Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supporting Information

Enantioselective α-Hydroxylation of β-Ketoamides

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General Methods

All reactions requiring dry or inert conditions were conducted in flame dried glassware under a positive pressure of nitrogen. THF was freshly distilled prior to use from $LiAlH_4$, chloroform was dried over molecular sieves. Molecular sieves (Aldrich Molecular Sieves, 3 Å, 1.6 mm pellets) were activated under vacuum at 200°C overnight.

Reactions were monitored by thin layer chromatography (TLC) on Merck silica gel plates (0.25 mm) and visualized by UV light. Flash chromatography was performed on Merck silica gel (60, particle size: 0.040–0.063 mm). ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker DRX 400 spectrometer at room temperature in $CDCl_3$ as solvent. Chemical shifts for protons are reported using residual $CHCl_3$ as internal reference (δ=7.26 ppm). Carbon spectra were referenced to the shift of the ^{13}C signal of $CDCl_3$ (δ=77.0 ppm). Optical rotation measurement of compounds **3a-k** was performed on a Jasco Dip-1000 digital polarimeter using the Na lamp (582 nm). FTIR spectra were recorded as thin films on KBr plates using Bruker Vertex 70 spectrometer and absorption maxima are reported in wavenumber (cm^{-1}). ESI-MS was performed using a Bio-Q triple quadrupole mass spectrometer (Micromass, Manchester, UK) equipped with an electrospray ion source. Melting points were measured on a digital Electrothermal 9100 apparatus.

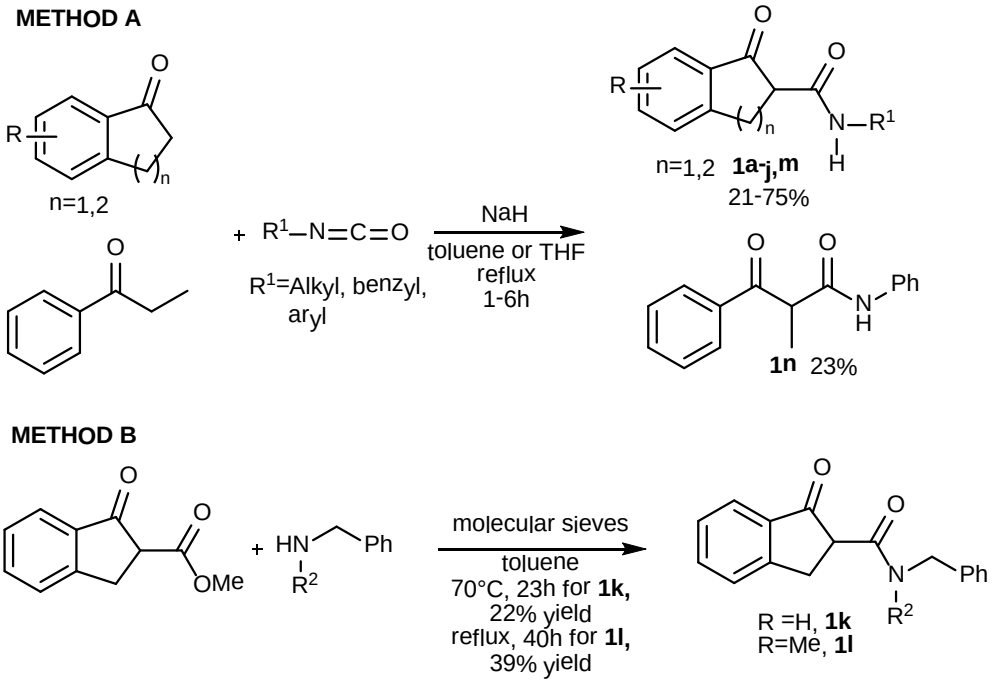
Petrol ether (PE) refers to light petroleum ether (boiling point 40-60°C). Anhydrous toluene, TBHP (5-6 M in decane), and all starting materials (unless otherwise noted) were purchased from Aldrich and used as received. 1-Isocyanato-4-(pentyloxy)benzene was synthesized according to procedures reported in the literature.[1] The cinchona derived thiourea **eHQNT** has been synthetized as reported in the literature.[2]

Enantiomeric excess of products **3** was determined by HPLC analysis (Waters-Breeze 2487, UV dual λ absorbance detector and 1525 Binary HPLC Pump) using Daicel chiral columns.

[1] (a) D. V. N., Hardy, *J. Chem. Soc.* **1934**, 2001. (b) N. Kihara, K. Hinoue, T. Takata, *Macromolecules* **2005**, *38*, 223. (c) H. Yi-Lin, H. Wie-Chung, L. Yi-Hung, P. Shie-Ming, C. Sheng-Hsien, *Angew. Chem. Int. Ed.* **2007**, *46*, 6629.
[2] B. Vakulya, S. Varga, A. Csámpai, T. Soós, *Org. Lett.* **2005**, *7*, 1967.

Experimental Procedures and Compounds Characterization

General procedure for the synthesis of β-ketoamides



METHOD A: β-ketoamides **1a-j**, **m** were prepared following a general procedure reported in the literature.[3]

In a two necked round bottom flask under a positive pressure of nitrogen, NaH (60% w/w dispersion in mineral oil, 10 mmol) was suspended in dry THF (10 mL) for 10 minutes under stirring. The suspension was allowed to settle and after removal of the supernatant, fresh THF (10 mL) was added. A solution of the appropriate indanone or α-tetralone (4 mmol) and isocyanate (4.8 mmol) in dry THF (1.5 mL) was added dropwise over 10 minutes to the refluxing suspension. After completion, monitored by TLC (eluent: PE/ AcOEt 8:2) the mixture was cooled to 0°C and 1 N HCl was added cautiously until the solid completely dissolved (≈ 15 mL). The solution was extracted with ethyl acetate (2 x 20 mL) and the organic phase was washed with saturated $NaHCO_3$ (20 mL), brine (20 mL), dried (Na_2SO_4) and concentrated. The residue was triturated with Et_2O to give the desired compound as yellow/white solid.

METHOD B: β-ketoamides **1k** and **1l** were prepared by using a general procedure reported in the literature.[4]

The β-ketoester (4 mmol) and appropriate benzylamine (8 mmol) in dry toluene (40 mL) were heated to reflux or to 70°C under nitrogen over molecular sieves for the necessary time (monitoring

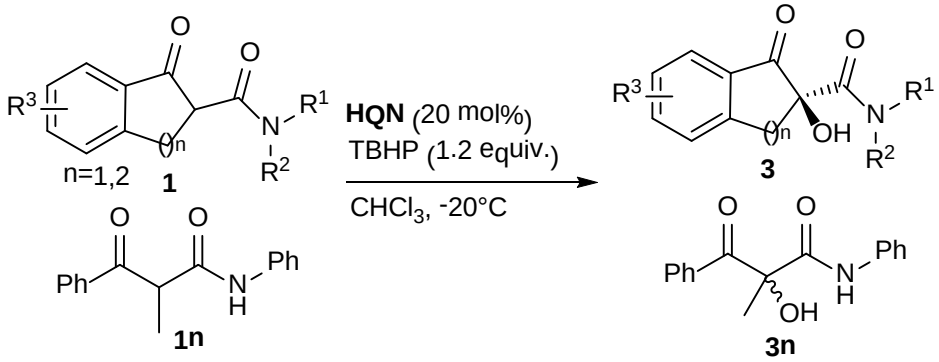
[3] T. A. Moss, A. Alba, D. Hepworth, D. J. Dixon, *Chem. Commun.*, **2008**, 2474.
[4] A. Russo, G. Galdi, G. Croce, A. Lattanzi, *Chem. Eur. J.* **2012**, *18*, 6152.

by TLC, PE/AcOEt 8:2 as eluent). Then molecular sieves were filtered off, and the mixture was purified by flash chromatography, using PE/AcOEt 9:1 to 7:3 as eluent, to give compounds **1k**, **1l**.

General procedure for the racemic hydroxylation of compounds 1

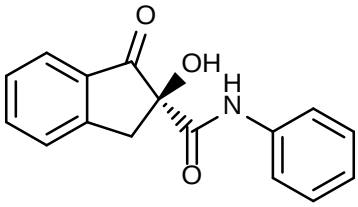
In a sample vial, the appropriate β-ketoamide **1** (0.10 mmol), TBHP (0.12 mmol), and 2-piperidinemethanol (3.5 mg, 0.03 mmol) were dissolved in dry $CHCl_3$ or anhydrous toluene (0.5 mL). The reaction was stirred at room temperature for 17-41 h until completion, monitored by TLC (PE/AcOEt 8:2 or 7:3). After removing the solvent under vacuum, the mixture was directly purified by flash chromatography (PE/AcOEt 9:1 to 7:3) to give products **3** in 34-97%.

General procedure for the asymmetric hydroxylation of compounds 1a-n



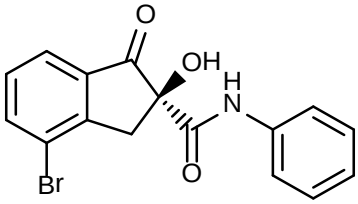
To a sample vial charged with the appropriate β-ketoamide **1** (0.10 mmol) and the hydroquinine (6.5 mg, 0.02 mmol) in anhydrous chloroform (2.0 mL), TBHP (0.12 mmol) was added and the reaction was stirred at –20 °C for 64-144 h until completion (monitored by TLC, PE/AcOEt 8:2 or 7:3). The solvent was removed under vacuum and the product **3** was isolated by flash chromatography (PE/AcOEt 9:1 to 7:3). The absolute configuration of compounds **3** was assigned to be (*S*) by analogy to the structure determined by single-crystal X-ray analysis performed on compound **3b** (see the X-ray analysis section). Crystallization using *n*-hexane/$CHCl_3$ or *n*-pentane/$CHCl_3$ mixtures performed at room temperature gave needle-shaped crystals in an enantioenriched form.

(*S*)-2-hydroxy-1-oxo-*N*-phenyl-2,3-dihydro-1*H*-indene-2-carboxamide (3a)



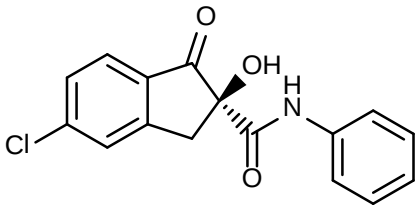
White solid (83% yield, 66% after crystallization), **mp** 149.9-151.3 °C. **[α]$_D^{25}$** = +6.4 (*c* 0.6, $CHCl_3$), *ee* 87%. **FTIR** ν_{max} (KBr)/cm^{-1} 3342, 1719, 1654, 1599, 1533, 1445, 750 . **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 8.83 (bs, 1H), 7.77 (d, 1H, *J*= 7.7 Hz), 7.67 (t, 1H, *J*= 7.2 Hz), 7.52-7.50 (m, 3H), 7.42 (t, 1H, *J*= 7.2 Hz), 7.29 (t, 2H, *J*= 7.5 Hz), 7.11 (t, 1H, *J*= 7.1 Hz), 4.36 (bs, 1H), 3.87 (d, 1H, *J*= 16.8 Hz), 3.18 (d, 1H, *J*= 16.8 Hz). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 203.2, 168.4, 153.1, 136.9, 136.5, 133.7, 129.0, 128.1, 126.4, 125.2, 124.7, 119.7, 82.6, 40.8. **MS** (ESI *m/z*) 268.10 [MH^+, 100%], 290.09 [MNa^+, 85%]. HPLC analysis with Chiralcel ODH column, 70:30 *n*-hexane:2-propanol, 1 mL/min, detection at 254 nm; minor enantiomer t_R = 9.1 min, major enantiomer t_R = 6.4 min.

(*S*)-4-bromo-2-hydroxy-1-oxo-*N*-phenyl-2,3-dihydro-1*H*-indene-2-carboxamide (3b)



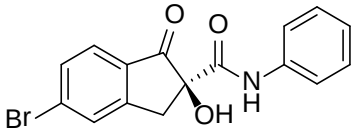
White solid (88% yield, 66% after crystallization), **mp** 171.9-173.6 °C. **[α]$_D^{25}$** = +50.0 (*c* 0.6, $CHCl_3$), *ee* 96%. **FTIR** ν_{max} (KBr)/cm^{-1} 3339, 1728, 1657, 1598, 1533, 1445, 1267, 1120, 943, 753, 692. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 8.70 (bs, 1H), 7.84 (d, 1H, *J*= 7.8 Hz), 7.76 (d, 1H, *J*= 7.6 Hz), 7.53 (d, 2H, J = 8.4 Hz), 7.36-7.29 (m, 3H), 7.15-7.11 (m, 1H), 3.84 (d, 1H, *J*= 17.3 Hz), 3.72 (bs, 1H), 3.12 (d, 1H, *J*= 17.3 Hz) **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 202.6, 168.0, 152.7, 139.1, 136.7, 135.7, 129.8, 129.0, 124.9, 123.9, 121.7, 119.7, 82.2, 41.9. **MS** (ESI *m/z*) 346.00 [MH^+, 100%], 368.05 [MNa^+, 25%]. HPLC analysis with Chiralcel ODH column, 80:20 *n*-hexane:2-propanol, 1 mL/min, detection at 254 nm; minor enantiomer t_R = 8.5 min, major enantiomer t_R = 9.4 min.

(*S*)-5-chloro-2-hydroxy-1-oxo-*N*-phenyl-2,3-dihydro-1*H*-indene-2-carboxamide (3c)



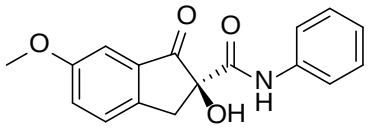
Pale yellow solid (85% yield), **mp** 182.7-183.1 °C. **[α]$_D^{23}$** = +48.9 (*c* 0.6, $CHCl_3$), *ee* 79%. **FTIR** ν_{max} (KBr)/cm^{-1} 3307, 1732, 1646, 1449, 1081, 759. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 8.70 (bs, 1H), 7.73 (d, 1H, *J*= 8.2 Hz), 7.53-7.51 (m, 3H), 7.41 (d, 1H, *J*= 7.9 Hz), 7.33-7.29 (m, 2H), 7.13 (t, 1H, *J*= 7.4 Hz), 3.84 (d, 1H, *J*= 16.9 Hz), 3.80 (bs, 1H), 3.17 (d, 1H, *J*= 16.9 Hz) **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 201.6, 167.8, 154.3, 143.3, 136.7, 132.1, 129.1, 126.7, 126.2, 124.9, 119.7, 82.8, 40.6. **MS** (ESI *m/z*) 301.97 [MH^+, 8%], 324.02 [MNa^+, 100%]. HPLC analysis with Chiralcel ODH column, 70:30 *n*-hexane:2-propanol, 1 mL/min, detection at 254 nm; minor enantiomer t_R = 9.6 min, major enantiomer t_R = 7.0 min.

(*S*)-5-bromo-2-hydroxy-1-oxo-*N*-phenyl-2,3-dihydro-1*H*-indene-2-carboxamide (3d)



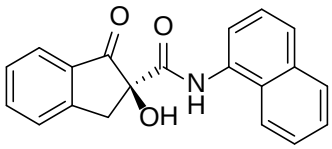
White solid (87% yield), **mp** 187.1-188.3 °C. **[α]$_D^{26}$**=+45.1 (*c* 0.9, $CHCl_3$), *ee* 78%. **FTIR** ν_{max} (KBr)/cm^{-1} 3355, 1723, 1659, 1595, 1532, 1445, 1219, 772. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 8.70 (bs, 1H), 7.71 (s, 1H), 7.66 (d, 1H, *J*= 8.2 Hz), 7.58 (d, 1H, *J*= 8.0 Hz), 7.52 (d, 2H, *J*= 8.6 Hz), 7.33-7.30 (m, 2H), 7.15-7.11 (m, 1H), 3.84 (d, 1 H, *J*= 17.1 Hz), 3.75 (bs, 1H), 3.18 (d, 1H, *J*= 17.1 Hz) **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 201.8, 167.8, 154.3, 136.8, 132.5, 132.2, 131.9, 129.7, 129.1, 126.2, 124.9, 119.7, 82.8, 40.5 **MS** (ESI *m/z*) 367.91 [MNa^+, 100%]. HPLC analysis with Chiralcel ODH column, 70:30 *n*-hexane:2-propanol, 1 mL/min, detection at 254 nm; minor enantiomer t_R =10.0 min, major enantiomer t_R =7.8 min.

(*S*)-2-hydroxy-6-methoxy-1-oxo-*N*-phenyl-2,3-dihydro-1*H*-indene-2-carboxamide (3e)



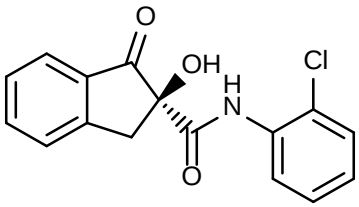
White solid (84% yield, 60% after crystallization), **mp** 146.0-147.2 °C. **[α]$_D^{20}$**= -31.3 (*c* 0.9, $CHCl_3$), *ee* 98%. **FTIR** ν_{max} (KBr)/cm^{-1} 3343, 1717, 1661, 1600, 1532, 1494, 1445, 1281, 1241, 1026, 754. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 8.79 (bs, 1H), 7.48 (d, 2H, *J*= 7.7 Hz), 7.36 (d, 1H, *J*= 8.4 Hz), 7.29-7.27 (m, 1H), 7.25-7.23 (m, 2H) 7.15 (d, 1H, *J*= 2.5 Hz), 7.09 (t, 1H, *J*= 7.4 Hz), 4.40 (bs, 1H), 3.80 (s, 3H), 3.75 (d, 1H, *J*= 16.6 Hz), 3.08 (d, 1H, *J*= 16.5 Hz). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 203.1, 168.5, 159.7, 146.1, 136.9, 134.8, 128.9, 127.1, 125.9, 124.7, 119.7, 106.1, 83.2, 55.6, 40.2, **MS** (ESI *m/z*) 297.95 [MH^+, 17%], 320.07 [MNa^+, 100%], 336.07 [MK^+, 8%]. HPLC analysis with Chiralcel ODH column, 70:30 *n*-hexane:2-propanol, 1 mL/min, detection at 254 nm; minor enantiomer t_R = 10.9 min, major enantiomer t_R = 7.5 min.

(*S*)-2-hydroxy-*N*-(naphthalen-1-yl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxamide (3f)



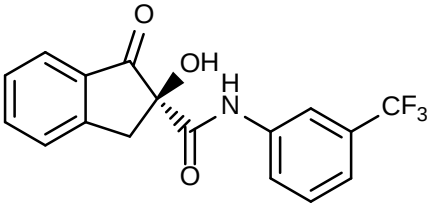
Pale yellow solid (82% yield), **mp** 166.2-167.5 °C. **[α]$_D^{21}$**=+28.9 (*c* 0.6, $CHCl_3$), *ee* 74%. **FTIR** ν_{max} (KBr)/cm^{-1} 3368, 1722, 1661, 1538, 1532, 1500, 1219, 772. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 9.23 (bs, 1H), 7.98 (d, 1H, *J*= 7.5 Hz), 7.89-7.81 (m, 3H), 7.68-7.66 (m, 2H), 7.57-7.48 (m, 3H), 7.44-7.40 (m, 2H), 4.09 (bs, 1H), 3.94 (d, 1H, *J*= 16.7 Hz), 3.26 (d, 1H, *J*= 16.7 Hz) **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 203.0, 168.6, 153.0, 136.5, 134.0, 133.7, 131.3, 128.7, 128.2, 126.53, 126.48, 126.42, 126.0, 125.8, 125.6, 125.3, 120.2, 119.6, 83.1, 40.8 **MS** (ESI *m/z*) 318.10 [MH^+, 40%], 340.09 [MNa^+, 100%], 355.90 [MK^+, 25%]. HPLC analysis with Chiralpak ASH column, 70:30 *n*-hexane:2-propanol, 0.8 mL/min, detection at 254 nm; minor enantiomer t_R = 12.4 min, major enantiomer t_R =16.4 min.

(*S*)-*N*-(2-chlorophenyl)-2-hydroxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxamide (3g)



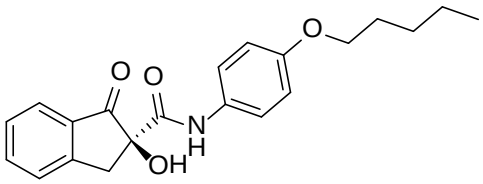
White solid (76% yield, 48% after crystallization), **mp** 90.3-93.0 °C. **[α]$_D^{21}$** = +22.8 (*c* 0.6, $CHCl_3$), *ee* 99%. **FTIR** ν_{max} (KBr)/cm^{-1} 3352, 1723, 1685, 1594, 1529, 1443, 1304, 1214, 751. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 9.31 (bs, 1H), 8.31 (dd, 1H, J_1= 8.2, J_2=1.3 Hz), 7.84 (d, 1H, *J*= 7.8 Hz), 7.73-7.69 (m, 1H), 7.54 (d, 1H, *J*= 7.8 Hz), 7.48-7.44 (m, 1H), 7.38 (dd, 1H, J_1= 8.1, J_2=1.3 Hz), 7.23-7.21 (m, 1H), 7.08-7.03 (m, 1H), 3.86 (d, 1H, *J*= 16.8 Hz), 3.78 (bs, 1H), 3.27 (d, 1H, *J*= 16.8 Hz) **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 202.6, 168.6, 152.7, 136.5, 133.7, 129.1, 128.2, 127.7, 126.4, 125.3, 125.1, 123.2, 121.0, 82.9, 40.8 **MS** (ESI *m/z*) 302.10 [MH^+, 13%], 324.02 [MNa^+, 100%], 340.03 [MK^+, 5%]. HPLC analysis with Chiralcel ODH column, 80:20 *n*-hexane:2-propanol, 1 mL/min, detection at 254 nm; minor enantiomer t_R = 6.4 min, major enantiomer t_R = 7.4 min.

(*S*)-2-hydroxy-1-oxo-*N*-(3-(trifluoromethyl)phenyl)-2,3-dihydro-1*H*-indene-2-carboxamide (3h)



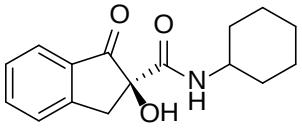
Pale yellow solid (88% yield), **mp** 138.4-139.8 °C. **[α]$_D^{26}$**=+9.7 (*c* 0.5, $CHCl_3$), *ee* 56%. **FTIR** ν_{max} (KBr)/cm^{-1} 3333, 1719, 1682, 1603, 1542, 1449, 1333, 1167, 1125, 772, 698. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 8.93 (bs, 1H), 7.93 (s, 1H), 7.80 (d, 1H, *J*= 7.7 Hz), 7.72-7.68 (m, 1H), 7.64 (d, 1H, *J*= 7.9 Hz), 7.52 (d, 1H, *J*= 7.7 Hz), 7.46-7.41 (m, 1H), 7.39-7.35 (m, 2H), 3.95 (bs, 1H), 3.88 (d, 1H, *J*= 16.7 Hz), 3.21 (d, 1H, *J*= 16.7 Hz) **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 202.8, 168.6, 152.9, 137.4, 136.7, 133.5, 131.5 (q, *J*=32 Hz), 129.5, 128.3, 126.4, 125.3, 122.6, 121.3 (d, *J*=36 Hz), 116.5 (d, *J*=36 Hz), 82.9, 40.8 **MS** (ESI *m/z*) 336.06 [MH^+, 5%], 358.04 [MNa^+, 100%]. HPLC analysis with Chiralpak ASH column, 70:30 *n*-hexane:2-propanol, 0.8 mL/min, detection at 254 nm; minor enantiomer t_R = 6.5 min, major enantiomer t_R = 8.1 min.

(*S*)-2-hydroxy-1-oxo-*N*-(4-(pentyloxy)phenyl)-2,3-dihydro-1*H*-indene-2-carboxamide (3i)



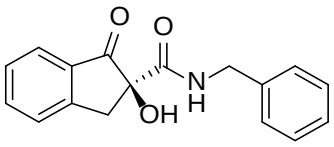
White solid (89% yield), **mp** 125.6-127.0 °C. **[α]$_D^{23}$**=+2.8 (*c* 0.6, $CHCl_3$), *ee* 76%. **FTIR** ν_{max} (KBr)/cm^{-1} 3325, 2930, 1721, 1645, 1512, 1220, 828, 772. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 8.70 (bs, 1H), 7.74 (d, 1H, *J*= 7.7 Hz), 7.66-7.62 (m, 1H), 7.46 (d, 1H, *J*= 7.7 Hz), 7.40-7.35 (m, 3H), 6.77 (d, 2H, J= 9.0 Hz), 4.35 (bs, 1H), 3.88 (t, 2H, *J*= 6.6 Hz), 3.82 (d, 1H, *J*= 16.8 Hz), 3.13 (d, 1H, *J*= 16.8 Hz), 1.79-1.73 (m, 2H), 1.44-1.34 (m, 4H), 0.92 (t, 3H, *J*= 7.0 Hz). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 203.4, 168.1, 156.2, 153.2, 136.4, 133.7, 129.9, 128.0, 126.4, 125.1, 121.3, 114.7, 82.5, 68.2, 40.8, 28.9, 28.1, 22.4, 14.0. **MS** (ESI *m/z*) 354.24 [MH^+, 100%], 376.17 [MNa^+, 10%]. HPLC analysis with Chiralcel ODH column, 70:30 *n*-hexane:2-propanol, 1 mL/min, detection at 254 nm; minor enantiomer t_R = 7.3 min, major enantiomer t_R = 8.7 min.

(S)-*N*-cyclohexyl-2-hydroxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxamide (3j)



White wax (37% yield). **[α]$_D^{30}$**= -7.2 (*c* 0.7, $CHCl_3$), *ee* 40%. **FTIR** ν_{max} (KBr)/cm^{-1} 3353, 2930, 2855, 1723, 1646, 1530, 1465, 1215, 752. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.76 (d, 1H, *J*= 7.7 Hz), 7.64 (t, 1H, *J*= 7.0 Hz), 7.47 (d, 1H, *J*= 7.7 Hz), 7.40 (t, 1H, *J*= 7.5 Hz), 6.69 (d, 1H, *J*= 6.6 Hz), 3.79 (bs, 1H), 3.72 (d, 1H, *J*= 16.8 Hz), 3.68-3.63 (m, 1H), 3.10 (d, 1H, *J*= 16.8 Hz), 1.89-1.86 (m, 2H), 1.70-1.57 (m, 4H), 1.36-1.14 (m, 4H). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 203.4, 169.2, 152.9, 136.2, 133.9, 128.0, 126.3, 125.1, 82.1, 48.4, 40.7, 32.83, 32.77, 29.7, 25.4, 24.7. **MS** (ESI *m/z*) 274.13 [MH^+, 97%], 296.06 [MNa^+, 100%]. HPLC analysis with Chiralcel ODH column, 80:20 *n*-hexane:2-propanol, 1 mL/min, detection at 254 nm; minor enantiomer t_R = 5.3 min, major enantiomer t_R = 6.2 min.

(*S*)-*N*-benzyl-2-hydroxy-1-oxo-2,3-dihydro-1*H*-indene-2-carboxamide (3k)



Yellow wax (50% yield). **[α]$_D^{23}$**= -4.1 (*c* 0.6, $CHCl_3$), *ee* 29%. **FTIR** ν_{max} (KBr)/cm^{-1} 3394, 2924, 1722, 1653, 1608, 1528, 1455, 1218, 928, 772, 699. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.77 (d, 1H, *J*= 7.6 Hz), 7.65 (t, 1H, *J*= 7.5 Hz), 7.47 (d, 1H, *J*= 7.6 Hz), 7.40 (t, 1H, *J*= 7.5 Hz), 7.35-7.29 (m, 2H), 7.27-7.25 (m, 3H), 7.18 (bs, 1H), 4.41 (d, 2H, *J*= 5.9Hz), 3.83 (bs, 1H), 3.77 (d, 1H, *J*= 16.8 Hz), 3.13 (d, 1H, *J*= 16.8 Hz). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 203.2, 170.3, 153.0, 137.6, 136.3, 133.8, 128.7, 128.1, 127.7, 127.6, 126.4, 125.2, 82.2, 43.4, 40.7 **MS** (ESI *m/z*) 282.00 [MH^+, 10%], 304.05 [MNa^+, 100%]. HPLC analysis with Chiralcel ODH column, 80:20 *n*-hexane:2-propanol, 1 mL/min, detection at 254 nm; minor enantiomer t_R = 10.1 min, major enantiomer t_R = 12.1 min.

X-Ray Data for the Absolute Configuration Assignment of Compound 3b

X-ray diffraction quality single crystals of **3b** were obtained by slow evaporation of a solution of **3b** in *n*-pentane/$CHCl_3$ mixture performed at room temperature.

A suitable crystal of **3b** was selected and glued on a glass fiber and measured at room temperature with a Rigaku AFC7S diffractometer equipped with a Mercury CCD detector using Mo$K\alpha$ radiation. Data reduction was performed with the crystallographic package CrystalClear.[5] Data have been corrected for Lorentz, polarization and absorption. The structures were solved by direct methods using the program SIR2002[6] and refined by means of full matrix least-squares based on F^2 using the program SHELXL97. [7]

All non-hydrogen atoms were refined anisotropically, hydrogen atoms were positioned geometrically and included in structure factors calculations but not refined.

A total of 190 refinable parameters were finally considered, final disagreement indices are R = 0.079 (2339 reflections $F^2>2\sigma F^2$), $_wR2$= 0.199 (all 3466 independent. reflections).

Flack parameter is 0.018(19).

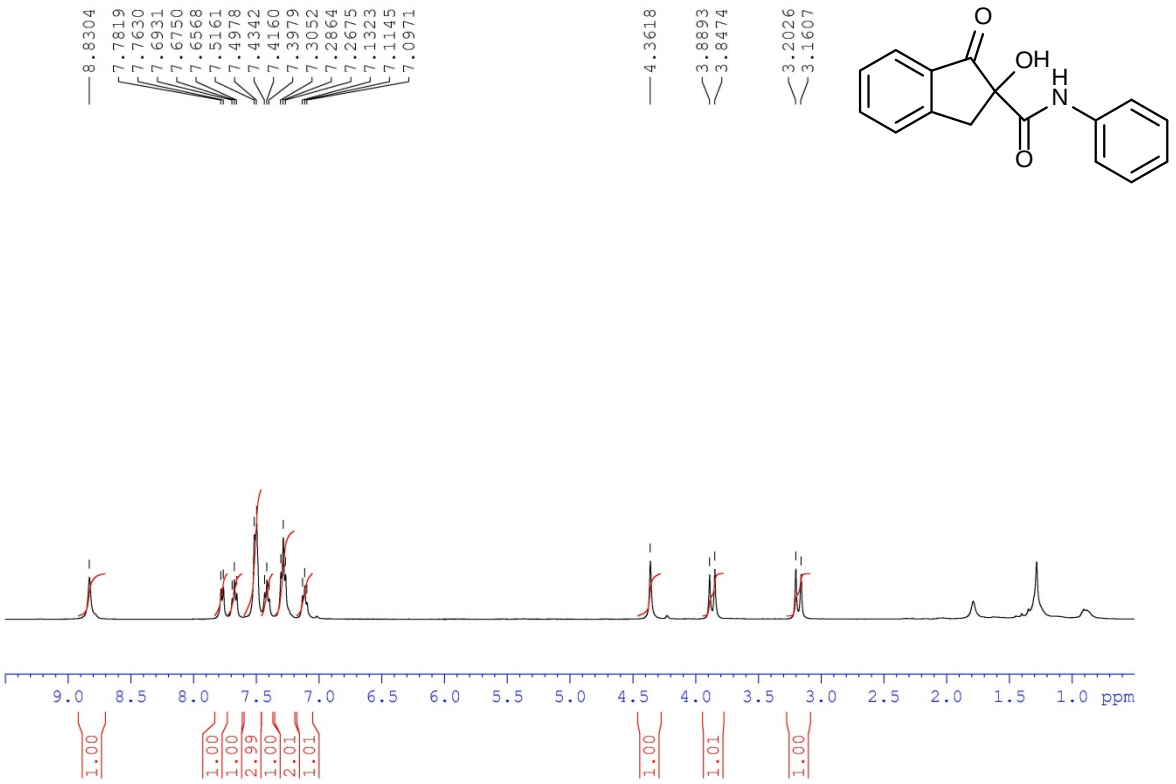
ORTEP plot is obtained by means of the program ORTEP32.[8]

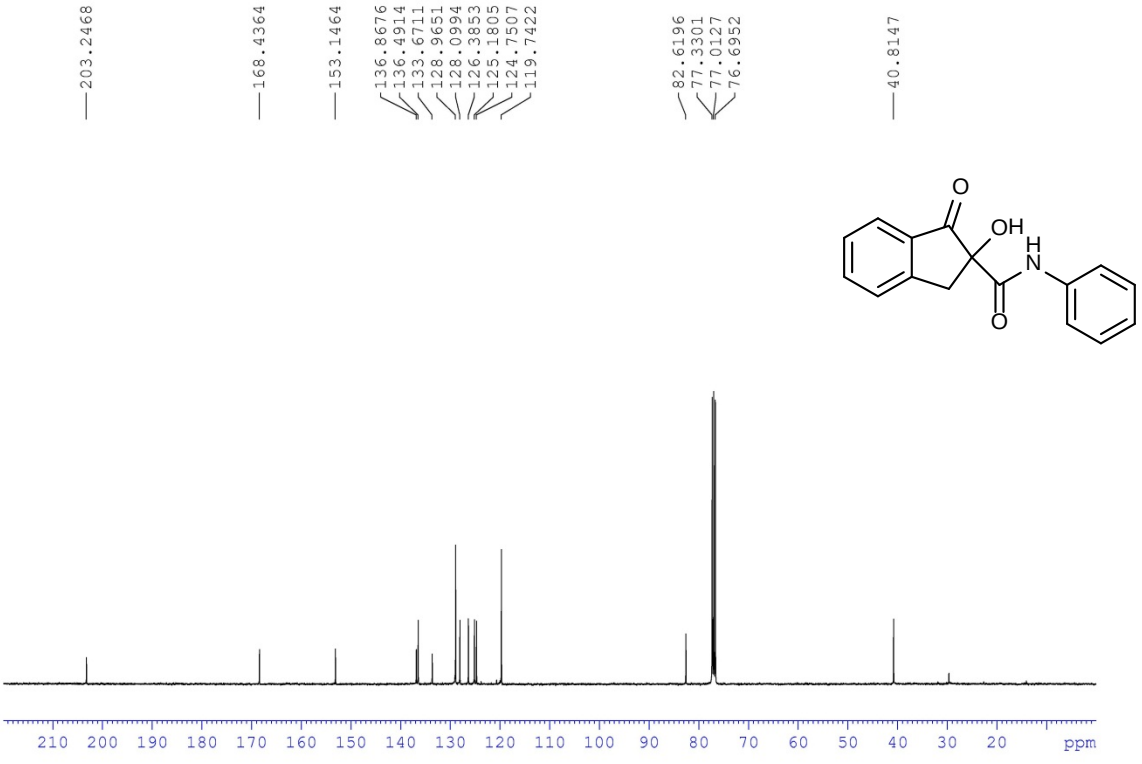
Crystal data:

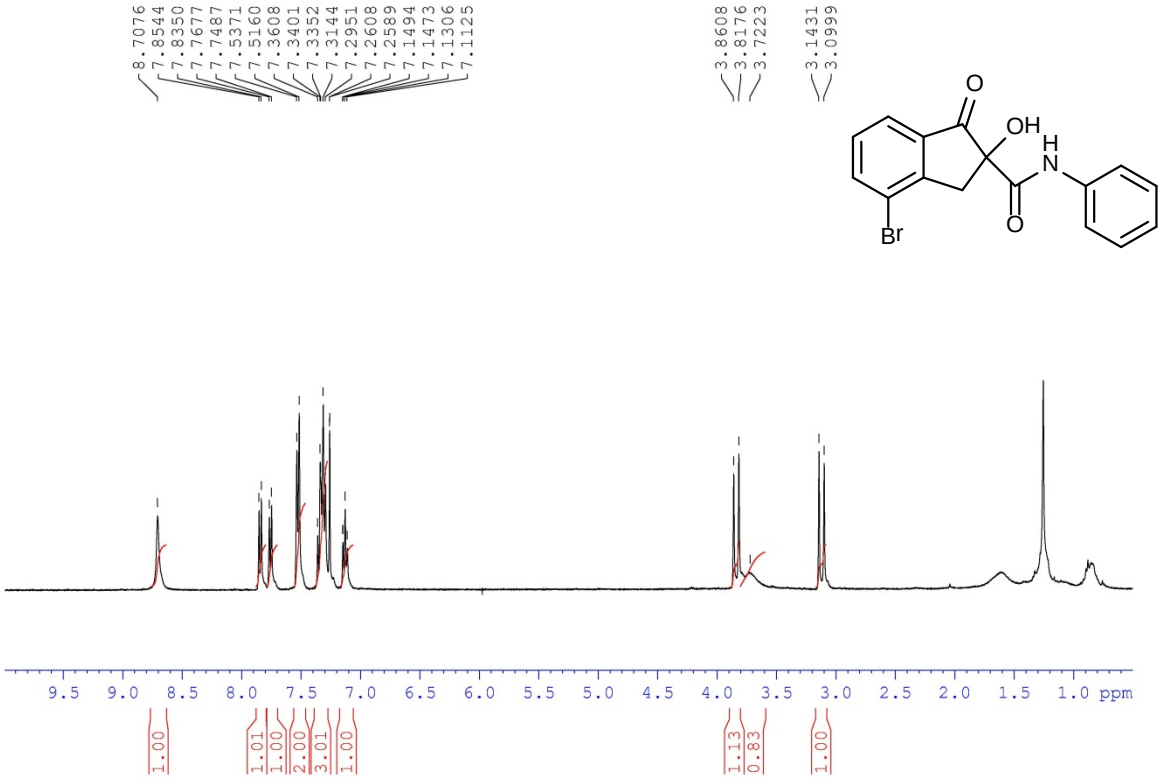
$C_{16}H_{12}BrNO_3$, orthorhombic, space group $P2_12_12_1$, Z= 4, a = 9.801(3)Å, b = 10.969(3) Å, c = 14.070(4) Å, V=1512.6(8)Å^3, D_x = 1.520 g cm^{-3}, μ_{calc} = 2.73 mm^{-1}.

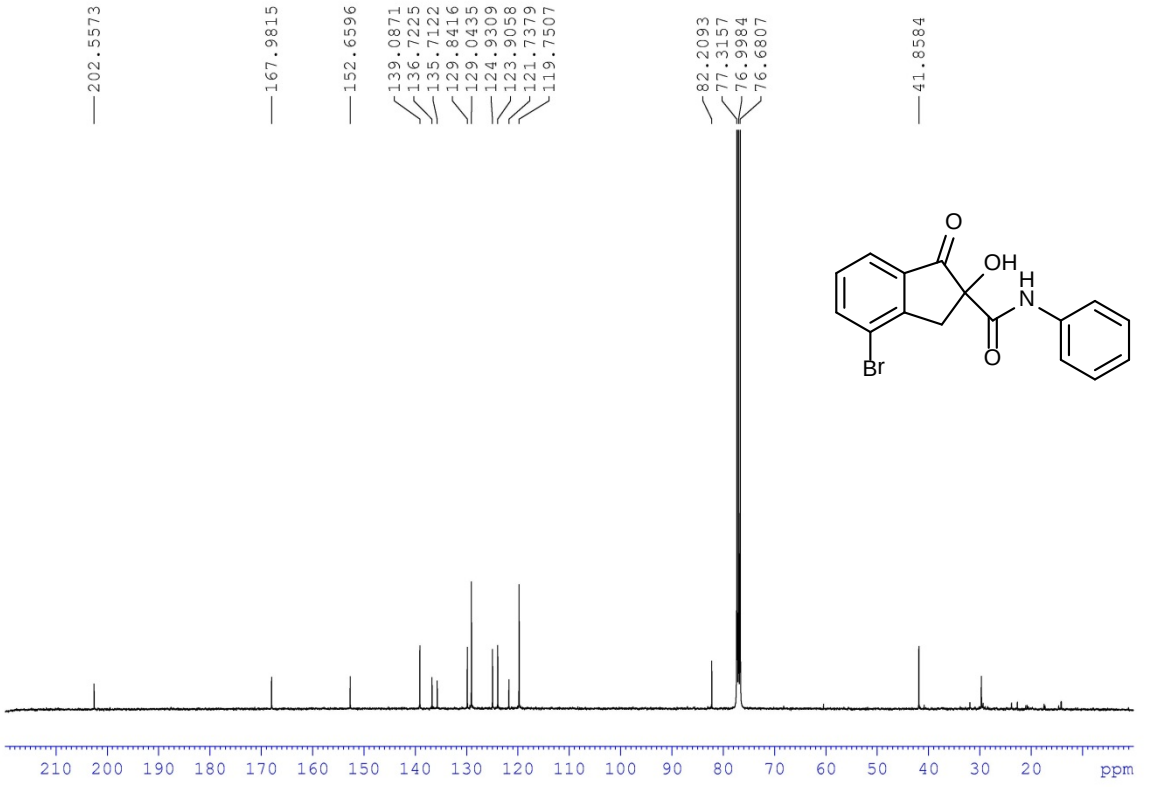
[5] CrystalClear, Crystal Structure Analysis Package, Rigaku-Molecular Structure Corp.
[6] M. C. Burla, M. Camalli, B. Carrozzini, G. Cascarano, C. Giacovazzo, G. Polidori, R. Spagna *J. Appl. Cryst.* **2001**, *34*, 523.
[7] G. M. Sheldrick, *Acta Cryst*. **2008**, *A64*, 112.
[8] L. J. Farrugia, *J. Appl. Cryst.* **1997**, *30*, 565

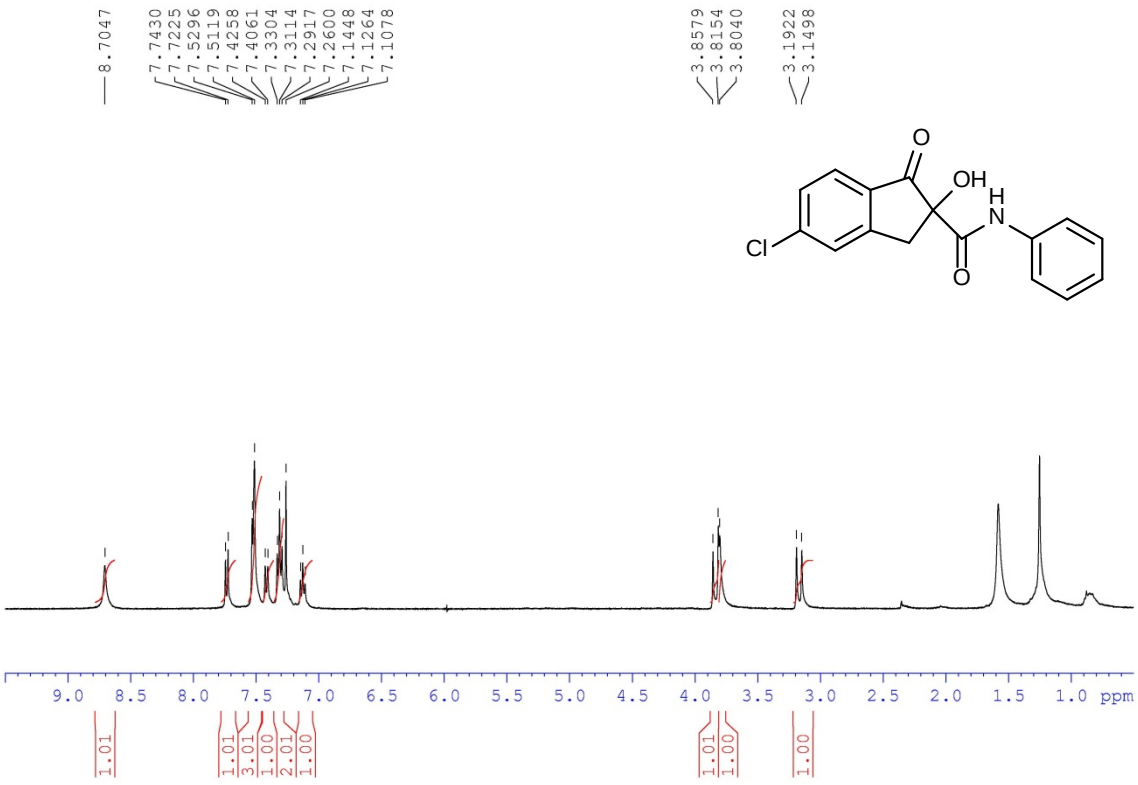
NMR Spectra

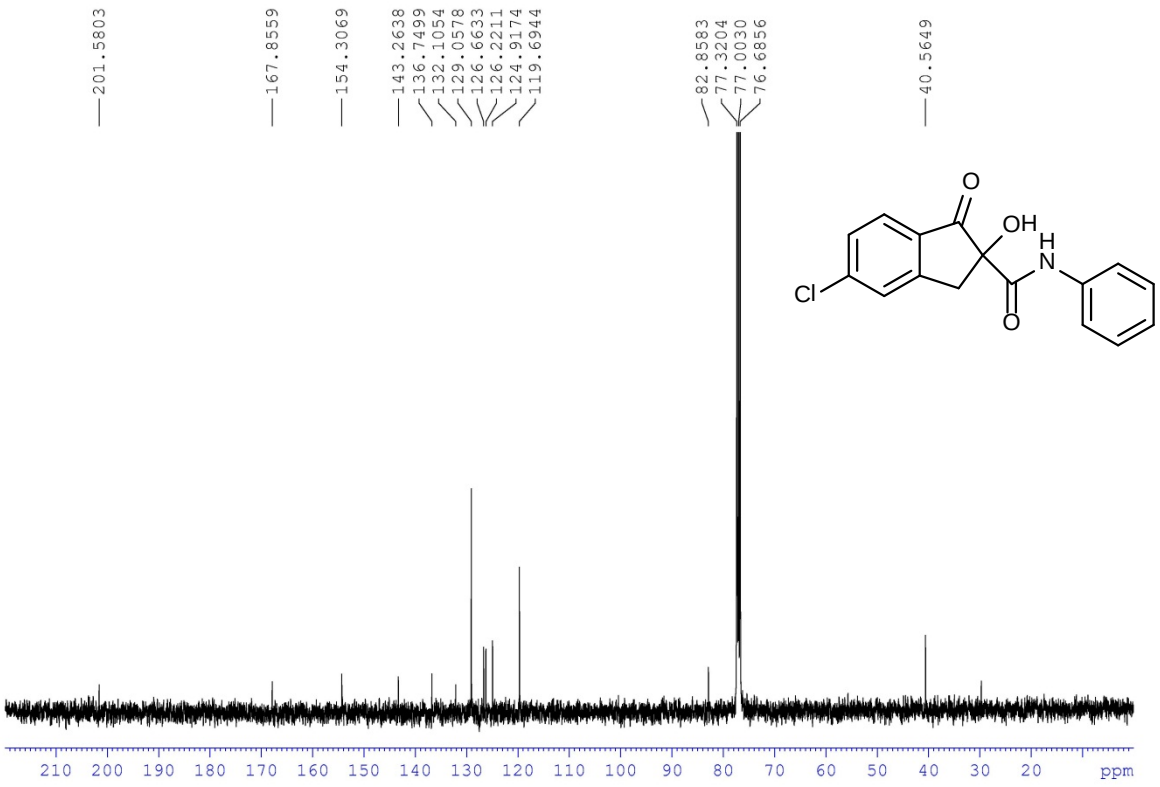


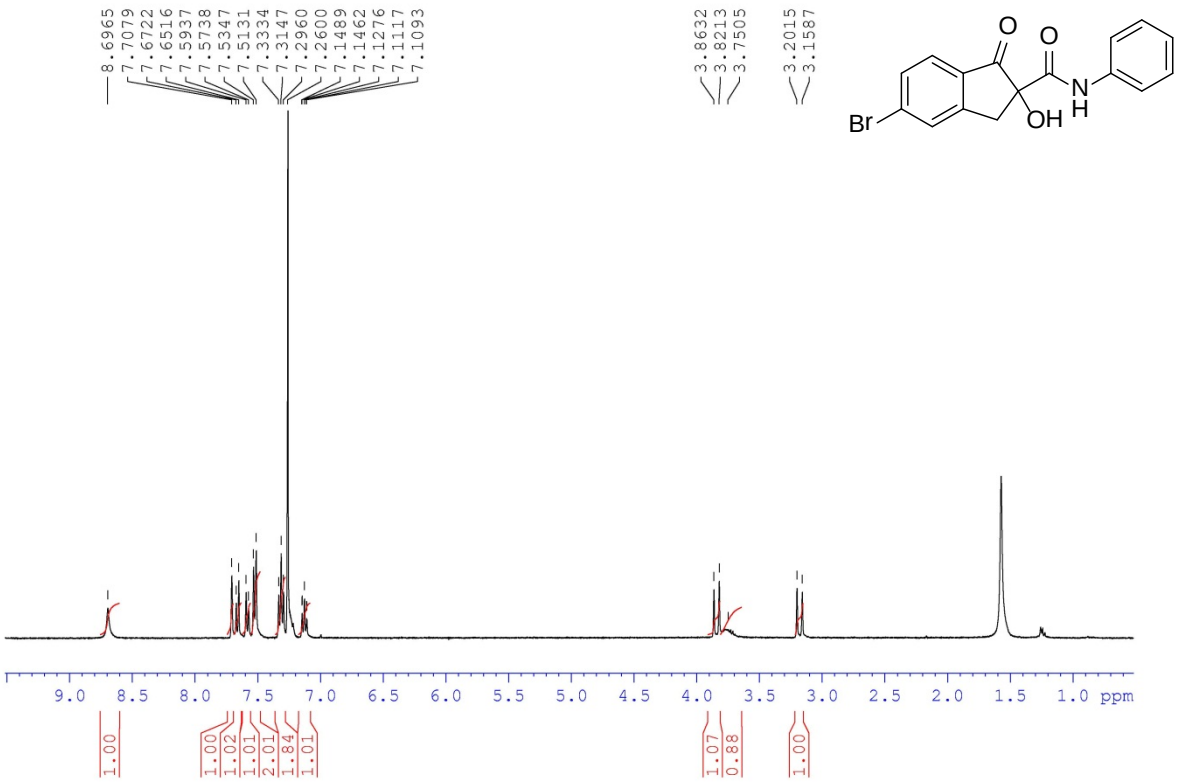


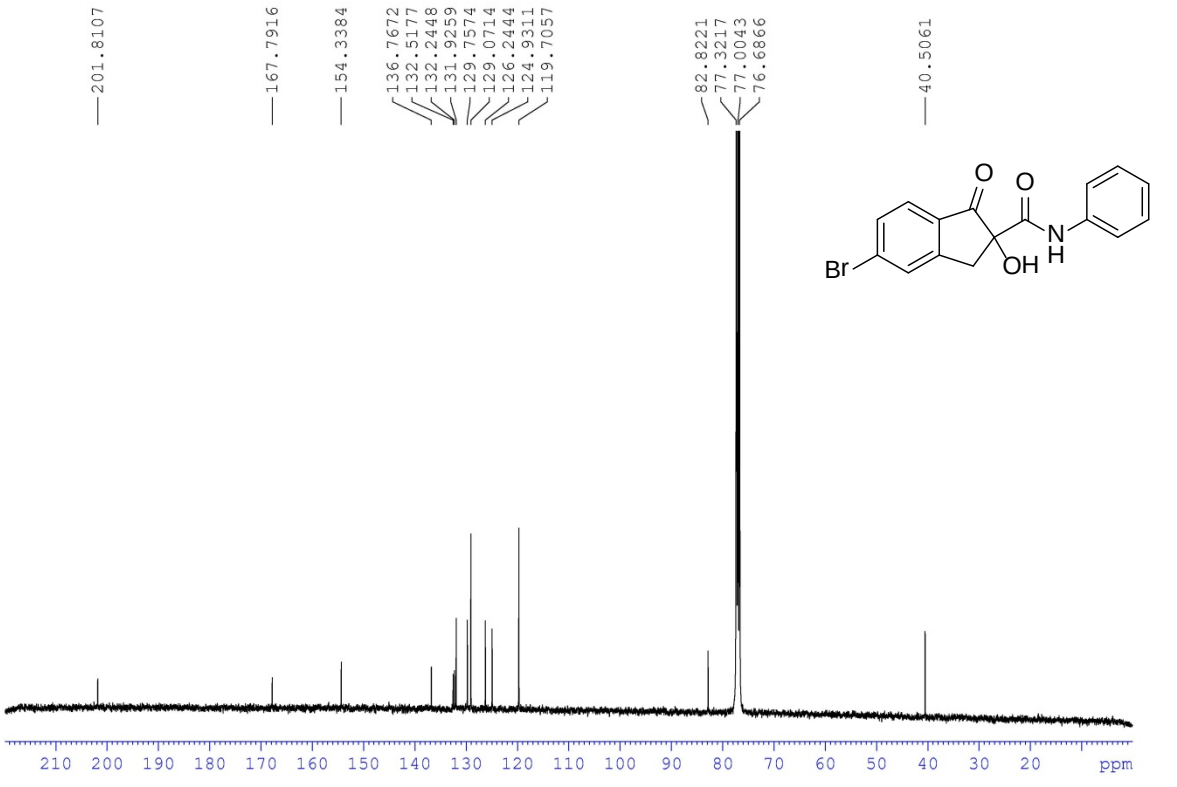


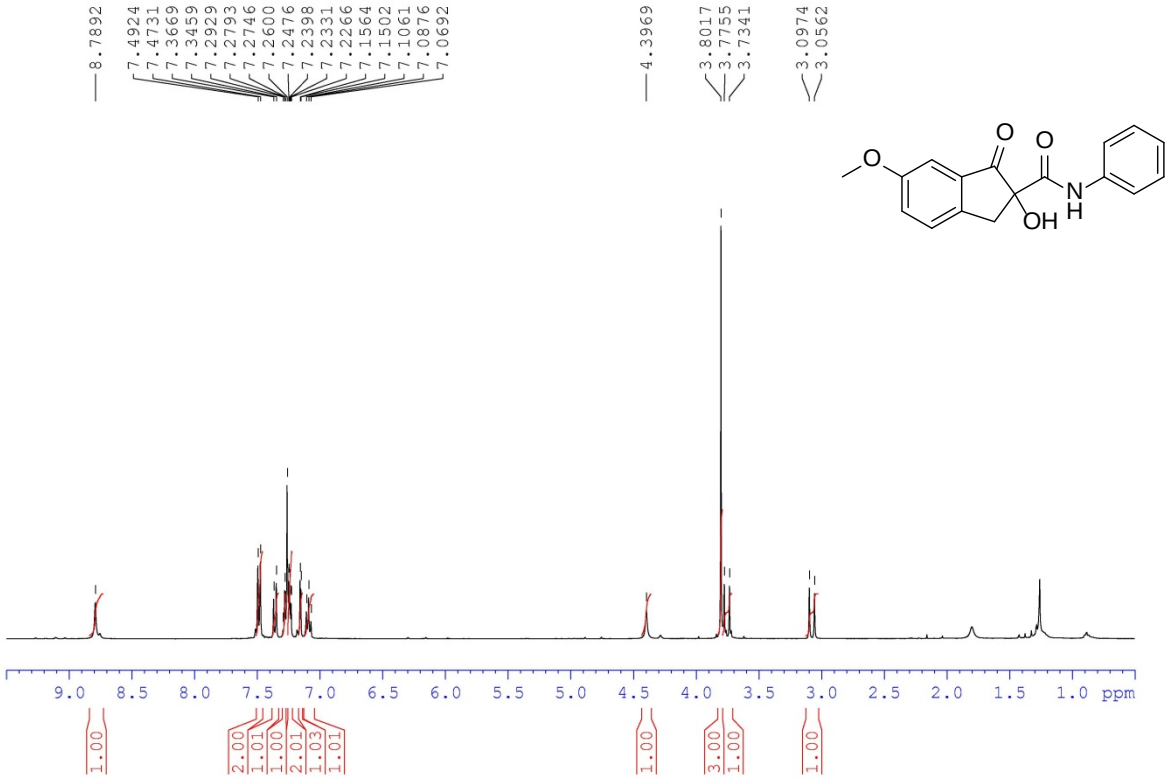


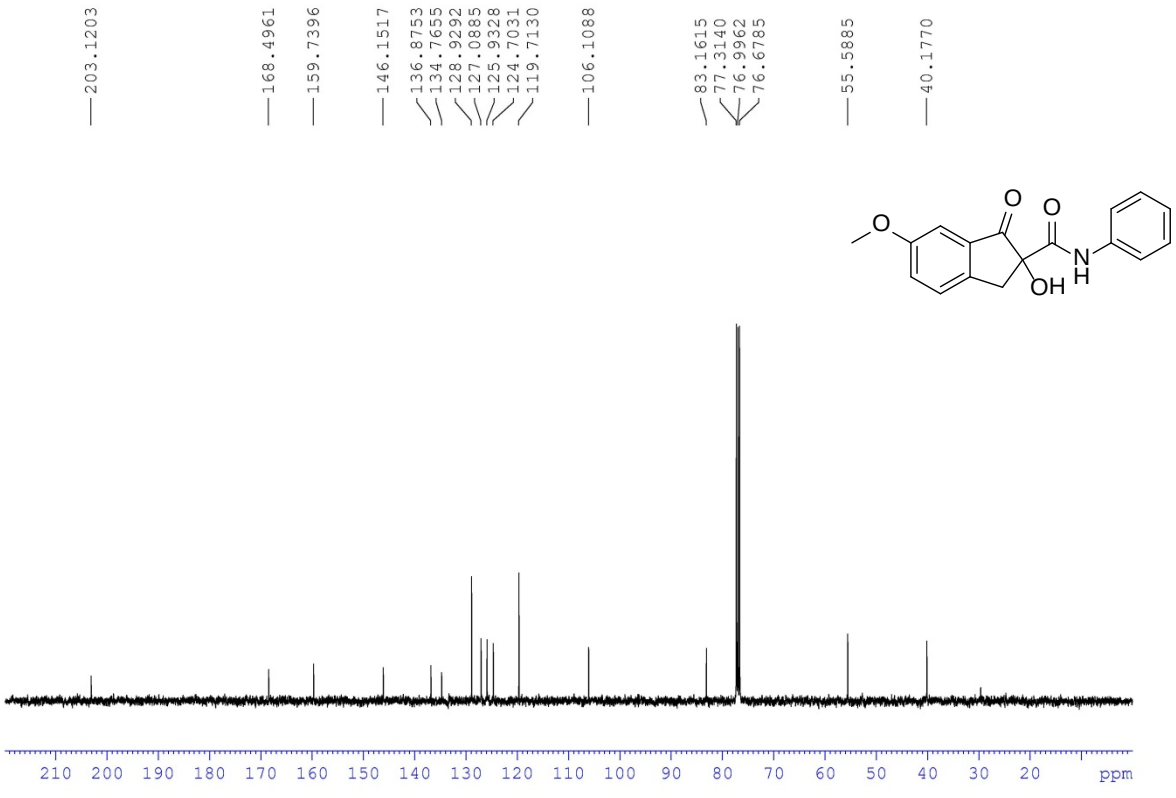


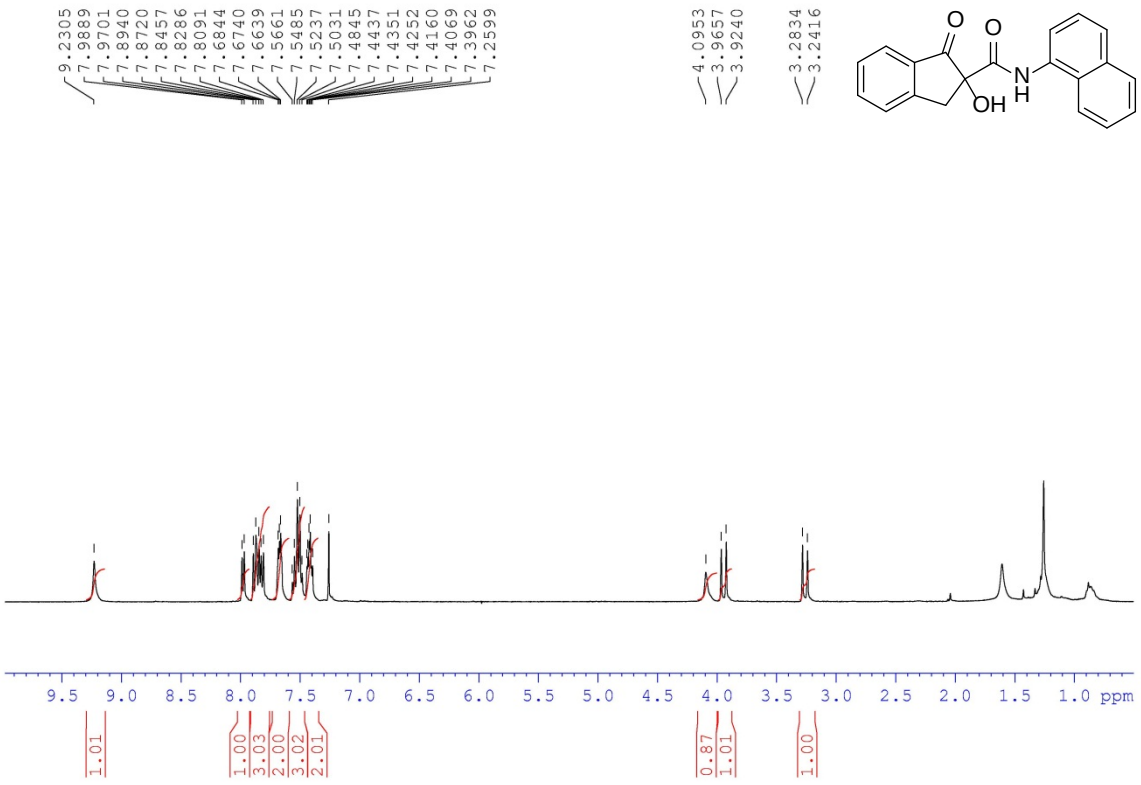


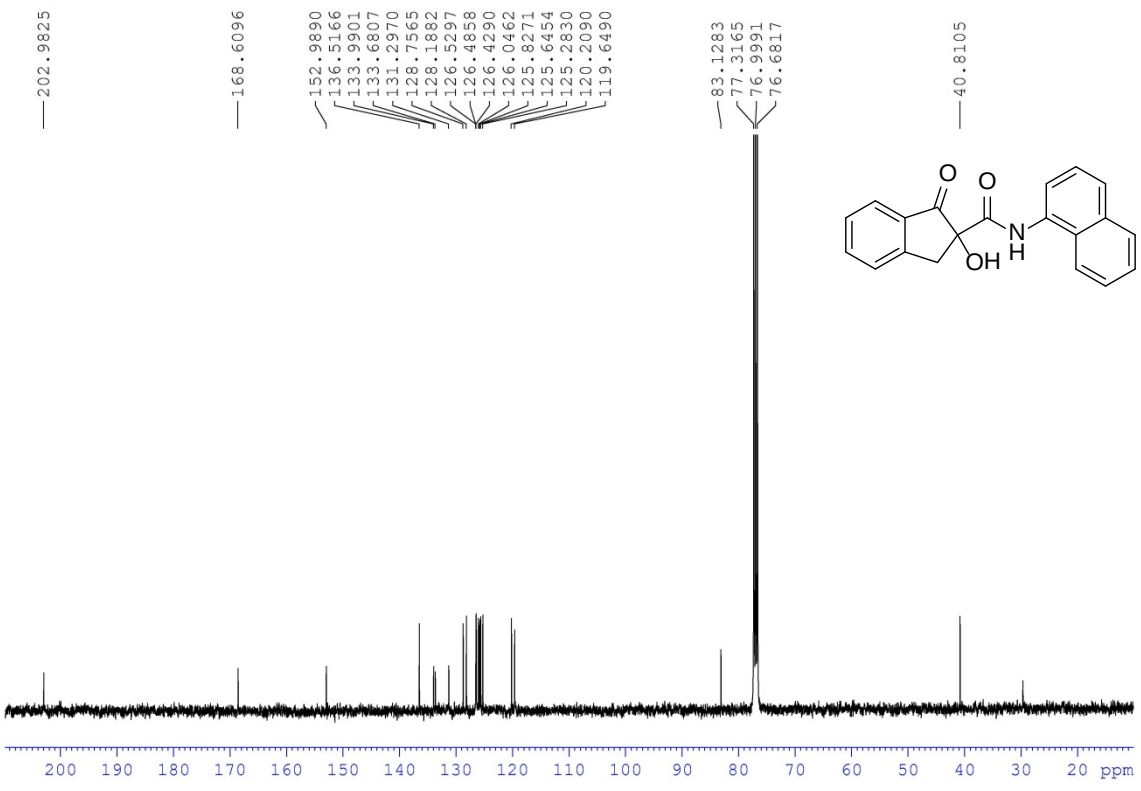


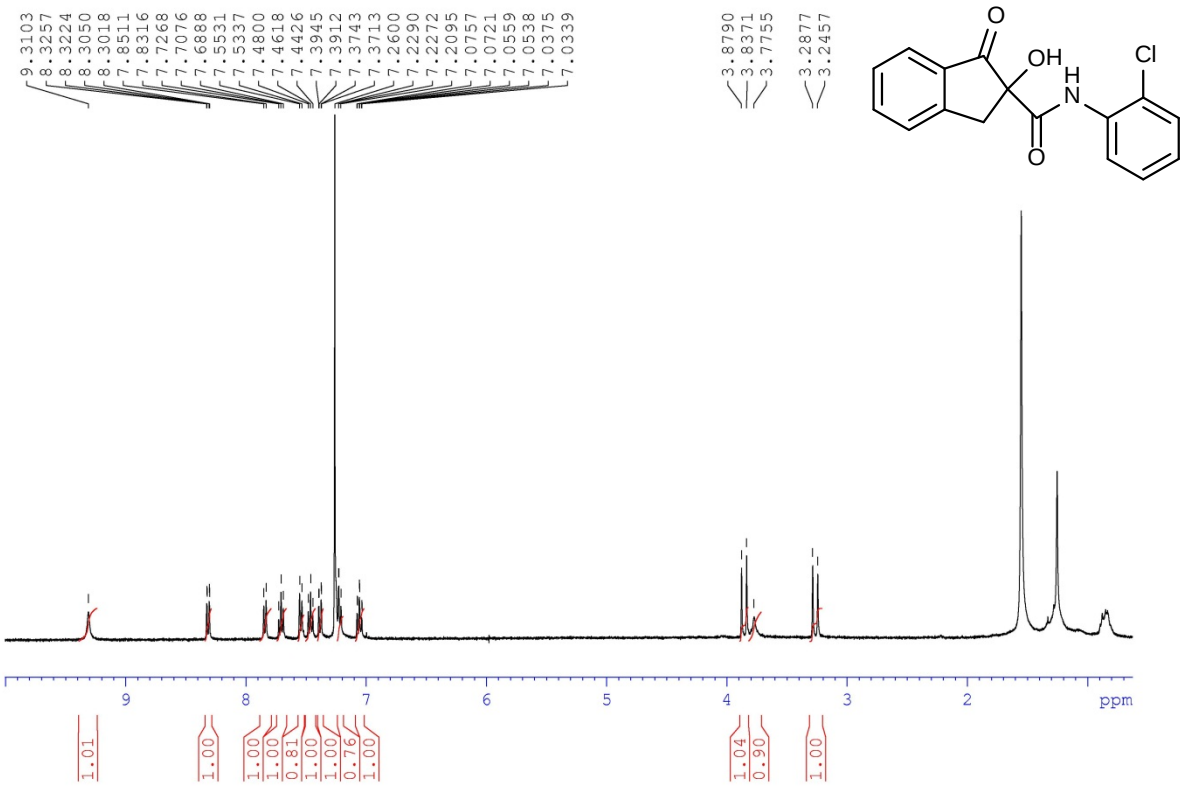


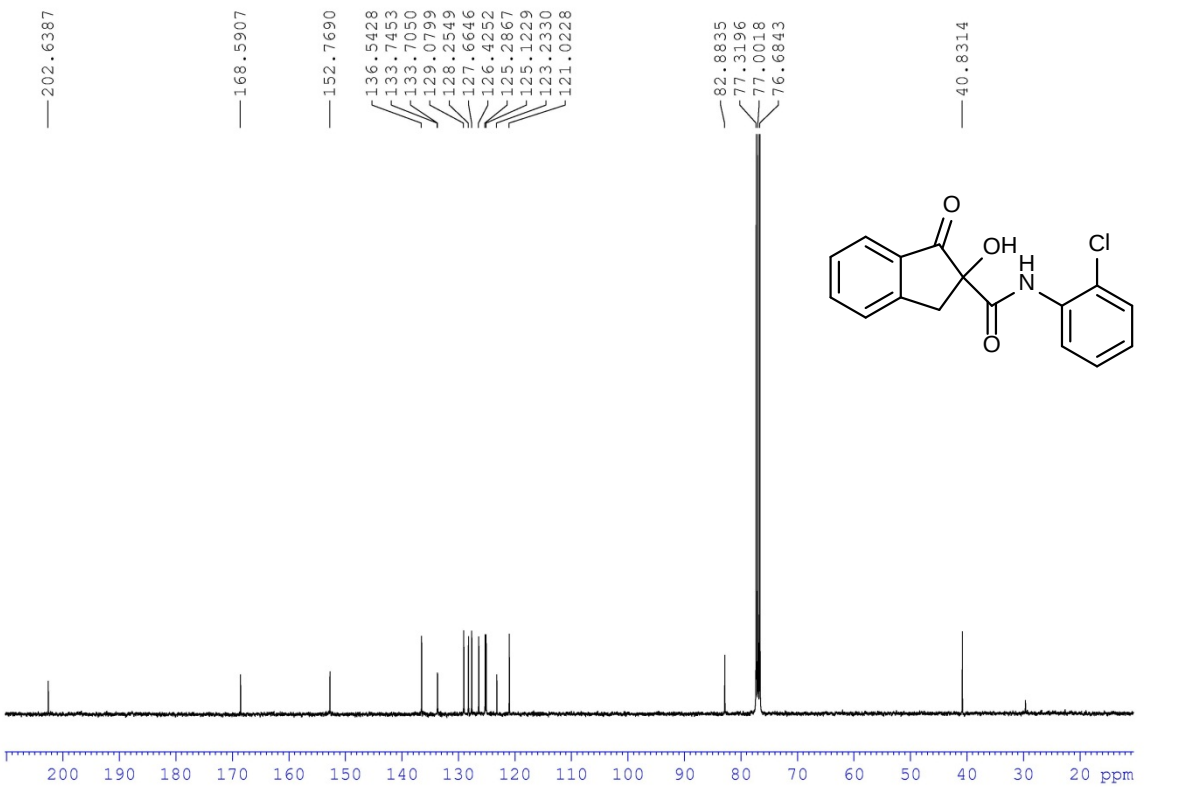


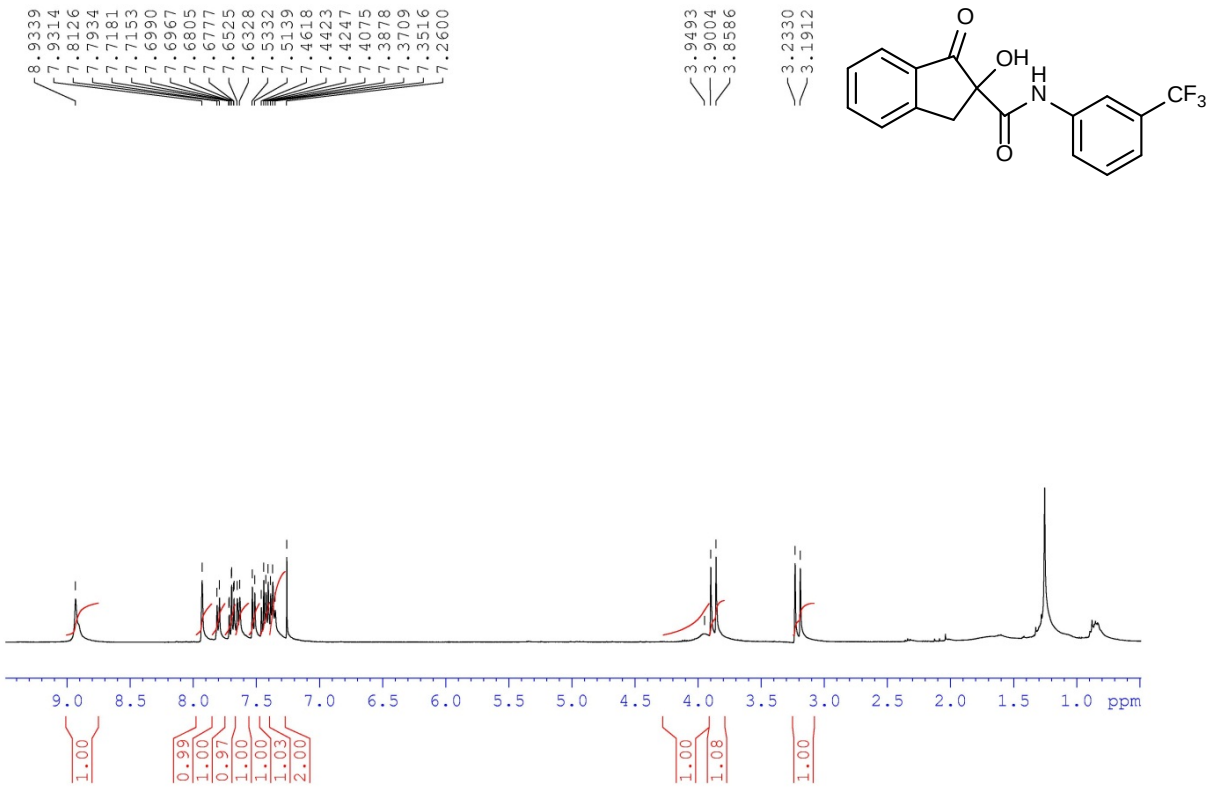


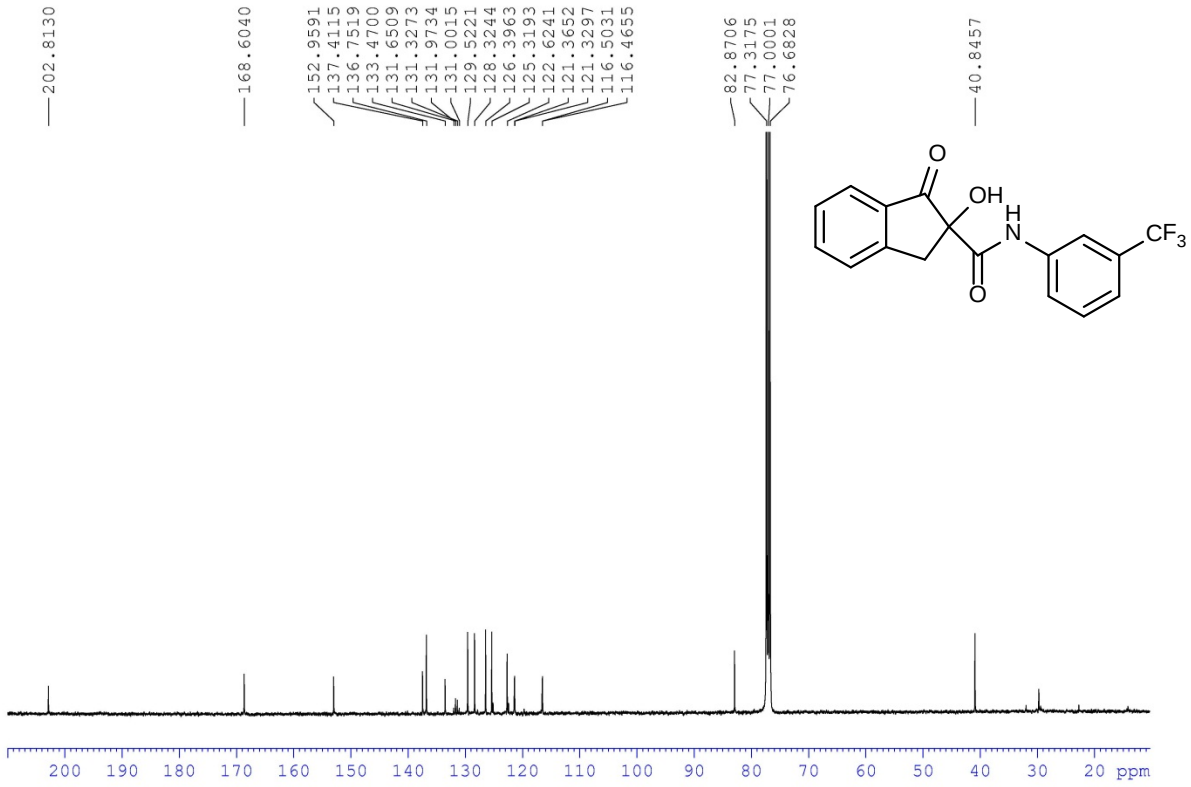


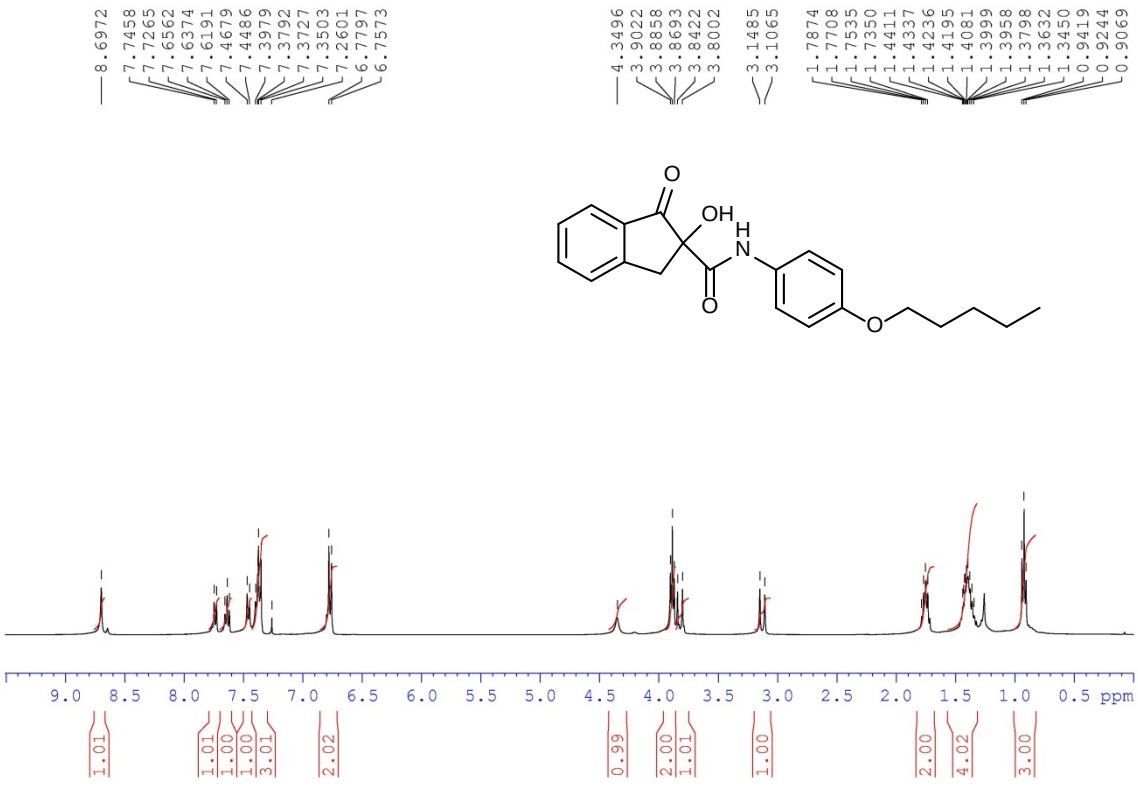


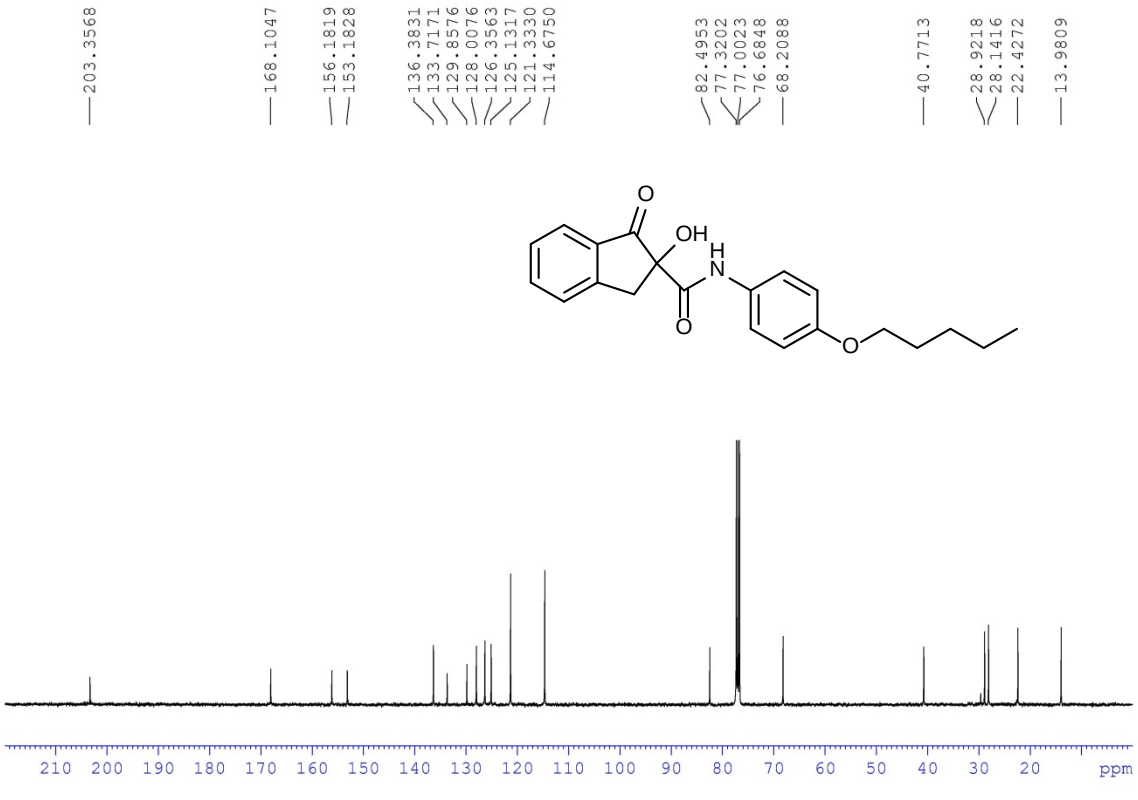


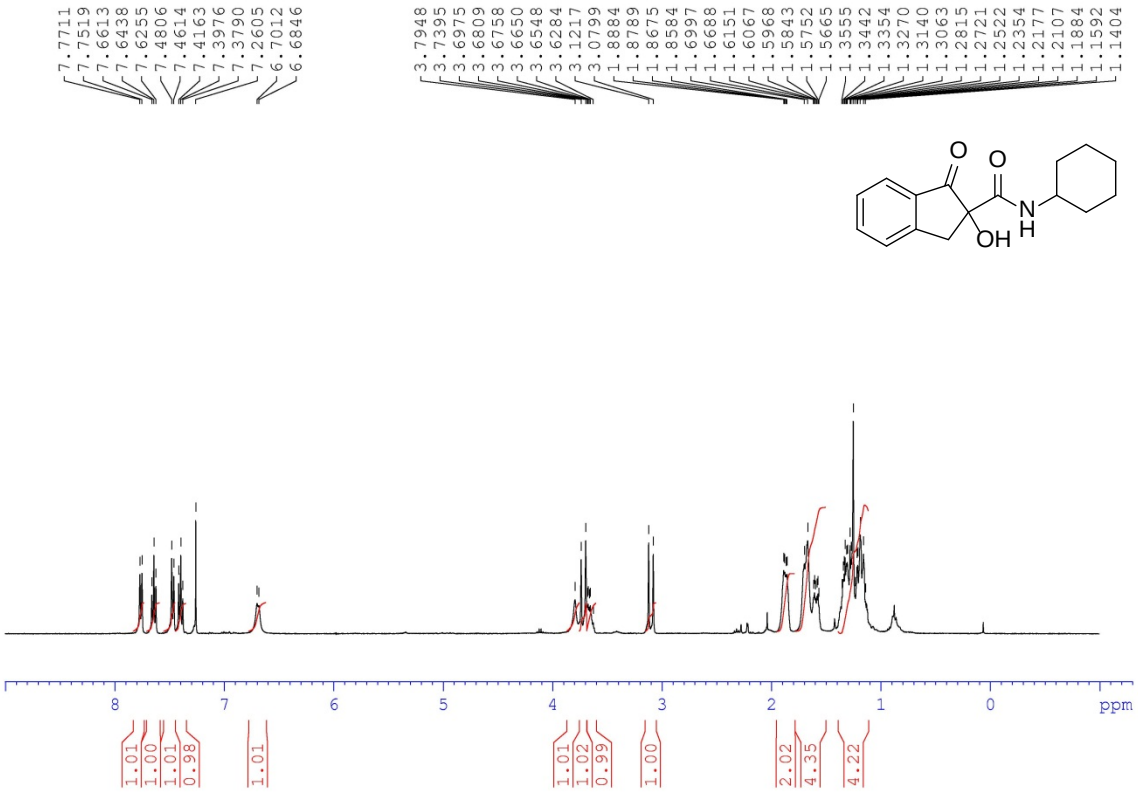


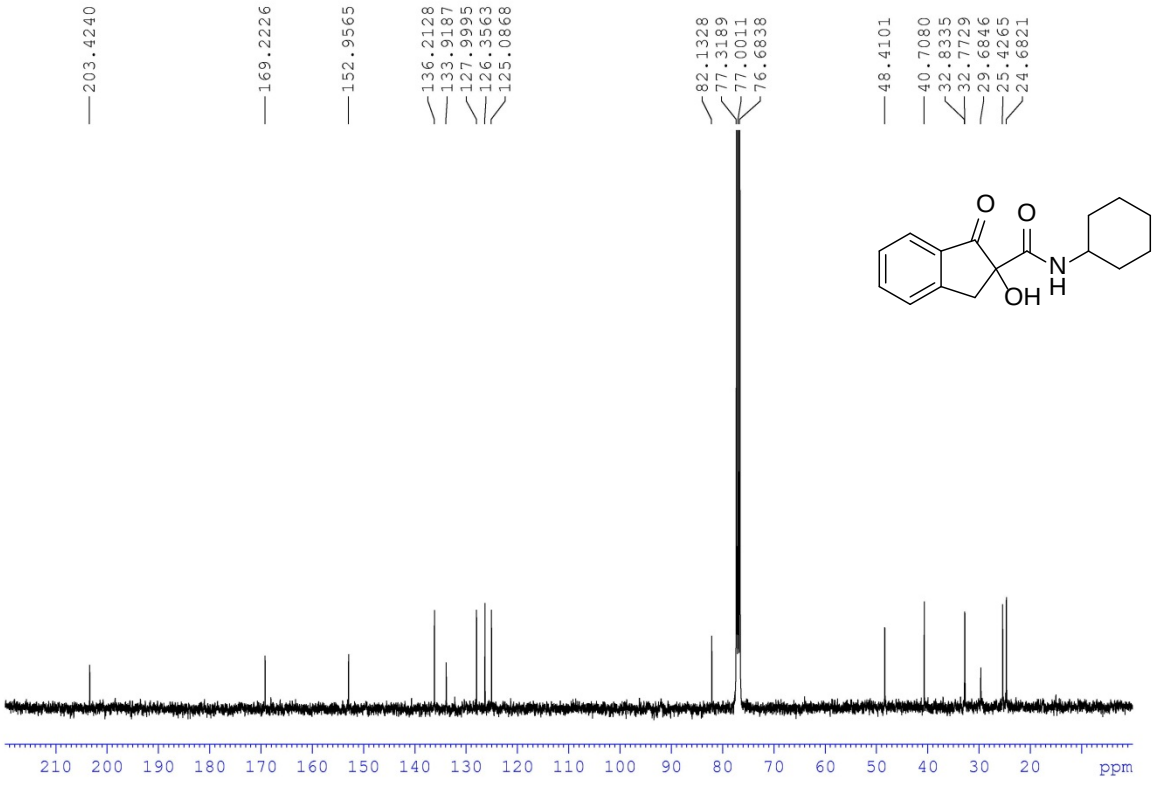


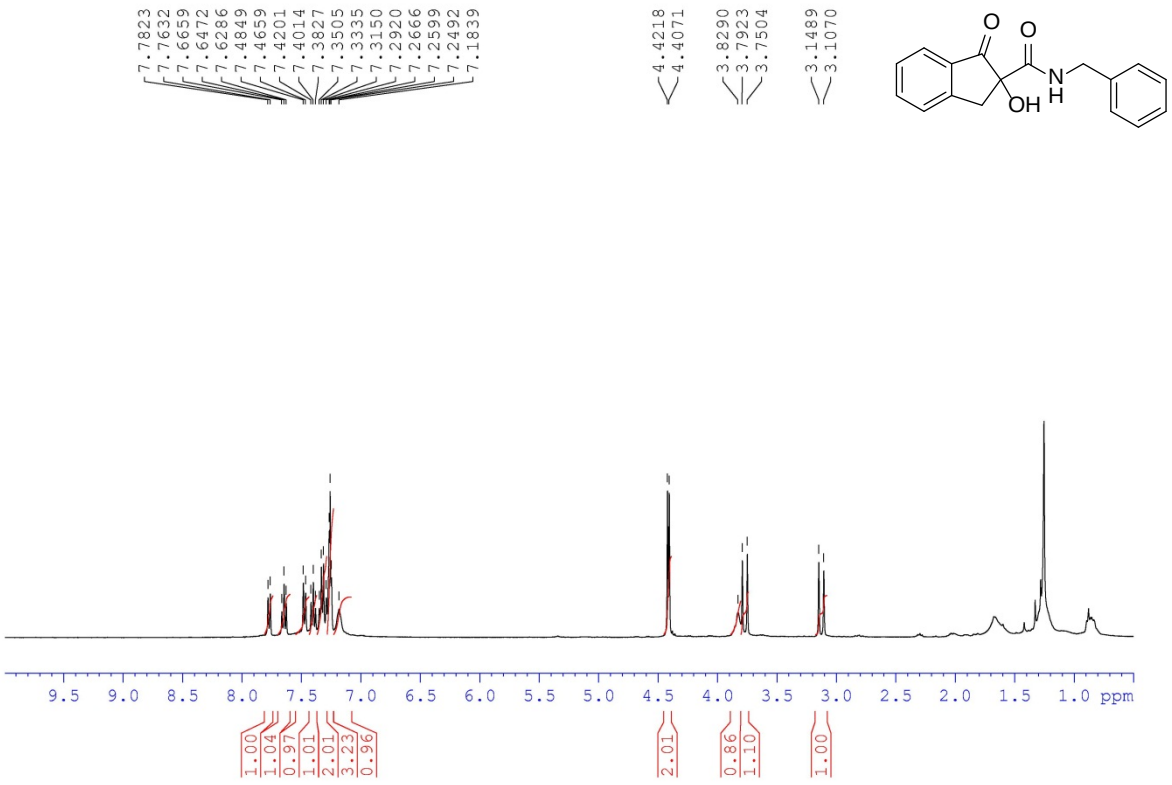


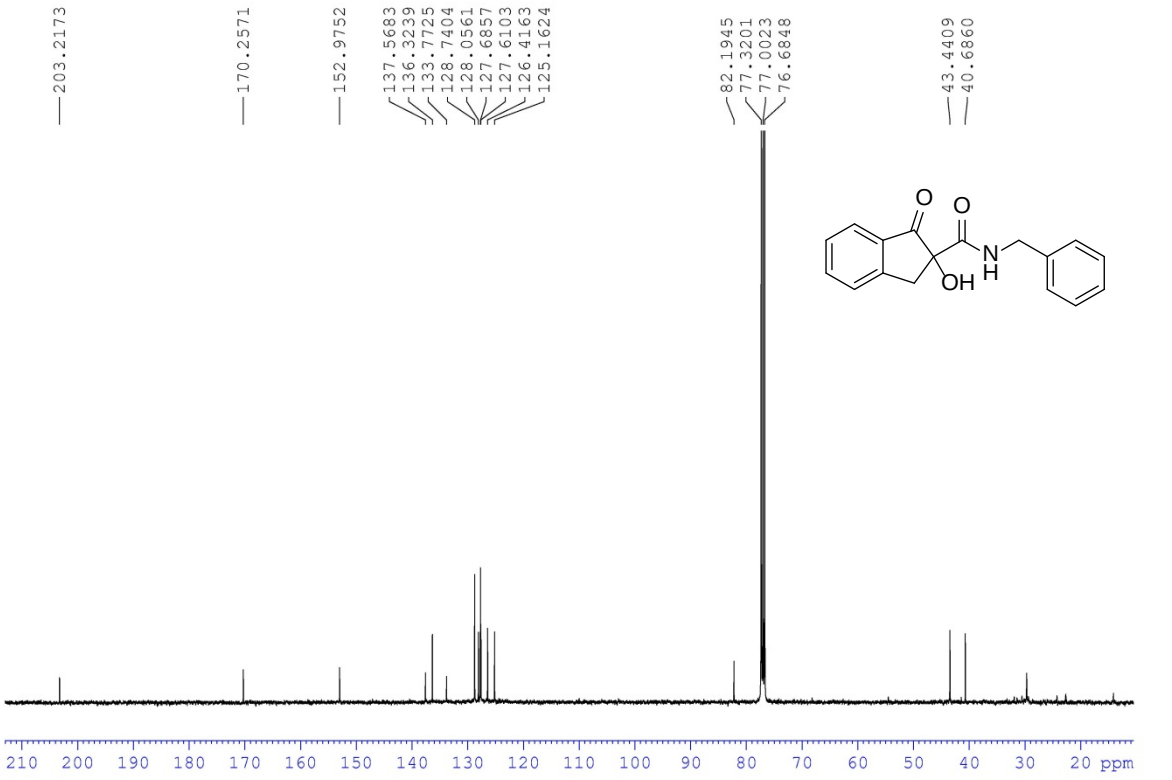




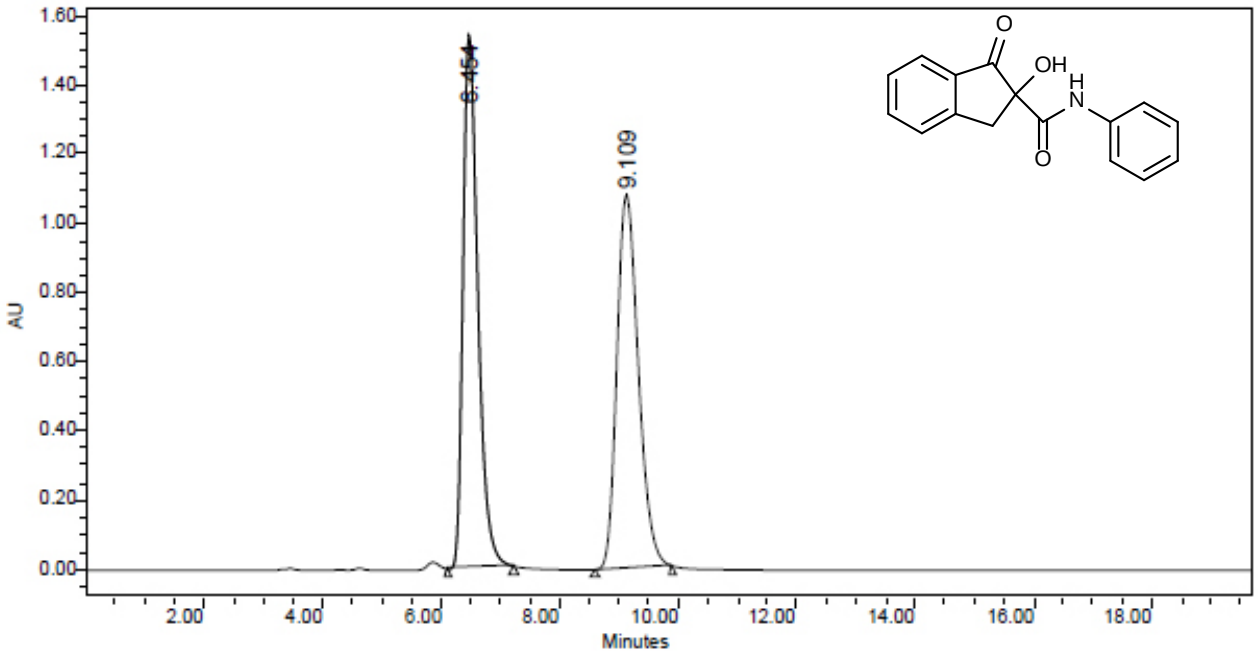




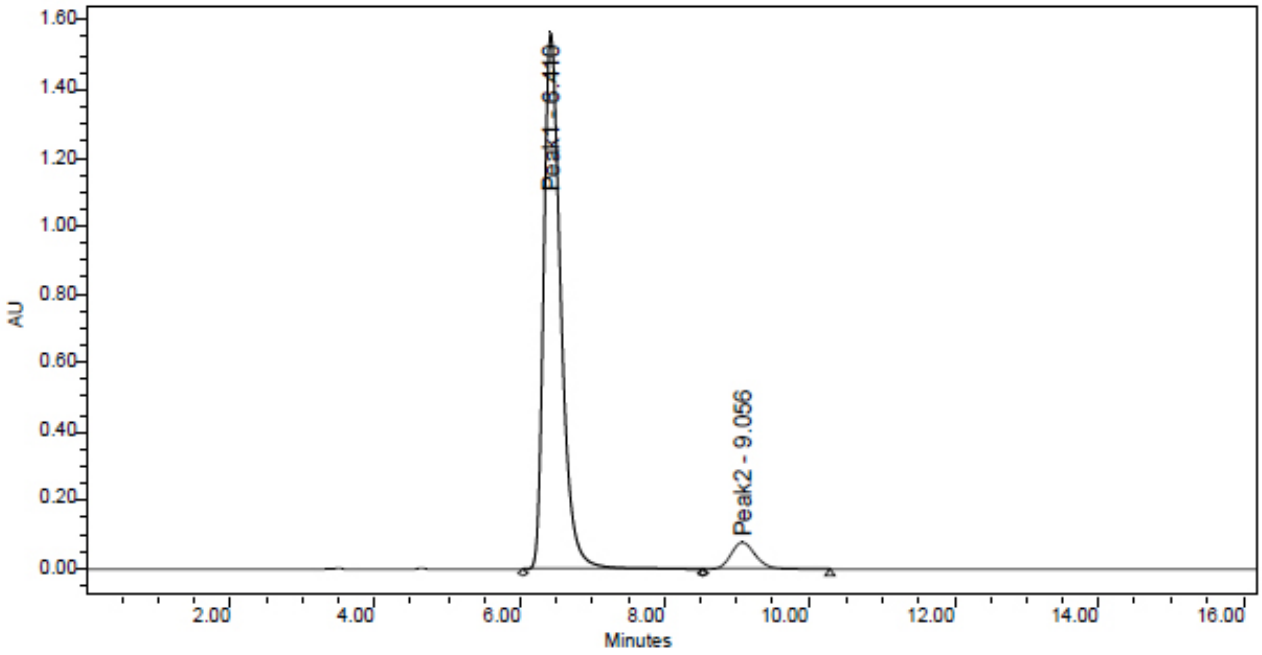




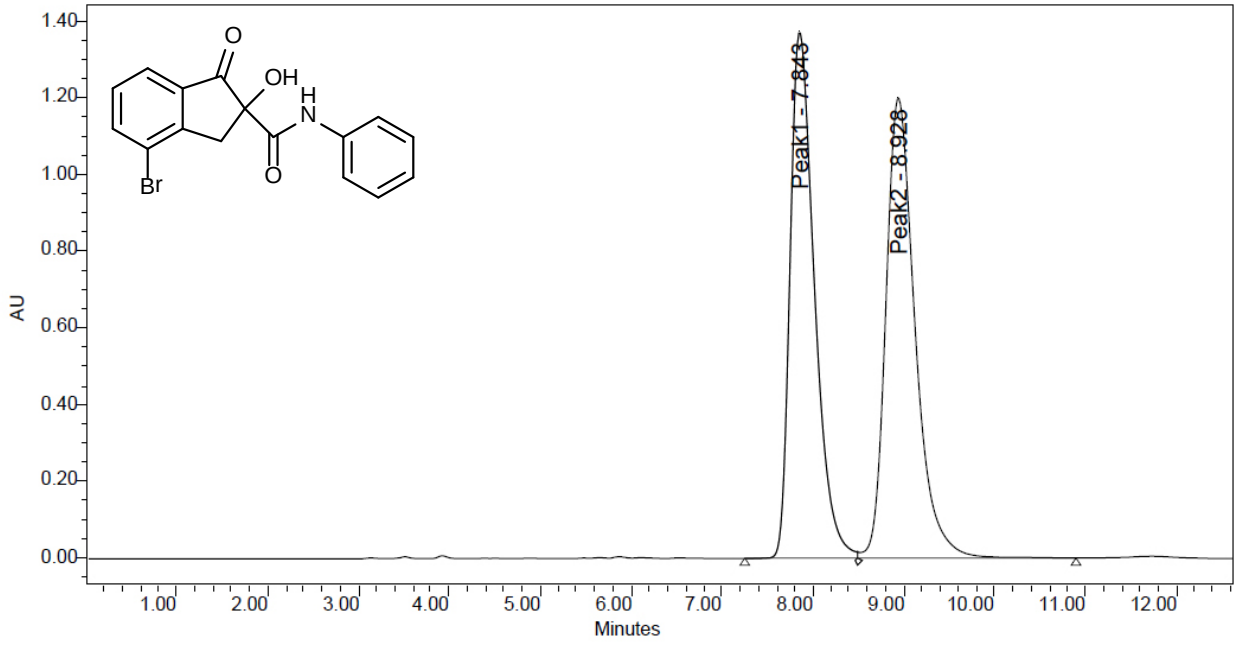
HPLC Chromatograms



	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	6.454	26864286	49.62	1542077	58.83
2	9.109	27277915	50.38	1079291	41.17



	Peak Name	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	Peak1	6.410	25823329	93.28	1568291	95.23
2	Peak2	9.056	1859265	6.72	78469	4.77



	Peak Name	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	Peak1	7.843	25570330	48.78	1372284	53.34
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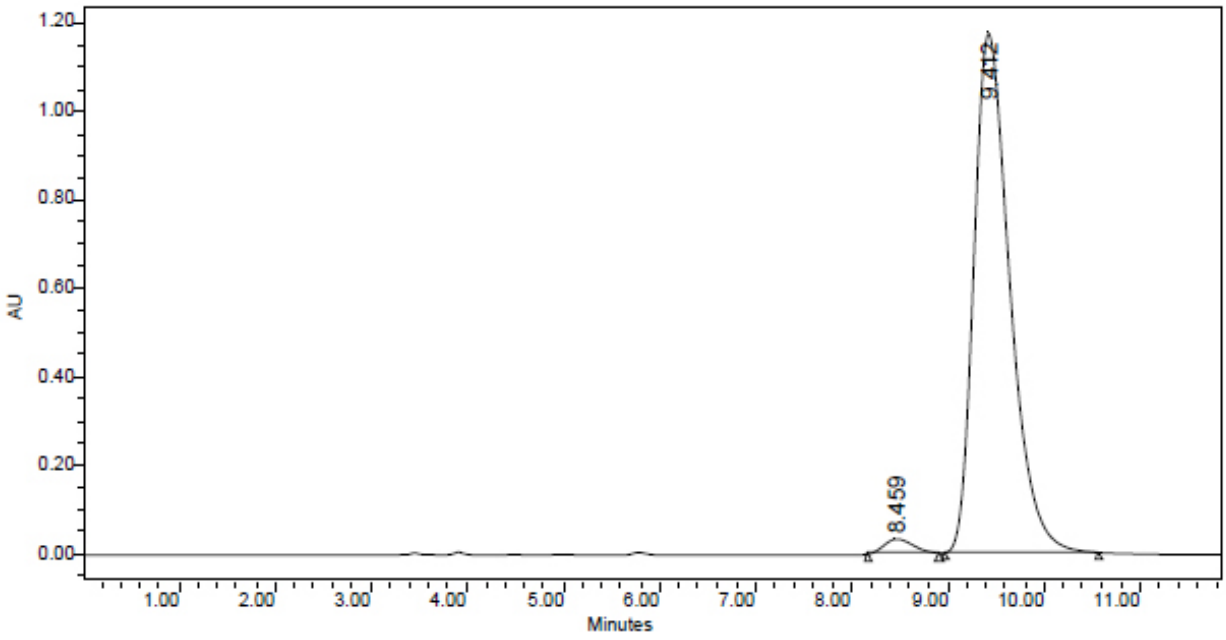
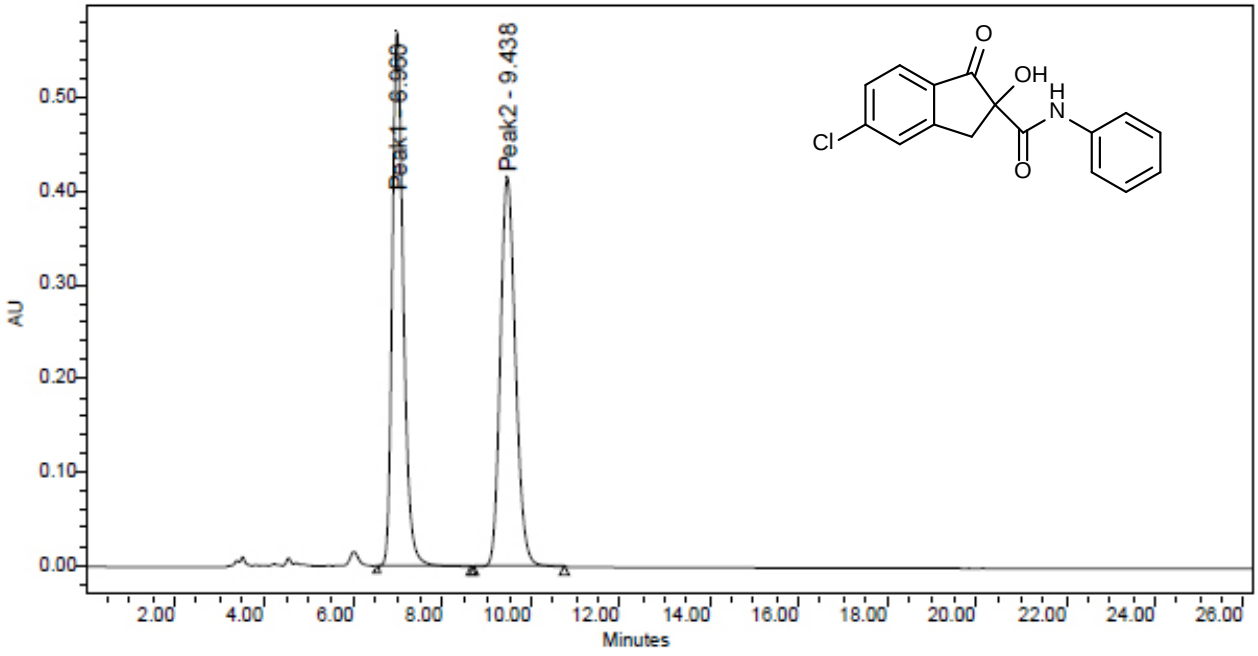


	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	8.459	693274	2.23	33195	2.75
2	9.412	30462791	97.77	1172708	97.25



	Peak Name	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
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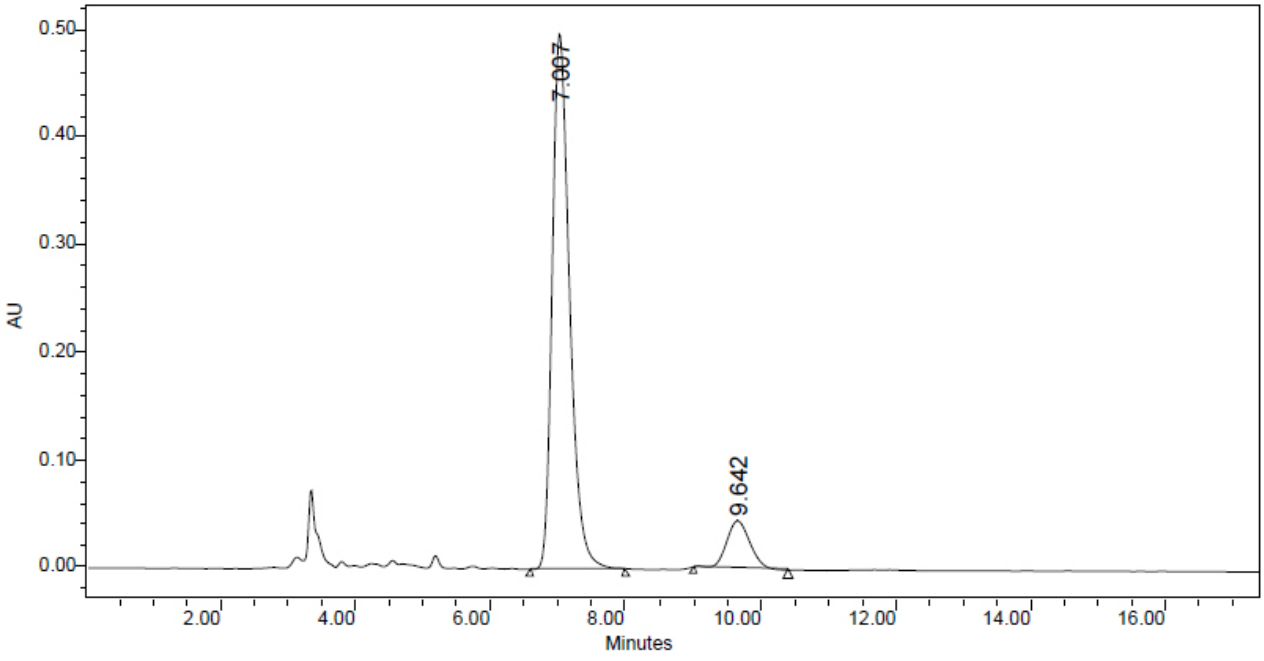
2	Peak2	9.438	9841928	49.96	415973	42.20



	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
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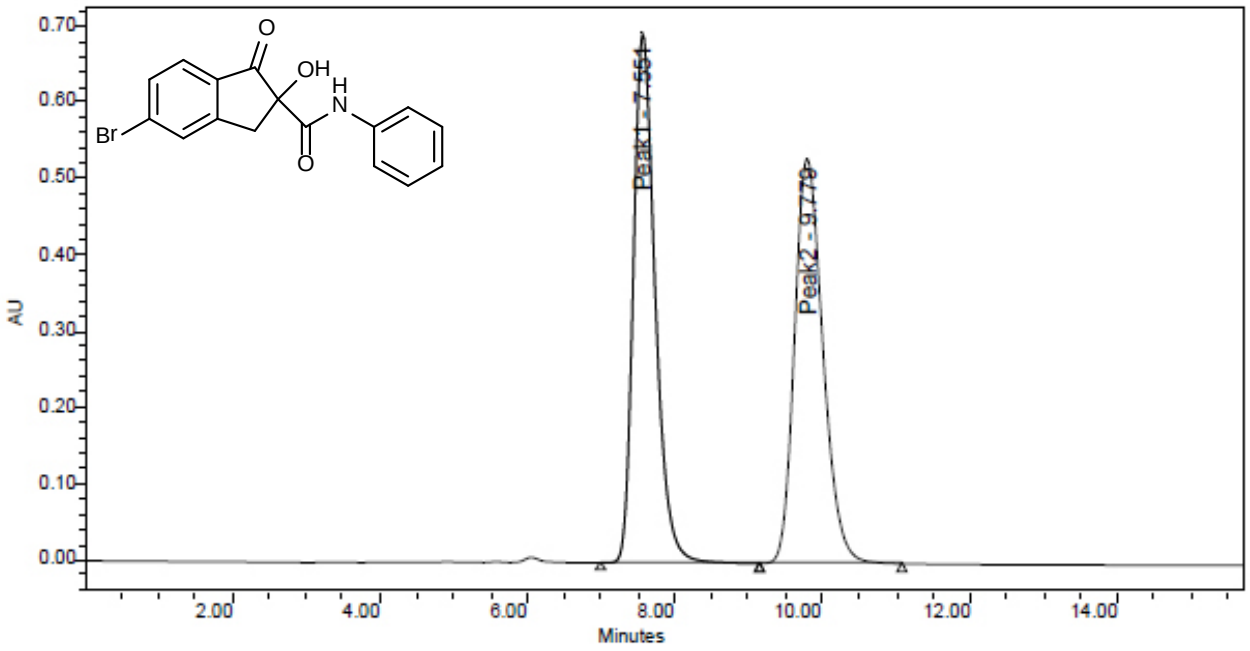
2	9.642	1059413	10.65	44221	8.15



	Peak Name	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	Peak1	7.551	14210802	49.99	693117	56.63
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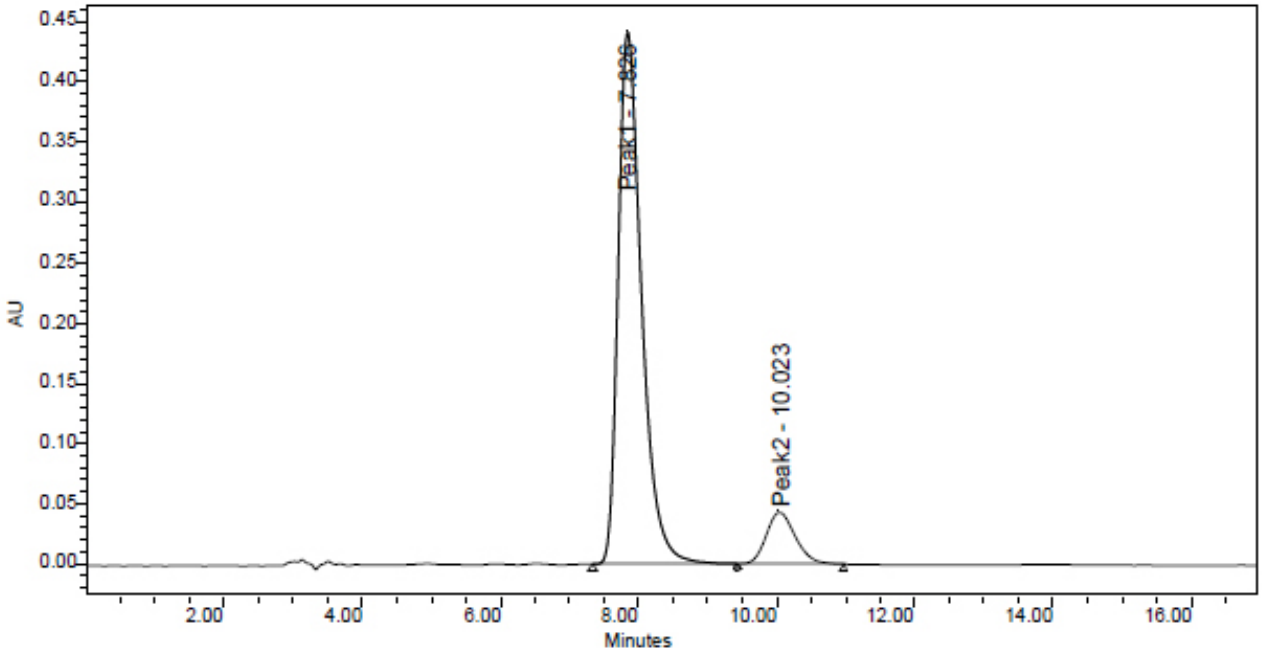

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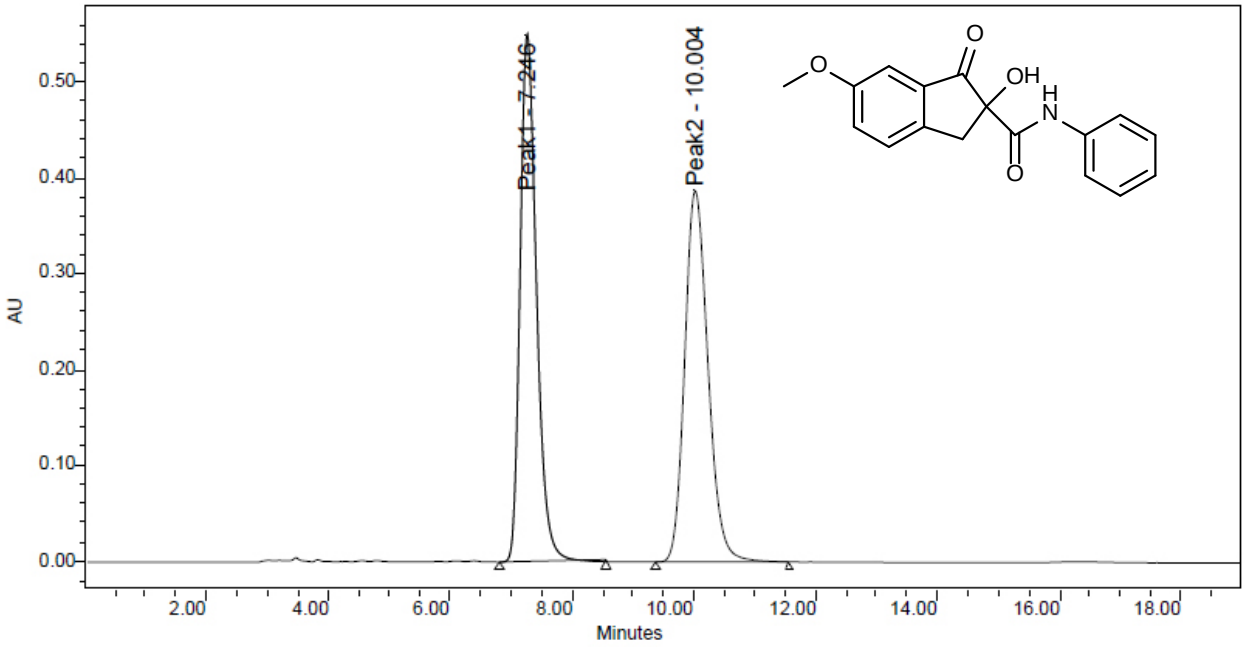
2	Peak2	10.023	1264265	10.85	42892	8.87



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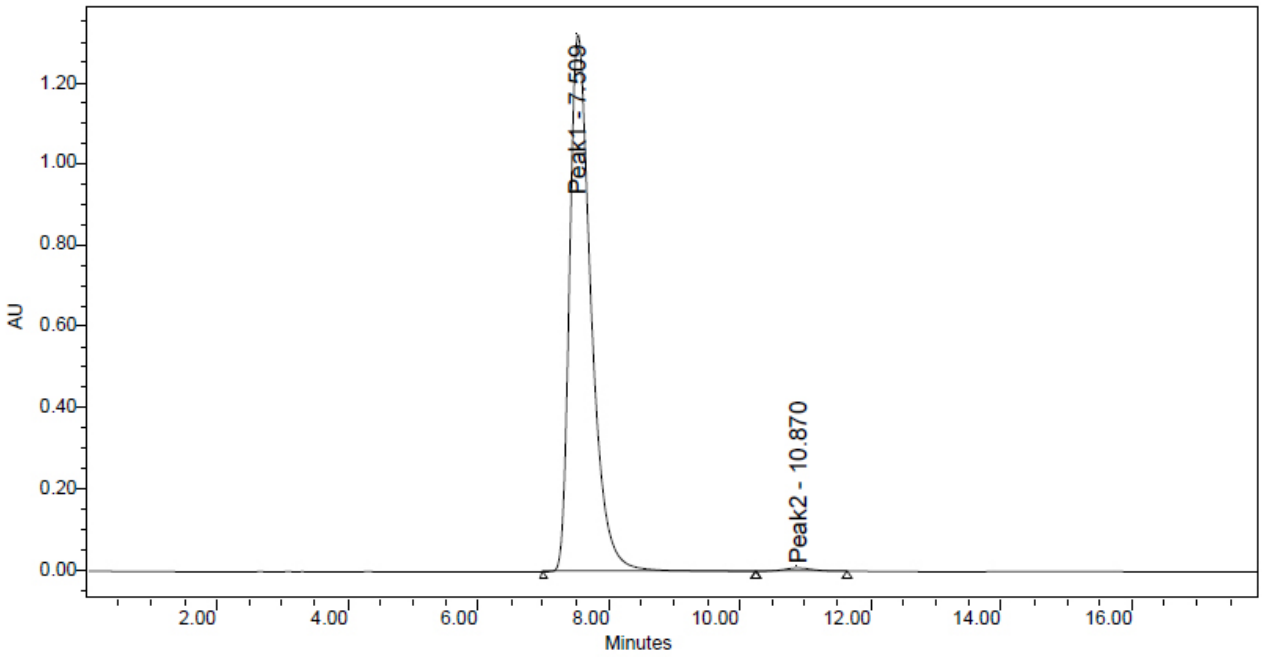

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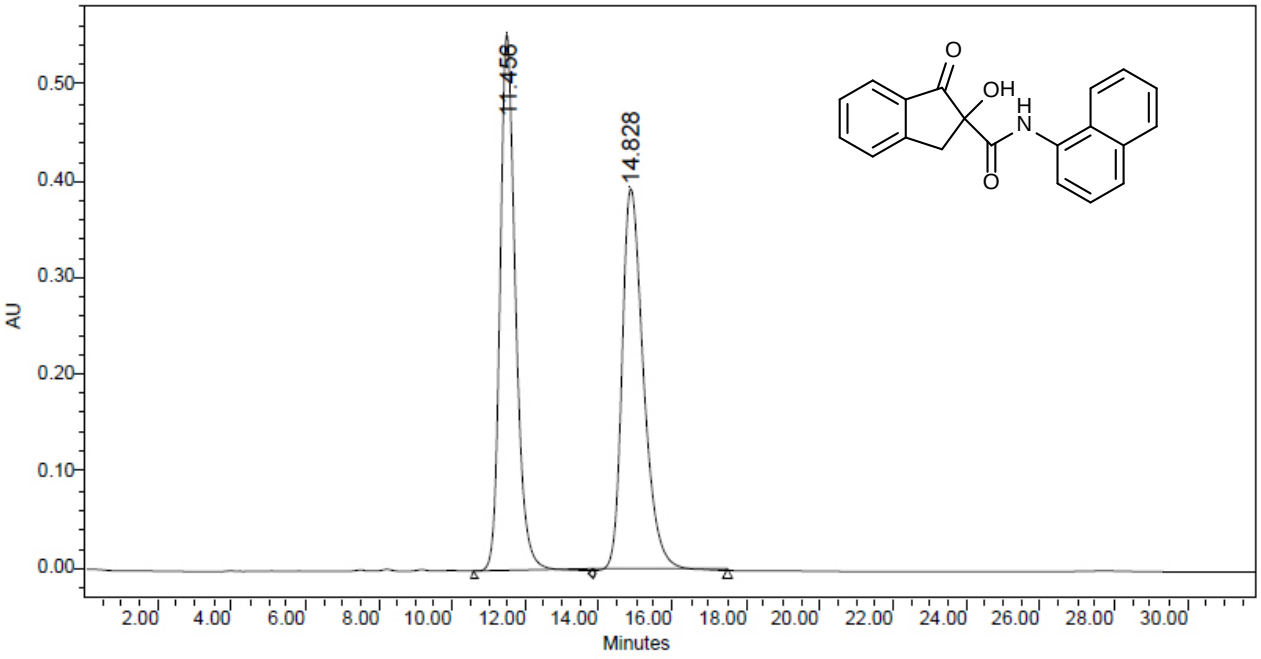
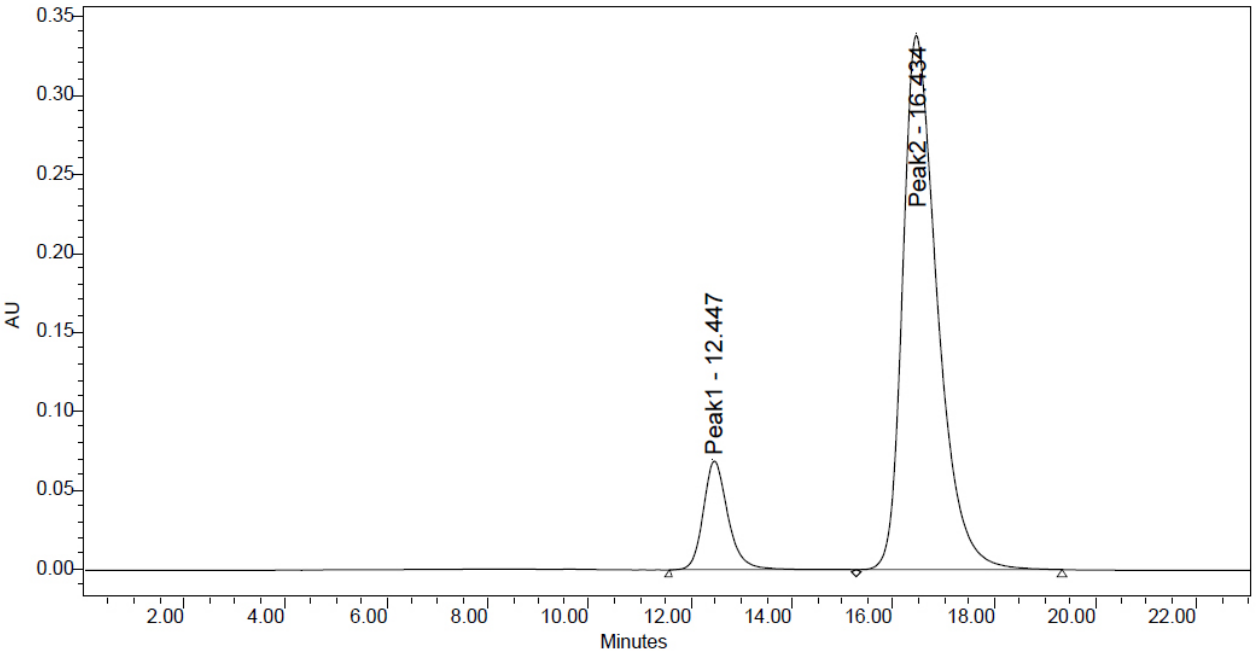
2	Peak2	10.870	251310	0.82	8148	0.61



	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	11.456	16291743	50.26	554776	58.42
2	14.828	16123642	49.74	394874	41.58



	Peak Name	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
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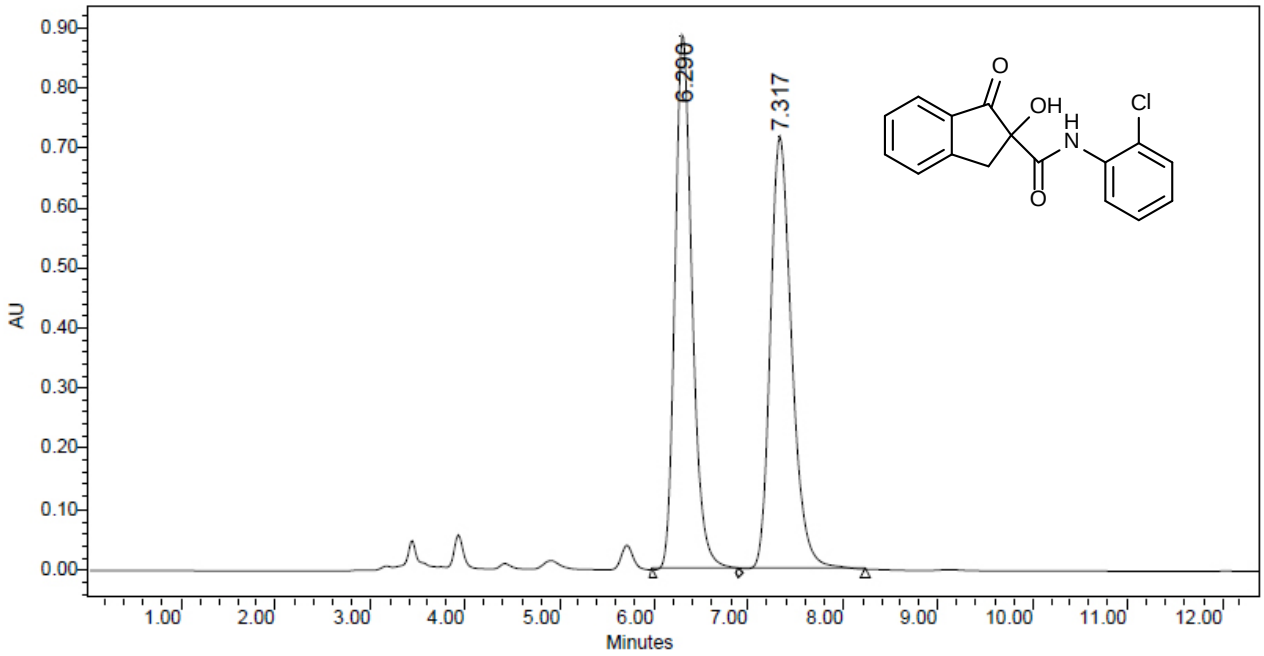
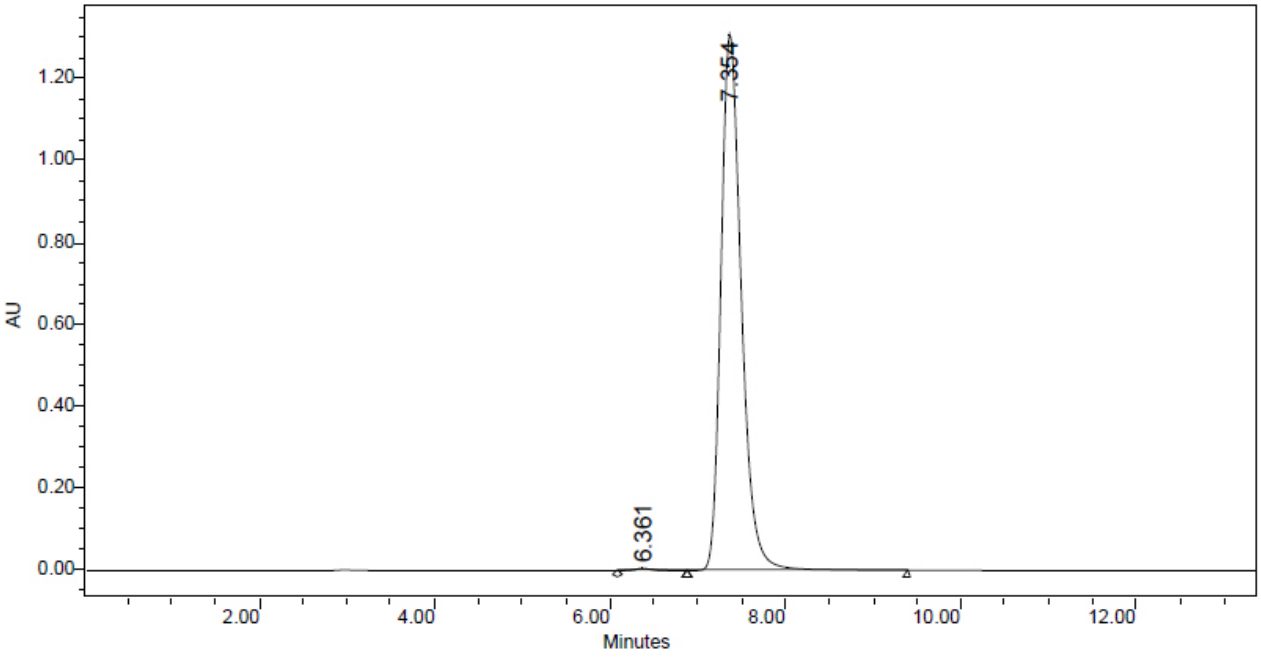
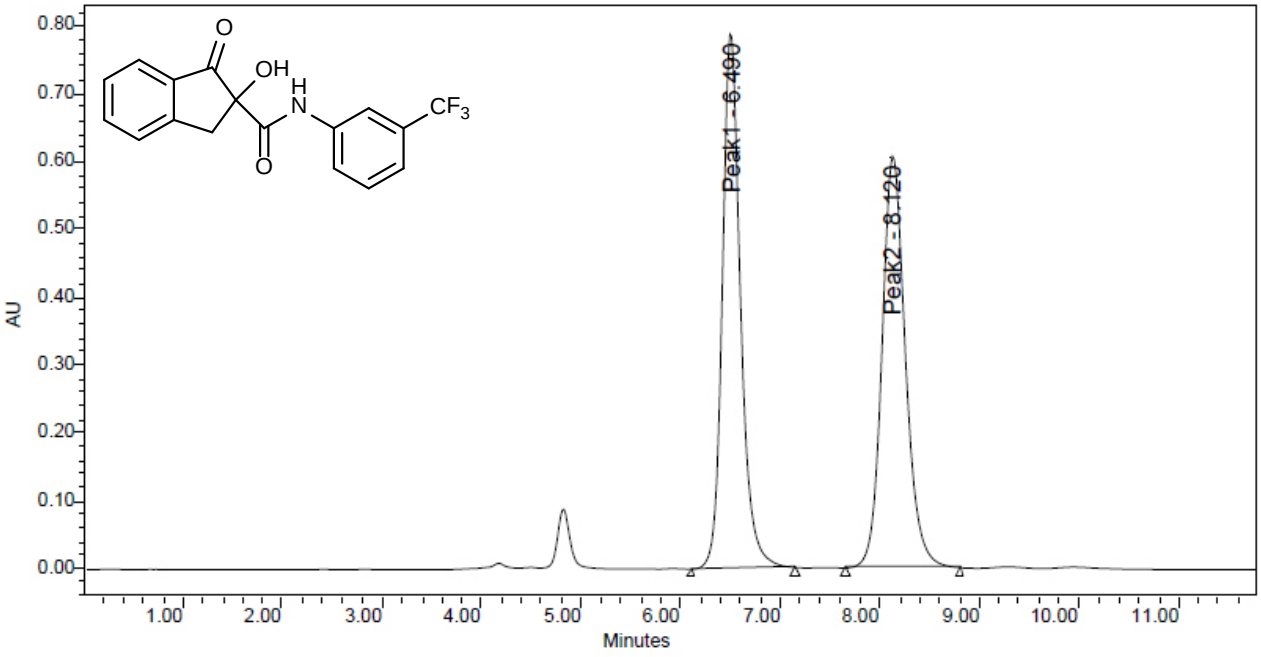


	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	6.290	11286427	49.77	892536	55.34
2	7.317	11390151	50.23	720289	44.66



	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	6.361	62431	0.29	4695	0.36
2	7.354	21220248	99.71	1312583	99.64



	Peak Name	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
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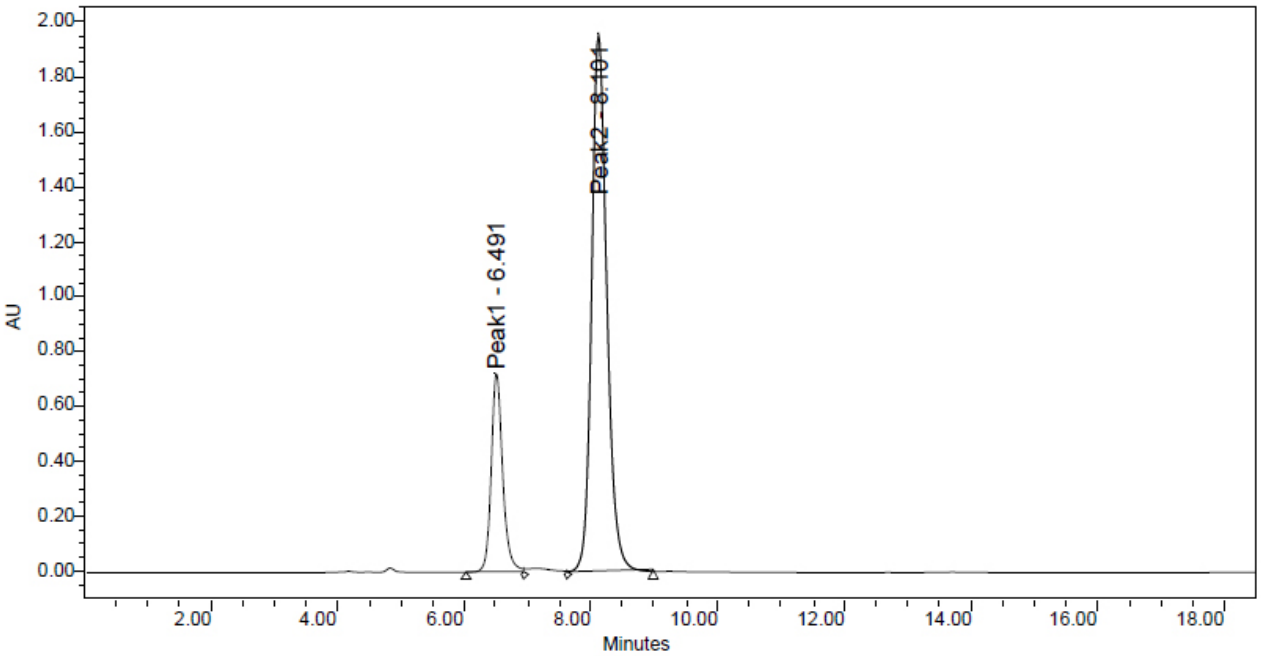
2	Peak2	8.120	9935166	49.77	607191	43.43



	Peak Name	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
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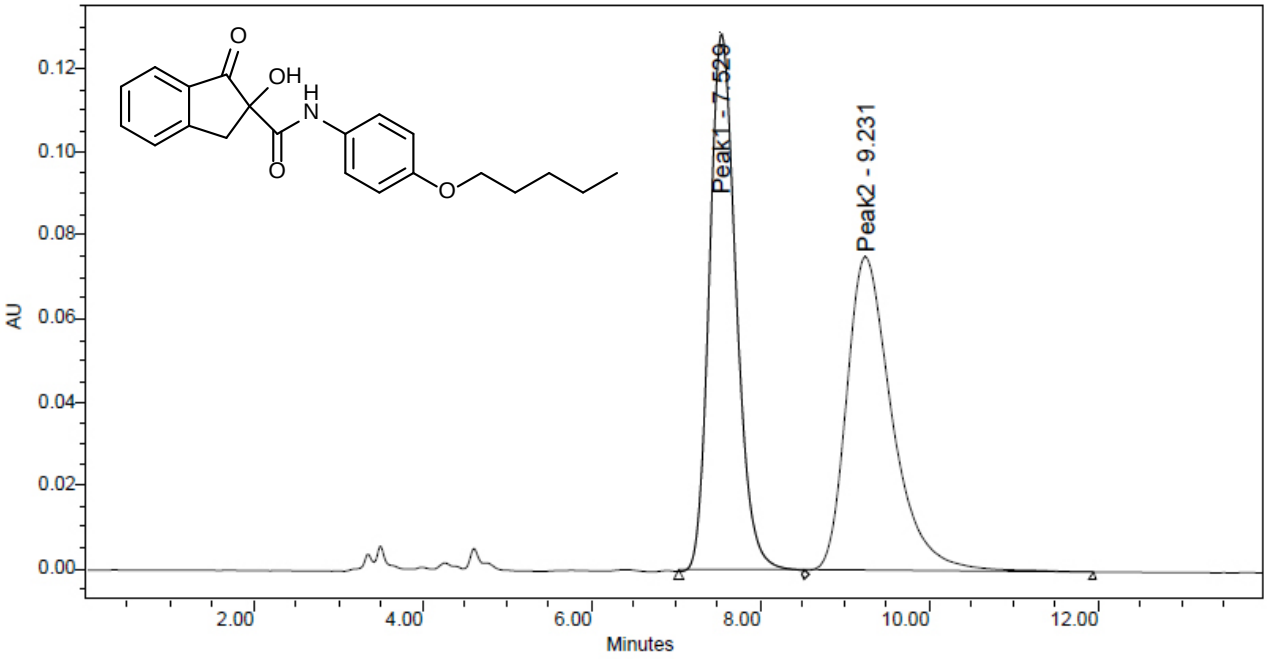
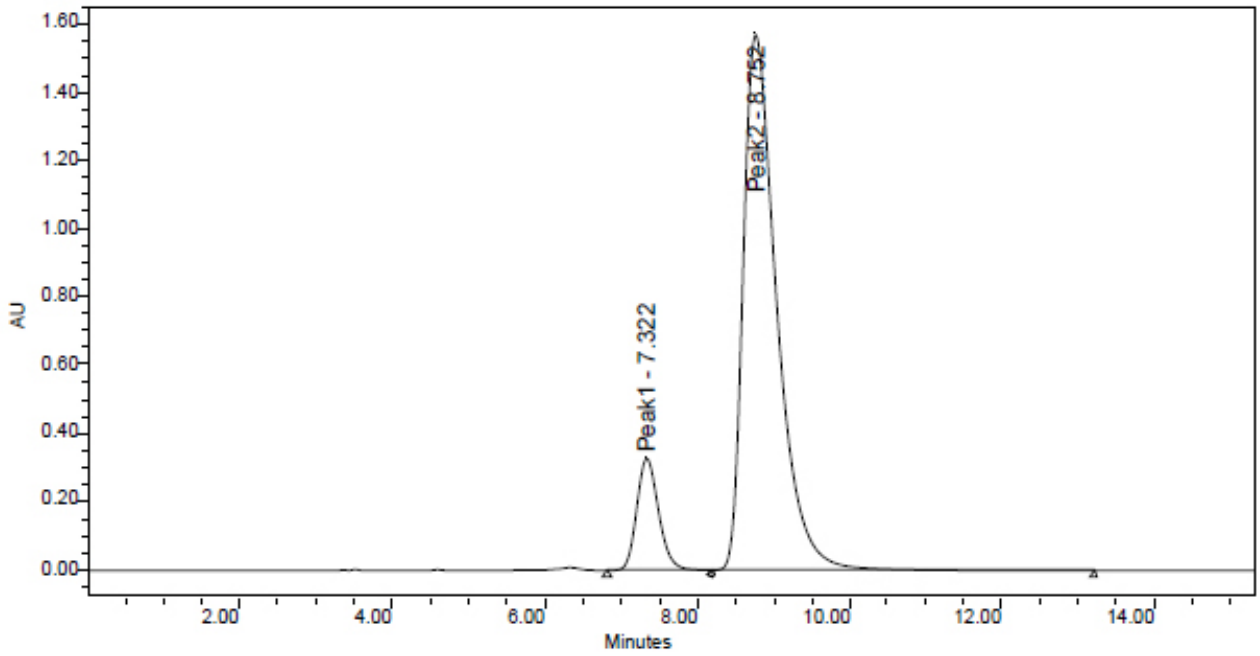
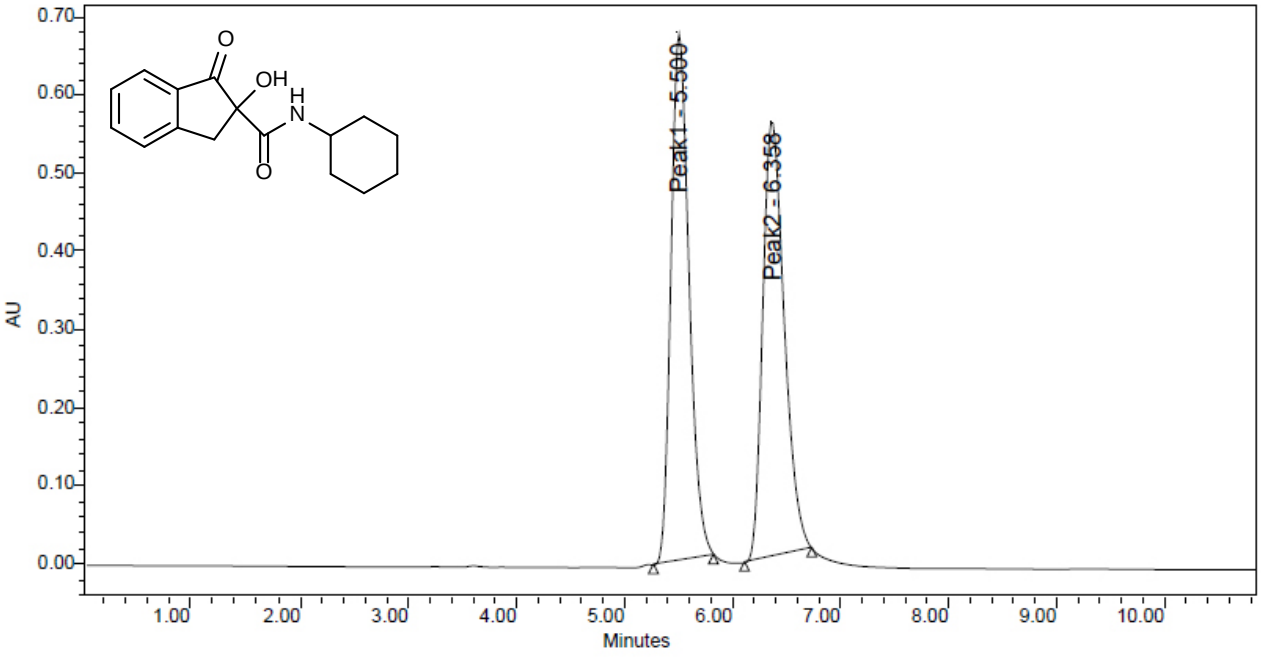
2	Peak2	8.101	32490831	78.07	1948876	72.93



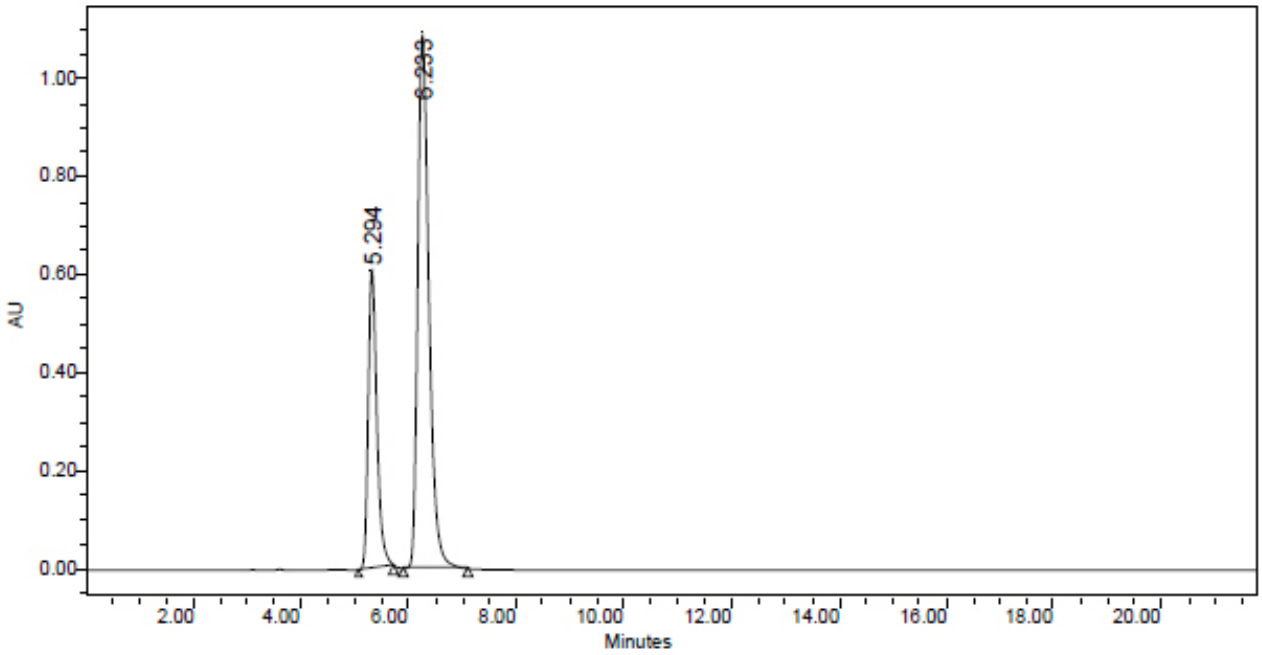
	Peak Name	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	Peak1	7.529	2850108	49.94	129028	63.06
2	Peak2	9.231	2856829	50.06	75589	36.94



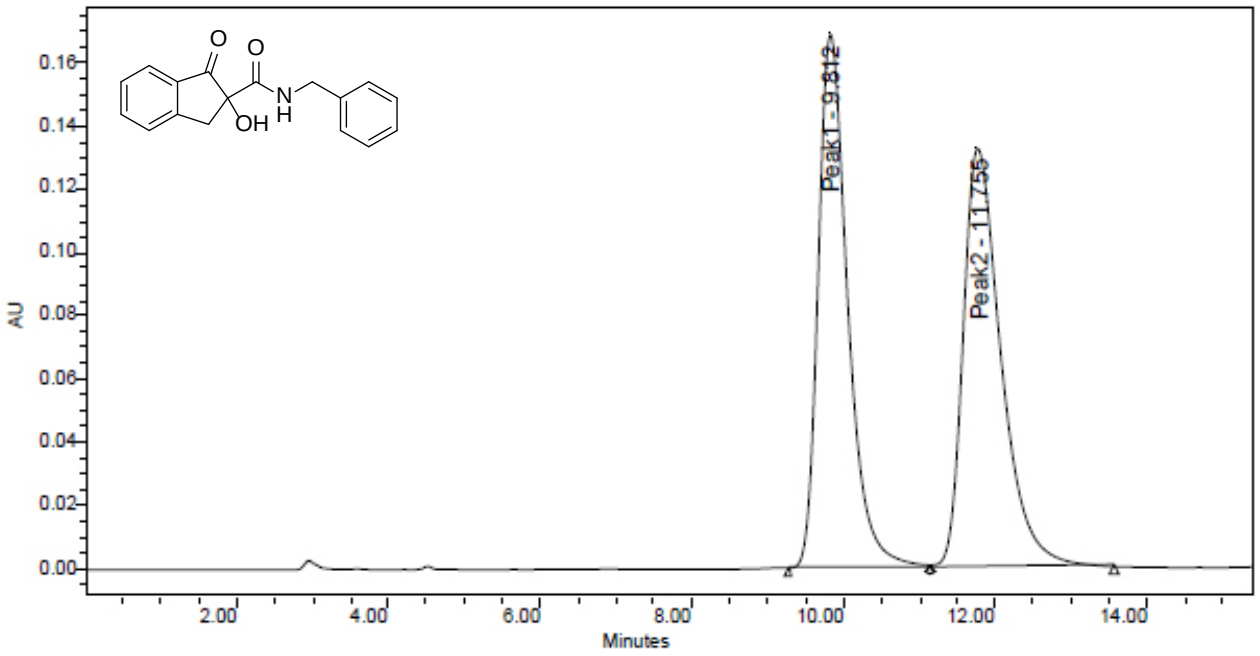
	Peak Name	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	Peak1	7.322	6545223	12.00	327689	17.26
2	Peak2	8.752	48005075	88.00	1570418	82.74



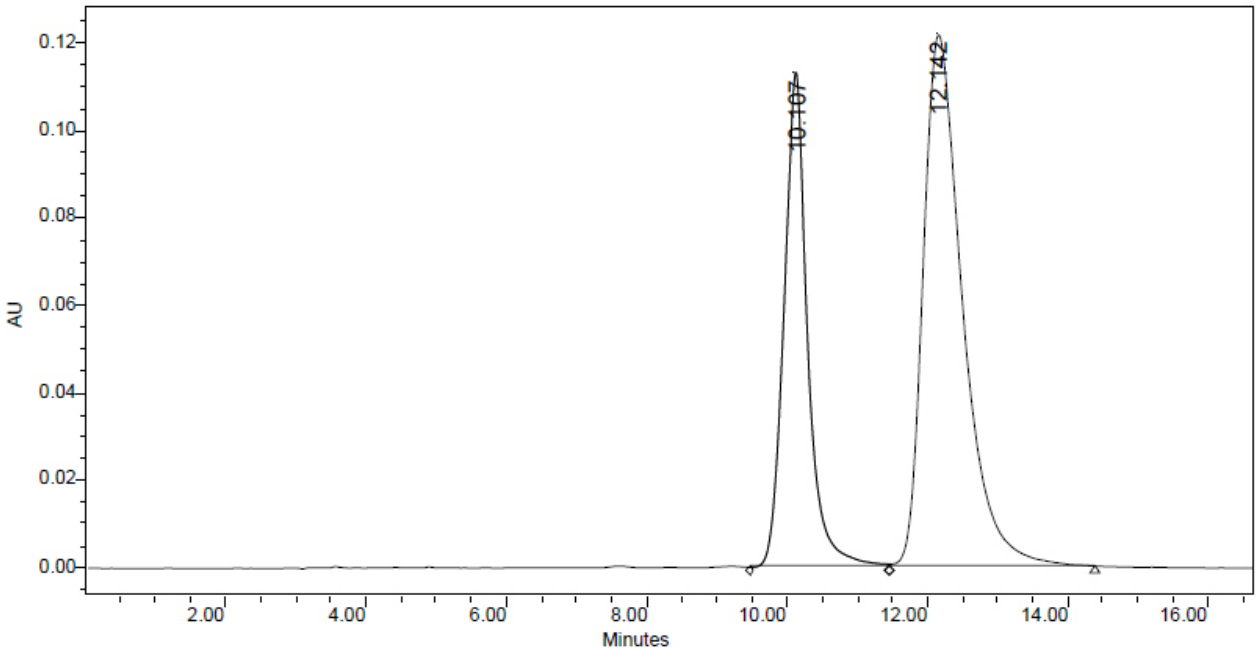
	Peak Name	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	Peak1	5.500	7856069	50.41	674088	54.68
2	Peak2	6.358	7727144	49.59	558787	45.32



	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	5.294	6833475	30.25	609975	35.89
2	6.233	15759411	69.75	1089580	64.11



	Peak Name	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	Peak1	9.812	4563934	49.81	168646	56.01
2	Peak2	11.755	4598046	50.19	132471	43.99



	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	10.107	2644555	35.75	113518	48.23
2	12.142	4752319	64.25	121835	51.77