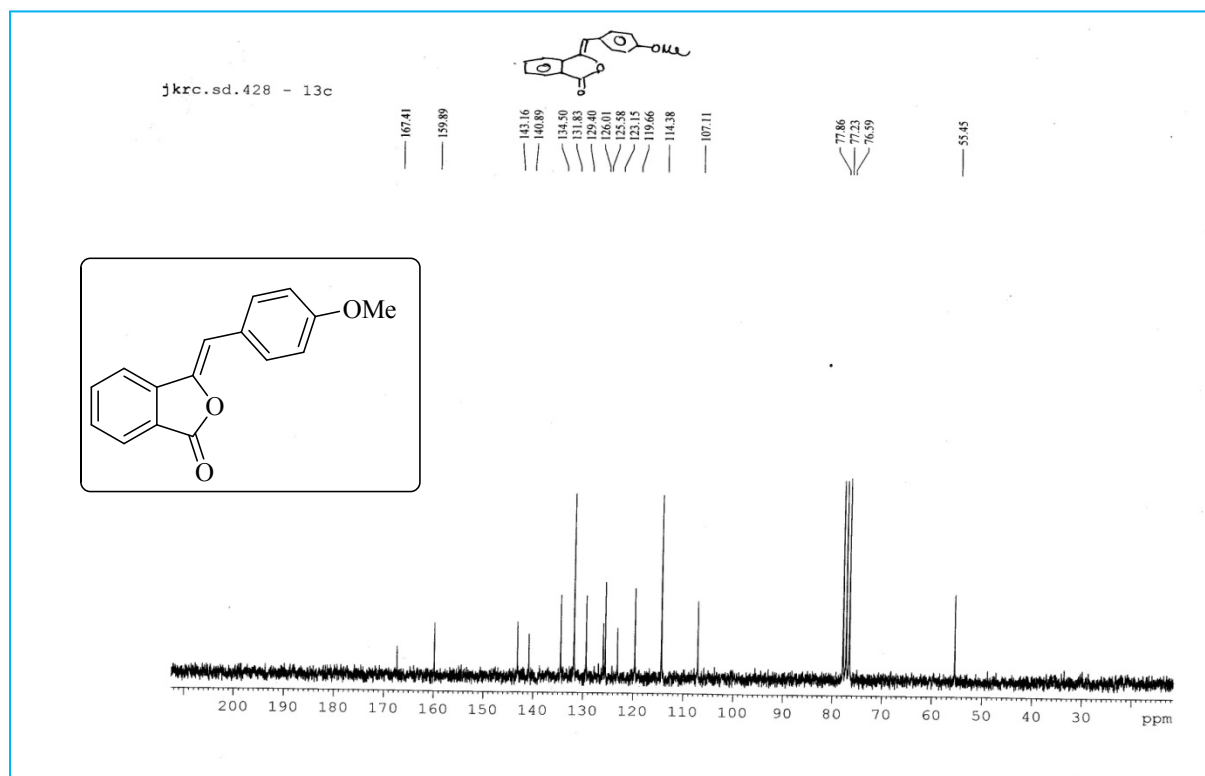
¹³C NMR (CDCl₃, 50 MHz) of Compound (3c):



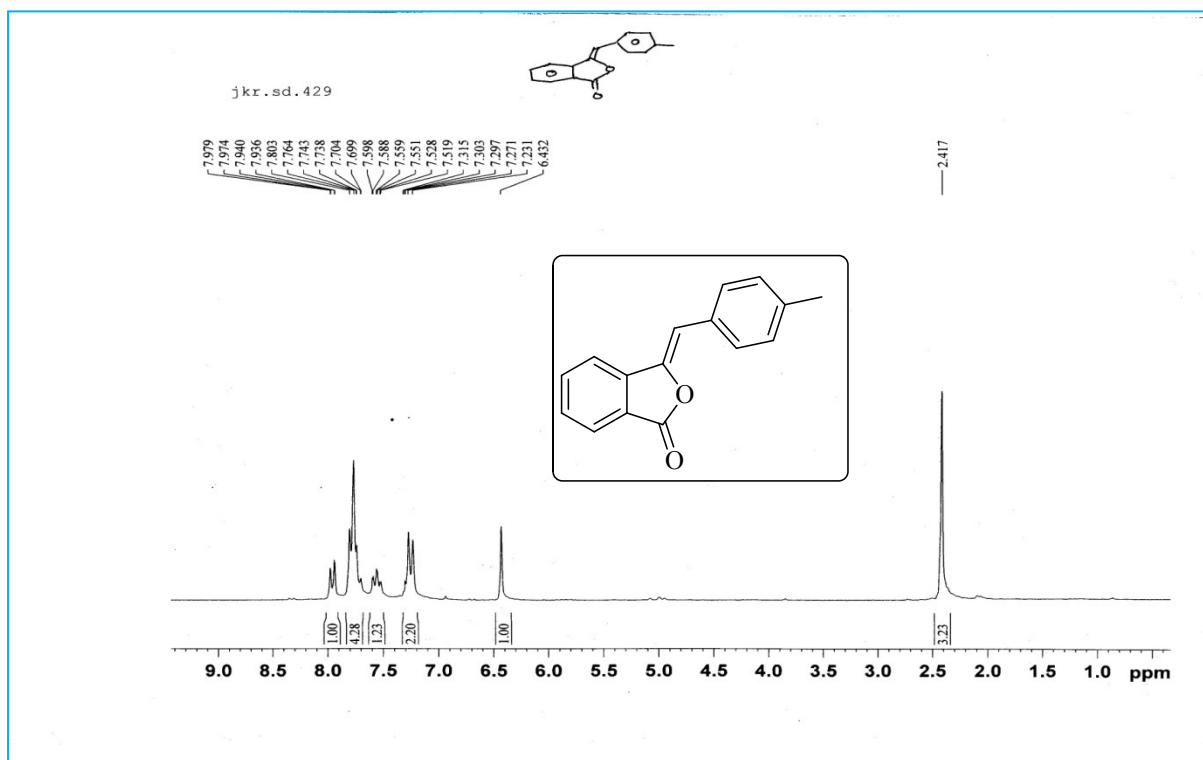
¹H NMR (CDCl₃, 200 MHz) of Compound (3d):



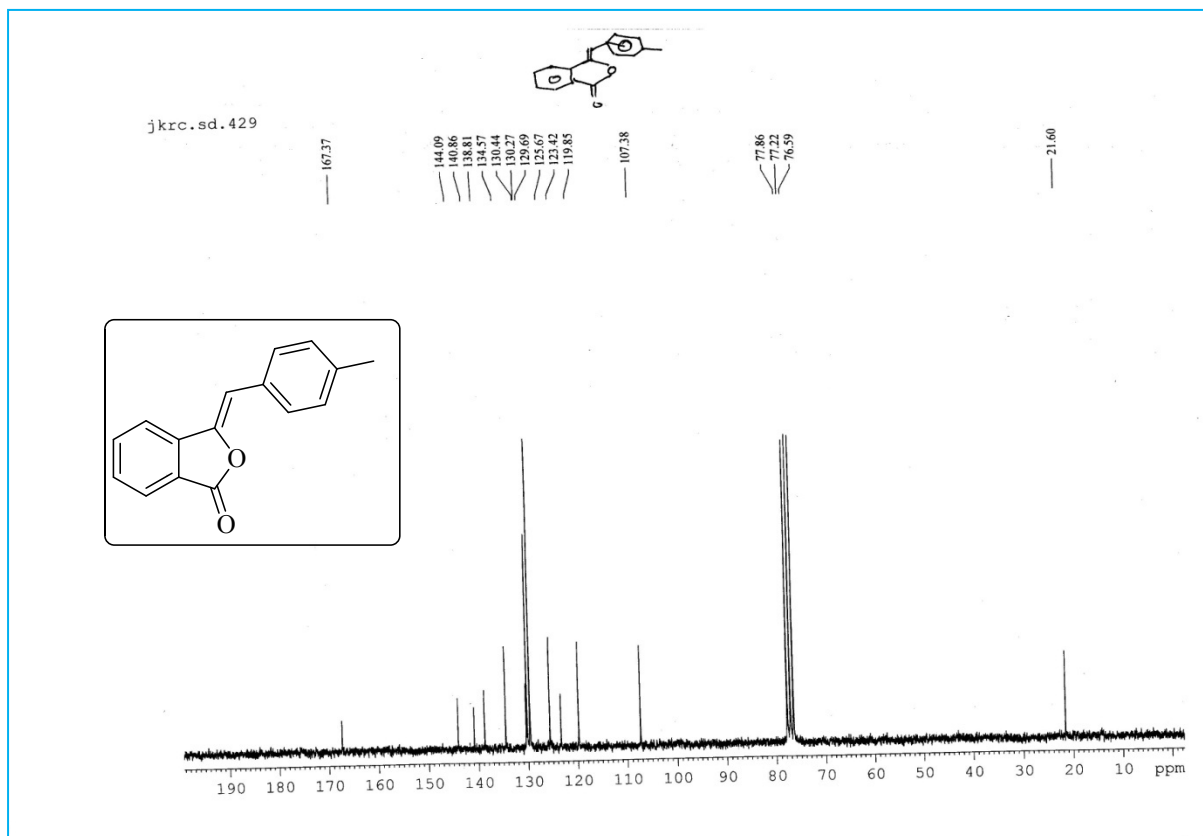
¹³C NMR (CDCl₃, 50 MHz) of Compound (3d):



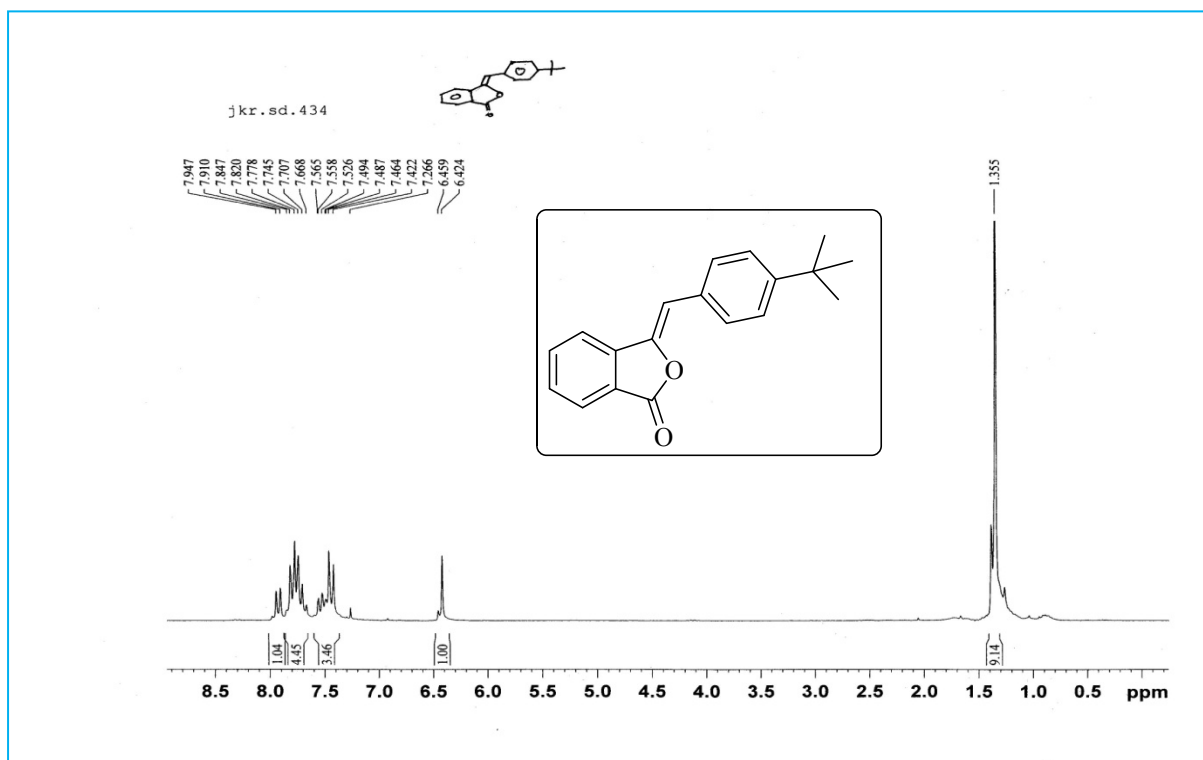
¹H NMR (CDCl₃, 200 MHz) of Compound (3e):



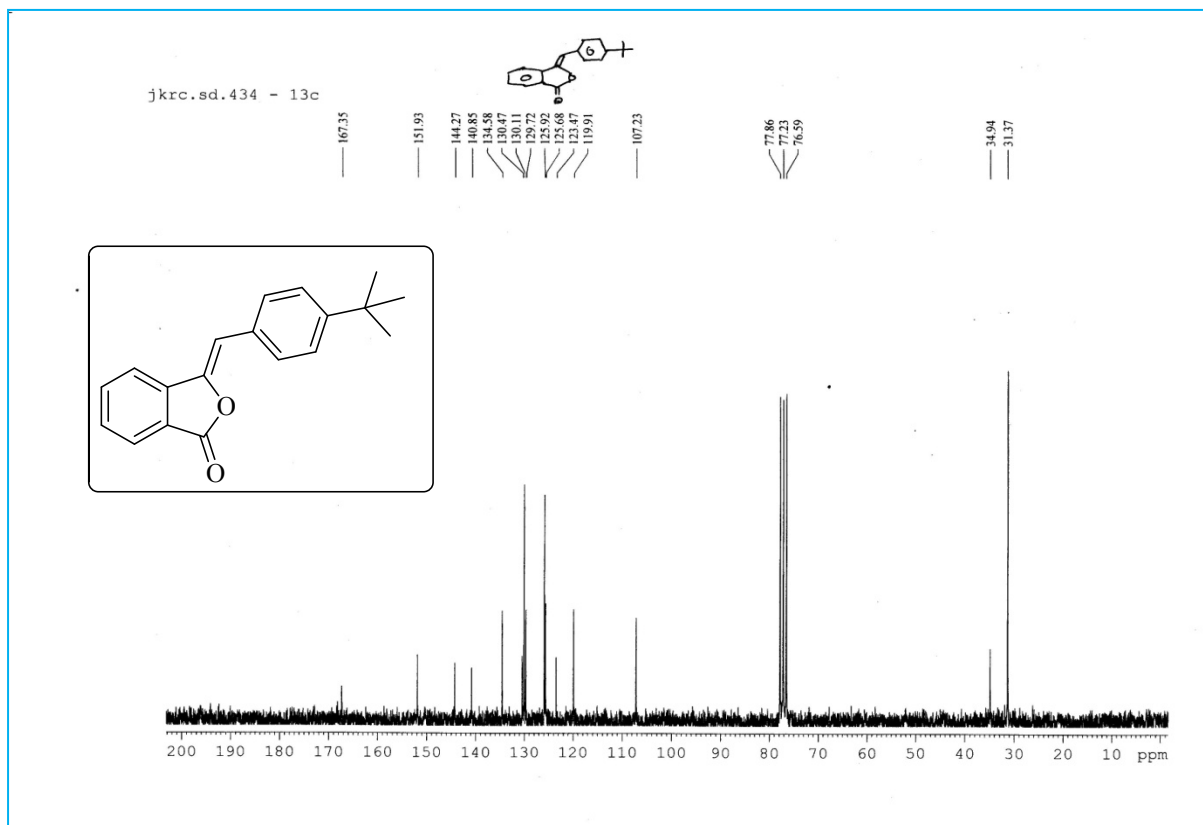
¹³C NMR (CDCl₃, 50 MHz) of Compound (3e):



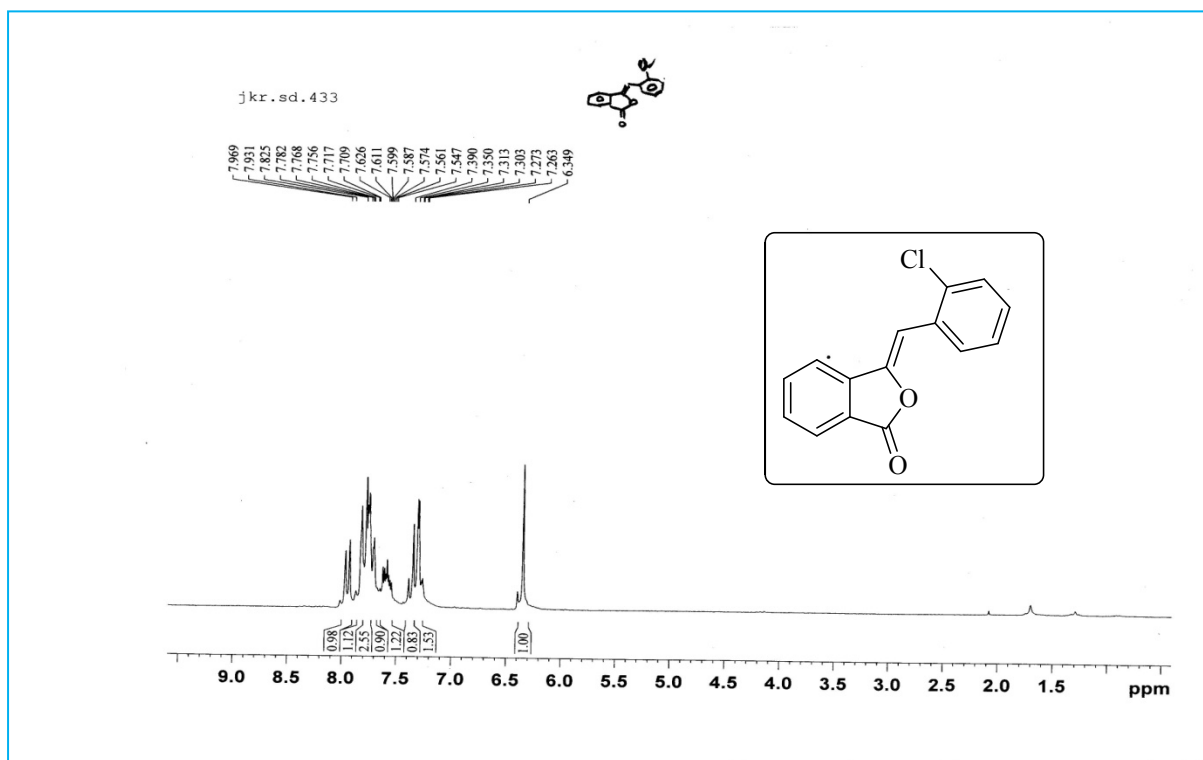
¹H NMR (CDCl₃, 200 MHz) of Compound (3f):



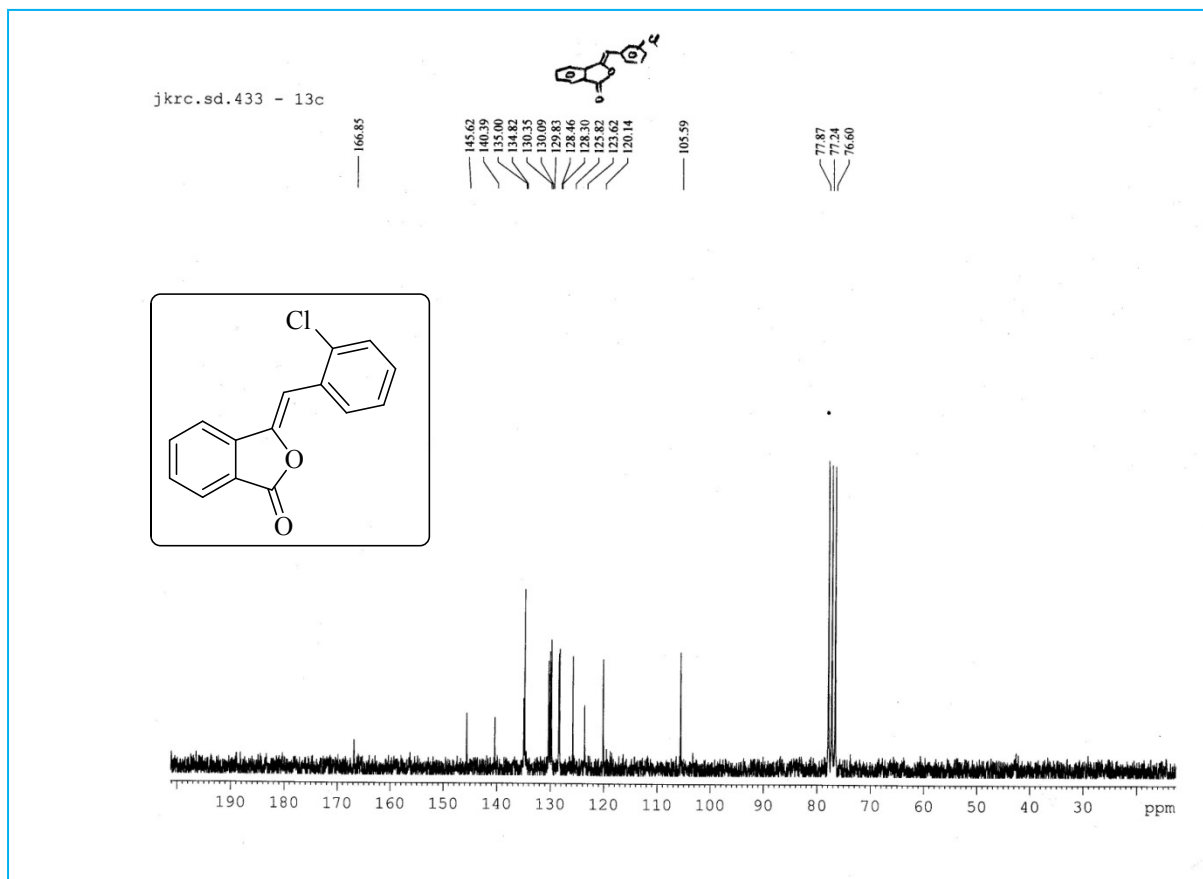
¹³C NMR (CDCl₃, 50 MHz) of Compound (3f):



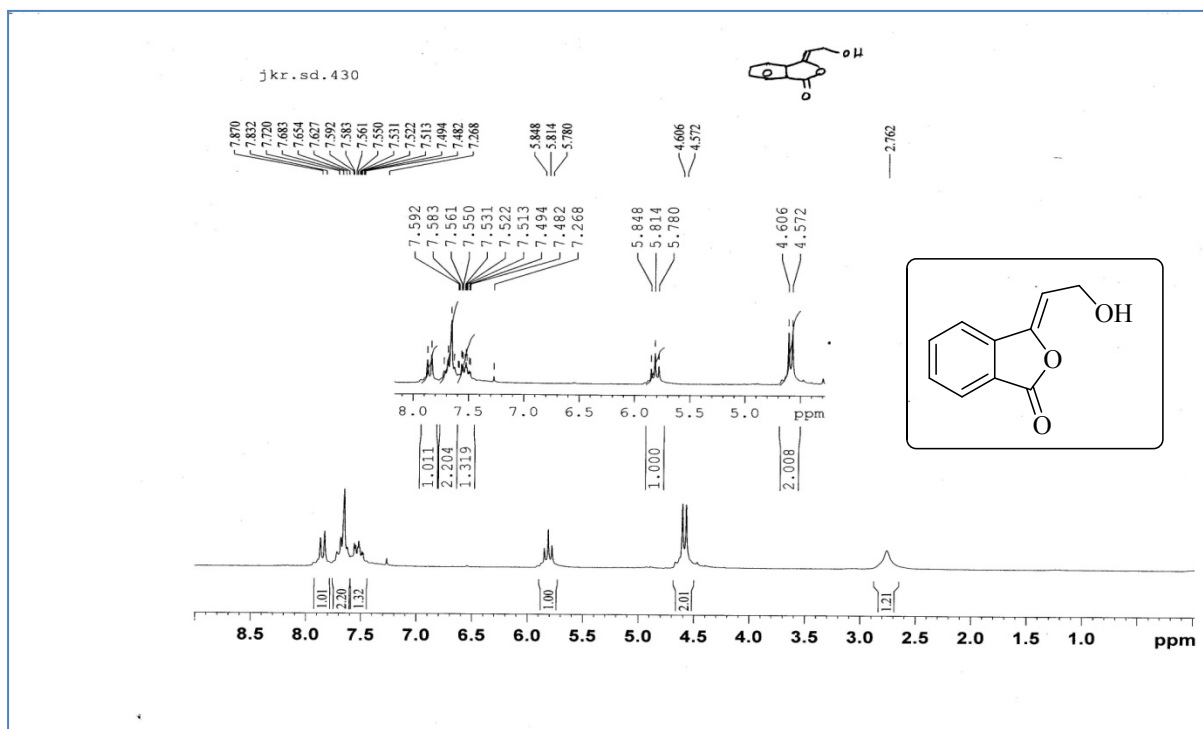
¹H NMR (CDCl₃, 200 MHz) of Compound (3g):



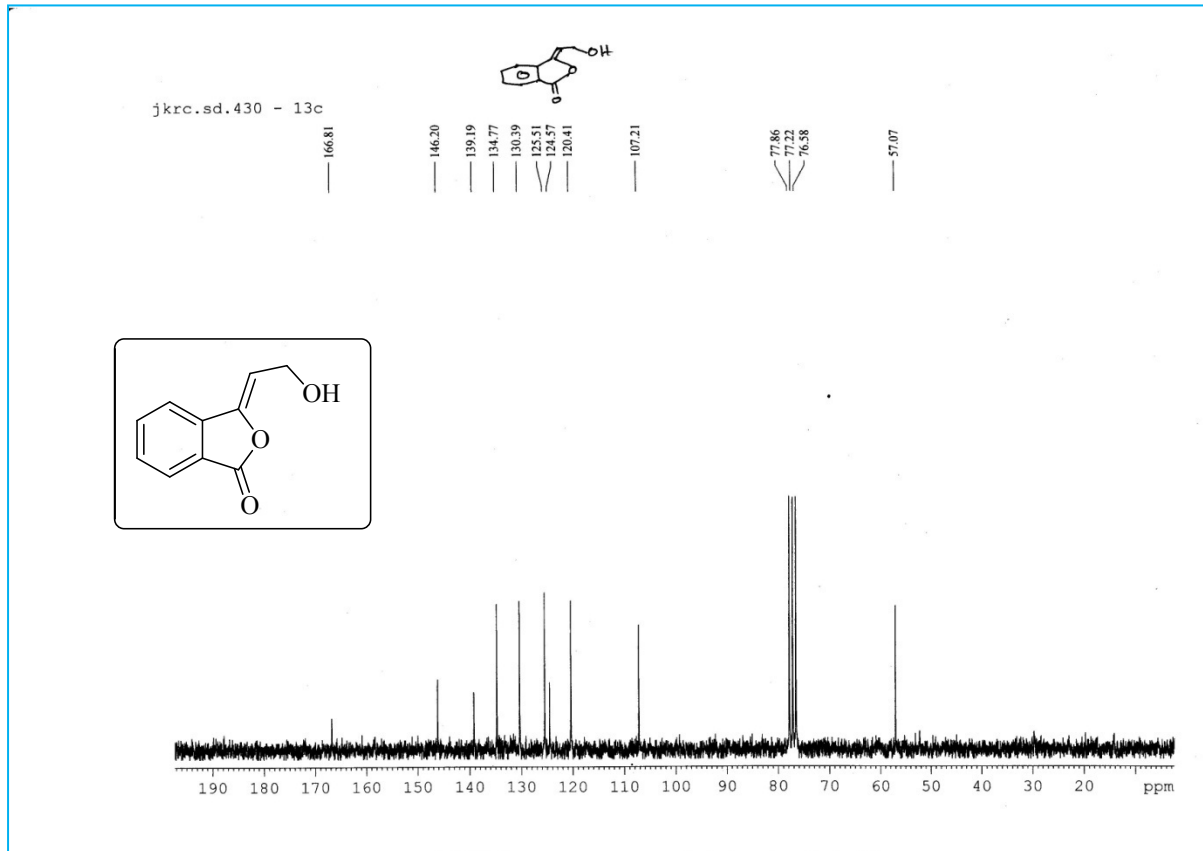
¹³C NMR (CDCl₃, 50 MHz) of Compound (3g):



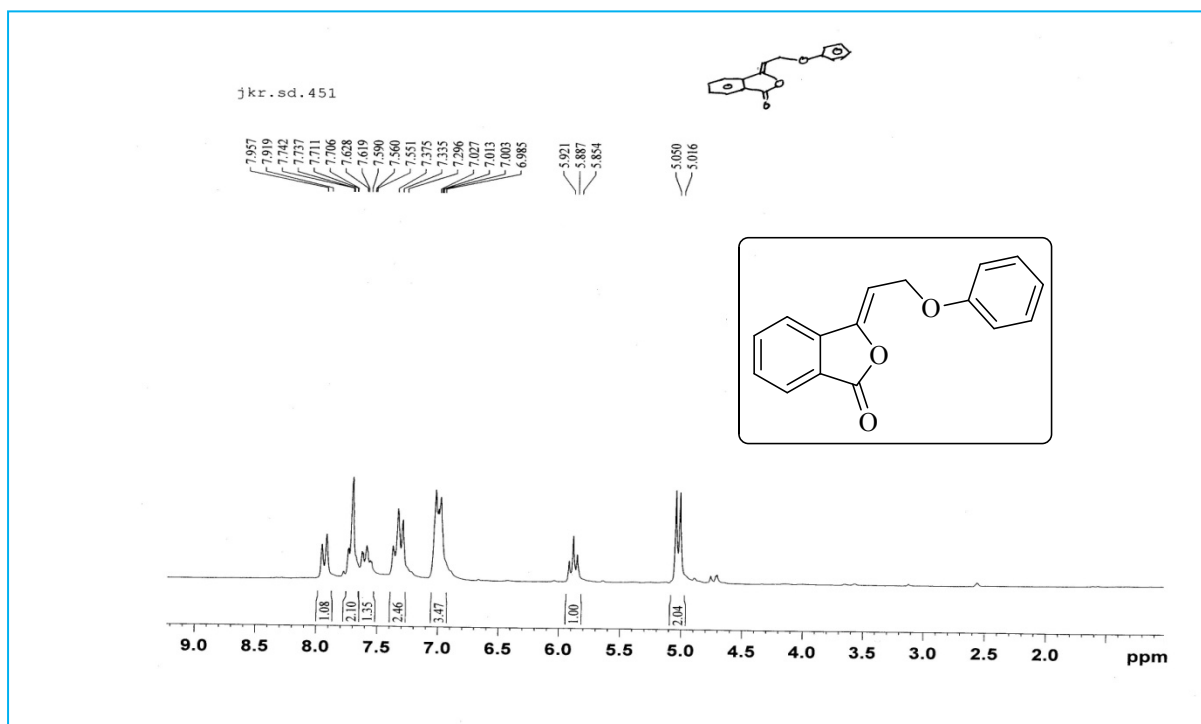
¹H NMR (CDCl₃, 200 MHz) of Compound (3h):



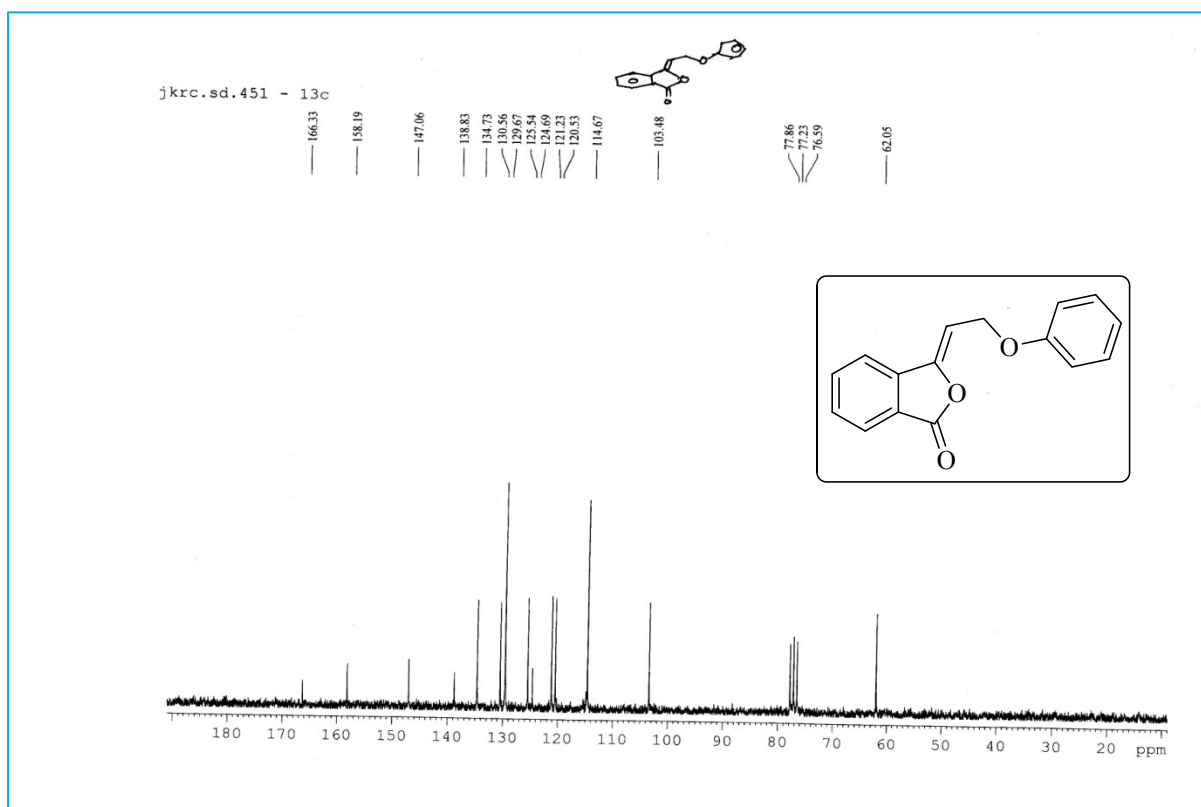
¹³C NMR (CDCl₃, 50 MHz) of Compound (3h):



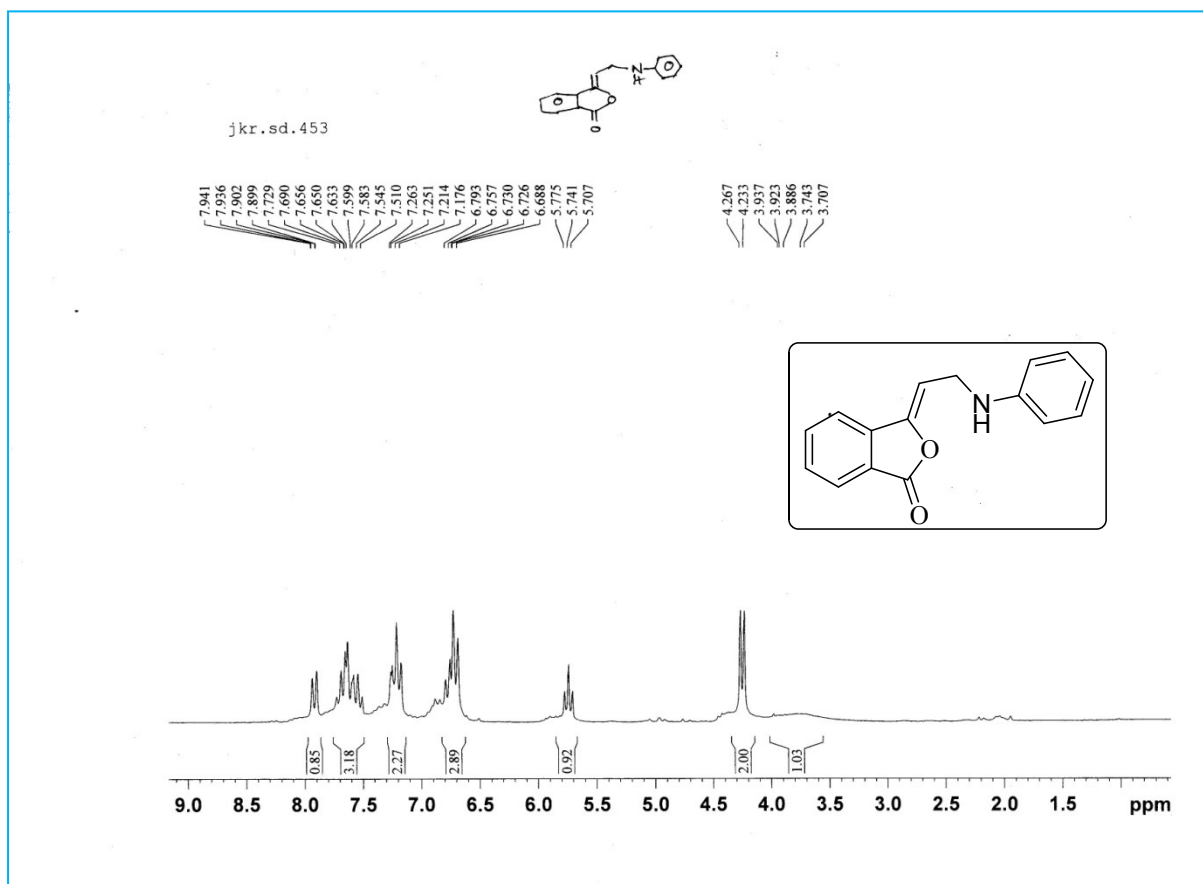
¹H NMR (CDCl₃, 200 MHz) of Compound (3i):



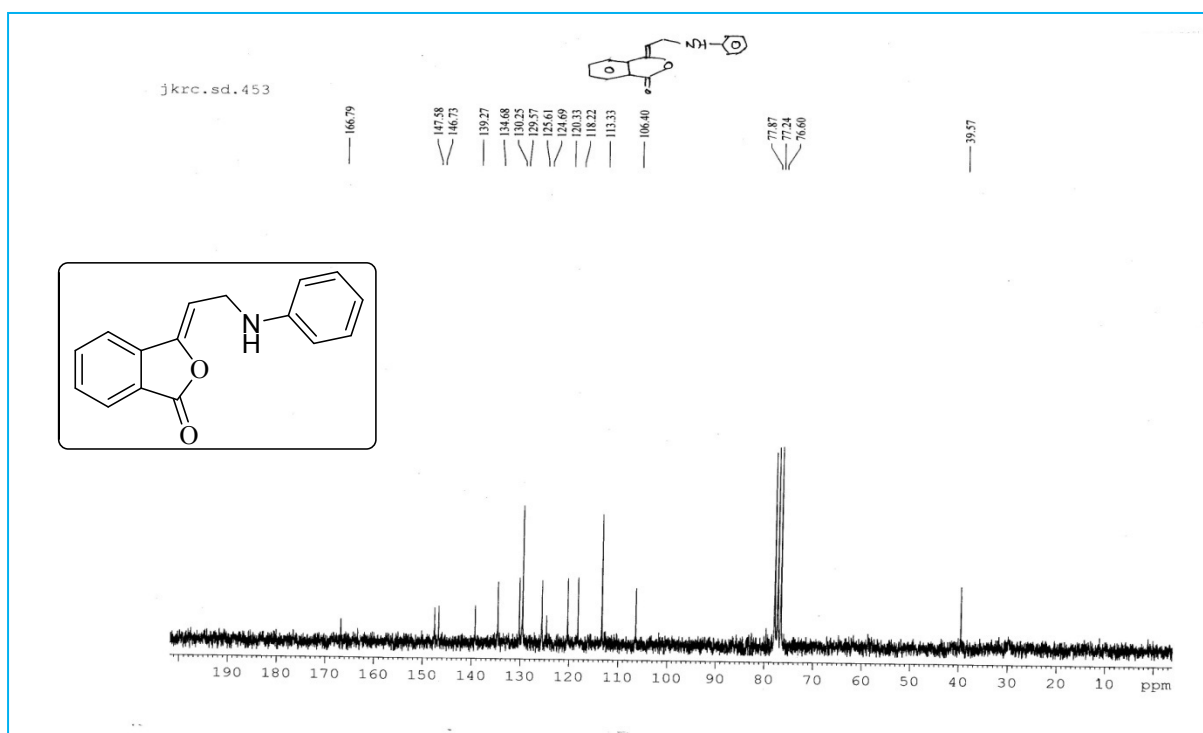
¹³C NMR (CDCl₃, 50 MHz) of Compound (3i):



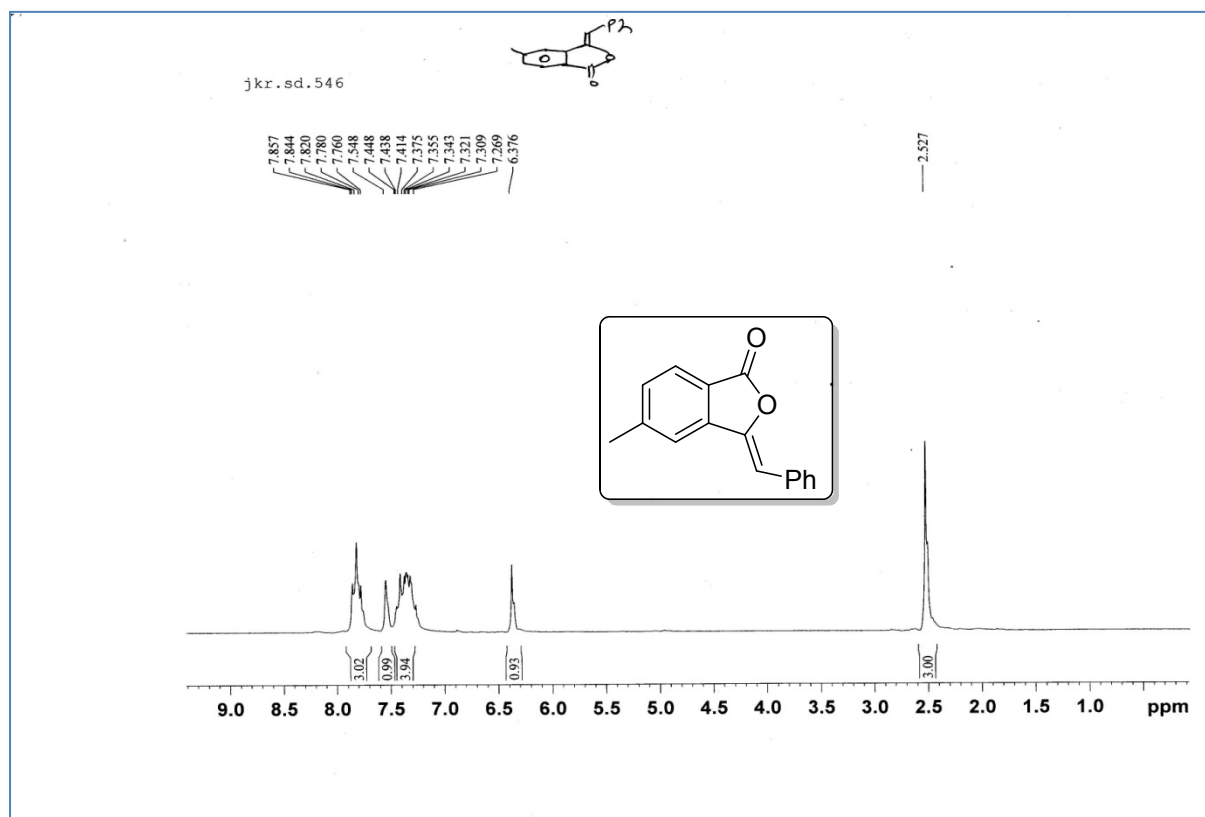
¹H NMR (CDCl₃, 200 MHz) of Compound (3j):



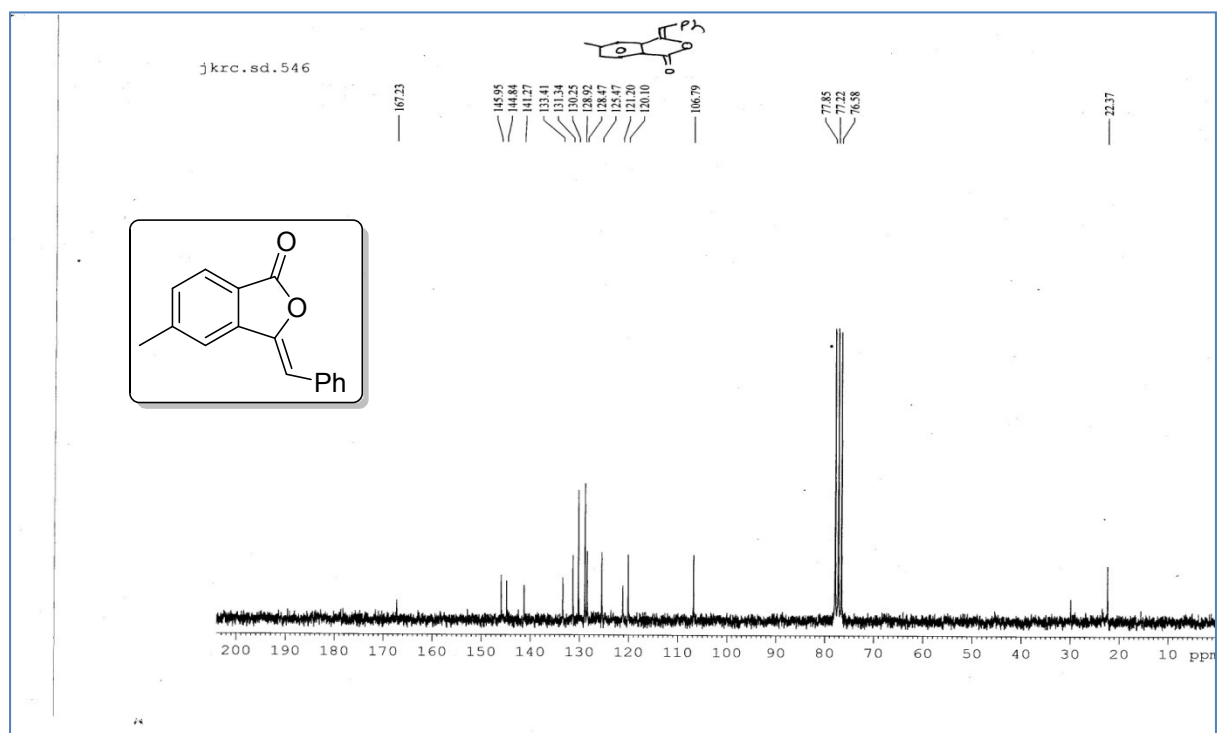
¹³C NMR (CDCl₃, 50 MHz) of Compound (3j):



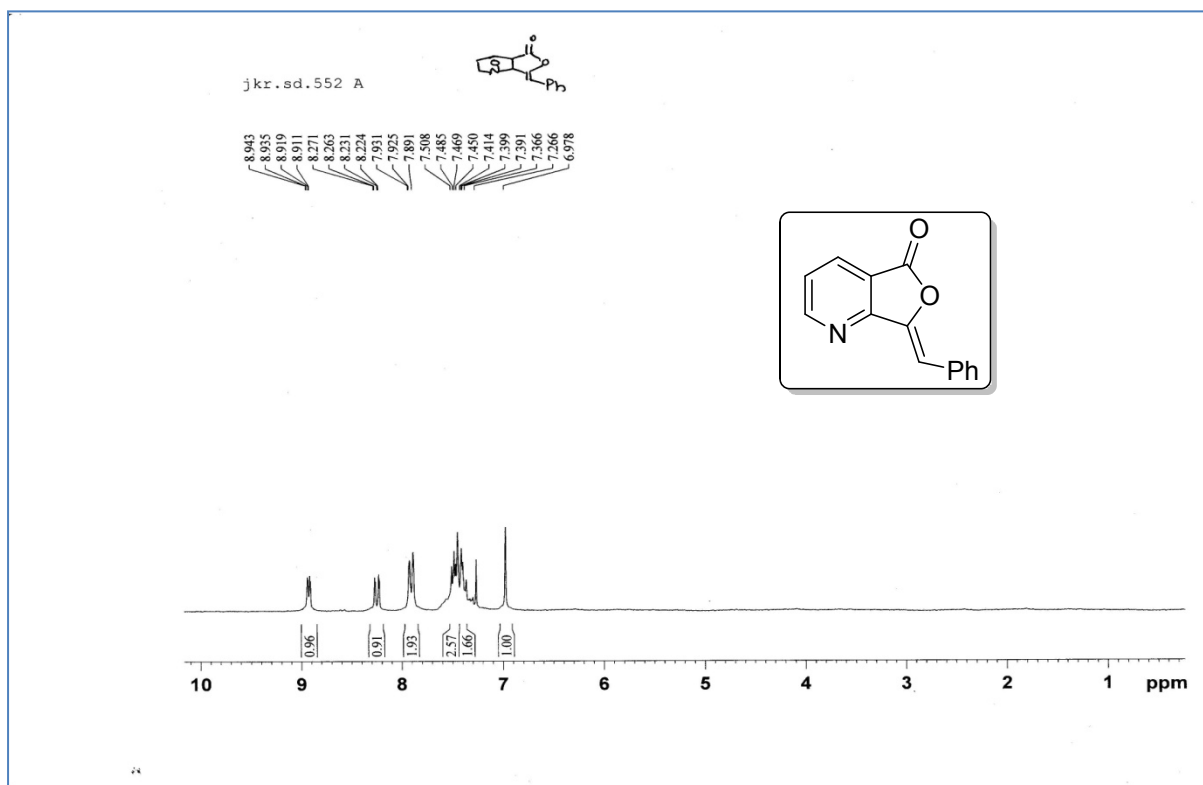
¹H NMR (CDCl₃, 200 MHz) of Compound (3k):



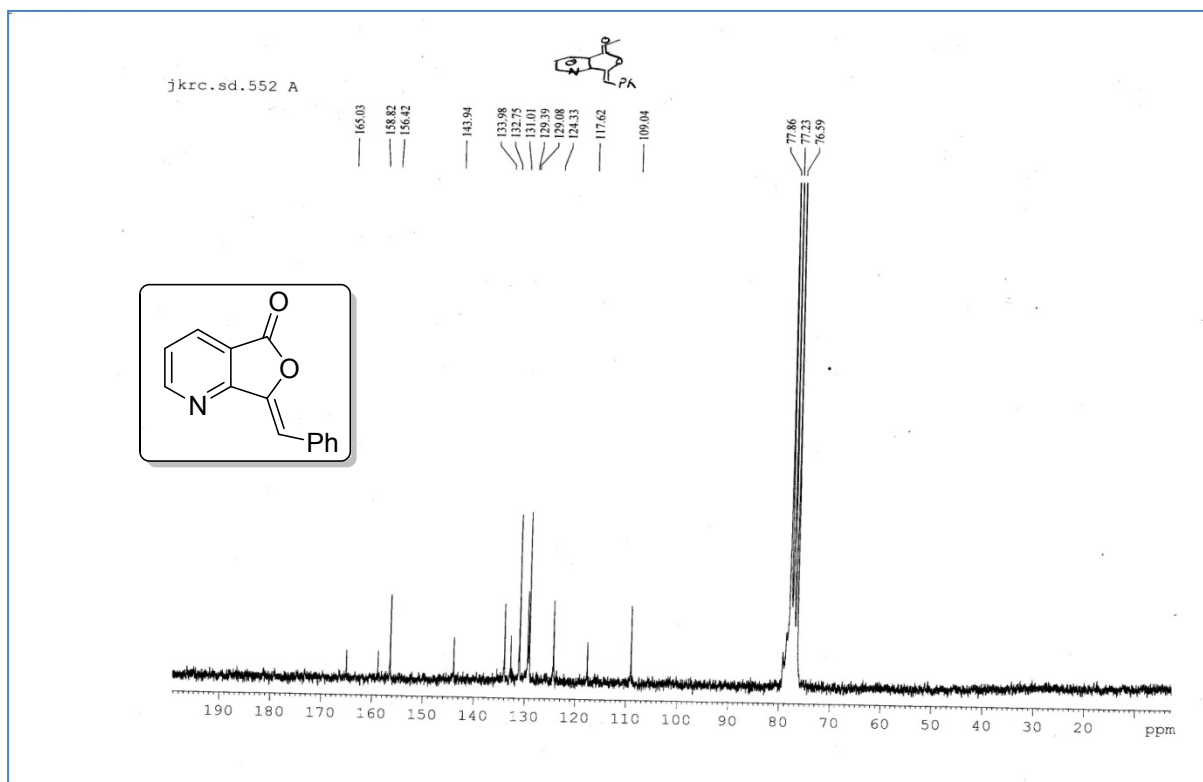
¹³C NMR (CDCl₃, 50 MHz) of Compound (3k):



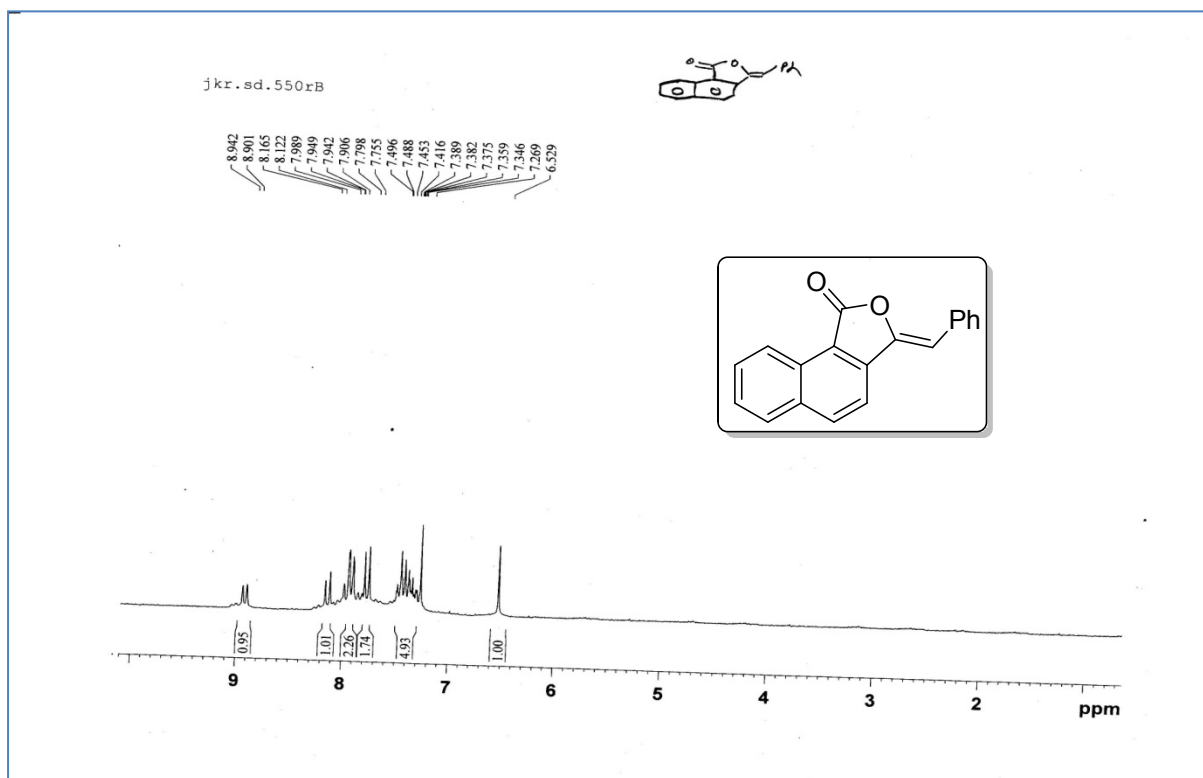
¹H NMR (CDCl₃, 200 MHz) of Compound (3l):



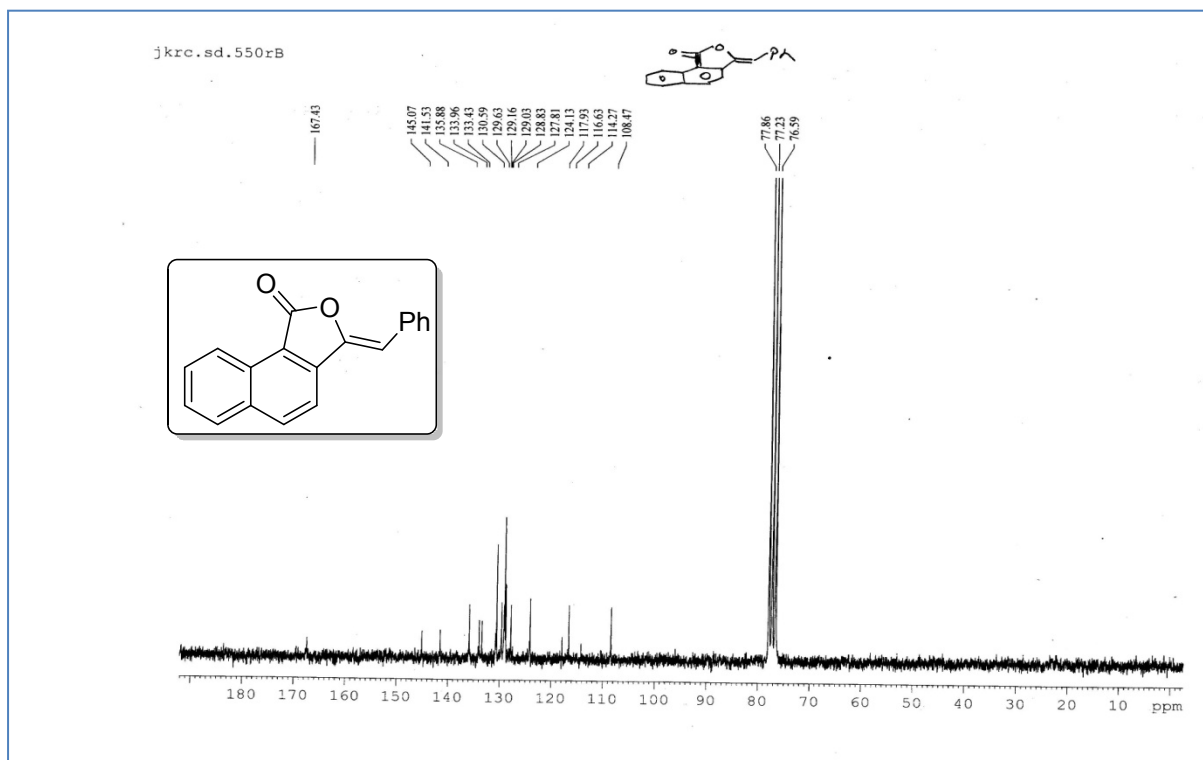
¹³C NMR (CDCl₃, 50 MHz) of Compound (3l):



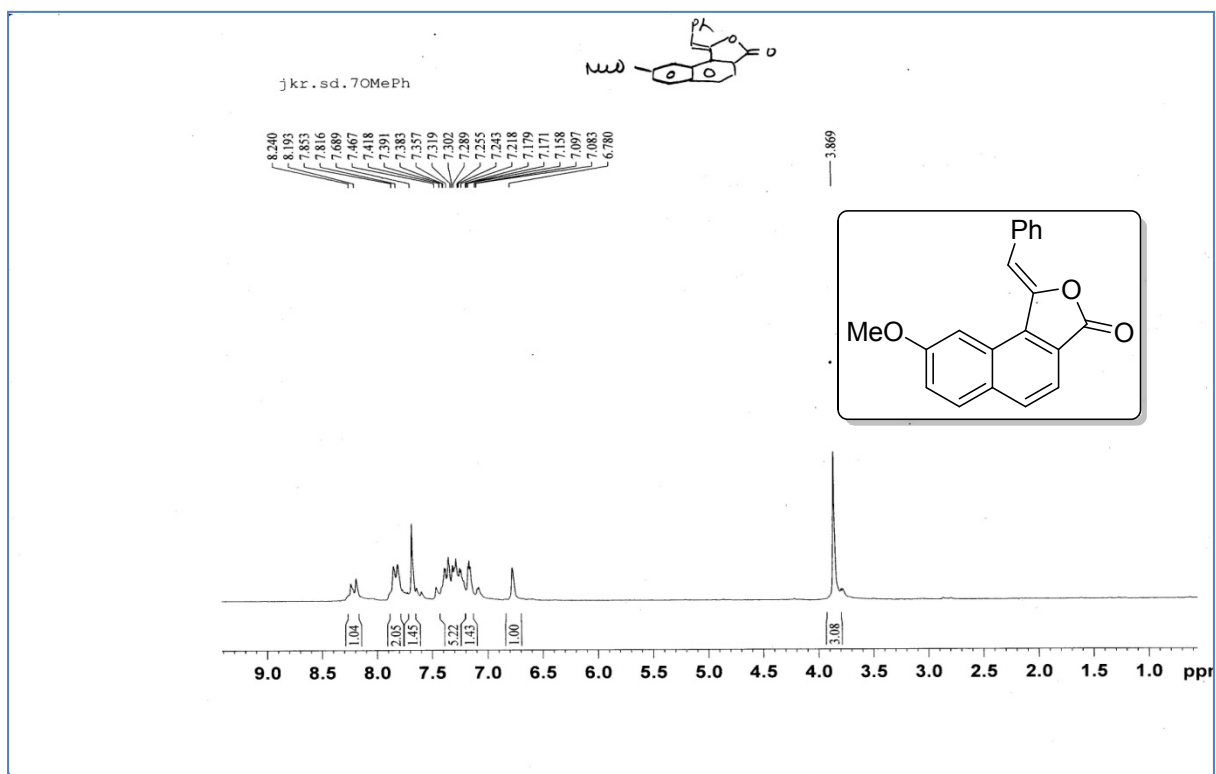
¹H NMR (CDCl₃, 200 MHz) of Compound (3m):



¹³C NMR (CDCl₃, 50 MHz) of Compound (3m):



¹H NMR (CDCl₃, 200 MHz) of Compound (3n):



¹³C NMR (CDCl₃, 50 MHz) of Compound (3n):

