

SUPPLEMENTARY MATERIAL TO
**Synthesis of novel phthalimido oxime pseudoesters and
 evaluation of their cytotoxicity**

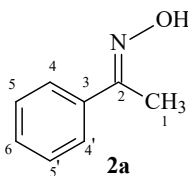
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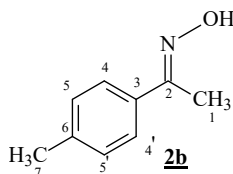
CHARACTERIZATION DATA

(*E*)-Acetophenone oxime (**2a**).



The product was isolated upon column chromatography (SiO₂, eluent hexane/ethyl acetate gradient 8/2). Yield 91 %; white powder; m.p.: 55±2 °C, ¹H-NMR (300 MHz, CDCl₃, 27°C, δ / ppm): 9.44 (1H, s, OH) 7.69–7.66 (2H, m, H4 & H4'), 7.44–7.42 (3H, m, H5, H5' & H6), 2.36 (3H, s, CH₃); ¹³C-NMR (75MHz, CDCl₃, 27°C, δ / ppm): 155.5 (C2), 136.0 (C3), 128.8 (C4), 127.7 (C6), 125.6 (C5), 11.9 (C1).

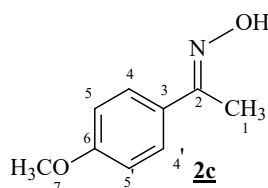
(*E*)-4-Methylacetophenone oxime (**2b**).



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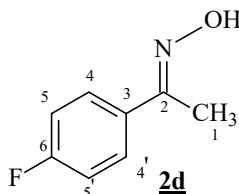
The product was isolated upon column chromatography (SiO₂, eluent hexane/ethyl acetate gradient 7/3). Yield: 96 %; white powder; m.p.: 62±2 °C; ¹H-NMR (300 MHz, CDCl₃, 27°C, δ / ppm): 8.45 (1H, *s*, OH) 7.57–7.54 (2H, *m*, H4 & H4'), 7.23–7.21 (3H, *m*, H5, H5' & H6), 2.40 (3H, *s*, OCH₃), 2.32 (3H, *s*, CH₃); ¹³C-NMR (75 MHz, CDCl₃, 27°C, δ / ppm): 155.4 (C2), 138.8 (C6), 133.1 (C3), 128.7 (C4), 125.4 (C5), 20.7 (C7), 11.7 (C1).

(*E*)-4-Methoxyacetophenone oxime (**2c**).



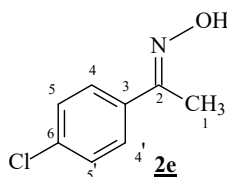
The product was isolated upon column chromatography (SiO₂, eluent hexane/ethyl acetate gradient 8.5/1.5). Yield: 95 %; white powder; m.p.: 92±2 °C; ¹H-NMR (300 MHz, CDCl₃, 27 °C, δ / ppm): 8.45 (1H, *s*, OH), 7.57 (2H, *d*, *J*_{4,5} = 8,1 Hz, H4 & H4'), 6.90 (2H, *d*, *J*_{5,4} = 8,1 Hz, H5 & H5'), 3.83 (3H, *s*, H₃CO), 2.29 (3H, *s*, H₁); ¹³C-NMR (75 MHz, CDCl₃, 27°C, δ / ppm): 160.0 (C2), 155.0 (C6), 128.5 (C3), 126.9 (C4), 113.7 (C5), 54.8 (C7), 11,7 (C1).

(*E*)-4-Fluoroacetophenone oxime (**2d**).



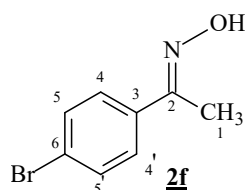
The product was isolated upon column chromatography (SiO₂, eluent hexane/ethyl acetate gradient 8/2). Yield: 82 %; white powder; m.p. 94±2 °C, ¹H-NMR (300 MHz, CDCl₃, 27°C, δ / ppm): 9.11 (1H, *s*, OH) 7.60 (2H, *d*, *J*_{4,5} = 8.7 Hz, H4 & H4'), 7.06 (2H, *d*, *J*_{5,4} = 8.7 Hz, H5 & H5'), 2.31 (3H, *s*, CH₃); ¹³C-NMR (75 MHz, CDCl₃, 27 °C, δ / ppm): 164.6 (C2), 154.7 (C6), 132.0 (C3), 127.4 (C4), 115.0 (C5), 11.9 (C1).

(*E*)-4-Chloroacetophenone oxime (**2e**).



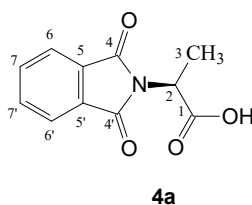
The product was isolated upon column chromatography (SiO₂, eluent hexane/ethyl acetate gradient 7/3). Yield: 94 %, white powder, m.p.: 108±2 °C; ¹H-NMR (300 MHz, CDCl₃, 27 °C, δ / ppm): 9.24 (1H, *s*, OH), 7.53 (2H, *d*, *J*_{4,5} = 8.7 Hz, H4 & H4'), 7.33 (2H, *d*, *J*_{5,4} = 8.7 Hz, H5 & H5'), 2.27 (3H, *s*, CH₃); ¹³C-NMR (75 MHz, CDCl₃, 27 °C, δ / ppm): 154.7 (C2), 134.8 (C6), 134.3 (C3), 128.2 (C4), 126.8 (C5), 11.7 (C1).

(*E*)-4-Bromoacetophenone oxime (**2f**).



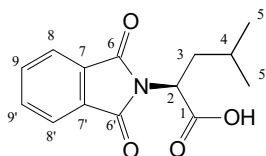
The product was isolated upon column chromatography (SiO₂, eluent hexane/ethyl acetate gradient 8.5/1.5). Yield: 94 %; white powder; m.p. 107±2 °C, ¹H-NMR (300 MHz, CDCl₃, 27 °C, δ / ppm): 8.30 (1H, *s*, OH) 7.66 (2H, *d*, *J*_{4,5} = 8.5 Hz, H4 & H4'), 7.48 (2H, *d*, *J*_{5,4} = 8.5 Hz, H5 & H5'), 2.26 (3H, *s*, CH₃); ¹³C-NMR (75 MHz, CDCl₃, 27 °C, δ / ppm): 154.7 (C2), 134.8 (C6), 131.2 (C3), 127.1 (C4), 123.1 (C5), 11.6 (C1).

(*S*)-2-(1,3-Dioxisoindolin-2-yl)propanoic acid (**4a**).

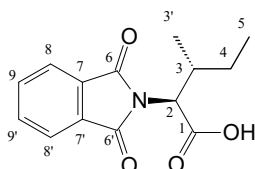


4a

Product was isolated upon column chromatography (SiO₂, eluent ethyl acetate/hexane gradient 8/2). Yield: 95 %; white powder; m.p.: 138±2 °C; Anal. Calcd. for C₁₁H₉NO₄: C, 60.27; H, 4.10; N, 6.39; O, 29.22 %. Found: C, 60.34; H, 4.12; N, 6.28 %; IR (KBr, cm⁻¹): 2931 (CH), 1721 (C=O), 1345 (C-N); ¹H-NMR (300 MHz, CDCl₃, 27°C, δ / ppm): 11.26 (1H, *s*, COOH) 7.80–7.76 (2H, *m*, H6 & H6'), 7.68–7.63 (2H, *m*, H7 & H7'), 5.00 (1H, *q*, *J*_{2,3} = 7.5 Hz, H2), 1.65 (3H, *d*, *J*_{3,2} = 7.2 Hz, CH₃); ¹³C-NMR (75 MHz, CDCl₃, 27°C, δ / ppm): 174.9 (C1), 166.8 (C4), 133.7 (C7), 131.3 (C5), 123.0 (C6), 46.7 (C2), 14.4 (C3); [α]_D²⁵ (c: 1×10⁻³ g mL⁻¹, CHCl₃): -43.2.

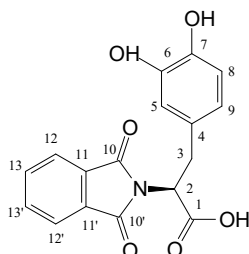
(S)-2-(1,3-Dioxoisindolin-2-yl)-4-methyl-pentanoic acid (**4b**).**4b**

The product was isolated upon column chromatography (SiO₂, eluent ethyl acetate/hexane gradient 8/2). Yield: 89 %; white powder; m.p.: 123±2 °C, Anal. Calcd. for C₁₄H₁₅NO₄: C, 64.36; H, 5.74; N, 5.36; O, 24.52 %. Found: C, 64.42; H, 5.70; N, 5.37 %; IR (KBr, cm⁻¹): 1708 (C=O), 1465 (CH₂), 1328 (C–N); ¹H-NMR (300 MHz, CDCl₃, 27 °C, δ / ppm): 10.20 (1H, *s*, COOH), 7.87–7.83 (2H, *m*, H8 & H8'), 7.75–7.70 (2H, *m*, H9 & H9'), 4.97 (1H, *dd*, *J*_{2,3} = 11.1 & *J*_{2,3'} = 4.5 Hz, H2), 2.40–2.30 (1H, *m*, H4), 2.03–1.94 (1H, *m*, H3), 1.56–1.51 (1H, *m*, H3'), 0.97 (6H, *dd*, *J*_{5,4} = *J*_{5',4'} = 6.6 Hz, H5, H5'); ¹³C-NMR (75 MHz, CDCl₃, 27 °C, δ / ppm): 174 (C1), 167 (C6), 133.5 (C9), 131.3 (C7), 127 (C8), 49.9 (C2), 36.6 (C3), 24.6 (C5), 20.5 (C4); [α]_D²⁵ (*c*: 1×10⁻³ g mL⁻¹, CHCl₃): –35.

(2S,3R)-(1,3-Dioxoisindolin-2-yl)-3-methyl-2-pentanoic acid (**4c**).**4c**

The product was isolated upon column chromatography (SiO₂, eluent ethyl acetate/hexane gradient 8/2). Yield: 85 %; white crystals; m.p.: 134±2 °C; Anal. Calcd. for C₁₄H₁₅NO₄: C, 64.36; H, 5.74; N, 5.36; O, 24.52 %. Found: C, 64.39; H, 5.71; N, 5.38 %; IR (KBr, cm⁻¹): 1718 (C=O), 1460 (CH₂), 1320 (C–N); ¹H-NMR (CDCl₃, 300 MHz, 27 °C, δ / ppm): 8.84 (1H, *s*, COOH) 7.87–7.83 (2H, *m*, H8 & H8'), 7.75–7.70 (2H, *m*, H9 & H9'), 4.73 (1H, *d*, *J*_{2,3} = 9 Hz, H2), 2.61–2.54 (1H, *m*, H3), 1.56–1.43 (1H, *m*, H4), 1.18 (3H, *d*, *J*_{3',3} = 8.1 Hz, H3'), 0.89 (3H, *t*, *J*_{5,4} = 7.5 Hz, H5); ¹³C-NMR (75 MHz, CDCl₃, 27 °C, δ / ppm): 172.8 (C1), 167.2 (C6), 133.6 (C9), 131.2 (C7), 125.7 (C8), 56.6 (C2), 33.9 (C3), 25.3 (C4), 16.1 (C3'), 10.2 (C5); [α]_D²⁵ (*c*: 1×10⁻³ g mL⁻¹, CHCl₃): –19.7.

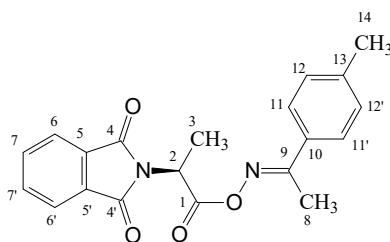
(S)-3-(3,4-Dihydroxyphenyl)-2-(1,3-dioxisoindolin-2-yl)propanoic acid (**4d**).



4d

The product was isolated upon column chromatography (SiO₂, eluent ethyl acetate/hexane gradient 8/2). Yield: 76 %; white powder; 185±2 °C; Anal. Calcd. for C₁₇H₁₃NO₆: C, 62.29; H, 3.97; N, 4.28; O, 29.35 %. Found: C, 62.39; H, 3.91; N, 4.27 %; IR (KBr, cm⁻¹): 3290 (OH), 1721 (C=O), 1460 (CH₂), 1332 (C–N); ¹H-NMR (300 MHz, DMSO-*d*₆, 27 °C, δ / ppm): 13.13 (1H, *s*, COOH); 8.54 (2H, *s*, 2(OH)), 7.83–7.62 (4H, *m*, H12, H12', H13 & H13'), 6.68 (1H, *s*, H5), 6.52 (1H, *d*, *J*_{9,8} = 5.7 Hz, H9), 6.33 (1H, *d*, *J*_{8,9} = 5.7 Hz, H8), 4.97 (1H, *dd*, *J*_{2,3} = 11.4 Hz & *J*_{2,3'} = 5.1 Hz, H2), 3.32–3.14 (2H, *m*, H3); ¹³C-NMR (75 MHz, DMSO-*d*₆, 27 °C, δ(ppm)): 170 (C1), 167 (C10), 144.9 (C6), 143.7 (C7), 134.7 (C4), 130.8 (C13), 128.0 (C11), 123.2 (C12), 119.3 (C9), 116 (C8), 115.5 (C5), 53.3 (C2), 33.2 (C3); [α]_D²³ (c: 1×10⁻³ g mL⁻¹, DMSO): -45.6,

(S)-2-[1-Methyl-2-(((1-(4-methylphenyl)ethylidene)amino)oxy)-2-oxoethyl]-1H-isoindole-1,3(2H)-dione (**5a**).

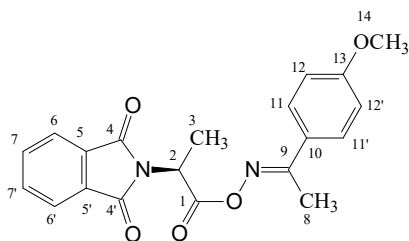


5a

The product was isolated upon column chromatography (SiO₂, eluent ethyl acetate/hexane gradient 8/2). Yield: 63 %; yellow oil; Anal. Calcd. for C₂₀H₁₈N₂O₄: C, 68.57; H, 5.14; N, 8.00; O, 18.28 %. Found: C, 68.54; H, 5.19; N, 8.01 %; IR (KBr, cm⁻¹): 1770 (C=O), 1595 (C=N), 1088 (O=CON), 985 (N–O); ¹H-NMR (300 MHz, CDCl₃, 27 °C, δ / ppm): 7.88–7.85 (2H, *m*, H6 & H6'), 7.74–7.71 (2H, *m*, H7, H7'), 7.64 (2H, *d*, *J*_{11,12} = 7.8 Hz, H11 & H11'), 6.88 (2H, *d*, *J*_{12,11} = 7.8 Hz, H12 & H12'), 5.19 (1H, *q*, *J*_{2,3} = 7.2 Hz, H2), 2.27 (3H, *s*, H14), 2.18 (3H, *s*, H8), 1.81 (3H, *d*, *J*_{3,2} = 7.2 Hz, H3); ¹³C-NMR (75 MHz, CDCl₃, 27 °C, δ / ppm): 166.2 (C1), 163.0 (C4), 161.2 (C9), 133.6 (C13),

131.4 (C7), 128.1 (C5), 126.2 (C10), 125.7 (C12), 122.9 (C11), 113.4 (C6), 46.7 (C2), 21.2 (C14), 14.7 (C8), 13.5 (C3); $[\alpha]_D^{25}$ (*c*: 1×10^{-3} g mL⁻¹, CHCl₃): -78.2.

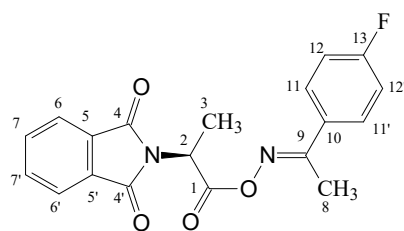
(*S*)-2-[2-(((1-(4-Methoxyphenyl)ethylidene)amino)oxy)-1-methyl-2-oxoethyl]-1*H*-isoindole-1,3(2*H*)-dione (**5b**).



5b

The product was isolated upon column chromatography (SiO₂, eluent hexane/ethyl acetate gradient 8/2). Yield: 52 %; white powder; m.p.: 150±2 °C; Anal. Calcd. for C₂₀H₁₈N₂O₅: C, 65.57; H, 4.95; N, 7.65; O, 21.84 %. Found: C, 65.76; H, 4.82; N, 7.61 %; IR (KBr, cm⁻¹): 2938 (OCH₃), 1751 (C=O), 1592 (C=N), 1051 (O=CON), 987 (N-O); ¹H-NMR (300 MHz, CDCl₃, 27 °C, δ / ppm): 7.88–7.85 (2H, *m*, H6 & H6'), 7.75–7.72 (2H, *m*, H7, H7'), 7.70 (2H, *d*, $J_{11,12} = 8.4$ Hz, H11, H11'), 6.84 (2H, *d*, $J_{12,11} = 8.4$ Hz, H12 & H12'), 5.21 (1H, *q*, $J_{2,3} = 7.2$ Hz, H2), 3.80 (3H, *s*, OCH₃), 2.20 (3H, *s*, H8), 1.82 (3H, *d*, $J_{3,2} = 7.2$ Hz, H3); ¹³C-NMR (75MHz, CDCl₃, 27 °C, δ / ppm): 166.7 (C1), 166.2 (C4), 163.0 (C13), 133.6 (C9), 131.4 (C7), 129.2 (C5), 128.1 (C11), 126.2 (C6), 122.9 (C10), 113.4 (C12), 54.7 (OCH₃), 46.6 (C2), 14.8 (C8), 13.9 (C3); $[\alpha]_D^{22}$ (*c*: 1×10^{-3} g mL⁻¹, CHCl₃): -40.2.

(*S*)-2-[2-(((1-(4-Fluorophenyl)ethylidene)amino)oxy)-1-methyl-2-oxoethyl]-1*H*-isoindole-1,3(2*H*)-dione (**5c**).

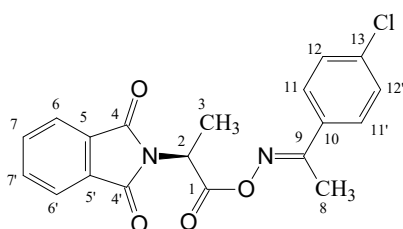


5c

The product was isolated upon column chromatography (SiO₂, eluent hexane/ethyl acetate gradient 8/2). Yield: 60 %; white crystals; m.p.: 166±2 °C; Anal. Calcd. for C₁₉H₁₅FN₂O₄: C, 64.40; H, 4.23; F, 5.36; N, 7.90; O, 18.07 %. Found: C, 64.38; H, 4.32; F, 5.32; N, 7.94 %; IR (KBr, cm⁻¹): 1737 (C=O), 1589 (C=N), 1062 (O=CON), 1001 (N-O); ¹H-NMR (300 MHz, CDCl₃, 27 °C, δ / ppm): 7.90–7.85 (2H, *m*, H6, H6'), 7.77–7.73 (2H, *m*, H7 & H7'), 7.69

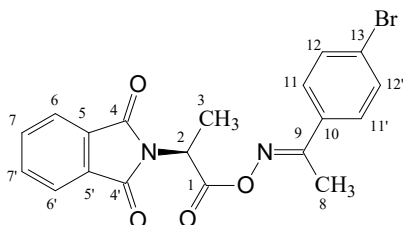
(2H, *d*, $J_{11,12}$ = 8.4 Hz, H11 & H11'), 7.09 (2H, *d*, $J_{12,11}$ = 8.4 Hz, H12 & H12'), 5.22 (1H, *q*, $J_{2,3}$ = 7.2 Hz, H2), 2.21 (3H, *s*, H8), 1.84 (3H, *d*, $J_{3,2}$ = 7.2 Hz, H3); ^{13}C -NMR (75 MHz, CDCl_3 , 27 °C, δ / ppm): 166.7 (C1), 166.0 (C4), 162.5 (C13), 133.7 (C9), 131.4 (C7), 128.7 (C5), 128.6 (C11), 123.0 (C10), 115.2 (C6), 114.9 (C12), 46.6 (C2), 14.7 (C8), 13.5 (C3); $[\alpha]_{\text{D}}^{23}$ (*c*: 1×10^{-3} g mL $^{-1}$, CHCl_3): -60.1.

(*S*)-2-[2-(((1-(4-Chlorophenyl)ethylidene)amino)oxy)-1-methyl-2-oxoethyl]-1*H*-isoindole-1,3(2*H*)-dione (**5d**).

**5d**

The product was isolated upon column chromatography (SiO_2 , eluent hexane/ethyl acetate gradient 8/2). Yield: 76 %; white powder; m.p.: 140 ± 2 °C, Anal. Calcd. for $\text{C}_{19}\text{H}_{15}\text{ClN}_2\text{O}_4$: C, 61.53; H, 4.04; Cl, 9.58; N, 7.55; O, 17.27 %. Found: C, 61.57; H, 4.07; Cl, 8.91; N, 7.48 %; IR (KBr, cm^{-1}): 1739 (C=O), 1516 (C=N), 1068 (O=CON), 963 (N-O); ^1H -NMR (300 MHz, CDCl_3 , 27 °C, δ / ppm): 7.87–7.83 (2H, *m*, H6 & H6'), 7.75–7.72 (2H, *m*, H7 & H7'), 7.45 (2H, *d*, $J_{11,12}$ = 8.2 Hz, H11 & H11'), 7.25 (2H, *d*, $J_{12,11}$ = 8.2 Hz, H12 & H12'), 5.05 (1H, *q*, $J_{2,3}$ = 7.2 Hz, H2), 2.19 (3H, *s*, H8), 1.81 (3H, *d*, $J_{3,2}$ = 7.2 Hz, H3); ^{13}C -NMR (75 MHz, CDCl_3 , 27 °C, δ / ppm): 167.9 (C1), 167.4 (C4), 136.0 (C9), 134.4 (C13), 131.7 (C7), 129.7 (C5), 128.9 (C10), 123.6 (C11), 122.7 (C12), 121.4 (C6), 50.9 (C2), 15.3 (C8), 13.5 (C3); $[\alpha]_{\text{D}}^{25}$ (*c*: 1×10^{-3} g mL $^{-1}$, CHCl_3): -28.6.

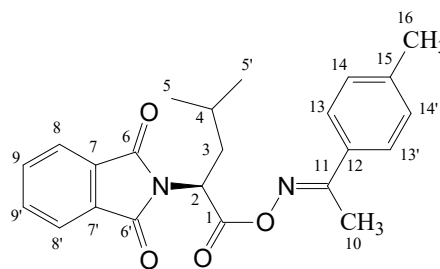
4(*S*)-2-[2-(((1-(4-Bromophenyl)ethylidene)amino)oxy)-1-methyl-2-oxoethyl]-1*H*-isoindole-1,3(2*H*)-dione (**5e**).

**5e**

The product was isolated upon column chromatography (SiO_2 , eluent hexane/ethyl acetate gradient 8/2). Yield: 75 %; white powder; m.p.: 96 ± 2 °C, Anal.

Calcd. for $C_{19}H_{15}BrN_2O_4$: C, 54.95; H, 3.61; Br, 19.25; N, 6.74; O, 15.42 %. Found: C, 54.88; H, 3.64; Br, 19.32 N, 6.78 %; IR (KBr, cm^{-1}): 1757 (C=O), 1591 (C=N), 1074 (O=CON), 999 (N-O); 1H -NMR (300 MHz, $CDCl_3$, 27°C, δ / ppm): 7.89–7.85 (2H, *m*, H6 & H6'), 7.76–7.73 (2H, *m*, H7 & H7'), 7.60 (2H, *d*, $J_{11,12}$ = 8.2 Hz, H11 & H11'), 7.52 (2H, *d*, $J_{12,11}$ = 8.2 Hz, H12 & H12'), 5.24 (1H, *q*, $J_{2,3}$ = 7.2 Hz, H2), 2.20 (3H, *s*, H8), 1.84 (3H, *d*, $J_{3,2}$ = 7.2 Hz, H3); ^{13}C -NMR (75 MHz, $CDCl_3$, 27°C, δ / ppm): 166.6 (C1), 166.0 (C4), 162.5 (C9), 133.7 (C10), 132.8 (C7), 131.4 (C5), 131.3 (C12), 128.0 (C11), 124.8 (C6), 123.0 (C13), 46.6 (C2), 14.7 (C8), 13.5 (C3); $[\alpha]_D^{22}$ (*c*: 1×10^{-3} g mL $^{-1}$, $CHCl_3$): -38.3.

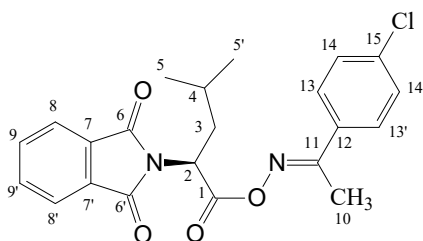
(*S*)-2-[3-Methyl-1-(((1-(4-methylphenyl)ethylidene)amino)oxy)carbonyl)butyl]-1*H*-isoindole-1,3(2*H*)-dione (**5f**).



5f

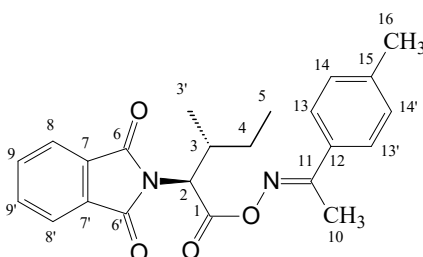
The product was isolated upon column chromatography (SiO_2 , eluent hexane/ethyl acetate gradient 9.5/0.5). Yield: 61 %; white oil; Anal. Calcd. for $C_{23}H_{24}N_2O_4$: C, 70.40; H, 6.12; N, 7.14; O, 16.32 %. Found: C, 70.42; H, 6.18; N, 7.12; IR (KBr, cm^{-1}): 1762 (C=O), 1595 (C=N), 1460 (CH_2), 1084 (O=CON), 989 (N-O); 1H -NMR (300 MHz, $CDCl_3$, 27 °C, δ / ppm): 7.89–7.86 (2H, *m*, H8 & H8'), 7.85–7.73 (2H, *m*, H9 & H9'), 7.60 (2H, *d*, $J_{13,14}$ = 8.2 Hz, H13 & H13'), 7.18 (2H, *d*, $J_{14,13}$ = 8.2 Hz, H14 & H14'), 5.19 (1H, *dd*, $J_{2,3}$ = 10.8 & $J_{2,3'}$ = 4.5 Hz, H2), 2.52–2.40 (1H, *m*, H3), 2.35 (3H, *s*, H16), 2.19 (3H, *s*, H10), 2.14–2.06 (1H, *m*, CH_2), 1.62–1.43 (1H, *m*, H4), 1.01 (3H, *d*, $J_{5,4}$ = 6.9 Hz, H5), 0.98 (3H, *d*, $J_{5',4'}$ = 6.9 Hz, H5'); ^{13}C -NMR (75 MHz, $CDCl_3$, 27 °C, δ / ppm): 167.0 (C1), 166.2 (C6), 163.4 (C11), 140.5 (C15), 133.6 (C9), 131.1 (C7), 128.7 (C12), 126.4 (C14), 122.9 (C13), 122.7 (C8), 49.9 (C2), 36.8 (C3), 24.6 (C16), 22.4 (C5), 20.7 (C4), 13.7 (C10); $[\alpha]_D^{26}$ (*c*: 1×10^{-3} g mL $^{-1}$, $CHCl_3$): -42.7.

(S)-2-[1-(((1-(4-Chlorophenyl)ethylidene)amino)oxy)carbonyl)-3-methylbutyl]-1H-isoindole-1,3(2H)-dione (**5g**).

**5g**

The product was isolated upon column chromatography (SiO₂, eluent hexane/ethyl acetate gradient 9.5/0.5). Yield: 69 %; white powder; m.p.: 116±2 °C, Anal. Calcd. for C₂₂H₂₄ClN₂O₄: C, 64.00; H, 5.09; Cl, 8.60; N, 6.78; O, 15.51 %. Found: C, 64.08; H, 5.12; Cl, 8.62; N, 6.64 %; IR (KBr, cm⁻¹): 1751 (C=O), 1595 (C=N), 1462 (CH₂), 1080 (O=CON), 991 (N-O); ¹H-NMR (300 MHz, CDCl₃, 27 °C, δ / ppm): 7.87–7.83 (2H, *m*, H8 & H8'), 7.76–7.71 (2H, *m*, H9 & H9'), 7.64 (2H, *d*, *J*_{13,14} = 8.2 Hz, H13 & H13'), 7.32 (2H, *d*, *J*_{14,13} = 8.2 Hz, H14 & H14'), 5.19 (1H, *dd*, *J*_{2,3} = 11.1 Hz & *J*_{2,3'} = 4.8 Hz, H2), 2.50–2.40 (1H, *m*, H4), 2.17 (3H, *s*, H10), 2.12–2.03 (1H, *m*, H3), 1.61–1.59 (1H, *m*, H3), 0.99 (3H, *d*, *J*_{5,4} = 7.2 Hz, H5), 0.97 (3H, *d*, *J*_{5',4'} = 7.2 Hz, H5'); ¹³C-NMR (75 MHz, CDCl₃, 27 °C, δ / ppm): 166.5 (C1), 166.0 (C6), 162.4 (C11), 136.4 (C15), 133.7 (C9), 131.2 (C7), 130.9 (C12), 128.2 (C13), 126.7 (C14), 122.9 (C8), 49.8 (C2), 36.9 (C3), 24.3 (C5), 22.4 (C4), 13.6 (C10); [α]_D²⁵ (c: 1×10⁻³ g mL⁻¹, CHCl₃): -40.5.

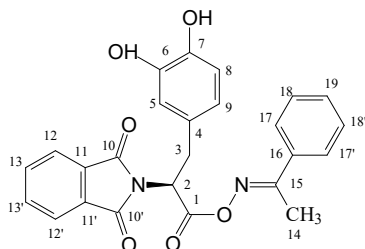
2-[(1S,2R)-2-Methyl-1-(((1-(4-methylphenyl)ethylidene)amino)oxy)carbonyl)-butyl]-1H-isoindole-1,3(2H)-dione (**5h**).

**5h**

The product was isolated upon column chromatography (SiO₂, eluent hexane/ethyl acetate gradient 9.5/0.5). Yield: 62 %; white crystals; m.p.: 92±2 °C, Anal. Calcd. for C₂₃H₂₄N₂O₄: C, 70.40; H, 6.12; N, 7.14; O, 16.32 %. Found: C, 70.43; H, 6.15; N, 7.15 %; IR (KBr, cm⁻¹): 1759 (C=O), 1595 (C=N), 1464 (CH₂), 1074 (O=CON), 993 (N-O); ¹H-NMR (300 MHz, CDCl₃,

27 °C, δ / ppm): 7.85–7.82 (2H, *m*, H8 & H8'), 7.72–7.70 (2H, *m*, H9, H9'), 7.57 (2H, *d*, $J_{13,14} = 8.2$ Hz, H13, H13'), 7.14 (*d*, $J_{14,13} = 8.2$ Hz, 2H, H14 & H14'), 4.82 (1H, *d*, $J_{2,3} = 9$ Hz, H2), 2.76–2.71 (1H, *m*, H3), 2.30 (3H, *s*, H16), 2.17 (3H, *s*, H10), 1.59–1.54 (1H, *m*, H4), 1.29 (3H, *d*, $J_{3',3} = 6.9$ Hz, H3'), 1.11–1.02 (1H, *m*, H4), 0.94 (3H, *t*, $J_{5,4} = 6.9$ Hz, H5); ^{13}C -NMR (75 MHz, CDCl_3 , 27 °C, δ / ppm): 167.0 (C1), 165.4 (C6), 163.1 (C11), 140.4 (C15), 133.7 (C9), 131.8 (C7), 128.6 (C12), 128.2 (C14), 126.4 (C13), 122.9 (C8), 55.5 (C2), 34.3 (C3), 25.7 (C4), 21.2 (C16), 16.2 (C10), 13.7 (C3'), 10.6 (C5); $[\alpha]_{\text{D}}^{25}$ (*c*: 1×10^{-3} g mL^{-1} , CHCl_3): -23.2.

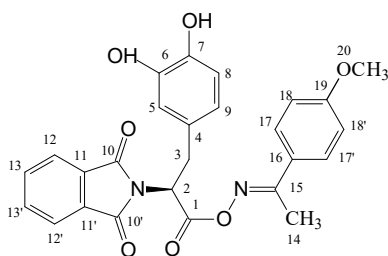
(*S*)-2-[2-(3,4-Dihydroxyphenyl)-1-(((1-(4-methylphenyl)ethylidene)amino)oxy)-carbonyl)ethyl]-1*H*-isoindole-1,3(2*H*)-dione (**5i**).



5i

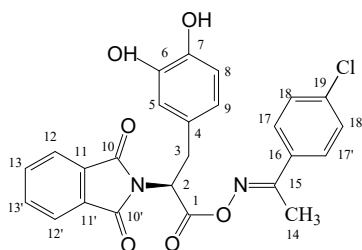
The product was isolated upon column chromatography (SiO_2 , eluent hexane/ethyl acetate gradient 9/1). Yield: 53 %; white crystals; m.p.: 166 ± 2 °C, Anal. Calcd. for $\text{C}_{25}\text{H}_{20}\text{N}_2\text{O}_6$: C, 67.56; H, 4.50; N, 6.30; O, 21.62 %. Found: C, 67.52; H, 4.54; N, 6.30 %; IR (KBr, cm^{-1}): 3373 (OH), 1743 (C=O), 1593 (C=N), 1424 (CH_2), 1080 (O=CON), 986 (N-O); ^1H -NMR (300 MHz, CDCl_3 , 27 °C, δ / ppm): 8.14 (2H, *2s*, 2(OH)), 7.80–7.26 (12H, *m*, Ar-H), 5.37 (1H, *dd*, $J_{2,3} = 9.6$ Hz & $J_{2,3'} = 6.9$ Hz, H2), 3.59–3.55 (2H, *m*, H3), 2.21 (3H, *s*, H14); ^{13}C -NMR (75 MHz, CDCl_3 , 27 °C, δ / ppm): 166.9 (C1), 165.7 (C10), 164.0 (C15), 143.2 (C6), 142.4 (C7), 133.8 (C16), 133.7 (C4), 131.0 (C13), 130.2 (C11), 128.4 (C19), 128.0 (C17), 126.5 (C18), 123.0 (C12), 120.8 (C9), 115.4 (C8), 114.5 (C5), 52.6 (C2), 26.4 (C3), 13.9 (C14); $[\alpha]_{\text{D}}^{23}$ (*c*: 1×10^{-3} g mL^{-1} , CHCl_3): -42.7.

(S)-2-[2-(3,4-Dihydroxyphenyl)-1-(((1-(4-methoxyphenyl)ethylidene)amino)oxy)carbonyl)ethyl]-1H-isoindole-1,3(2H)-dione (**5j**).

**5j**

The product was isolated upon column chromatography (SiO₂, eluent hexane/ethyl acetate gradient 9/1). Yield: 73 %; white crystals; m.p.: 180±2 °C; Anal. Calcd. for C₂₆H₂₃N₂O₇: C, 65.68; H, 4.84; N, 5.89; O, 23.57 %. Found: C, 65.74; H, 4.79; N, 5.87 %; IR (KBr, cm⁻¹): 3370 (OH), 2948 (OCH₃), 1758 (C=O), 1548 (C=N), 1416 (CH₂), 1076 (O=CON), 983 (N-O); ¹H-NMR (300 MHz, CDCl₃, 27 °C, δ / ppm): 8.54 (2H, 2s, 2(OH)), 7.84–6.63 (11H, m, Ar-H), 5.35 (1H, dd, J_{2,3} = 9.3 & J_{2,3'} = 7.2 Hz, H2), 3.84 (3H, s, OCH₃), 3.68–3.59 (2H, m, H3), 2.18 (3H, s, H14); ¹³C-NMR (75 MHz, CDCl₃, 27 °C, δ / ppm): 167.4 (C1), 166.1 (C10), 161.8 (C19), 142.7 (C15), 134.1 (C6), 131.6 (C7), 129.3 (C4), 128.6 (C13), 126.6 (C11), 123.4 (C17), 122.7 (C12), 121.5 (C16), 116.5 (C9), 115.0 (C8), 114.3 (C5), 114.0 (C18), 53.5 (OCH₃), 53.1 (C2), 34.0 (C3), 14.1 (CH₃); [α]_D²⁵ (c: 1×10⁻³ g mL⁻¹, CHCl₃): -57.2.

(S)-2-[2-(((1-(4-Chlorophenyl)ethylidene)amino)oxy)-1-((3,4-dihydroxyphenyl)methyl)-2-oxoethyl]-1H-isoindole-1,3(2H)-dione (**5k**).

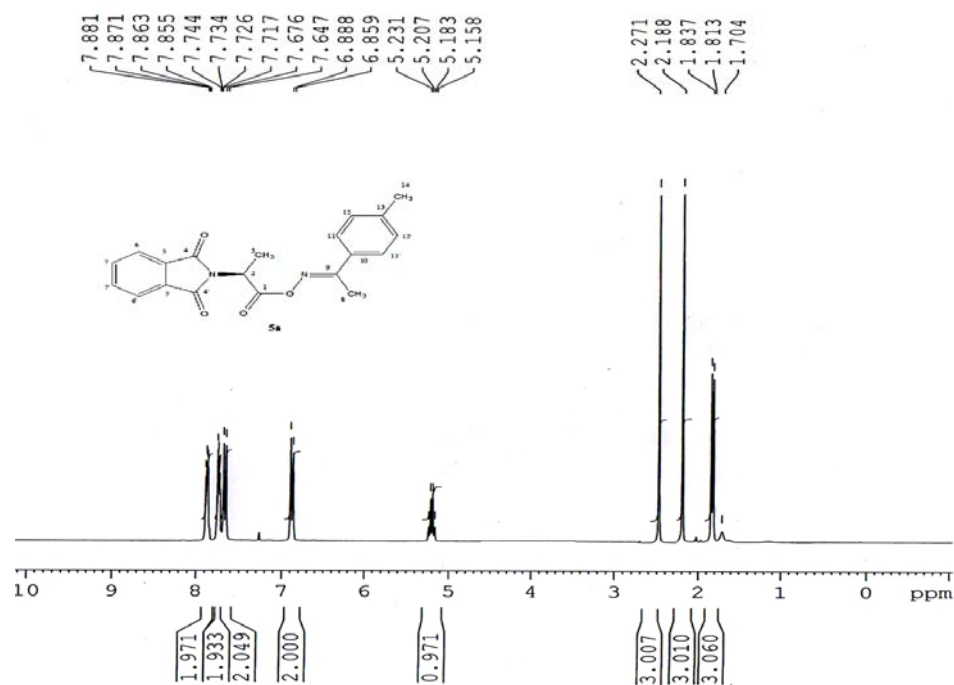
**5k**

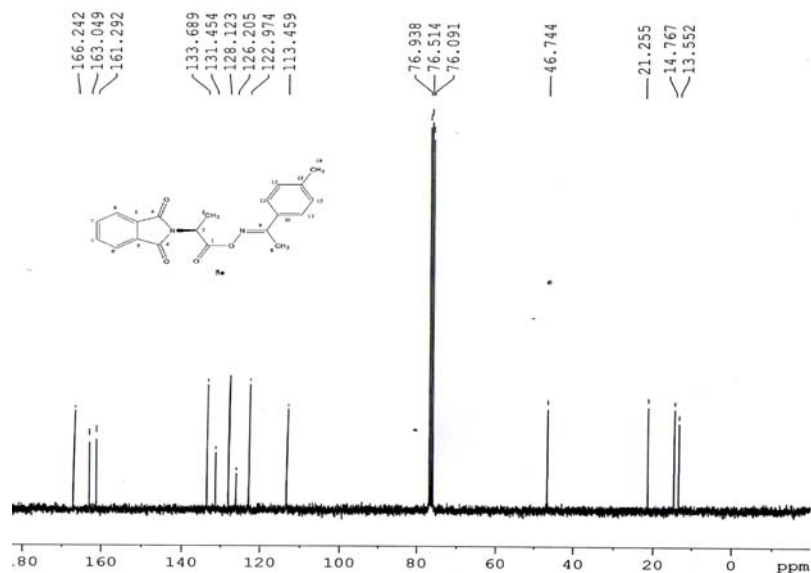
The product was isolated upon column chromatography (SiO₂, eluent hexane/ethyl acetate gradient 9/1). Yield: 67 %; white oil; Anal. Calcd. for C₂₅H₁₉ClN₂O₆: C, 62.69; H, 3.97; Cl, 7.41; N, 5.85; O, 20.06 %. Found: C, 62.72; H, 4.01; Cl, 7.46; N, 5.77 %; IR (KBr, cm⁻¹): 3368 (OH), 1741 (C=O), 1584 (C=N), 1462 (CH₂), 1076 (O=CON), 991 (N-O); ¹H-NMR (300 MHz, CDCl₃, 27 °C, δ / ppm): 8.65 (2H, 2s, 2(OH)); 7.82–6.60 (11H, m, Ar-H), 5.33 (1H, dd, J_{2,3} = 9.3 Hz & J_{2,3'} = 6.9 Hz, H2), 3.59–3.46 (2H, m, H3), 2.19 (3H, s,

CH₃); ¹³C-NMR (75 MHz, CDCl₃, 27°C, δ / ppm): 168.8 (C1), 165.9 (C10), 163.2 (C15), 142.7 (C6), 137.1 (C7), 134.2 (C19), 132.07(C4), 131.0 (C13), 129.6 (C11), 128.3 (C16), 126.8 (C17), 123.4 (C18), 121.4 (C12), 116.0 (C9), 115.3 (C8), 114.5 (C5), 53.1 (C2), 34.5 (C3), 14.7 (C14); [α]_D²⁰ (c: 1×10⁻³ g mL⁻¹, CHCl₃): -48.9.

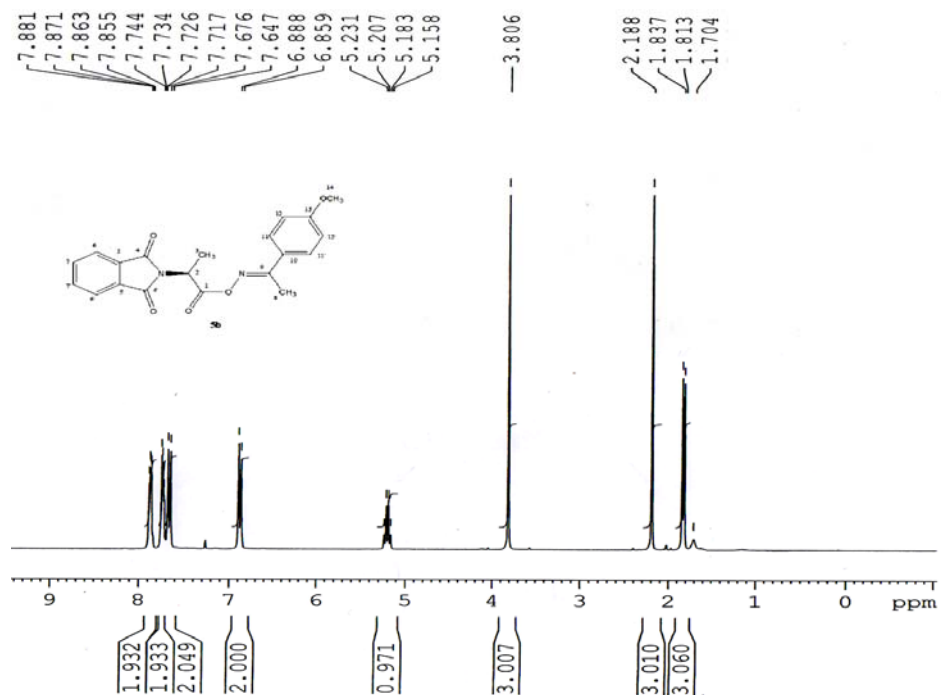
¹H- AND ¹³C-NMR SPECTRA OF COMPOUNDS **5a-k**

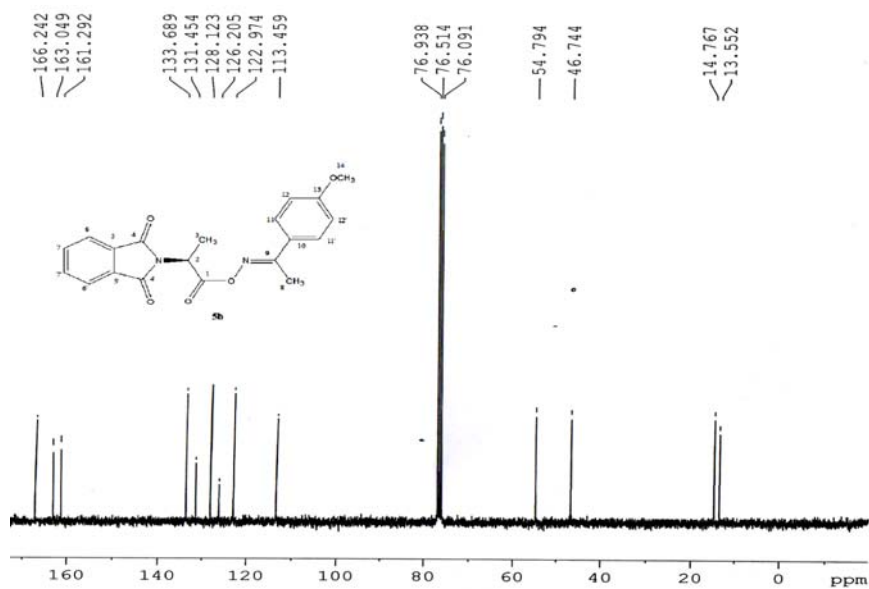
(*S*)-2-[1-Methyl-2-(((1-(4-methylphenyl)ethylidene)amino)oxy)-2-oxoethyl]-1*H*-isoindole-1,3(2*H*)-dione (**5a**)



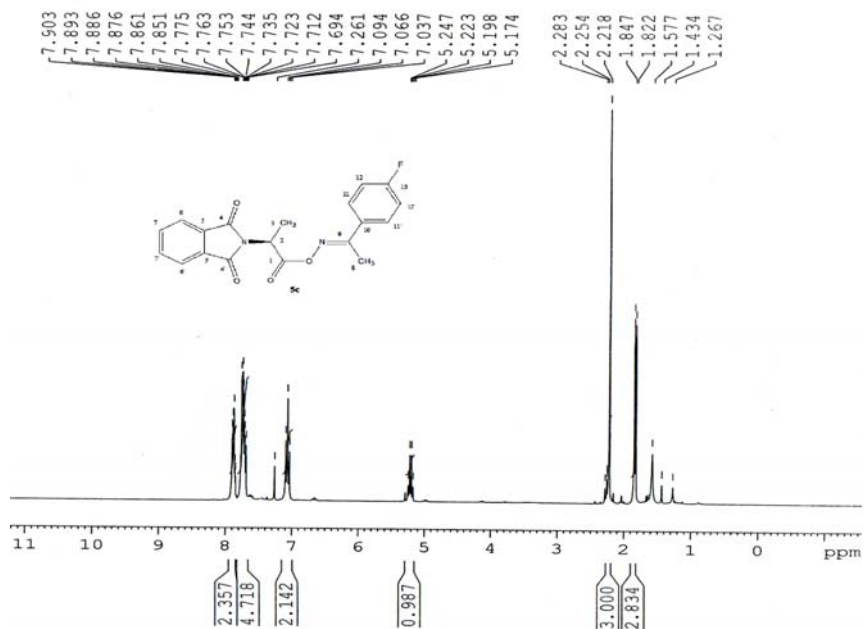


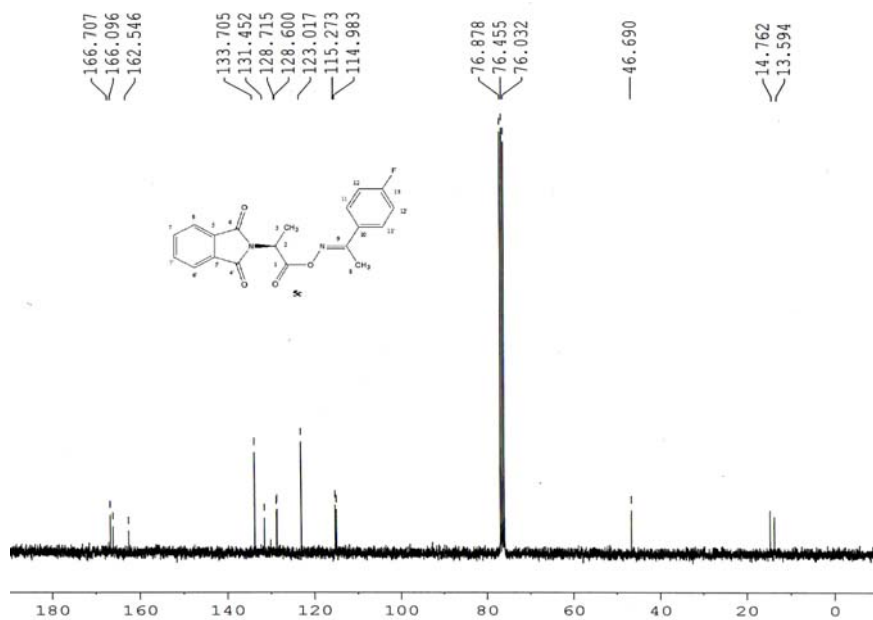
(S)-2-[2-(((1-(4-Methoxyphenyl)ethylidene)amino)oxy)-1-methyl-2-oxoethyl]-1H-isoindole-1,3(2H)-dione (**5b**)



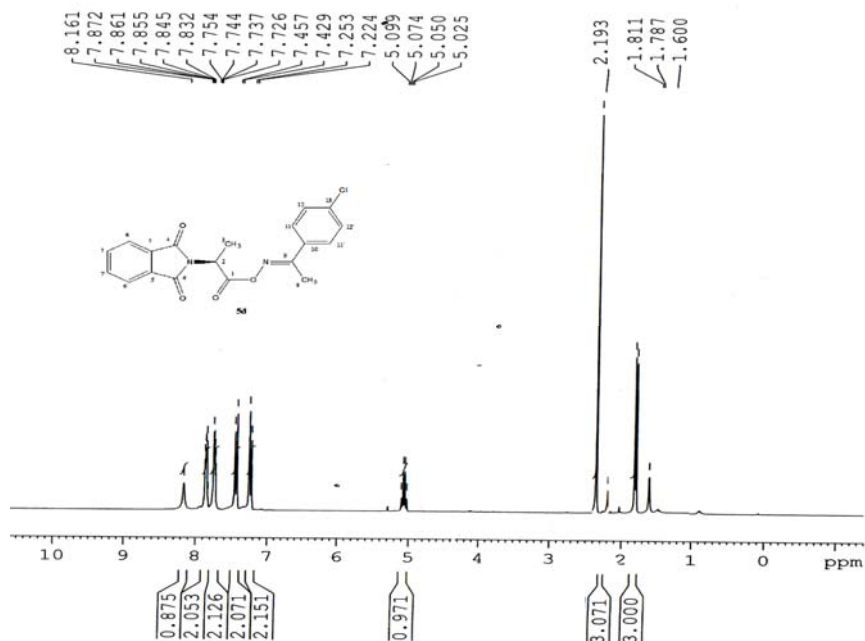


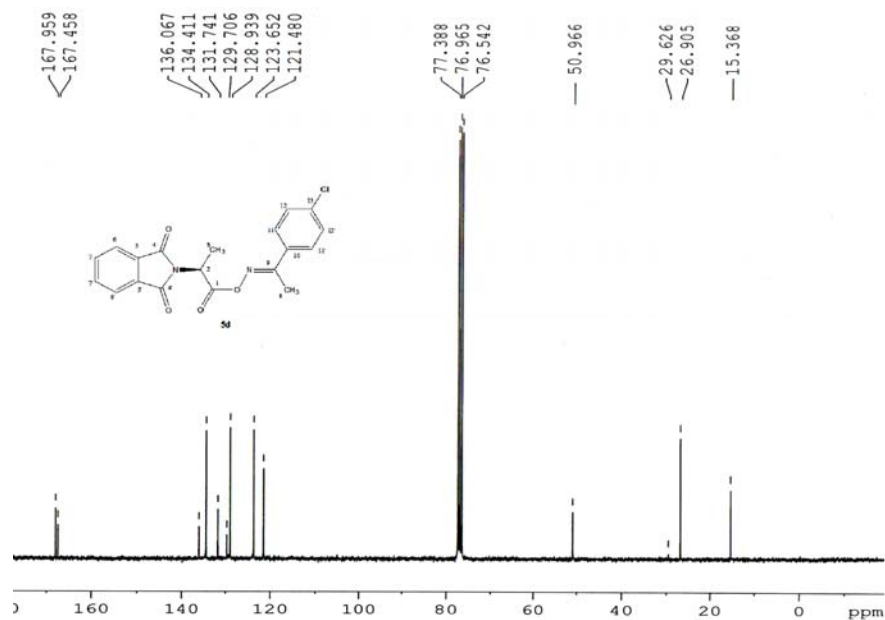
(*S*)-2-[2-(((1-(4-Fluorophenyl)ethylidene)amino)oxy)-1-methyl-2-oxoethyl]-1*H*-isoindole-1,3(2*H*)-dione (**5c**)



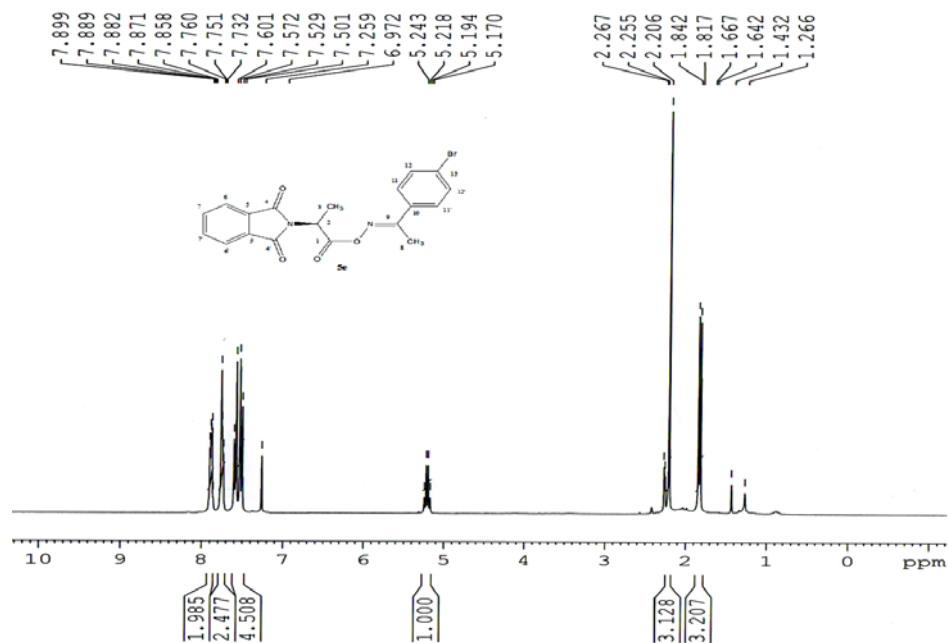


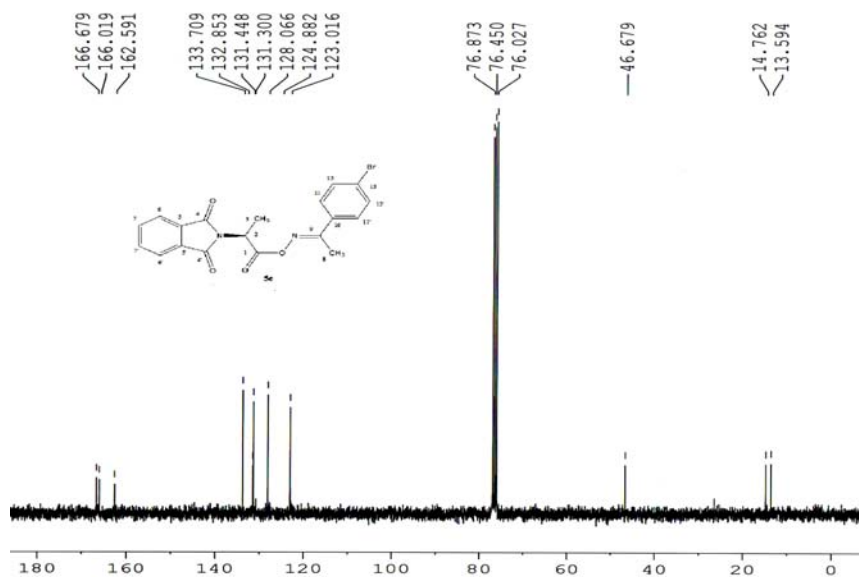
(S)-2-[2-(((1-(4-Chlorophenyl)ethylidene)amino)oxy)-1-methyl-2-oxoethyl]-1H-isoindole-1,3(2H)-dione (**5d**)



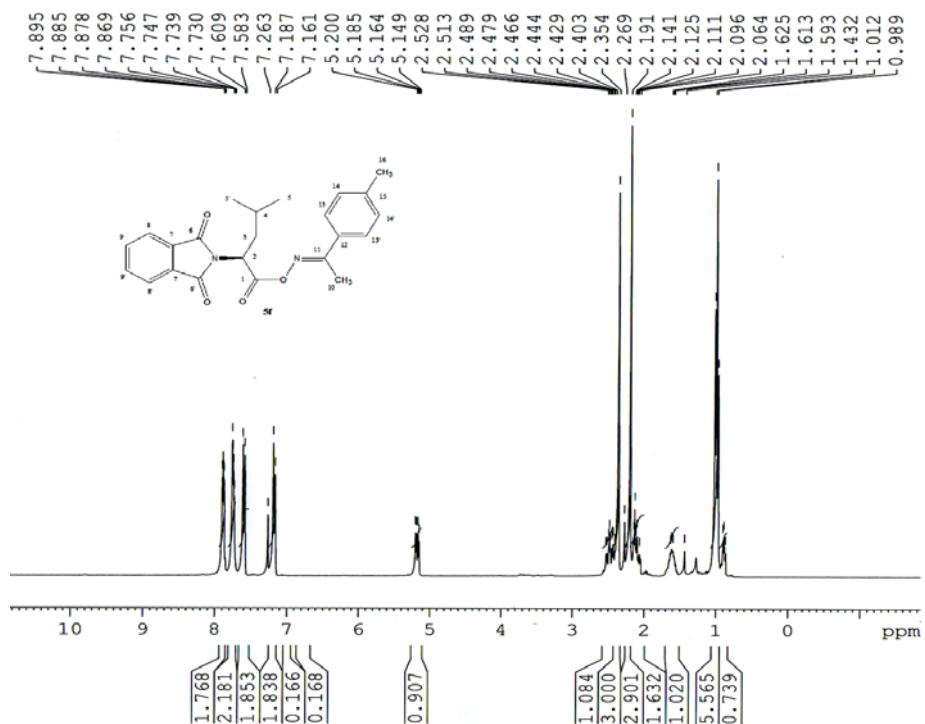


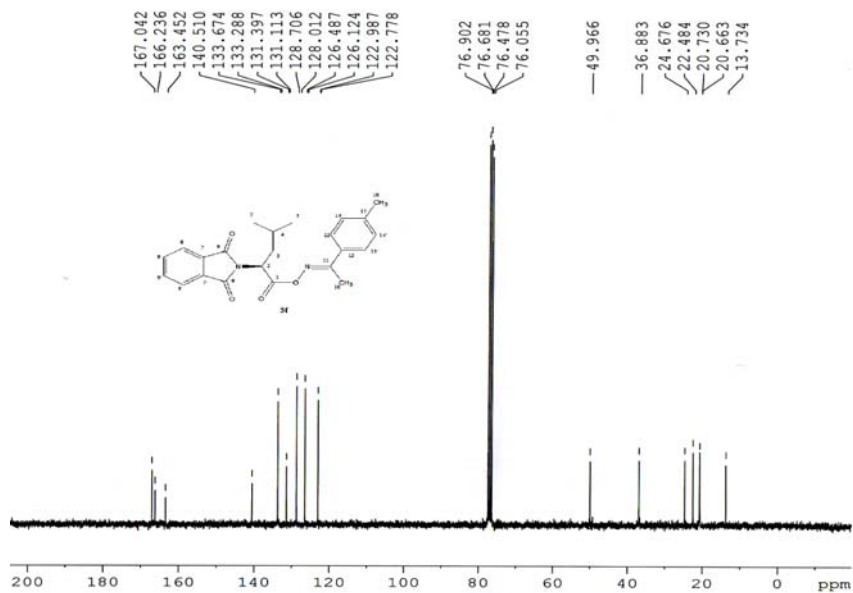
(*S*)-2-[2-(((1-(4-Bromophenyl)ethylidene)amino)oxy)-1-methyl-2-oxoethyl]-1*H*-isoindole-1,3(2*H*)-dione (**5e**)





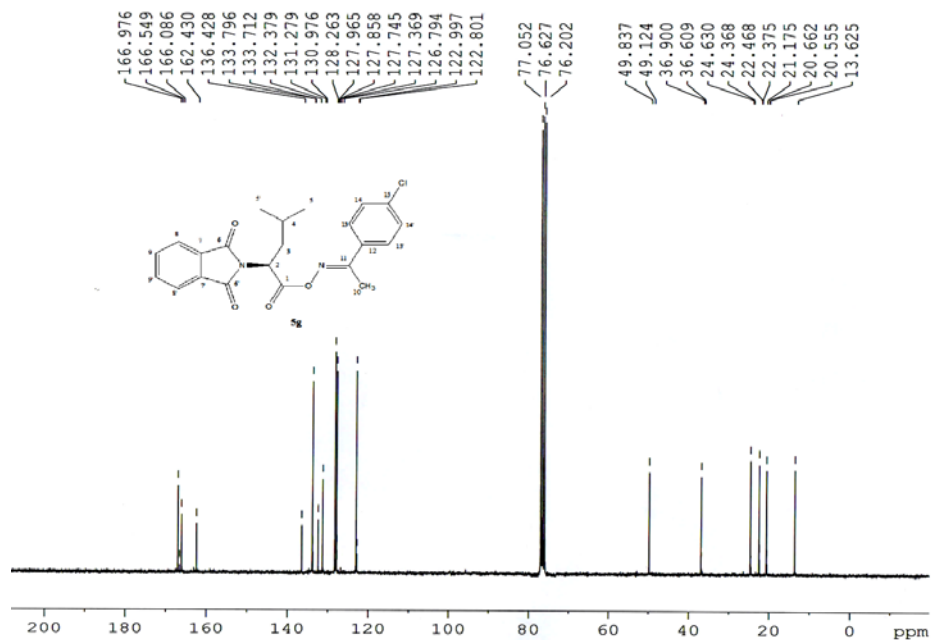
(S)-2-[3-Methyl-1-(((1-(4-methylphenyl)ethylidene)amino)oxy)carbonyl)butyl]-1H-isoindole-1,3(2H)-dione (**5f**)



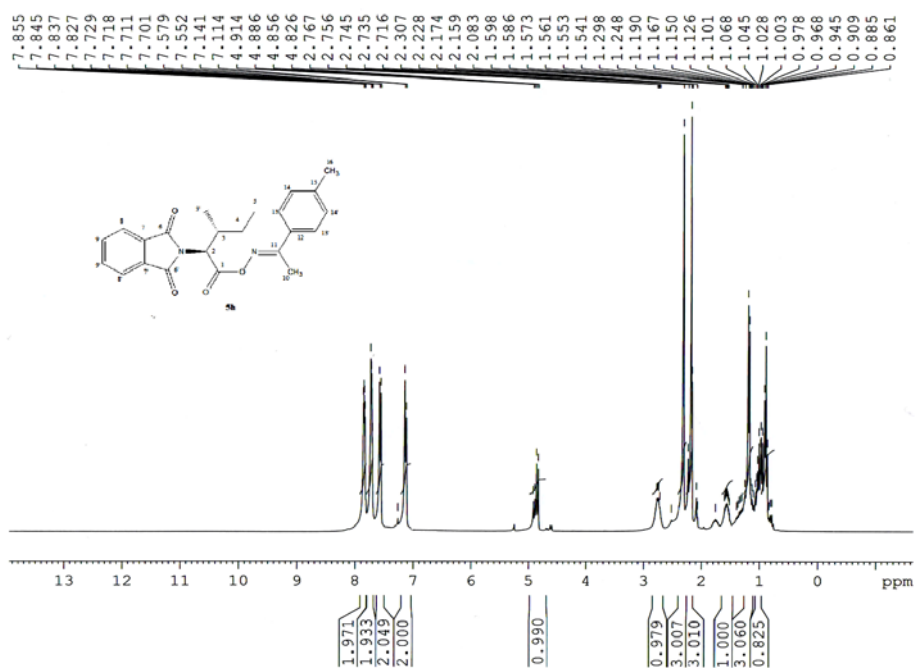


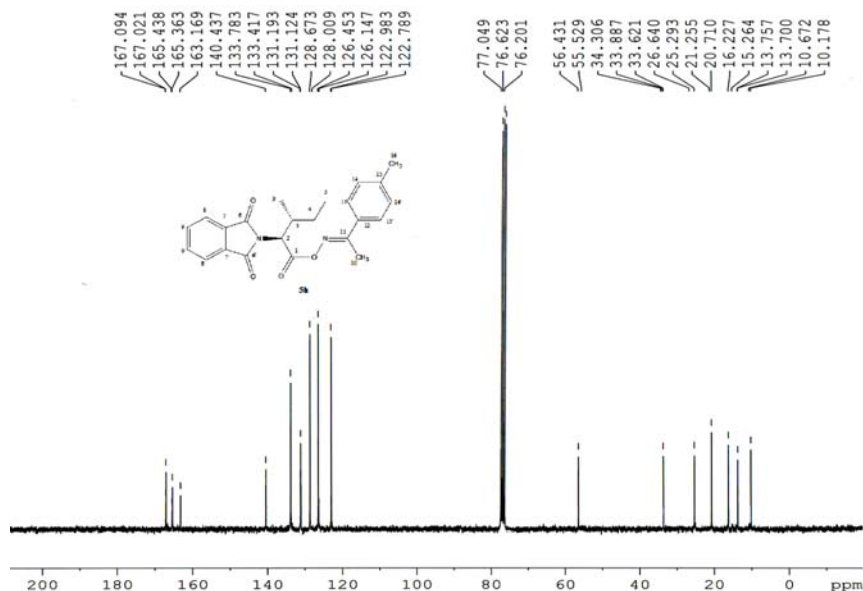
(*S*)-2-[1-(((1-(4-Chlorophenyl)ethylidene)amino)oxy)carbonyl)-3-methylbutyl]-1*H*-isoindole-1,3(2*H*)-dione (**5g**)



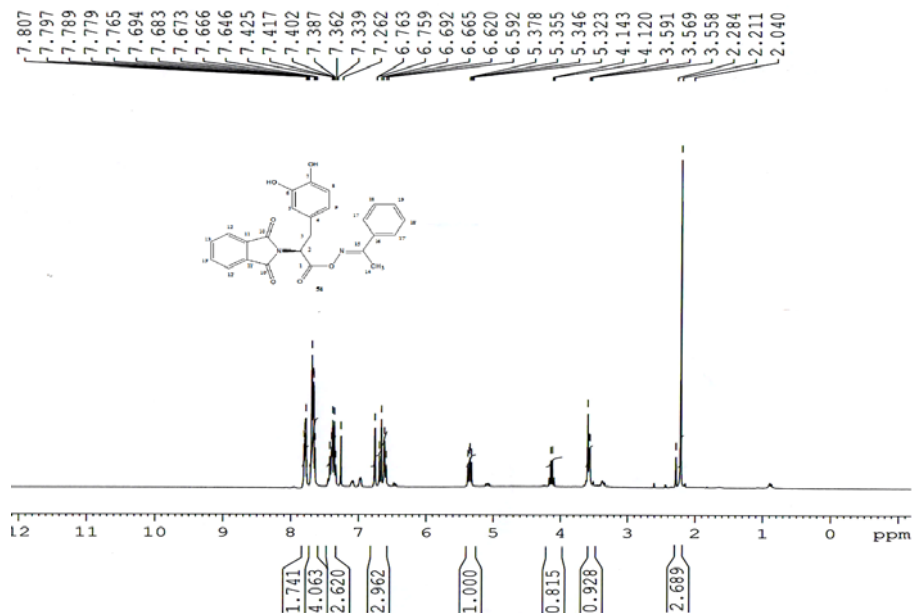


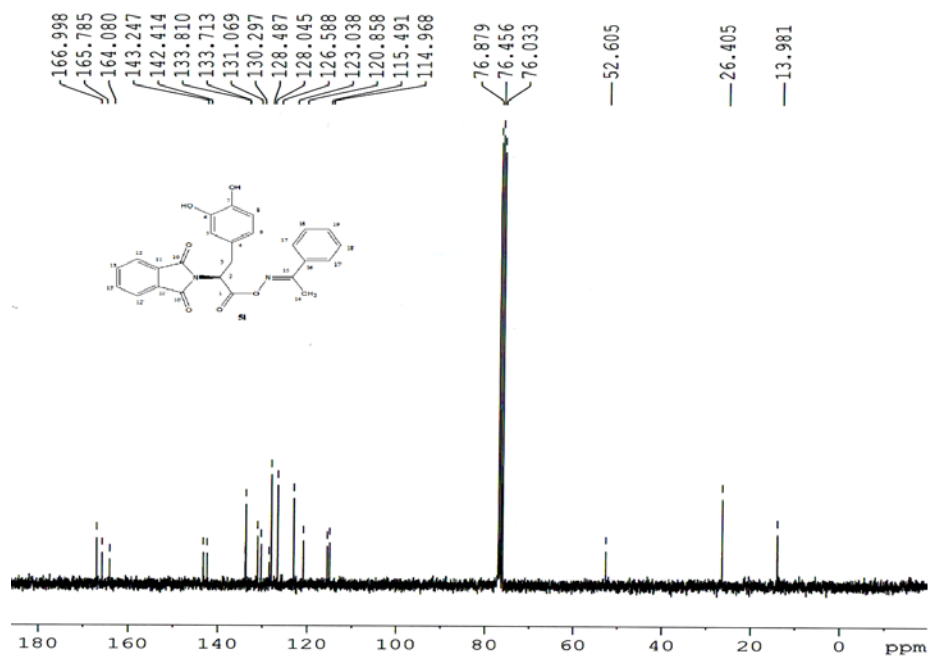
2-[(1*S*,2*R*)-2-Methyl-1-(((1-(4-methylphenyl)ethylidene)amino)oxy)carbonyl-butyl]-1*H*-isoindole-1,3(2*H*)-dione (**5h**)



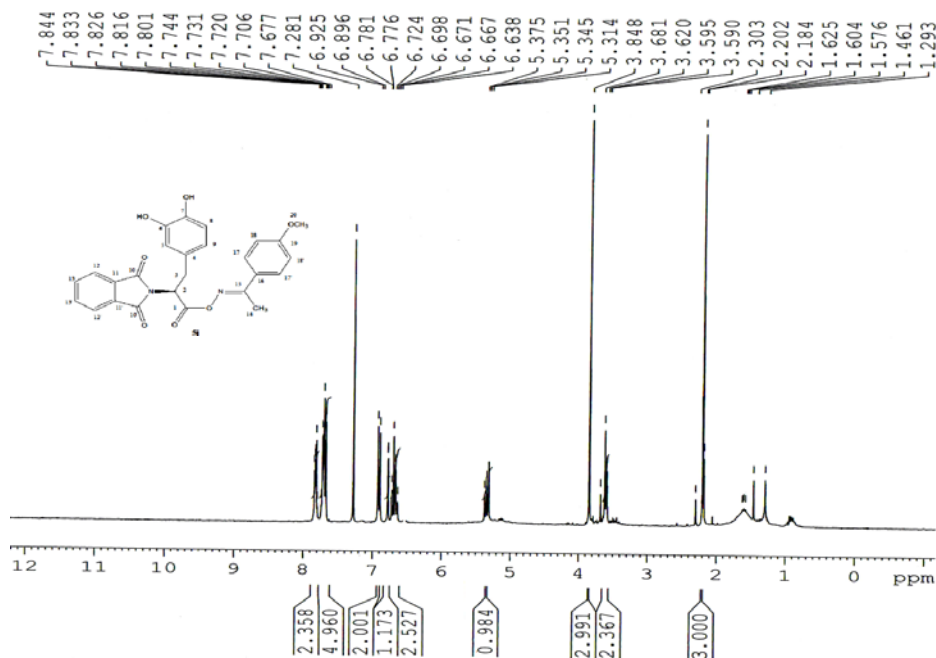


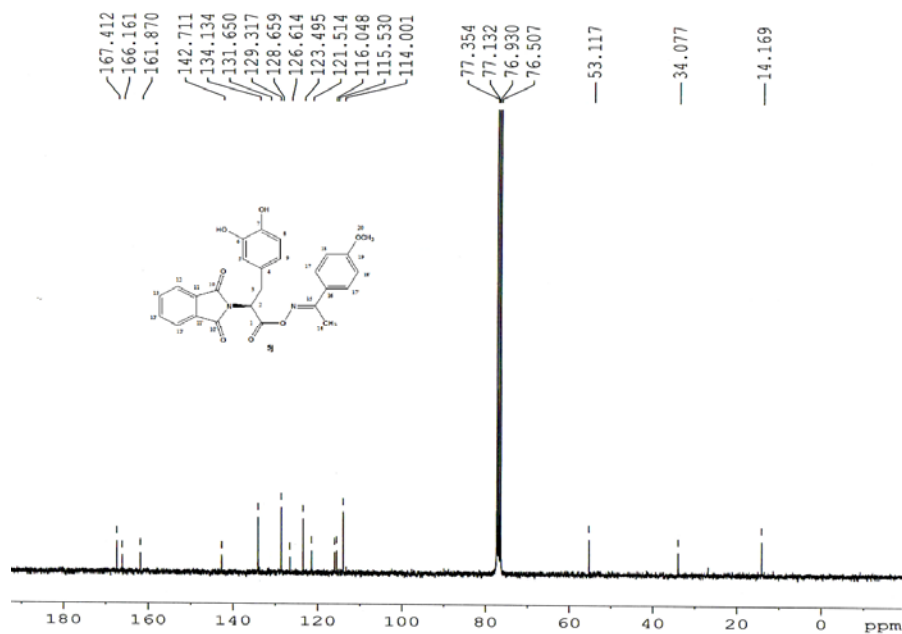
(S)-2-[2-(3,4-Dihydroxyphenyl)-1-(((1-(4-methylphenyl)ethylidene)amino)oxy)carbonyl)ethyl]-1H-isoindole-1,3(2H)-dione (**5i**)





(S)-2-[2-(3,4-Dihydroxyphenyl)-1-(((1-(4-methoxyphenyl)ethylidene)amino)-oxy)carbonyl)ethyl]-1H-isoindole-1,3(2H)-dione (**5j**)





(*S*)-2-[2-(((1-(4-Chlorophenyl)ethylidene)amino)oxy)-1-((3,4-dihydroxyphenyl)-methyl)-2-oxoethyl]-1*H*-isoindole-1,3(2*H*)-dione (**5k**)

