

Asymmetric Vinylogous Mukaiyama Aldol Reaction of Isatins under Bifunctional Organocatalysis: Enantioselective Synthesis of Substituted 3-Hydroxy-2-Oxindoles

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1. General Methods and Starting Materials

All solvents were dried using activated 4Å molecular sieves and stored under nitrogen. 4Å molecular sieves, 1.6-2.5 mm of particle size, were activated by microwave (700W) (3 x 60 sec) and subsequent cycles of vacuum/nitrogen. Catalyst **3a** and **3b** were acquired from commercial sources and catalysts **3c**, **3d**, **3e** and **3f** were synthesized following a procedure described in the literature.¹ For thin layer chromatography (TLC) silica gel plates with fluorescence indicator 254 nm were used and compounds were visualized by irradiation with UV light and/or by treatment with a solution of potassium permanganate in water followed by heating. Flash column chromatography was performed using Iatrobeds 6RS-8060 silica gel and compressed air. Celite® 512 medium was used for some filtrations. Cyclohexane, ethyl acetate, dichloromethane and diethyl ether for flash chromatography were acquired from commercial sources and were used without previous purification. Optical rotation was recorded in cells with 10 cm path length; the specific solvents and concentrations (in g/100 mL) are indicated. NMR spectra were acquired on a *Bruker Avance 300 MHz spectrometer*, running at 300, 75 and 282 MHz for ¹H, ¹³C and ¹⁹F respectively. Chemical shifts (δ) are reported in ppm relative to residual solvent signals (CDCl₃, 7.26 ppm for ¹H NMR and 77.2 ppm for ¹³C NMR respectively). ¹³C NMR spectra were acquired on a broad band decoupled mode. The following abbreviations are used to describe peak patterns when appropriate: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), m (multiplet), bs (broad singlet). Different methods have been used for measuring the exact mass (indicated for each case): MS (ESI) (Electrospray ionization mass spectroscopy) was acquired with an *Agilent Technologies 6120 Quadrupole LC/MS* and MS (EI) (Electron Ionization mass spectroscopy) was acquired with an *Agilent Technologies 5977B MSD*. In these two techniques, *MassWorks software ver. 4.0.0.0 (Cerno Bioscience)* was used for the formula identification. *MassWorks* is a MS calibration software which calibrates for isotope profile as well as for mass accuracy allowing highly accurate comparisons between calibrated and theoretical spectra.²

Enantiomeric excesses were determined in a Supercritical Fluid Chromatography (SFC) with chiral columns. The chromatograms were acquired with an *Agilent Technologies 1260 Infinity*

¹ C. Cassani, R. Martín-Rapún, E. Arceo, F. Bravo and P. Melchiorre, *Nature Protocols*. 2013, **8**, 325–344.

² a) Y. Wang and M. Gu, *Anal. Chem.* 2010, **82**, 7055-7062; b) Y. Wang, Methods for Operating MS Instrument Systems, United States Patent No. 6,983,213, **2006**; c) N. Ochiaia, K. Sasamoto, K. MacNamara *Journal of Chromatography A*, 2012, **1270**, 296-304; d) H.-P. Ho, R.-Y. Lee, C.-Y. Chen, S.-R. Wang, Z.-G. Li and M.-R. Lee, *Rapid Commun. Mass Spectrom.* 2011, **25**, 25-32.

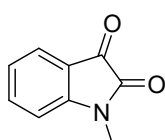
with a *SFC module* and a UV-vis detector. The chiral columns used were: Chiralpak IA, IB-3, IC, ID-3, IG-3 (see in each case).

2. Synthesis and characterization data of isatins 1

General procedure A: Synthesis of isatins 1

The corresponding isatin (1.25 mmol, 1.0 eq) and K_2CO_3 (519 mg, 3.75 mmol, 3.0 eq.) were dissolved in 6.0 mL of MeCN. Then, the corresponding alkylhalide (1.38 mmol, 1.1 eq.) was added and the reaction mixture was stirred for 24h at 80°C. The reaction was monitored by 1H NMR and, once completed, the solution was concentrated *in vacuo*. The crude mixture was dissolved in ethyl acetate, washed with water (3 x 10 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. The final products **1** were used without further purification.

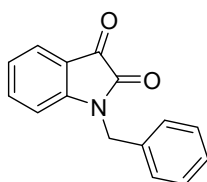
1-Methylindoline-2,3-dione (**1b**)³



Following general procedure A, isatin (184 mg, 1.25 mmol) and iodomethane (196 mg, 1.38 mmol) after 24h, gave **1b** as an orange solid (78% yield). The 1H -NMR is in accordance with the literature.

1H -NMR: δ 7.65 – 7.56 (m, 2H), 7.18 – 7.09 (m, 1H), 6.94 – 6.86 (m, 1H), 3.26 (s, 3H).

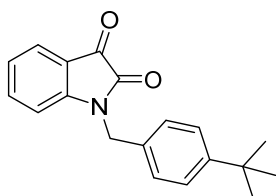
1-Benzylindoline-2,3-dione (**1c**)⁴



Following general procedure A, isatin (184 mg, 1.25 mmol) and benzyl bromide (236 mg, 1.38 mmol) after 24h, gave **1c** as an orange solid (81% yield). The 1H -NMR is in accordance with the literature.

1H -NMR: δ 7.64 – 7.56 (m, 1H), 7.49 (td, $J = 7.8, 1.4$ Hz, 1H), 7.40 – 7.24 (m, 5H), 7.08 (t, $J = 7.7$ Hz, 1H), 6.78 (d, $J = 7.9$ Hz, 1H), 4.90 (s, 2H).

1-[4-(*tert*-Butyl)benzyl]indoline-2,3-dione (**1d**)



Following general procedure A, isatin (184 mg, 1.25 mmol) and 1-(bromomethyl)-4-(*tert*-butyl)benzene (314 mg, 1.38 mmol) after 24h, gave **1d** as an orange solid (71% yield).

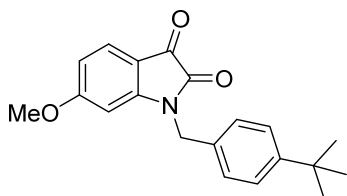
1H -NMR: δ 7.64 – 7.56 (m, 1H), 7.49 (td, $J = 7.8, 1.4$ Hz, 1H), 7.40 – 7.24 (m, 4H), 7.08 (td, $J = 7.6, 1.0$ Hz, 1H), 6.85 – 6.80 (m, 1H), 4.89 (s, 2H), 1.29 (s, 9H). ^{13}C -NMR: δ

³ A. A. Nagle, S. A. Reddy, H. Bertrand, H. Tajima, D. Truong-Minh, S. Wong, J. D. Hayes, G. Wells and E. Chew, *Chem. Med. Chem.* 2014, **9**, 1763-1774.

⁴ A. Kamal, K. S. Babu, M. V. P. S. V. Vardhan, S. M. A. Hussaini, R. Mahesh, S. P. Shaik and A. Alarifi, *Bioorg. Med. Chem. Lett.* 2015, **25**, 2199–2202.

183.5, 158.4, 151.4, 151.1, 138.4, 131.6, 127.4 (2C), 126.1 (2C), 125.5, 123.9, 117.9, 111.2, 43.9, 34.7, 31.4 (3C). **HRMS (ESI)**: calculated for $C_{19}H_{20}NO_2^+$ $[M+H]^+$: 294.1489; found: 294.1466.

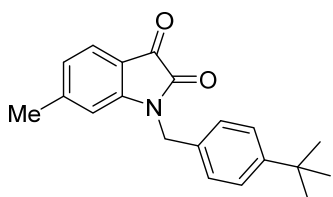
1-[4-(*tert*-Butyl)benzyl]-6-methoxyindoline-2,3-dione (**1e**)



Following general procedure A, 6-methoxyisatin (222 mg, 1.25 mmol) and 1-(bromomethyl)-4-(*tert*-butyl)benzene (314 mg, 1.38 mmol) after 24h, gave **1e** as an orange solid (66% yield).

¹H-NMR: δ 7.58 (d, $J = 8.4$ Hz, 1H), 7.38 – 7.33 (m, 2H), 7.28 – 7.23 (m, 2H), 6.53 – 6.49 (m, 1H), 6.30 (d, $J = 2.2$ Hz, 1H), 4.85 (s, 2H), 3.83 (s, 3H), 1.29 (s, 9H). **¹³C-NMR**: δ 180.8, 168.3, 159.8, 153.5, 151.3, 131.9, 128.1, 127.4 (2C), 126.1 (2C), 111.6, 108.0, 98.4, 56.2, 43.8, 34.7, 31.5 (3C). **HRMS (EI)**: calculated for $C_{20}H_{21}NO_3^+$ $[M]^+$: 323.1516; found: 323.1537.

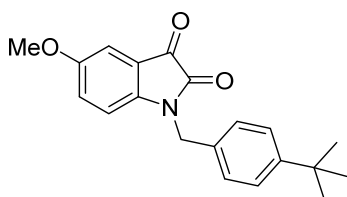
1-[4-(*tert*-Butyl)benzyl]-6-methylindoline-2,3-dione (**1f**)



Following general procedure A, 6-methylisatin (202 mg, 1.25 mmol) and 1-(bromomethyl)-4-(*tert*-butyl)benzene (314 mg, 1.38 mmol) after 48h, gave **1f** as an orange solid (61% yield).

¹H-NMR: δ 7.49 (d, $J = 7.6$ Hz, 1H), 7.36 (m, 2H), 7.28 – 7.24 (m, 2H), 6.90 – 6.86 (m, 1H), 6.64 – 6.61 (m, 1H), 4.86 (s, 2H), 2.36 (s, 3H), 1.30 (s, 9H). **¹³C-NMR**: δ 182.8, 159.1, 151.5, 151.3, 150.8, 131.9, 127.3 (2C), 126.1 (2C), 125.5, 124.6, 115.7, 111.8, 43.7, 34.7, 31.4, 23.2 (3C). **HRMS (ESI)**: calculated for $C_{20}H_{22}NO_2^+$ $[M+H]^+$: 308.1645; found: 308.1640.

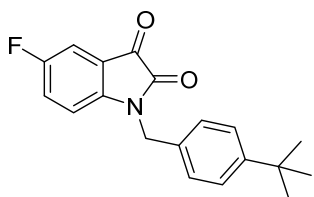
1-[4-(*tert*-Butyl)benzyl]-5-methoxyindoline-2,3-dione (**1g**)



Following general procedure A, 5-methoxyisatin (222 mg, 1.25 mmol) and 1-(bromomethyl)-4-(*tert*-butyl)benzene (314 mg, 1.38 mmol) after 24h, gave **1g** as a dark red solid (78% yield).

¹H-NMR: δ 7.39 – 7.21 (m, 4H), 7.13 (d, $J = 2.7$ Hz, 1H), 7.04 (dd, $J = 8.6, 2.7$ Hz, 1H), 6.72 (d, $J = 8.6$ Hz, 1H), 4.86 (s, 2H), 3.76 (s, 3H), 1.29 (s, 9H). **¹³C-NMR**: 183.9, 158.5, 156.7, 151.3, 144.9, 131.7, 127.4 (2C), 126.1 (2C), 124.8, 118.3, 112.2, 109.7, 56.1, 43.9, 34.7, 31.4 (3C). **HRMS (EI)**: calculated for $C_{20}H_{21}NO_3^+$ $[M]^+$: 323.1516; found: 323.1528.

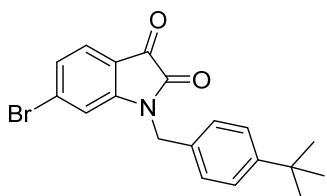
1-[4-(*tert*-Butyl)benzyl]-5-fluoroindoline-2,3-dione (**1h**)



Following general procedure A, 5-fluoroisatin (207 mg, 1.25 mmol) and 1-(bromomethyl)-4-(*tert*-butyl)benzene (314 mg, 1.38 mmol) after 24h, gave **1h** as a red solid (65% yield).

¹H-NMR: δ 7.41 – 7.13 (m, 6H), 6.77 (dd, J = 8.6, 3.6 Hz, 1H), 4.89 (s, 2H), 1.29 (s, 9H). **¹³C-NMR:** δ 182.9 (d, J = 2.3 Hz), 159.5 (d, J = 249.6 Hz), 158.2 (d, J = 1.5 Hz), 151.6, 147.1 (d, J = 2.2 Hz), 131.3, 127.4 (2C), 126.2 (2C), 124.8 (d, J = 24.1 Hz), 118.5 (d, J = 7.0 Hz), 112.6 (d, J = 17.5 Hz), 112.4, 44.0, 34.8, 31.4 (3C). **¹⁹F-NMR:** δ -118.2 ppm. **HRMS (EI):** calculated for C₁₉H₁₈NO₂F⁺ [M]⁺ : 311.1316; found: 311.1306.

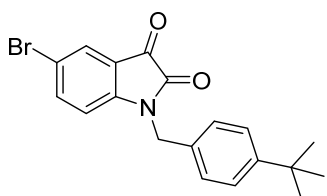
6-Bromo-1-[4-(*tert*-butyl)benzyl]indoline-2,3-dione (**1i**)



Following general procedure A, 6-bromoisatin (283 mg, 1.25 mmol) and 1-(bromomethyl)-4-(*tert*-butyl)benzene (314 mg, 1.38 mmol) after 24h, gave **1i** as an orange solid (70% yield).

¹H-NMR: δ 7.50 – 6.95 (m, 6H), 7.00 (s, 1H), 4.87 (s, 2H), 1.30 (s, 9H). **¹³C-NMR:** δ 182.2, 158.2, 151.8, 151.6, 133.7, 131.2, 127.4 (2C), 127.2, 126.4, 126.3 (2C), 116.5, 114.7, 44.1, 34.8, 31.4 (3C). **HRMS (EI):** calculated for C₁₉H₁₈BrNO₂⁺ [M]⁺ : 371.0515; found: 371.0541.

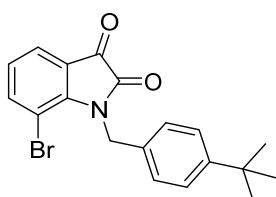
5-Bromo-1-[4-(*tert*-butyl)benzyl]indoline-2,3-dione (**1j**)



Following general procedure A, 5-bromoisatin (283 mg, 1.25 mmol) and 1-(bromomethyl)-4-(*tert*-butyl)benzene (314 mg, 1.38 mmol) after 24h, gave **1j** as an orange solid (82% yield).

¹H-NMR: δ 7.71 (d, J = 2.1 Hz, 1H), 7.59 (dd, J = 8.4, 2.1 Hz, 1H), 7.39 – 7.20 (m, 4H), 6.71 (d, J = 8.4 Hz, 1H), 4.88 (s, 2H), 1.29 (s, 9H). **¹³C-NMR:** δ 182.4, 157.7, 151.7, 149.7, 140.6, 131.2, 128.3, 127.4 (2C), 126.2 (2C), 119.1, 116.9, 112.9, 44.1, 34.8, 31.4 (3C) ppm. **HRMS (EI):** calculated for C₁₉H₁₈BrNO₂⁺ [M]⁺ : 371.0515; found: 371.0505.

7-Bromo-1-[4-(*tert*-butyl)benzyl]indoline-2,3-dione (**1k**)

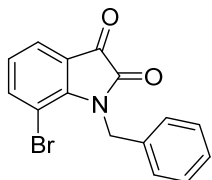


Following general procedure A, 7-bromoisatin (283 mg, 1.25 mmol) and 1-(bromomethyl)-4-(*tert*-butyl)benzene (314 mg, 1.38 mmol) after 24h, gave **1k** as an orange solid (61% yield).

¹H-NMR: δ 7.67 (dd, J = 8.1, 1.3 Hz, 1H), 7.61 (dd, J = 7.3, 1.3 Hz, 1H), 7.37 – 7.31 (m, 2H), 7.24 – 7.20 (m, 2H), 6.99 (dd, J = 8.1, 7.3 Hz, 1H), 5.41 (s, 2H), 1.29 (s, 9H). **¹³C-NMR:** δ 182.6, 159.2, 150.8, 148.1, 144.3, 133.1, 126.6 (2C), 125.8 (2C), 125.3, 124.9, 121.1,

104.6, 44.5, 34.7, 31.5 (3C). **HRMS (EI)**: calculated for $C_{19}H_{18}BrNO_2^+$ $[M]^+$: 371.0515; found: 371.0502.

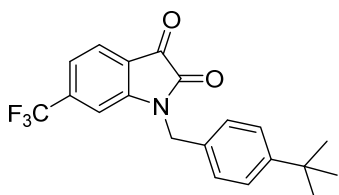
1-Benzyl-7-bromoindoline-2,3-dione (**1l**)



Following general procedure A, 7-bromoisatin (283 mg, 1.25 mmol) and benzyl bromide (236 mg, 1.38 mmol) after 24h, gave **1l** as an orange solid (79% yield).

¹H-NMR: δ 7.66 – 7.57 (m, 2H), 7.35 – 7.22 (m, 5H), 6.98 (t, J = 7.7 Hz, 1H), 5.42 (s, 2H). **¹³C-NMR**: δ 182.5, 159.2, 148.0, 144.3, 136.2, 128.9 (2C), 127.8, 126.6 (2C), 125.4, 124.9, 121.1, 104.6, 44.8. **HRMS (ESI)**: calculated for $C_{15}H_{11}NO_2Br^+$ $[M+H]^+$: 315.9968; found: 315.9950.

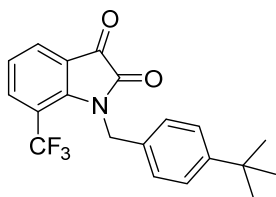
1-[4-(*tert*-Butyl)benzyl]-6-(trifluoromethyl)indoline-2,3-dione (**1m**)



Following general procedure A, 6-trifluoromethylisatin (269 mg, 1.25 mmol) and 1-(bromomethyl)-4-(*tert*-butyl)benzene (314 mg, 1.38 mmol) after 24h, gave **1m** as a yellow solid (66% yield).

¹H-NMR: δ 7.71 (d, J = 7.7 Hz, 1H), 7.43 – 7.35 (m, 3H), 7.30-7.25 (m, 2H), 7.04 (s, 1H), 4.93 (s, 2H), 1.30 (s, 9H). **¹³C-NMR**: δ 182.7, 157.7, 151.9, 151.2, 139.1 (q, J = 32.9 Hz), 130.9, 127.6 (2C), 126.3 (2C), 125.8, 122.9 (q, J = 274.0 Hz), 121.0 (q, J = 4.0 Hz), 120.0, 108.1 (q, J = 3.9 Hz), 44.2, 34.8, 31.4 (3C). **¹⁹F-NMR**: δ -63.9. **HRMS (EI)**: calculated for $C_{20}H_{18}F_3NO_2^+$ $[M]^+$: 361.1284; found: 361.1275.

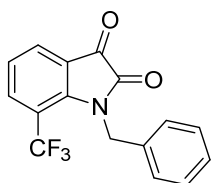
1-[4-(*tert*-Butyl)benzyl]-7-(trifluoromethyl)indoline-2,3-dione (**1n**)



Following general procedure A, 7-trifluoromethylisatin (269 mg, 1.25 mmol) and 1-(bromomethyl)-4-(*tert*-butyl)benzene (314 mg, 1.38 mmol) after 24h, gave **1n** as an orange solid (68% yield).

¹H-NMR: δ 7.85 (d, J = 7.7 Hz, 2H), 7.34 – 7.07 (m, 5H), 5.18 (s, 2H), 1.27 (s, 9H). **¹³C-NMR**: δ 181.6, 159.3, 150.4, 148.9, 135.8 (q, J = 6.0 Hz), 131.9, 128.9, 125.8 (2C), 125.5 (2C), 123.6, 122.5 (q, J = 271.8 Hz), 120.2, 114.9 (q, J = 33.7 Hz), 45.9 (q, J = 5.0 Hz), 34.5, 31.3 (3C). **¹⁹F-NMR**: δ -55.6. **HRMS (EI)**: calculated for $C_{20}H_{18}F_3NO_2^+$ $[M]^+$: 361.1284; found: 361.1288.

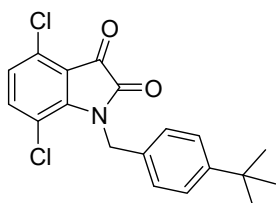
1-Benzyl-7-(trifluoromethyl)indoline-2,3-dione (**1o**)



Following general procedure A, 7-trifluoromethylisatin (269 mg, 1.25 mmol) and benzyl bromide (236 mg, 1.38 mmol) after 24h, gave **1o** as a brown solid (76% yield).

¹H-NMR: δ 7.87 – 7.81 (m, 2H), 7.30 – 7.11 (m, 6H), 5.20 (s, 2H). **¹³C-NMR:** δ 181.6, 159.4, 148.9 (q, J = 1.8 Hz), 136.0 (q, J = 6.0 Hz), 135.1 (q, J = 1.3 Hz), 129.1, 128.8 (2C), 127.6, 126.0 (2C), 123.8, 122.6 (q, J = 272.2 Hz), 120.4, 115.1 (q, J = 33.7 Hz), 46.3 (q, J = 5.0 Hz). **¹⁹F-NMR:** δ -55.6. **HRMS (ESI):** calculated for $C_{16}H_{10}NO_2NaF_3^+$ $[M+Na]^+$: 328.0556; found: 328.0594.

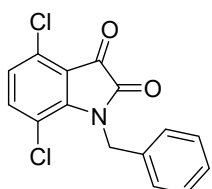
1-[4-(*tert*-Butyl)benzyl]-4,7-dichloroindoline-2,3-dione (**1p**)



Following general procedure A, 4,7-dichloroisatin (270 mg, 1.25 mmol) and 1-(bromomethyl)-4-(*tert*-butyl)benzene (314 mg, 1.38 mmol) after 24h, gave **1p** as an orange solid (63% yield).

¹H-NMR: δ 7.38 (d, J = 8.9 Hz, 1H), 7.34 (d, J = 8.3 Hz, 2H), 7.21 (d, J = 8.3 Hz, 2H), 7.01 (d, J = 8.9 Hz, 1H), 5.36 (s, 2H), 1.29 (s, 9H). **¹³C-NMR:** δ 179.5, 158.2, 151.1, 147.5, 140.8, 133.2, 132.9, 126.7 (2C), 126.6, 125.9 (2C), 117.2, 115.9, 45.1, 34.7, 31.5 (3C). **HRMS (EI):** calculated for $C_{19}H_{17}ClNO_2^+$ $[M-Cl]^+$: 326.0942; found: 326.0885.

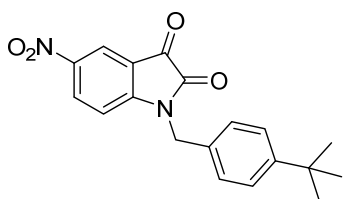
1-Benzyl-4,7-dichloroindoline-2,3-dione (**1q**)



Following general procedure A, 4,7-dichloroisatin (270 mg, 1.25 mmol) and benzyl bromide (236 mg, 1.38 mmol) after 24h, gave **1q** as an orange solid (77% yield).

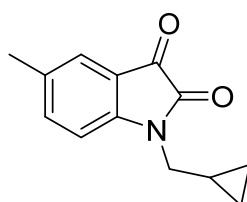
¹H-NMR: δ 7.40 – 7.23 (m, 6H), 7.02 (d, J = 8.7 Hz, 1H), 5.39 (s, 2H) ppm. **¹³C-NMR:** δ 179.4, 158.2, 147.3, 140.8, 136.0, 133.2, 129.0 (2C), 128.0, 126.7 (2C), 126.7, 117.2, 115.9, 45.4 ppm. **HRMS (ESI):** calculated for $C_{15}H_9NO_2Cl_2Na^+$ $[M+Na]^+$: 327.9903; found: 327.9870.

1-[4-(*tert*-Butyl)benzyl]-5-nitroindoline-2,3-dione (**1r**)⁵



It was prepared following the procedure described in the literature:⁵ 5-Nitroindoline-2,3-dione (384 mg, 2.0 mmol, 1.0 eq) was dissolved in 3.0 mL of DMF and the solution was cooled to 0°C. NaH (60% dispersion in mineral oil, 96 mg, 2.0 mmol, 1.0 eq.) was added and the reaction mixture was stirred for 1h at 0°C. Then, 1-(bromomethyl)-4-(*tert*-butyl)benzene (455 mg, 2.0 mmol, 1.0 eq.) was added and the reaction was stirred for 24h at room temperature. After that, ethyl acetate (20 mL) and cold water (10 mL) were added and the organic layer was washed with water (3 x 10 mL), dried over MgSO₄, filtered and the solvent was evaporated under reduced pressure. **1r** was used without further purification (orange solid, 73% yield). ¹H-NMR: δ 8.46 (d, *J* = 2.4 Hz, 1H), 8.43 (dd, *J* = 8.7, 2.4 Hz, 1H), 7.44 – 7.33 (m, 2H), 7.30 – 7.20 (m, 2H), 6.97 (d, *J* = 8.7 Hz, 1H), 4.97 (s, 2H), 1.30 (s, 9H). ¹³C-NMR: δ 181.4, 158.1, 155.1, 152.1, 144.4, 133.6, 130.5, 127.5 (2C), 126.4 (2C), 121.1, 117.5, 111.5, 44.5, 34.8, 31.4 (3C). HRMS (ESI): calculated for C₁₉H₁₉N₂O₄⁺ [M+H]⁺: 339.1339; found: 339.1389.

1-(Cyclopropylmethyl)-5-methylindoline-2,3-dione (**1s**)⁶



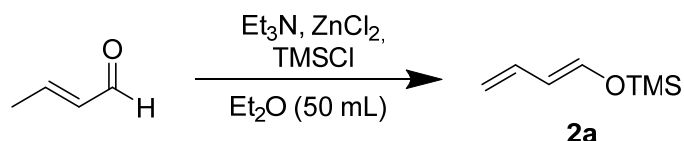
It was prepared following a procedure described in the literature:⁶ 5-Methylisatin (202 mg, 1.25 mmol, 1.0 eq) and Cs₂CO₃ (652 mg, 2.00 mmol, 1.6 eq.) were dissolved in 20 mL of DMF. (Bromomethyl)-cyclopropane (224 mg, 1.66 mmol, 1.3 eq.) was added and the reaction mixture was stirred for 72h at room temperature. The solution was then diluted with ethyl acetate (30 mL) and washed with water (3 x 20 mL), dried over MgSO₄, filtered and the solvent was evaporated under reduced pressure. **1s** was used without further purification. (red solid, 77% yield). The ¹H-NMR in accordance with the literature. ¹H-NMR: δ 7.46 – 7.35 (m, 2H), 6.86 (d, *J* = 8.0 Hz, 1H), 3.59 (d, *J* = 7.0 Hz, 2H), 2.34 (s, 3H), 1.22 – 1.10 (m, 1H), 0.61 – 0.53 (m, 2H), 0.44 – 0.37 (m, 2H).

⁵ R. Romagnoli, P. Giovanni Baraldi, O. Cruz-Lopez, D. Preti, J. Bermejo and F. Estévez, *ChemMedChem* 2009, **4**, 1668-1676.

⁶ X. Jia, Y. Zhu, Y. Yuan, X. Zhang, S. Lü, L. Zhang and L. Luo, *ACS Catal.* 2016, **6**, 6033-6036.

3. Synthesis and characterization data of silyl dienol ethers 2

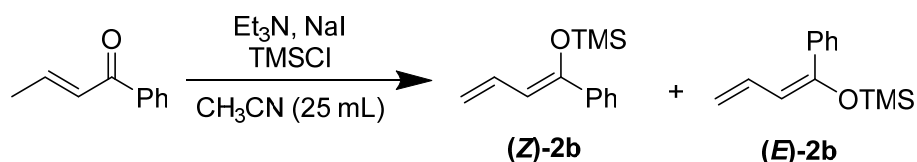
(E)-(Buta-1,3-dien-1-yloxy)trimethylsilane (**2a**)⁷



It was prepared following a modified procedure described in the literature:⁷ To a two-neck round bottom flask charged with a condenser previously oven-dried was added a magnetic stirrer and anhydrous powder zinc chloride (204 mg, 1.5 mmol, 0.03 eq.) under nitrogen atmosphere. Then, Et₃N (10.1 mL, 73 mmol, 1.5 eq.) was added and the mixture was stirred at room temperature for 1h. A solution of crotonaldehyde (4.1 mL, 50 mmol, 1.0 eq.) in anhydrous diethylether (50 mL) and was added under nitrogen atmosphere. Then TMSCl (12.7 mL, 100 mmol, 2.0 eq.) was added dropwise and the reaction mixture was refluxed for 24h. The solvent was evaporated under reduced pressure and pentane was added. The mixture was filtered through latrobeads silica gel and the filtrate was concentrated under reduced pressure. Purification by Kugelrohr distillation (b.p. 40-45°C, 25 mmHg) gave **2a** as colorless liquid (82% yield). The ¹H-NMR is in accordance with the literature.

¹H-NMR: δ 6.54 (d, *J* = 11.9 Hz, 1H), 6.22 (dt, *J* = 16.9, 10.6 Hz, 1H), 5.72 (t, *J* = 11.4 Hz, 1H), 5.03 – 4.95 (m, 2H), 4.86 – 4.80 (m, 1H), 0.21 (s, 9H).

Trimethyl[(1-phenylbuta-1,3-dien-1-yl)oxy]silane (**2b**)⁸



It was prepared according to a modified procedure described in the literature:⁸ To a round bottom flask previously oven-dried was charged with a magnetic stirrer and the 1-phenyl-2-buten-1-one (1.02 g, 7 mmol, 1.0 eq.) under nitrogen atmosphere. Then, Et₃N (1.2 mL, 8.7 mmol, 1.3 eq.) and TMSCl (1.1 mL, 8.7 mmol, 1.3 eq.) were added. Next, a solution of NaI (1.3 g, 8.7 mmol, 1.3 eq.) in 25 mL of CH₃CN was added dropwise under nitrogen atmosphere. The reaction mixture was heated at 80°C and stirred at this temperature for 24h. After that, the mixture was cooled, 50 mL of pentane were added and the organic layer was washed with water (3x50 mL), dried over MgSO₄, filtered and the solvent was evaporated under reduced pressure. Purification

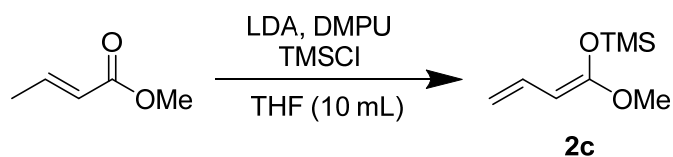
⁷ Y. Cui, H. Jiang, Z. Li, N. Wu, Z. Yang and J. Quan, *Org. Lett.*, 2009, **11**, 4628–4631.

⁸ S. E. Denmark and J. R. Heemstra, *J. Org. Chem.*, 2007, **72**, 5668–5688.

by Kugelrohr distillation (b.p. 65-70°C, 25 mmHg) gave **2b** as a colorless liquid (78% yield, mixture of isomers *Z:E*, 60:40). The ¹H-NMR is in accordance with the literature.

¹H-NMR: δ 7.58 – 7.48 (m, 2H), 7.47 – 7.37 (m, 2H), 7.40 – 7.23 (m, 6H), 6.74 (dt, *J* = 17.0, 10.6 Hz, 1H, *Z*), 6.48 (dt, *J* = 16.8, 10.6 Hz, 1H, *E*), 6.06 (d, *J* = 10.8 Hz, 1H, *Z*), 5.78 (d, *J* = 11.1 Hz, 1H, *E*), 5.27 – 5.19 (m, 1H, *Z*), 5.14 – 5.07 (m, 1H, *E*), 5.05 – 5.00 (m, 1H, *Z*), 4.89 – 4.82 (m, 1H, *E*), 0.18 (s, 9H, *E*), 0.17 (s, 9H, *Z*) ppm.

(*Z*)-[(1-Methoxybuta-1,3-dien-1-yl)oxy]trimethylsilane (2c**)⁹**

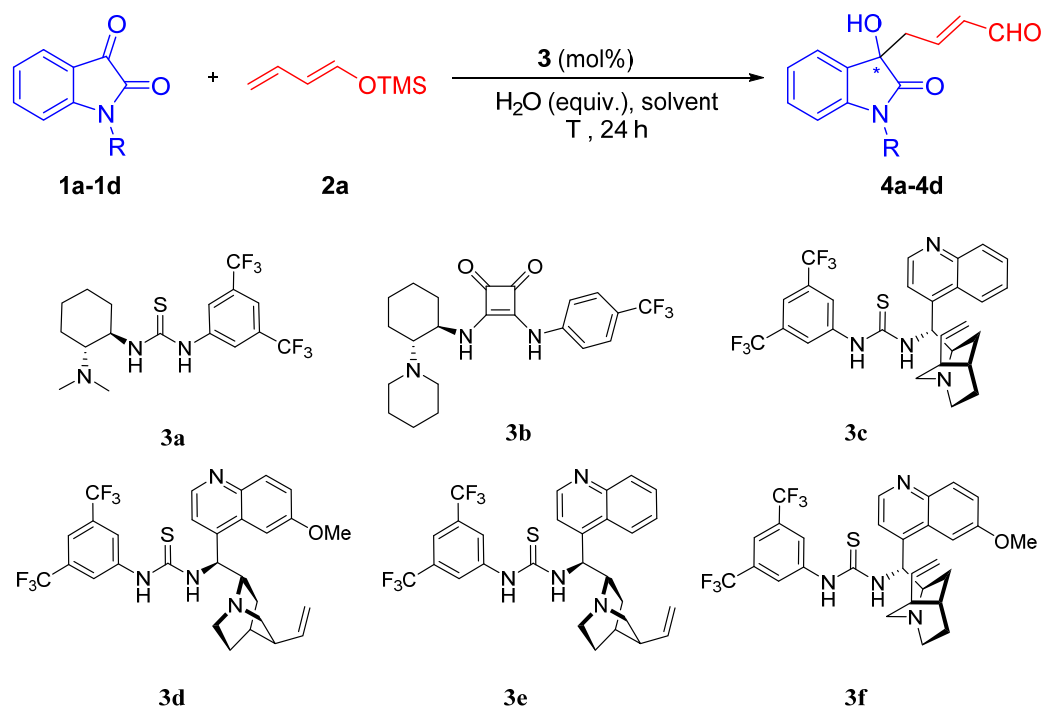


It was prepared according to a modified procedure described in the literature: To a round bottom flask previously oven-dried was charged with a magnetic stirrer under nitrogen atmosphere. Then, anhydrous THF (10 mL) and distilled diisopropylamine (2.5 mL, 18 mmol, 1.8 eq.) were added and the solution was cooled to 0°C. Subsequently, *n*-BuLi (7.8 mL, 1.6M in hexanes, 12.5 mmol, 1.3 eq.) was added dropwise and the solution was stirred at 0°C for 15 minutes. Then, the mixture was cooled to -78°C and DMPU (1.5 mL, 12.5 mmol, 1.3 eq.), the methyl (*E*)-but-2-enoate (1.0 mL, 10 mmol, 1.0 eq.) and the TMSCl (1.9 mL, 15 mmol, 1.5 eq.) were added dropwise keeping the temperature at -78°C. The reaction mixture was warmed to room temperature and stirred for 2h. Next, the solvent was evaporated under reduced pressure. Pentane was added and the mixture was filtered through a short pad of celite and the filtrate was concentrated under reduced pressure. Purification by Kugelrohr distillation (b.p. 70-75°C, 25 mmHg) gave **2c** as a colorless liquid (64% yield). The ¹H-NMR is in accordance with the literature.

¹H-NMR: δ 6.48 (dt, *J* = 17.2, 10.4 Hz, 1H), 4.85 (dd, *J* = 17.2, 2.0 Hz, 1H), 4.60 (dd, *J* = 10.2, 2.2 Hz, 1H), 4.49 (d, *J* = 10.4 Hz, 1H), 3.58 (s, 3H), 0.19 (s, 9H) ppm.

⁹ M. Frias, R. Mas-Ballesté, S. Arias, C. Alvarado, J. Alemán, *J. Am. Chem. Soc.*, **2017**, *139*, 672–679.

4. Optimisation table



Entry	R	3 (mol%)	H ₂ O (equiv.)	Solvent	T (°C)	Conversion (%) ^b	ee (%) ^c
1	H	3a (20)	3	DCM	r.t	100	30:70
2	Me	3a (20)	3	DCM	r.t	100	19:81
3	Bn	3a (20)	3	DCM	r.t	100	13:87
4	Bn	3a (10)	3	DCM	r.t	100	13:87
5	Bn	3b (10)	3	DCM	r.t	100	33:67
6	Bn	3c (10)	3	DCM	r.t	100	87:14
7	Bn	3d (10)	3	DCM	r.t	100	89:11
8	Bn	3e (10)	3	DCM	r.t	100	12:88
9	Bn	3f (10)	3	DCM	r.t	100	12:88
10	Bn	3d (10)	3	Dioxane	r.t	100	88:12
11	Bn	3d (10)	3	THF	r.t	100	91:2
12	Bn	3d (10)	3	TBME	r.t	100	87:13
13	Bn	3d (10)	3	DME	r.t	100	90:10
14	Bn	3d (10)	3	DCM	r.t	100	89:11
15	Bn	3d (10)	3	DCE	r.t	100	88:12
16	Bn	3d (10)	3	Toluene	r.t	100	85:15

17	Bn	3d (10)	3	Xylene	r.t	100	87:13
18	Bn	3d (10)	3	THF	0	100	92:8
19	Bn	3d (10)	3	THF	-30	100	93:7
20	Bn	3d (10)	3	THF	-78	35	93:7
21	Bn	3d (10)	0	THF	-30	5	-
22	Bn	3d (10)	1	THF	-30	57	92:8
23	Bn	3d (10)	6	THF	-30	56	92:8
24	-CH₂C₆H₄- p^tBu	3d (10)	3	THF	-30	100	99:1

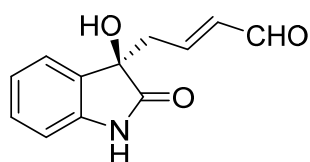
^a All the reactions were performed in 0.1 mmol with 0.3 mL of solvent . ^b Determined by ¹H NMR analysis of the crude. ^c Determined by SFC chromatography.

5. Synthesis and characterization data of 3-hydroxy-2-oxoindolin-3-ylbut-2-enals 4

General procedure B: vinylogous Mukaiyama aldol reaction to isatins. Synthesis of 3-hydroxy-2-oxoindolin-3-ylbut-2-enals

Catalyst **3d** (6.0 mg, 0.01 mmol, 0.1 equiv) and the corresponding isatin **1** (0.1 mmol, 1.0 eq.) were dissolved in anhydrous tetrahydrofuran (0.3 mL) in an oven-dried vial. Then, after cooling the reaction to the corresponding temperature if needed, the silyl dienol ether **2** (0.3 mmol, 3.0 equiv.) and water (5 μ L, 3.0 equiv.) were added. The reaction was stirred for the indicated time. The mixture was then concentrated *in vacuo*. Finally, the crude mixture was purified by flash column chromatography using Iatrobeads silica gel and eluting with the solvent indicated in each case.

(*R,E*)-4-(3-Hydroxy-2-oxoindolin-3-yl)but-2-enal (**4a**)



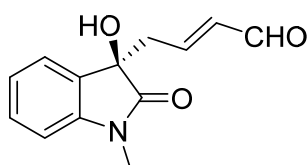
Following general procedure B, isatin **1a** (14.7 mg, 0.1 mmol) and silyl dienol ether **2a** (53 μ L, 0.3 mmol) after 24h at room temperature, gave **4a** (64% yield) as a white solid. Eluent: cyclohexane: ethyl acetate; 3:1.

$[\alpha]_{\text{D}}^{20} = +1.5$ (c 0.77, CHCl₃).

¹H-NMR (*d*⁶-DMSO): δ 10.33 (s, 1H), 9.45 (d, *J* = 7.9 Hz, 1H), 7.29 (d, *J* = 7.5 Hz, 1H), 7.22 (td, *J* = 7.7, 1.3 Hz, 1H), 6.97 (td, *J* = 7.5, 1.1 Hz, 1H), 6.94 – 6.85 (m, 1H), 6.82 (d, *J* = 7.5 Hz, 1H), 6.22 (s,

1H), 6.03 (dd, $J = 15.5, 7.9$ Hz, 1H), 2.84 (dd, $J = 14.2, 6.8$ Hz, 1H, CH_2), 2.71 (dd, $J = 14.2, 7.9$ Hz, 1H, CH_2). ^{13}C -NMR (d^6 -DMSO): δ 194.4, 178.2, 152.4, 141.3, 135.3, 131.2, 129.2, 124.2, 121.6, 109.7, 74.6, 40.6. **HRMS (ESI)⁺**: calculated for $C_{12}H_{10}NO_2^+$ [M-OH]⁺: 200.0706; found 200.0698. The enantiomeric ratio was determined by SFC using a Chiralpak IG-3 column [CO₂/MeOH from 95:5 to 60:40 in 8 min, flow rate 2.0 mL/min], $\tau_{major} = 5.21$ min, $\tau_{minor} = 6.84$ min (e.r. = 70:30).

(*R,E*)-4-(3-Hydroxy-1-methyl-2-oxoindolin-3-yl)but-2-enal (4b)

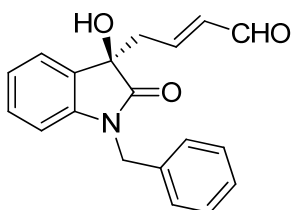


Following general procedure B, isatin **1b** (16.1 mg, 0.1 mmol) and silyl dienol ether **2a** (53 μ L, 0.3 mmol) after 24h at room temperature, gave **4b** (74% yield) as a colorless oil. Eluent: cyclohexane: ethyl acetate; 3:1.

$[\alpha]_D^{20} = +15.6$ (c 0.65, CHCl₃).

1H -NMR: δ 9.44 (d, $J = 7.8$ Hz, 1H), 7.42-7.32 (m, 2H), 7.17-7.06 (m, 1H), 6.87 (d, $J = 7.6$ Hz, 1H), 6.85-6.76 (m, 1H), 6.11 (dd, $J = 15.6, 7.8$ Hz, 1H), 3.20 (s, 3H), 3.11-2.75 (m, 2H), 2.91 (bs, 1H, OH). ^{13}C -NMR: δ 193.4, 177.1, 149.7, 143.1, 136.8, 130.4, 129.1, 124.2, 123.6, 108.9, 75.5, 41.6, 26.5. **HRMS (ESI)**: calculated for $C_{13}H_{12}NO_2^+$ [M-OH]⁺: 214.0863; found 214.0881. The enantiomeric ratio was determined by SFC using a Chiralpak IG-3 column [CO₂/MeOH from 95:5 to 60:40 in 8 min, flow rate 2.0 mL/min], $\tau_{major} = 4.65$ min, $\tau_{minor} = 4.93$ min (e.r. = 82:18).

(*R,E*)-4-(1-Benzyl-3-hydroxy-2-oxoindolin-3-yl)but-2-enal (4c)

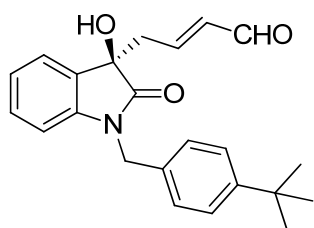


Following general procedure B, isatin **1c** (23.7 mg, 0.1 mmol) and silyl dienol ether **2a** (53 μ L, 0.3 mmol) after 24h at -30 °C, gave **4c** (74% yield) as a colorless oil. Eluent: cyclohexane: ethyl acetate; 3:1.

$[\alpha]_D^{20} = -1.4$ (c 0.71, CHCl₃).

1H -NMR: 9.37 (d, $J = 7.8$ Hz, 1H), 7.38 (d, $J = 7.4$ Hz, 1H), 7.31 – 7.22 (m, 6H), 7.09 (t, $J = 7.4$ Hz, 1H), 6.77 (d, $J = 7.8$ Hz, 1H), 6.67 (m, 1H), 6.11 (dd, $J = 15.7, 7.8$ Hz, 1H), 5.01 (d, $J = 15.7$ Hz, 1H, CH_2), 4.71 (d, $J = 15.6$ Hz, 1H, CH_2), 3.04 (dd, $J = 13.8, 6.4$ Hz, 1H, CH_2), 2.93 (dd, $J = 13.8, 8.5$ Hz, 1H, CH_2). ^{13}C -RMN δ 193.4, 177.2, 149.4, 142.3, 136.8, 135.3, 130.4, 129.1 (2C), 129.0, 128.1, 127.5 (2C), 124.2, 123.7, 110.0, 75.6, 44.1, 41.8. **HRMS (ESI)**: calculated for $C_{19}H_{18}NO_3^+$ [M+H]⁺: 308.1281; found 308.1270. The enantiomeric ratio was determined by SFC using a Chiralpak IC column [CO₂/MeOH from 95:5 to 60:40 in 8 min, flow rate 3.0 mL/min], $\tau_{major} = 5.27$ min, $\tau_{minor} = 4.82$ min (e.r. = 93:7).

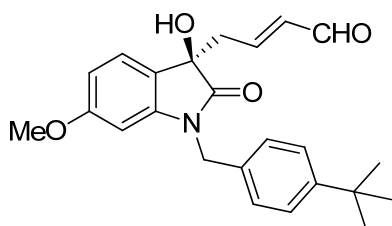
(*R,E*)-4-{1-[4-(*tert*-Butyl)benzyl]-3-hydroxy-2-oxoindolin-3-yl}but-2-enal (4d**)**



Following general procedure B, isatin **1d** (29.3 mg, 0.1 mmol) and silyl dienol ether **2a** (53 μ L, 0.3 mmol) after 24h at -30 $^{\circ}$ C, gave **4d** (82% yield) as a colorless oil. Eluent: cyclohexane: ethyl acetate; 3:1. $[\alpha]_D^{20} = -8.4$ (*c* 0.99, CHCl_3).

$^1\text{H-NMR}$: δ 9.36 (d, *J* = 7.8 Hz, 1H), 7.37 (d, *J* = 7.3 Hz, 1H), 7.34 – 7.17 (m, 5H), 7.09 (t, *J* = 7.5 Hz, 1H), 6.82 (d, *J* = 7.8 Hz, 1H), 6.74 – 6.62 (m, 1H), 6.10 (dd, *J* = 15.7, 7.8 Hz, 1H), 4.98 (d, *J* = 15.5 Hz, 1H, CH_2), 4.68 (d, *J* = 15.5 Hz, 1H, CH_2), 3.15 (s, 1H, OH), 3.03 (dd, *J* = 13.9, 6.6 Hz, 1H, CH_2), 2.92 (dd, *J* = 13.9, 8.4 Hz, 1H, CH_2), 1.28 (s, 9H). $^{13}\text{C-RMN}$ δ 193.4, 177.1, 151.1, 149.5, 142.5, 136.8, 132.3, 130.4, 129.0, 127.3 (2C), 125.9 (2C), 124.2, 123.6, 110.0, 75.6, 43.8, 41.9, 34.7, 31.4 (3C). **HRMS (ESI)**: calculated for $\text{C}_{23}\text{H}_{25}\text{NO}_3\text{Na}^+$ [$\text{M}+\text{Na}$] $^+$: 386.1727; found 386.1735. The enantiomeric ratio was determined by SFC using a Chiralpak IG-3 column [CO_2/MeOH 80:20, flow rate 2.0 mL/min] $\tau_{\text{major}} = 6.85$ min, $\tau_{\text{minor}} = 12.76$ min (e.r. = 99:1).

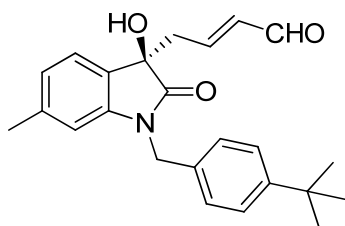
(*R,E*)-4-(1-(4-(*tert*-Butyl)benzyl)-3-hydroxy-6-methoxy-2-oxoindolin-3-yl)but-2-enal (4e**)**



Following general procedure B, isatin **1e** (32.3 mg, 0.1 mmol) and silyl dienol ether **2a** (53 μ L, 0.3 mmol) after 24h at -30 $^{\circ}$ C, gave **4e** (75% yield) as a colorless oil. Eluent: dichloromethane: diethyl ether; 9:1. $[\alpha]_D^{20} = -18.8$ (*c* 0.88, CHCl_3).

$^1\text{H-NMR}$: δ 9.36 (d, *J* = 7.8 Hz, 1H), 7.34 – 7.27 (m, 3H), 7.18 (d, *J* = 8.3 Hz, 2H), 6.72 – 6.60 (m, 1H), 6.55 (dd, *J* = 8.2, 2.2 Hz, 1H), 6.38 (d, *J* = 2.2 Hz, 1H), 6.10 (dd, *J* = 15.6, 7.7 Hz, 1H), 4.95 (d, *J* = 15.6 Hz, 1H, CH_2), 4.64 (d, *J* = 15.4 Hz, 1H, CH_2), 3.76 (s, 3H), 3.01 (dd, *J* = 13.9, 6.4 Hz, 1H, CH_2), 2.90 (dd, *J* = 13.9, 8.5 Hz, 1H, CH_2), 1.28 (s, 9H). $^{13}\text{C-RMN}$ δ 193.4, 177.5, 161.7, 151.1, 149.8, 144.0, 136.7, 132.3, 127.3 (2C), 126.0 (2C), 125.1, 120.9, 106.9, 98.2, 75.3, 55.7, 43.8, 41.9, 34.7, 31.4 (3C). **HRMS (ESI)**: calculated for $\text{C}_{24}\text{H}_{31}\text{N}_2\text{O}_4^+$ [$\text{M}+\text{NH}_4$] $^+$: 411.2278; found 411.2284. The enantiomeric ratio was determined by SFC using a Chiralpak IC column [CO_2/MeOH from 95:5 to 60:40 in 8 min, flow rate 3.0 mL/min], $\tau_{\text{major}} = 5.22$ min, $\tau_{\text{minor}} = 4.78$ min (e.r. = 93:7).

(*R,E*)-4-{1-[4-(*tert*-Butyl)benzyl]-3-hydroxy-2-oxo-6-methylindolin-3-yl}but-2-enal (4f**)**

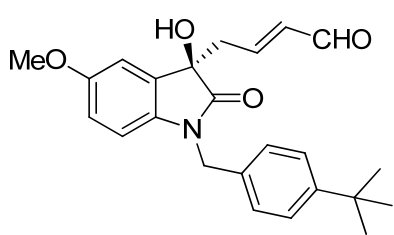


Following general procedure B, isatin **1f** (30.7 mg, 0.1 mmol) and silyl dienol ether **2a** (53 μ L, 0.3 mmol) after 24h at -30 $^{\circ}$ C, gave **4f** (74% yield) as a colorless oil. Eluent: dichloromethane: diethyl ether; 9:1.

$[\alpha]_D^{20} = -16.8$ (c 0.88, CHCl_3).

$^1\text{H-NMR}$: δ 9.36 (d, $J = 7.8$ Hz, 1H), 7.36 – 7.28 (m, 2H), 7.21 (t, $J = 8.2$ Hz, 3H), 6.89 (d, $J = 7.5$ Hz, 1H), 6.74 – 6.65 (m, 1H), 6.64 (bs, 1H), 6.09 (dd, $J = 15.7, 7.8$ Hz, 1H), 4.96 (d, $J = 15.5$ Hz, 1H, CH_2), 4.66 (d, $J = 15.5$ Hz, 1H, CH_2), 3.02 (dd, $J = 13.8, 6.6$ Hz, 1H, CH_2), 2.98 (bs, 1H), 2.90 (dd, $J = 13.8, 8.4$ Hz, 1H, CH_2), 2.32 (s, 3H), 1.29 (s, 9H). **$^{13}\text{C-RMN}$** : δ 193.4, 177.3, 151.1, 149.7, 142.7, 140.8, 136.7, 132.5, 127.2 (2C), 126.1, 126.0 (2C), 124.1, 123.9, 110.7, 75.4, 43.7, 41.9, 34.7, 31.4 (3C), 22.1. **HRMS (ESI)**: calculated for $\text{C}_{24}\text{H}_{27}\text{NO}_3\text{Na}^+$ $[\text{M}+\text{Na}]^+$: 400.1883; found 400.1863. The enantiomeric ratio was determined by SFC using a Chiralpak IC column [CO_2/MeOH from 95:5 to 60:40 in 8 min, flow rate 3.0 mL/min], $\tau_{\text{major}} = 5.11$ min, $\tau_{\text{minor}} = 4.72$ min (e.r. = 96:4).

(*R,E*)-4-{1-[4-(*tert*-Butyl)benzyl]-3-hydroxy-5-methoxy-2-oxoindolin-3-yl}but-2-enal (4g**)**

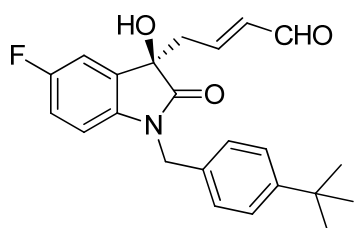


Following general procedure B, isatin **1g** (32.3 mg, 0.1 mmol) and silyl dienol ether **2a** (53 μ L, 0.3 mmol) after 24h at -30 $^{\circ}$ C, gave **4g** (84% yield) as a colorless oil. Eluent: dichloromethane: diethyl ether; 10:1.

$[\alpha]_D^{20} = +15.8$ (c 1.07, CHCl_3).

$^1\text{H-NMR}$: δ 9.34 (d, $J = 7.8$ Hz, 1H), 7.31 (d, $J = 8.3$ Hz, 2H), 7.18 (d, $J = 8.3$ Hz, 2H), 6.99 (d, $J = 2.5$ Hz, 1H), 6.77 (dd, $J = 8.6, 2.5$ Hz, 1H), 6.70 (d, $J = 8.6$ Hz, 1H), 6.68 – 6.59 (m, 1H), 6.10 (dd, $J = 15.7, 7.8$ Hz, 1H), 4.96 (d, $J = 15.5$ Hz, 1H, CH_2), 4.65 (d, $J = 15.5$ Hz, 1H, CH_2), 3.76 (s, 3H), 3.61 (s, 1H, OH), 3.02 (dd, $J = 13.9, 6.7$ Hz, 1H, CH_2), 2.93 (dd, $J = 13.9, 8.4$ Hz, 1H, CH_2), 1.28 (s, 9H). **$^{13}\text{C-RMN}$** δ 193.4, 177.0, 156.7, 151.1, 149.5, 136.8, 135.6, 132.4, 130.4, 127.3 (2C), 125.9 (2C), 114.7, 111.3, 110.6, 76.0, 55.9, 43.8, 41.9, 34.7, 31.4 (3C). **HRMS (ESI)**: calculated for $\text{C}_{24}\text{H}_{27}\text{NO}_4\text{Na}^+$ $[\text{M}+\text{Na}]^+$: 416.1832; found 416.1806. The enantiomeric ratio was determined by SFC using a Chiralpak IB-3 column [CO_2/MeOH from 95:5 to 60:40 in 8 min, flow rate 2.0 mL/min], $\tau_{\text{major}} = 5.09$ min, $\tau_{\text{minor}} = 4.82$ min (e.r. = 95:5).

(*R,E*)-4-{1-[4-(*tert*-Butyl)benzyl]-5-fluoro-3-hydroxy-2-oxoindolin-3-yl}but-2-enal (4h**)**

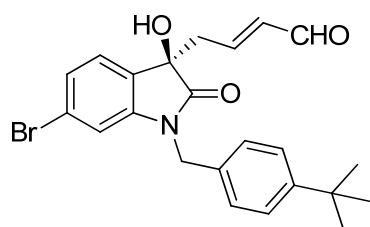


Following general procedure B, isatin **1h** (31.4 mg, 0.1 mmol) and silyl dienol ether **2a** (53 μ L, 0.3 mmol) after 24h at -30 $^{\circ}$ C, gave **4h** (74% yield) as a colorless oil. Eluent: dichloromethane: diethyl ether; 9:1.

$[\alpha]_{\text{D}}^{20} = -7.2$ (c 1.01, CHCl_3).

$^1\text{H-NMR}$: δ 9.37 (d, $J = 7.8$ Hz, 1H), 7.32 (d, $J = 8.3$ Hz, 2H), 7.17 (d, $J = 8.3$ Hz, 2H), 7.13 (dd, $J = 7.5, 2.6$ Hz, 1H), 6.96 (td, $J = 8.8, 2.6$ Hz, 1H), 6.73 (dd, $J = 8.6, 4.0$ Hz, 1H), 6.70 – 6.60 (m, 1H), 6.12 (dd, $J = 15.7, 7.8$ Hz, 1H), 4.97 (d, $J = 15.5$ Hz, 1H, CH_2), 4.67 (d, $J = 15.5$ Hz, 1H, CH_2), 3.02 (dd, $J = 13.9, 6.7$ Hz, 1H, CH_2), 2.93 (dd, $J = 13.9, 8.4$ Hz, 1H, CH_2), 1.28 (s, 9H). **$^{13}\text{C-RMN}$** δ 193.2, 176.9, 159.6 (d, $J = 243.2$ Hz), 151.3, 148.6, 138.3 (d, $J = 2.2$ Hz), 137.0, 131.9, 130.6 (d, $J = 7.7$ Hz), 127.2 (2C), 126.1 (2C), 116.7 (d, $J = 23.5$ Hz), 112.4 (d, $J = 24.8$ Hz), 110.8 (d, $J = 7.9$ Hz), 75.7, 43.9, 41.9, 34.7, 31.4 (3C). **$^{19}\text{F-RMN}$** δ 118.6. **HRMS (ESI)**: calculated for $\text{C}_{23}\text{H}_{28}\text{N}_2\text{O}_3\text{F}^+$ [$\text{M}+\text{NH}_4$] $^+$: 399.2078 found 399.2071. The enantiomeric ratio was determined by SFC using a Chiralpak IC column [CO_2/MeOH from 95:5 to 60:40 in 8 min, flow rate 3.0 mL/min], $\tau_{\text{major}} = 4.66$ min, $\tau_{\text{minor}} = 4.18$ min (e.r. = 93:7).

(*R,E*)-4-{6-Bromo-1-[4-(*tert*-butyl)benzyl]-3-hydroxy-2-oxoindolin-3-yl}but-2-enal (4i**)**

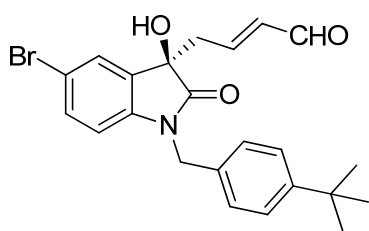


Following general procedure B, isatin **1i** (37.2 mg, 0.1 mmol) and silyl dienol ether **2a** (53 μ L, 0.3 mmol) after 24h at -30 $^{\circ}$ C, gave **4i** (73% yield) as a colorless oil. Eluent: dichloromethane: diethyl ether; 9:1.

$[\alpha]_{\text{D}}^{20} = -5.2$ (c 1.33, CHCl_3).

$^1\text{H-NMR}$: δ 9.38 (d, $J = 7.7$ Hz, 1H), 7.34 (d, $J = 8.2$ Hz, 2H), 7.26 – 7.22 (m, 2H), 7.18 (d, $J = 8.2$ Hz, 2H), 6.97 (s, 1H), 6.74 – 6.50 (m, 1H), 6.11 (dd, $J = 16.1, 7.7$ Hz, 1H), 4.96 (d, $J = 15.5$ Hz, 1H, CH_2), 4.64 (d, $J = 15.5$ Hz, 1H, CH_2), 3.00 (dd, $J = 14.3, 5.9$ Hz, 1H, CH_2), 2.89 (dd, $J = 14.3, 8.6$ Hz, 1H, CH_2), 1.30 (s, 9H). **$^{13}\text{C-RMN}$** δ 193.2, 176.8, 151.4, 148.6, 143.8, 137.1, 131.8, 127.9, 127.2 (2C), 126.5, 126.2 (2C), 125.5, 124.2, 113.4, 75.2, 43.9, 41.7, 34.7, 31.4 (3C). **HRMS (ESI)**: calculated for $\text{C}_{23}\text{H}_{24}\text{NO}_3\text{BrNa}^+$ [$\text{M}+\text{Na}$] $^+$: 464.0832; found 464.0820. The enantiomeric ratio was determined by SFC using a Chiralpak IC column [CO_2/MeOH from 95:5 to 60:40 in 8 min, flow rate 3.0 mL/min], $\tau_{\text{major}} = 4.98$ min, $\tau_{\text{minor}} = 4.62$ min (e.r. = 94:6).

(*R,E*)-4-{5-Bromo-1-[4-(*tert*-butyl)benzyl]-3-hydroxy-2-oxoindolin-3-yl}but-2-enal (4j**)**

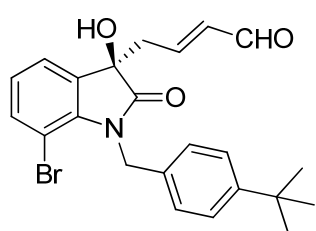


Following general procedure B, isatin **1j** (37.2 mg, 0.1 mmol) and silyl dienol ether **2a** (53 μ L, 0.3 mmol) after 24h at -30 $^{\circ}$ C, gave **4j** (84% yield) as a colorless oil. Eluent: dichloromethane: diethyl ether; 16:1.

$[\alpha]_{D}^{20} = -12.4$ (c 1.24, CHCl_3).

$^1\text{H-NMR}$: δ 9.35 (d, $J = 7.7$ Hz, 1H), 7.50 (d, $J = 2.0$ Hz, 1H), 7.38 (dd, $J = 8.3, 2.0$ Hz, 1H), 7.33 – 7.24 (m, 2H), 7.15 (d, $J = 8.3$ Hz, 2H), 6.67 (d, $J = 8.3$ Hz, 1H), 6.65 – 6.54 (m, 1H), 6.12 (dd, $J = 15.7, 7.7$ Hz, 1H), 4.95 (d, $J = 15.5$ Hz, 1H, CH_2), 4.65 (d, $J = 15.5$ Hz, 1H, CH_2), 3.42 (s, 1H, OH), 3.06 – 2.89 (m, 2H), 1.28 (s, $J = 6.2$ Hz, 9H). **$^{13}\text{C-RMN}$** δ 193.2, 176.6, 151.4, 148.5, 141.4, 137.0, 133.2, 131.8, 131.1, 127.5, 127.2 (2C), 126.1 (2C), 116.4, 111.6, 75.6, 43.9, 41.8, 34.7, 31.4 (3C). **HRMS (ESI)**: calculated for $\text{C}_{23}\text{H}_{24}\text{NO}_3\text{BrNa}^+$ $[\text{M}+\text{Na}]^+$: 464.0832; found 464.0852. The enantiomeric ratio was determined by SFC using a Chiralpak IB-3 column [CO_2/MeOH from 95:5 to 60:40 in 8 min, flow rate 2.0 mL/min], $\tau_{\text{major}} = 5.18$ min, $\tau_{\text{minor}} = 4.68$ min (e.r. = 92:8).

(*R,E*)-4-(7-Bromo-1-[4-(*tert*-butyl)benzyl]-3-hydroxy-2-oxoindolin-3-yl)but-2-enal (4k**)**

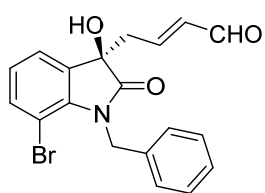


Following general procedure B, isatin **1k** (37.2mg, 0.1 mmol) and silyl dienol ether **2a** (53 μ L, 0.3 mmol) after 24h at -30 $^{\circ}$ C, gave **4k** (79% yield) as a colorless oil. Eluent: dichloromethane: diethyl ether; 19:1.

$[\alpha]_{D}^{20} = -5.2$ (c 1.33, CHCl_3).

$^1\text{H-NMR}$: δ 9.40 (d, $J = 7.8$ Hz, 1H), 7.45 (dd, $J = 8.2, 1.2$ Hz, 1H), 7.35 – 7.29 (m, 3H), 7.15 (d, $J = 8.4$ Hz, 2H), 6.98 (dd, $J = 8.2, 7.3$ Hz, 1H), 6.74 – 6.56 (m, 1H), 6.10 (dd, $J = 16.1, 7.6$ Hz, 1H), 5.40 (d, $J = 16.1$ Hz, 1H, CH_2), 5.30 (d, $J = 16.1$ Hz, 1H, CH_2), 3.03 – 2.96 (m, 1H, CH_2), 2.96 (s, 1H), 2.95 – 2.86 (m, 1H, CH_2), 1.28 (s, 9H). **$^{13}\text{C-RMN}$** δ 193.2, 177.9, 150.6, 148.6, 140.1, 137.1, 136.4, 133.8, 132.3, 126.5 (2C), 125.8 (2C), 124.9, 123.4, 103.4, 74.7, 44.5, 42.1, 34.6, 31.4 (3C). **HRMS (ESI)**: calculated for $\text{C}_{23}\text{H}_{28}\text{N}_2\text{O}_3\text{Br}^+$ $[\text{M}+\text{NH}_4]^+$: 459.1278; found 459.1324. The enantiomeric ratio was determined by SFC using a Chiralpak IC column: [CO_2/MeOH from 95:5 to 60:40 in 8 min, flow rate 3.0 mL/min], $\tau_{\text{major}} = 5.48$ min, $\tau_{\text{minor}} = 4.90$ min (e.r. = 85:15).

(*R,E*)-4-(1-Benzyl-7-bromo-3-hydroxy-2-oxoindolin-3-yl)but-2-enal (4l**)**

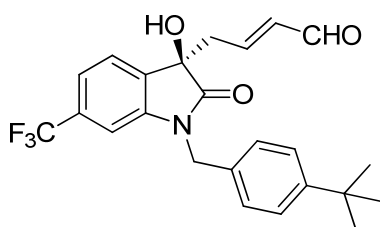


Following general procedure B, isatin **1l** (31.6 mg, 0.1 mmol) and silyl dienol ether **2a** (53 μ L, 0.3 mmol) after 24h at -30 $^{\circ}$ C, gave **4l** (83% yield) as a colorless oil. Eluent: dichloromethane: diethyl ether; 9:1.

$[\alpha]_D^{20} = -55.5$ (c 1.07, CHCl_3).

$^1\text{H-NMR}$: δ 9.40 (d, $J = 7.8$ Hz, 1H), 7.44 – 7.29 (m, 4H), 7.19 – 7.16 (m, 2H), 7.02 – 6.93 (m, 2H), 6.69 – 6.59 (m, 1H), 6.08 (dd, $J = 15.6, 7.7$ Hz, 1H), 5.40 (d, $J = 16.4$ Hz, 1H, CH_2), 5.30 (d, $J = 16.4$ Hz, 1H, CH_2), 2.99 (dd, $J = 13.9, 7.0$ Hz, 1H, CH_2), 2.91 (dd, $J = 13.9, 8.3$ Hz, 1H, CH_2). **$^{13}\text{C-RMN}$** : δ 193.3, 178.1, 148.6, 139.9, 137.1, 136.8, 136.3, 132.4, 128.8 (2C), 127.6, 126.6 (2C), 125.0, 123.4, 103.4, 74.8, 44.8, 42.1. **HRMS (ESI)**: calculated for $\text{C}_{19}\text{H}_{16}\text{NO}_3\text{BrNa}^+$ $[\text{M}+\text{Na}]^+$: 408.0206; found 408.0193. The enantiomeric ratio was determined by SFC using a Chiralpak IG-3 column: CO_2/MeOH 80:20, flow rate 2.0 mL/min, $\tau_{\text{major}} = 11.00$ min, $\tau_{\text{minor}} = 8.08$ min, **e.r.** = 93:7.

(*R,E*)-4-{1-[4-(*tert*-Butyl)benzyl]-3-hydroxy-2-oxo-6-(trifluoromethyl)indolin-3-yl}but-2-enal (4m**)**

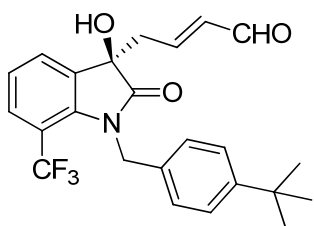


Following general procedure B, isatin **1m** (36.1 mg, 0.1 mmol) and silyl dienol ether **2a** (53 μ L, 0.3 mmol) after 24h at -30 $^{\circ}$ C, gave **4m** (65% yield) as a colorless oil. Eluent: dichloromethane: diethyl ether; 9:1.

$[\alpha]_D^{20} = -9.4$ (c 1.20, CHCl_3).

$^1\text{H-NMR}$: δ 9.39 (d, $J = 7.7$ Hz, 1H), 7.48 (d, $J = 7.7$ Hz, 1H), 7.42 – 7.31 (m, 3H), 7.20 (d, $J = 8.2$ Hz, 2H), 7.02 (s, 1H), 6.74 – 6.60 (m, 1H), 6.13 (dd, $J = 15.6, 7.7$ Hz, 1H), 5.01 (d, $J = 15.5$ Hz, 1H, CH_2), 4.71 (d, $J = 15.5$ Hz, 1H, CH_2), 3.32 (s, 1H), 3.04 (dd, $J = 14.1, 6.4$ Hz, 1H, CH_2), 2.91 (dd, $J = 14.1, 8.5$ Hz, 1H, CH_2), 1.29 (s, 9H). **$^{13}\text{C-RMN}$** δ 193.1, 176.9, 151.6, 148.2, 143.2, 137.2, 132.6 (q, $J = 32.7$ Hz), 132.5, 131.6, 127.3 (2C), 126.2 (2C), 124.6, 123.6 (q, $J = 273.1$ Hz), 120.7 (q, $J = 4.1$ Hz), 106.7 (q, $J = 3.9$ Hz), 75.3, 44.0, 41.7, 34.7, 31.4. **$^{19}\text{F-RMN}$** : -62.79 . **HRMS (ESI)**: calculated for $\text{C}_{24}\text{H}_{28}\text{N}_2\text{O}_3\text{F}_3^+$ $[\text{M}+\text{NH}_4]^+$: 449.2047; found 449.2040. The enantiomeric ratio was determined by SFC using a Chiralpak IC column: $[\text{CO}_2/\text{MeOH}$ 95:5, flow rate 3.0 mL/min], $\tau_{\text{major}} = 6.92$ min, $\tau_{\text{minor}} = 6.09$ min (**e.r.** = 94:6).

(*R,E*)-4-(1-(4-(*tert*-Butyl)benzyl)-3-hydroxy-2-oxo-7-(trifluoromethyl)indolin-3-yl)but-2-enal (4n)

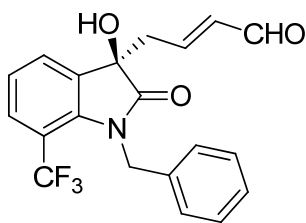


Following general procedure B, isatin **1n** (36.1 mg, 0.1 mmol) and silyl dienol ether **2a** (53 μ L, 0.3 mmol) after 24h at -30 $^{\circ}$ C, gave **4n** (73% yield) as a colorless oil. Eluent: dichloromethane: diethyl ether; 15:1.

$[\alpha]_D^{20} = -22.3$ (*c* 1.33, CHCl_3).

$^1\text{H-NMR}$: δ 9.44 (d, *J* = 7.8 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.29 (s, 2H), 7.22 (t, *J* = 7.9 Hz, 1H), 7.03 (d, *J* = 8.1 Hz, 2H), 6.77 – 6.64 (m, 1H), 6.09 (dd, *J* = 15.7, 7.8 Hz, 1H), 5.13 (s, 2H), 2.98 (dd, *J* = 14.1, 6.6 Hz, 1H, CH_2), 2.90 (dd, *J* = 14.1, 8.5 Hz, 1H, CH_2), 1.27 (s, 9H). **$^{13}\text{C-RMN}$** : δ 193.1, 178.7, 150.4, 148.3, 140.8, 137.2, 132.7, 132.0, 128.5 (q, *J* = 6.2 Hz), 127.9, 125.8 (q, *J* = 272.3 Hz), 125.8 (2C), 125.6 (2C), 123.2, 113.9 (q, *J* = 33.0 Hz), 73.5, 45.6, 42.0, 34.6, 31.4 (3C). **$^{19}\text{F-RMN}$** : -55.03. **HRMS (ESI)**: calculated for $\text{C}_{24}\text{H}_{24}\text{NO}_3\text{F}_3\text{Na}^+$ [$\text{M}+\text{Na}$] $^+$: 454.1600; found 454.1549. The enantiomeric ratio was determined by SFC using a Chiralpak IC column [CO_2/MeOH 95:5, flow rate 3.0 mL/min], $\tau_{\text{major}} = 8.50$ min, $\tau_{\text{minor}} = 7.17$ min (**e.r.** = 85:15).

(*R,E*)-4-(1-Benzyl-3-hydroxy-2-oxo-7-(trifluoromethyl)indolin-3-yl)but-2-enal (4o)

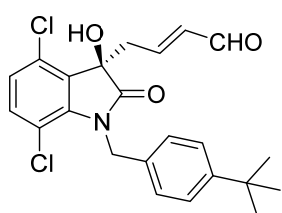


Following general procedure B, isatin **1o** (30.5 mg, 0.1 mmol) and silyl dienol ether **2a** (53 μ L, 0.3 mmol) after 24h at -30 $^{\circ}$ C, gave **4o** (72% yield) as a colorless oil. Eluent: dichloromethane: diethyl ether; 19:1.

$[\alpha]_D^{20} = -44.4$ (*c* 0.70, CHCl_3).

$^1\text{H-NMR}$: δ 9.47 (d, *J* = 7.8 Hz, 1H), 7.68 – 7.58 (m, 3H), 7.31 – 7.27 (m, 1H), 7.26 – 7.20 (m, 2H), 7.10 (d, *J* = 6.2 Hz, 2H), 6.76 – 6.65 (m, 1H), 6.11 (dd, *J* = 15.8, 7.8 Hz, 1H), 5.17 (s, 2H), 3.04 – 2.87 (m, 3H). **$^{13}\text{C-RMN}$** : δ 193.3, 178.8, 148.5, 140.6, 137.1, 135.7, 132.1, 128.6 (2C), 128.4 (q, *J* = 6.1 Hz), 128.0, 127.4, 125.9 (2C), 123.3, 123.2 (q, *J* = 272.1 Hz), 113.9 (q, *J* = 33.1 Hz), 73.6, 45.9 (q, *J* = 4.8 Hz), 41.9. **$^{19}\text{F-RMN}$** : -55.08. **HRMS (ESI)**: calculated for $\text{C}_{20}\text{H}_{16}\text{NO}_3\text{F}_3\text{Na}^+$ [$\text{M}+\text{Na}$] $^+$: 398.0974; found 398.0947. The enantiomeric ratio was determined by SFC using a Chiralpak IG-3 column [CO_2/MeOH 85:15, flow rate 2.0 mL/min], $\tau_{\text{major}} = 11.62$ min, $\tau_{\text{minor}} = 13.95$ min (**e.r.** = 93:7).

(*R,E*)-4-{1-[4-(*tert*-Butyl)benzyl]-4,7-dichloro-3-hydroxy-2-oxoindolin-3-yl}but-2-enal (4p**)**

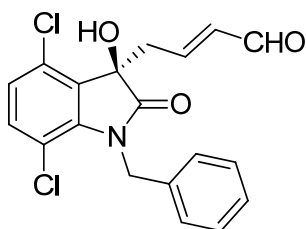


Following general procedure B, isatin **1p** (36.2 mg, 0.1 mmol) and silyl dienol ether **2a** (53 μ L, 0.3 mmol) after 24h at -30 $^{\circ}$ C, gave **4p** (84% yield) as a colorless oil. Eluent: dichloromethane: diethyl ether; 9:1.

$[\alpha]_D^{20} = -16.3$ (*c* 1.00, CHCl_3).

$^1\text{H-NMR}$: δ 9.25 (d, *J* = 7.6 Hz, 1H), 7.30 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 8.8 Hz, 1H), 7.15 (d, *J* = 8.3 Hz, 2H), 7.00 (d, *J* = 8.8 Hz, 1H), 6.42 – 6.32 (m, 1H), 6.08 (dd, *J* = 15.7, 7.7 Hz, 1H), 5.33 (d, *J* = 15.9 Hz, 1H, CH_2), 5.25 (d, *J* = 15.9 Hz, 1H, CH_2), 3.38 (dd, *J* = 13.6, 7.6 Hz, 1H, CH_2), 3.22 (dd, *J* = 13.6, 7.5 Hz, 1H, CH_2), 2.95 (bs, 1H, OH), 1.28 (s, 9H). **$^{13}\text{C-RMN}$** δ 193.1, 176.5, 150.9, 147.8, 140.4, 136.9, 134.0, 133.5, 130.5, 127.7, 126.7 (2C), 125.8 (2C), 125.5, 115.0, 76.0, 44.9, 39.2, 34.7, 31.4 (3C). **HRMS (ESI)**: calculated for $\text{C}_{23}\text{H}_{23}\text{NO}_3\text{Cl}_2\text{Na}^+$ [$\text{M}+\text{Na}$] $^+$: 454.0947; found 454.0980. The enantiomeric ratio was determined by SFC using a Chiralpak IC column [CO_2/MeOH from 95:5 to 60:40 in 8 min, flow rate 3.0 mL/min], $\tau_{\text{major}} = 4.88$ min, $\tau_{\text{minor}} = 4.46$ min (**e.r.** = 80:20).

(*R,E*)-4-(1-Benzyl-4,7-dichloro-3-hydroxy-2-oxoindolin-3-yl)but-2-enal (4q**)**

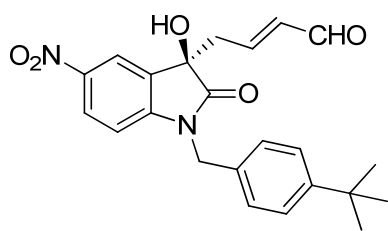


Following general procedure B, isatin **1q** (30.6 mg, 0.1 mmol) and silyl dienol ether **2a** (53 μ L, 0.3 mmol) after 24h at -30 $^{\circ}$ C, gave **4q** (75% yield) as a colorless oil. Eluent: dichloromethane: diethyl ether; 9:1.

$[\alpha]_D^{20} = -13.8$ (*c* 0.88, CHCl_3).

$^1\text{H-NMR}$: δ 9.29 (d, *J* = 7.6 Hz, 1H), 7.31 – 7.26 (m, 3H), 7.21 – 7.17 (m, 3H), 7.00 (d, *J* = 8.8 Hz, 1H), 6.44 – 6.33 (m, 1H), 6.09 (dd, *J* = 15.6, 7.6 Hz, 1H), 5.36 (d, *J* = 16.0 Hz, 1H, CH_2), 5.28 (d, *J* = 16.0 Hz, 1H, CH_2), 3.40 (dd, *J* = 13.5, 7.5 Hz, 1H, CH_2), 3.23 (dd, *J* = 13.5, 7.7 Hz, 1H, CH_2), 3.14 (bs, 1H). **$^{13}\text{C-RMN}$** : δ 193.1, 176.6, 147.7, 140.2, 136.9, 136.5, 134.0, 130.5, 128.9 (2C), 127.8, 127.7, 126.7 (2C), 125.6, 115.0, 76.0, 45.2, 39.2. **HRMS (ESI)**: calculated for $\text{C}_{19}\text{H}_{15}\text{NO}_3\text{Cl}_2\text{Na}^+$ [$\text{M}+\text{Na}$] $^+$: 398.0321; found 398.0340. The enantiomeric ratio was determined by SFC using a Chiralpak IG-3 column [CO_2/MeOH 85:15, flow rate 2.0 mL/min], $\tau_{\text{major}} = 3.63$ min, $\tau_{\text{minor}} = 2.88$ min (**e.r.** = 90:10).

(*R,E*)-4-{1-[4-(*tert*-Butyl)benzyl]-3-hydroxy-5-nitro-2-oxindolin-3-yl}but-2-enal (4r**)**

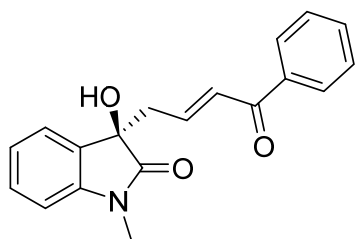


Following general procedure B, isatin **1r** (33.8 mg, 0.1 mmol) and silyl dienol ether **2a** (53 μ L, 0.3 mmol) after 48h at $-30\text{ }^{\circ}\text{C}$, gave **4r** (73% yield) as a colorless oil. Eluent: dichloromethane: diethyl ether; 9:1).

$[\alpha]_{\text{D}}^{20} = +32.5$ (c 1.23, CHCl_3).

$^1\text{H-NMR}$: δ 9.36 (d, $J = 7.7$ Hz, 1H), 8.28 (d, $J = 2.3$ Hz, 1H), 8.23 (dd, $J = 8.6, 2.3$ Hz, 1H), 7.33 (d, $J = 8.4$ Hz, 2H), 7.16 (d, $J = 8.4$ Hz, 2H), 6.90 (d, $J = 8.6$ Hz, 1H), 6.68 – 6.57 (m, 1H), 6.14 (dd, $J = 15.6, 7.7, 1.2$ Hz, 1H), 5.03 (d, $J = 15.5$ Hz, 1H, CH_2), 4.75 (d, $J = 15.5$ Hz, 1H, CH_2), 3.53 (bs, 1H, OH), 3.09 – 2.98 (m, 2H), 1.28 (s, 9H). **$^{13}\text{C-RMN}$** δ 192.9, 177.3, 151.8, 147.9, 147.4, 144.1, 137.4, 131.1, 129.9, 127.4, 127.3 (2C), 126.3 (2C), 120.1, 109.8, 75.2, 44.2, 41.6, 34.8, 31.4 (3C). **HRMS (ESI)**: calculated for $\text{C}_{23}\text{H}_{24}\text{N}_2\text{O}_5\text{Na}^+$ [$\text{M}+\text{Na}$] $^+$: 431.1577; found 431.1604. The enantiomeric ratio was determined by SFC using a Chiralpak IC column [CO_2/MeOH from 95:5 to 60:40 in 8 min, flow rate 3.0 mL/min], $\tau_{\text{major}} = 6.39$ min, $\tau_{\text{minor}} = 5.64$ min (e.r. = 94:6).

(*R,E*)-3-Hydroxy-1-methyl-3-(4-oxo-4-phenylbut-2-en-1-yl)indolin-2-one (4s**)¹⁰**



The Following general procedure B, isatin **1b** (23.7 mg, 0.1 mmol) and silyl dienol ether **2b** (59 μ L, 0.3 mmol) after 72h at room temperature, gave **4s** (74% yield) as a colorless oil. Eluent: cyclohexane: ethyl acetate; 3:1.

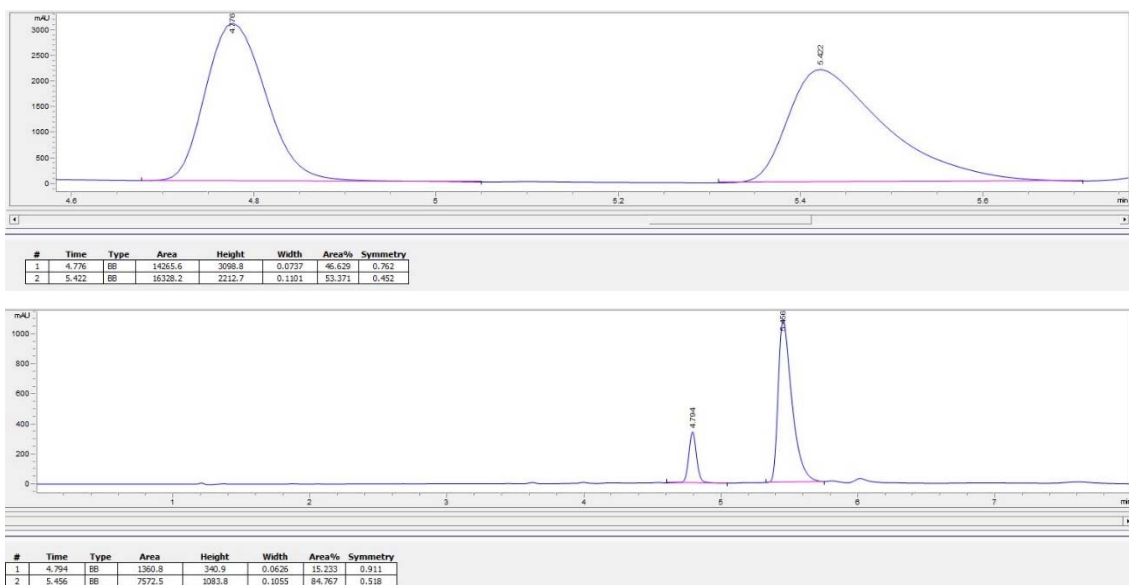
$[\alpha]_{\text{D}}^{20} = +15.1$ (c 0.61, CHCl_3). Lit.¹⁰ $+32.9$ (c 0.74, CHCl_3) for 92%

ee.

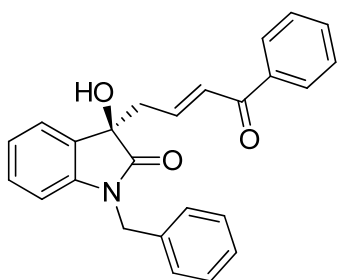
The $^1\text{H-NMR}$ is in accordance with the literature. **$^1\text{H-NMR}$** : δ 7.85 – 7.79 (m, 1H), 7.59 – 7.51 (m, 1H), 7.47 – 7.30 (m, 4H), 7.13 (t, $J = 7.4$ Hz, 1H), 6.93 – 6.72 (m, 3H), 3.19 (s, 3H), 3.01 (dd, $J = 13.7, 6.0$ Hz, 1H), 2.83 (dd, $J = 13.6, 7.8$ Hz, 1H). The enantiomeric ratio was determined by SFC using a Chiralpak IA column [CO_2/MeOH from 95:5 to 60:40 in 8 min, flow rate 3.0 mL/min], $\tau_{\text{major}} = 5.28$ min, $\tau_{\text{minor}} = 4.90$ min (e.r. = 85:15).

Major enantiomer is in accordance with HPLC chromatograms and optical rotation described in the literature.¹⁰ [ee determined by HPLC analysis; Chiralpak IA; Hexane/2-propanol = 92/8; flow rate 0.8 ml/min; 25 $^{\circ}\text{C}$; 254 nm; retention time: $\tau_{\text{major}} = 41.9$ min, $\tau_{\text{minor}} = 38.7$ min]

¹⁰ B. Zhu, W. Zhang, R. Lee, Z. Han, W. Yang, D. Tan, K.-W. Huang and Z. Jiang, *Angew. Chem. Int. Ed.* 2013, **52**, 6666-6670.



(*R,E*)-1-Benzyl-3-hydroxy-3-(4-oxo-4-phenylbut-2-en-1-yl)indolin-2-one (**4t**)

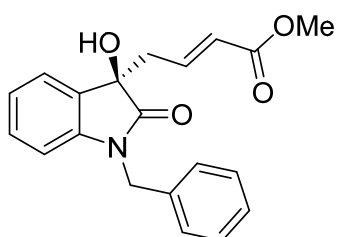


Following general procedure B, isatin **1t** (23.7 mg, 0.1 mmol) and silyl dienol ether **2b** (59 μ L, 0.3 mmol) after 48h at room temperature, gave **4t** (74% yield) as a colorless oil. Eluent: dichloromethane: diethyl ether; 7:1.

$[\alpha]_D^{20} = -3.8$ (*c* 1.08, CHCl_3).

$^1\text{H-NMR}$: δ 7.79 (d, *J* = 7.1 Hz, 2H), 7.56 – 7.50 (m, 1H), 7.47 – 7.36 (m, 4H), 7.27 – 7.18 (m, 5H), 7.13 – 7.07 (m, 1H), 6.93 (d, *J* = 15.4 Hz, 1H), 6.82 – 6.74 (m, 1H), 6.73 – 6.68 (m, 1H), 5.03 (d, *J* = 15.8 Hz, 1H, CH_2), 4.69 (d, *J* = 15.8 Hz, 1H, CH_2), 3.11 (dd, *J* = 13.4, 6.4 Hz, 1H, CH_2), 2.97 (dd, *J* = 13.4, 8.6 Hz, 1H, CH_2). $^{13}\text{C-RMN}$ δ 190.0, 177.5, 142.5, 140.4, 137.5, 135.2, 133.0, 130.6, 130.2, 129.2, 129.0 (2C), 128.7 (2C), 128.7 (2C), 127.8, 127.2 (2C), 124.4, 123.6, 110.0, 76.1, 44.1, 41.9 ppm. **HRMS (ESI)**: calculated for $\text{C}_{25}\text{H}_{21}\text{NO}_3\text{Na}^+$ [$\text{M}+\text{Na}$] $^+$: 406.1414; found 406.1438. The enantiomeric ratio was determined by SFC using a Chiralpak IA column [CO_2/MeOH 85:15, flow rate 3.0 mL/min], $\tau_{\text{major}} = 9.91$ min, $\tau_{\text{minor}} = 9.04$ min (**e.r.** = 80:20).

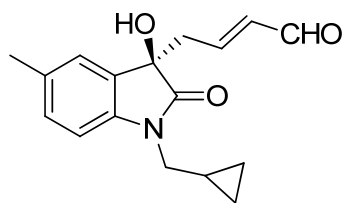
Methyl (*R,E*)-4-(1-benzyl-3-hydroxy-2-oxindolin-3-yl)but-2-enoate (**4u**)



The Following general procedure B, isatin **1c** (23.7 mg, 0.1 mmol) and silyl dienol ether **2c** (65 μ L, 0.3 mmol) after 24h at room temperature, gave **4u** (74% yield) as a colorless oil. Eluent: Cyclohexane: ethyl acetate; 3:1.

¹H-NMR: δ 7.38 (d, J = 7.3 Hz, 1H), 7.33 – 7.28 (m, 4H), 7.23 – 7.20 (m, 2H), 7.08 (t, J = 7.6 Hz, 1H), 6.85 – 6.74 (m, 1H), 6.72 (d, J = 7.5 Hz, 1H), 5.89 (d, J = 15.6 Hz, 1H), 5.04 (d, J = 15.7 Hz, 1H, CH_2), 4.73 (d, J = 15.7 Hz, 1H, CH_2), 3.70 (s, 3H), 2.96 (dd, J = 13.6, 6.6 Hz, 1H, CH_2), 2.85 – 2.74 (m, 2H). **¹³C-RMN** δ 177.3, 166.3, 142.5, 140.8, 135.4, 130.3, 129.1, 129.0 (2C), 127.9, 127.4 (2C), 126.0, 124.4, 123.6, 110.0, 75.8, 51.7, 44.1, 41.4. **HRMS (ESI):** calculated for $C_{20}H_{20}NO_4$ [M+H]⁺: 338.1387; found 338.1420. The enantiomeric ratio was determined by SFC using a Chiralpak IC column [CO₂/MeOH from 95:5 to 60:40 in 8 min, flow rate 3.0 mL/min], τ_{major} = 4.69 min, τ_{minor} = 5.35 min (e.r. = 50:50).

(*R,E*)-4-[1-(Cyclopropylmethyl)-3-hydroxy-5-methyl-2-oxoindolin-3-yl]but-2-enal (4v**)**

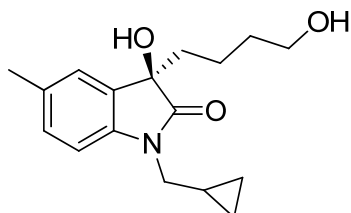


Following general procedure B, isatin **1s** (21.5 mg, 0.1 mmol) and silyl dienol ether **2a** (53 μ L, 0.3 mmol) after 72h at room temperature, gave **4v** (75% yield) as a colorless oil. Eluent: dichloromethane: ethyl acetate; 1:1.

$[\alpha]_D^{20}$ = -11.0 (c 0.99, CHCl₃).

¹H-NMR: δ 9.43 (d, J = 7.8 Hz, 1H), 7.23 – 7.10 (m, 2H), 6.83 (d, J = 8.0 Hz, 1H), 6.73 – 6.62 (m, 1H), 6.10 (dd, J = 15.6, 7.7 Hz, 1H), 3.60 (dd, J = 14.5, 7.2 Hz, 1H, CH_2), 3.50 (dd, J = 14.5, 6.6 Hz, 1H, CH_2), 3.03 – 2.65 (m, 3H), 2.35 (s, 3H), 1.19 – 1.06 (m, 1H), 0.59 – 0.47 (m, 2H), 0.39 – 0.25 (m, 2H). **¹³C-RMN** δ 193.4, 176.8, 149.7, 140.4, 136.7, 133.1, 130.6, 129.0, 125.0, 109.1, 75.7, 44.6, 41.9, 29.9, 21.2, 9.7, 4.1, 4.0 ppm. **HRMS (ESI):** calculated for $C_{17}H_{18}NO_2$ [M-OH]⁺: 268.1332; found 268.1330. The enantiomeric ratio was determined by SFC using a Chiralpak IC column [CO₂/MeOH from 95:5 to 60:40 in 8 min, flow rate 3.0 mL/min], τ_{major} = 5.28 min, τ_{minor} = 4.90 min (e.r. = 97:3).

(*R,E*)-1-(Cyclopropylmethyl)-3-hydroxy-3-(4-hydroxybutyl)-5-methylindolin-2-one (6**)**



Isatin **4v** (19 mg, 0.066 mmol, 1.0 eq.) was dissolved in methanol (1.0 mL) in an oven-dried vial. After cooling the reaction to 0 °C, sodium borohydride (51 mg, 1.33 mmol, 20 equiv.) was added and the reaction was stirred at 0 °C for 15 minutes and 5h at room temperature. The mixture was then extracted with EtOAc (3x5 mL), washed with water (3x5 mL), dried over MgSO₄, filtered and the solvent was evaporated under reduced pressure. The final product was used without further purification. The crude was then dissolved in methanol (4.0 mL) and added to an oven-dried vial containing

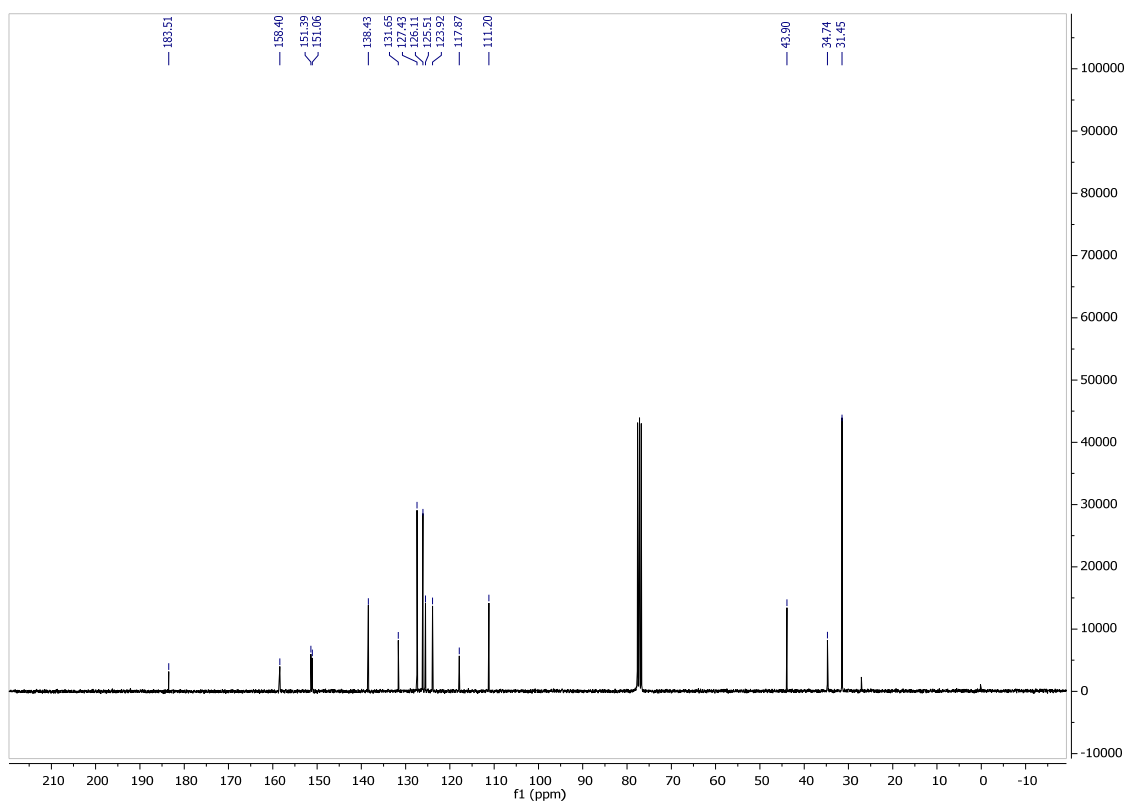
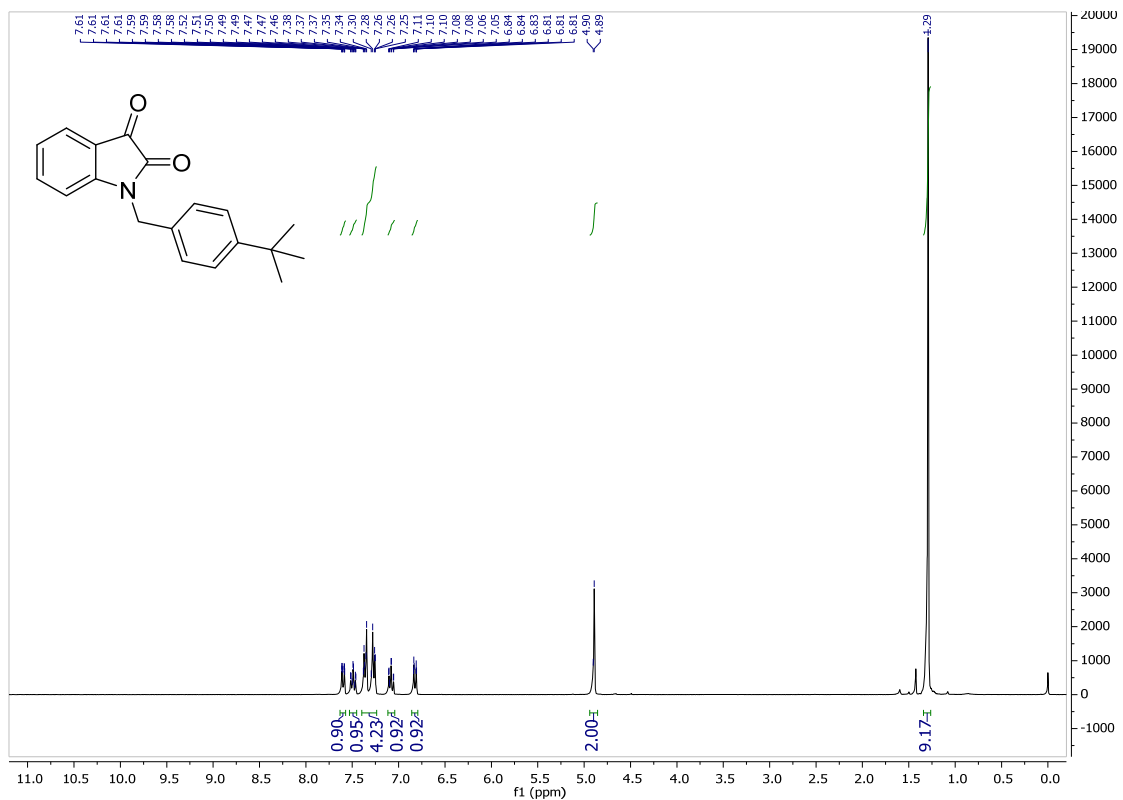
20 mol% Pd/C (10% w/w). The reaction mixture was purged with a balloon of H₂ and stirred for 90 minutes at room temperature under hydrogen atmosphere. The crude was filtered through a short pad of celite and the solvent was evaporated under reduced pressure. The product was obtained as a colorless oil (71% yield) after purification by flash chromatography (dichloromethane: ethyl acetate; 1:1).

$[\alpha]_D^{20} = -17.1$ (c 0.77, CHCl₃).

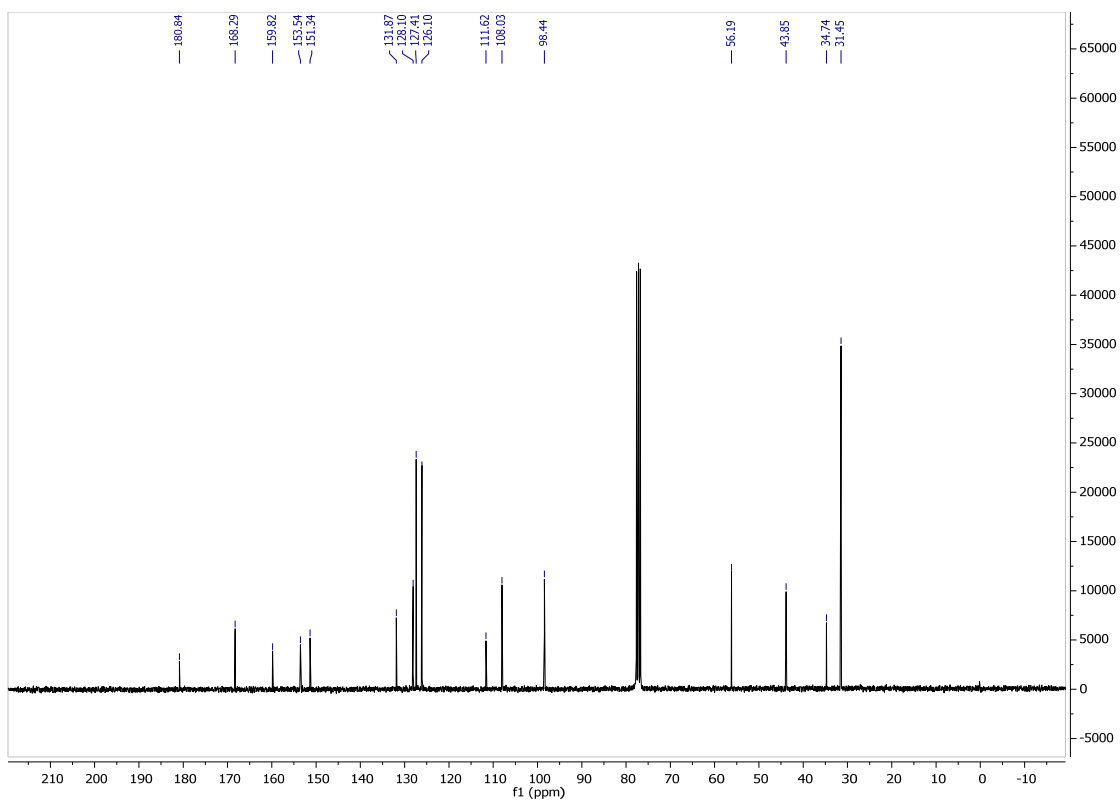
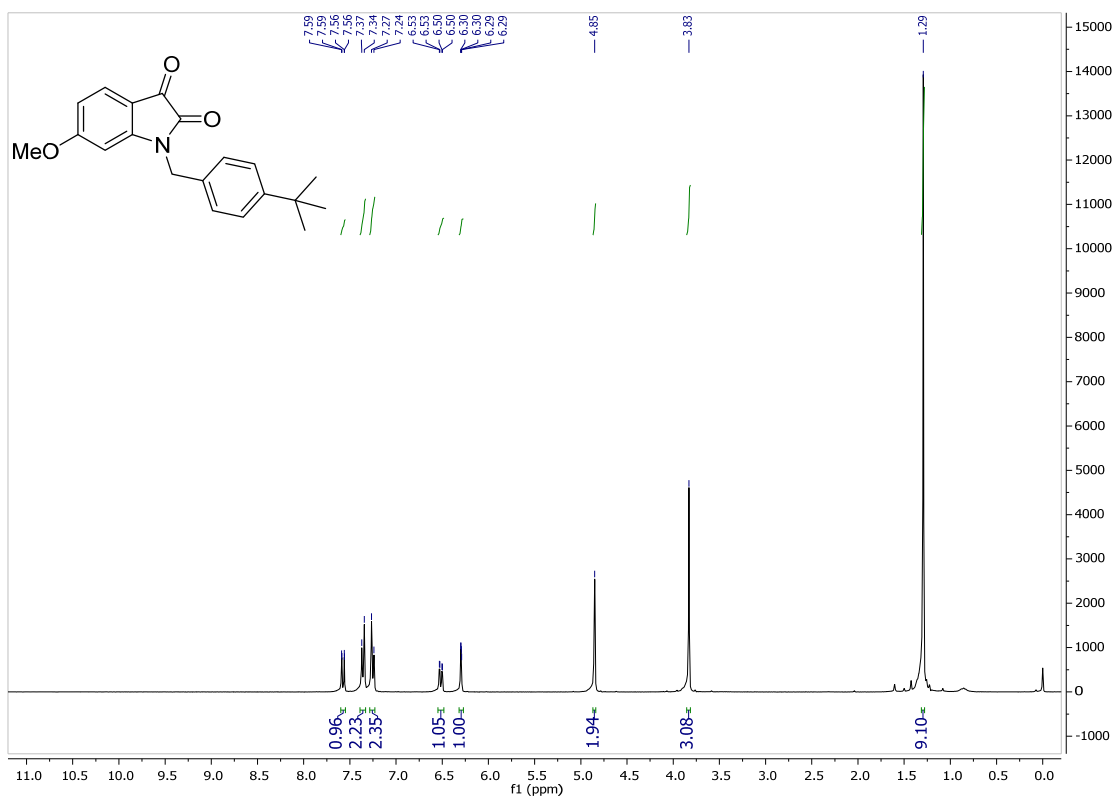
¹H-NMR: δ 7.20 (s, 1H), 7.12 (d, *J* = 7.9 Hz, 1H), 6.82 (d, *J* = 7.9 Hz, 1H), 3.67 – 3.44 (m, 4H), 2.71 (s, 1H, *OH*), 2.35 (s, 3H), 2.05 – 1.91 (m, 2H), 1.58 – 1.45 (m, 2H), 1.22 – 1.12 (m, 2H), 0.91 – 0.78 (m, 1H), 0.57 – 0.45 (m, 2H), 0.41 – 0.33 (m, 2H). **¹³C-RMN** δ 178.2, 140.8, 132.8, 130.1, 130.0, 124.9, 108.8, 62.6, 44.5, 38.6, 32.7, 21.3, 19.7, 9.8, 4.1, 4.0. **HRMS (ESI):** calculated for C₁₇H₂₄NO₃⁺ [M+H]⁺: 290.1751; found 290.1751. The enantiomeric ratio was determined by SFC using a Chiralpak IA column [CO₂/MeOH from 95:5 to 60:40 in 8 min, flow rate 3.0 mL/min], $\tau_{\text{major}} = 3.56$ min, $\tau_{\text{minor}} = 3.81$ min (e.r. = 97:3).

6. Spectroscopical data

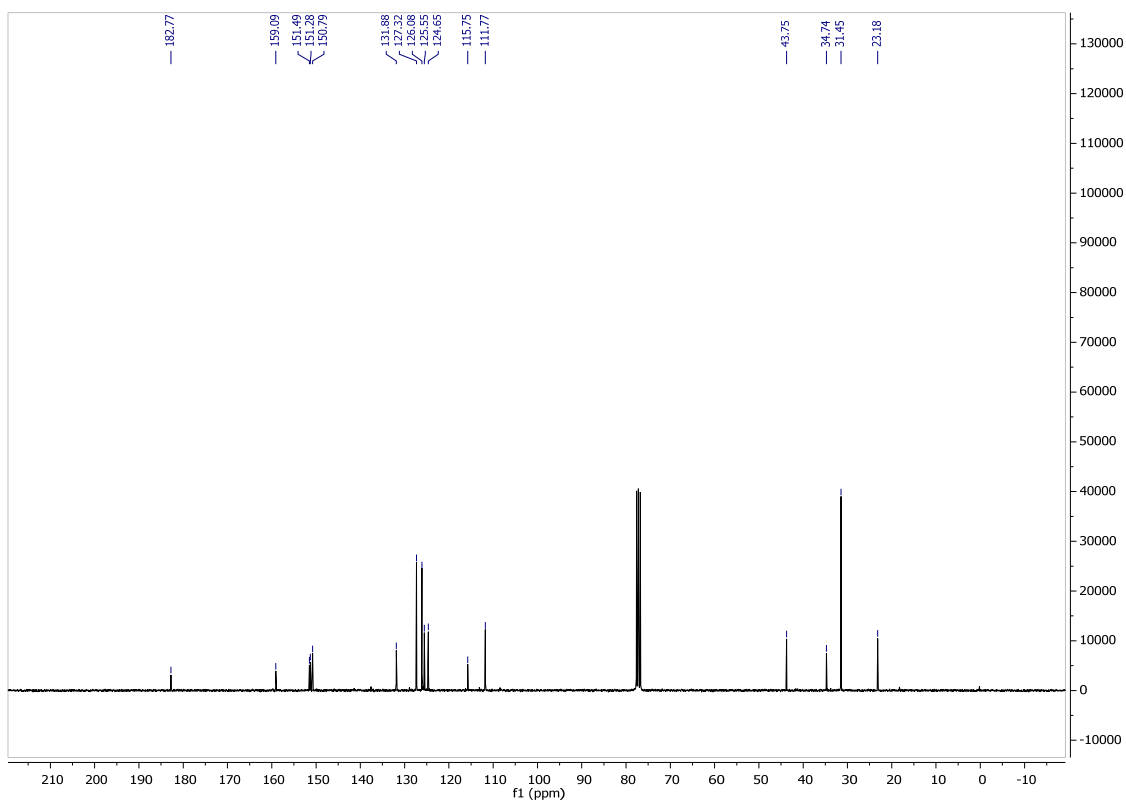
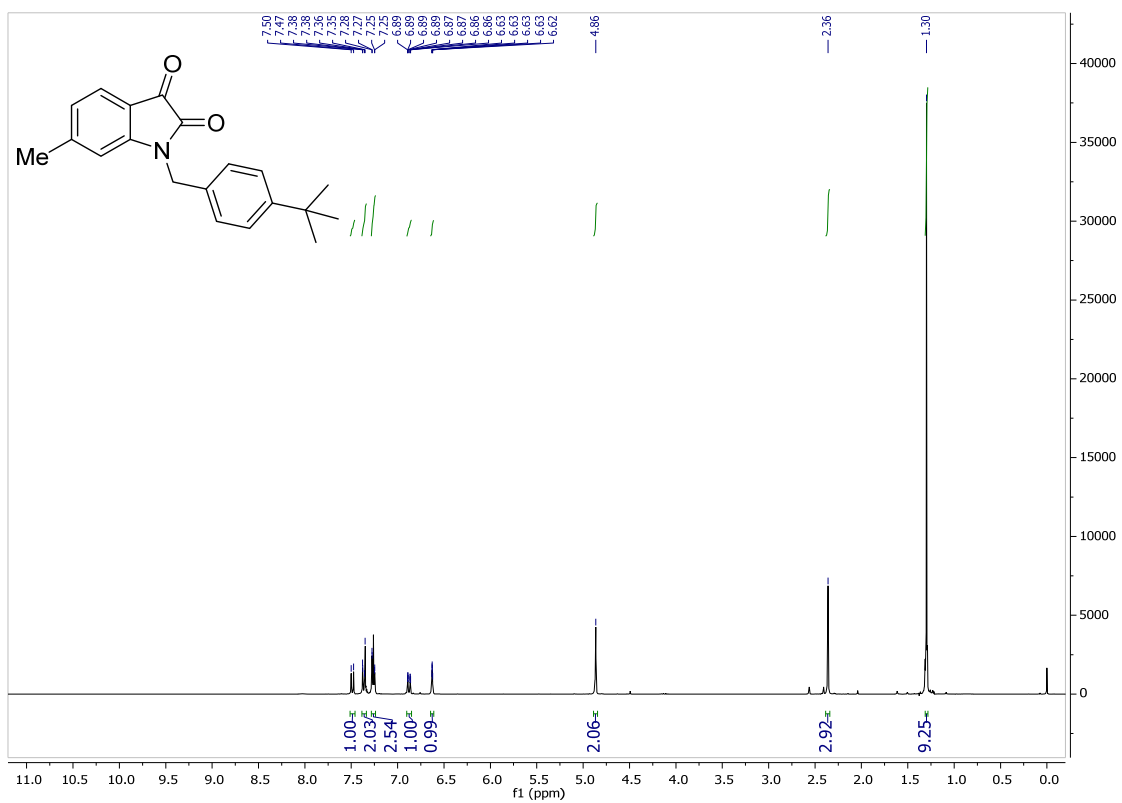
1-[4-(*tert*-Butyl)benzyl]indoline-2,3-dione (1d)



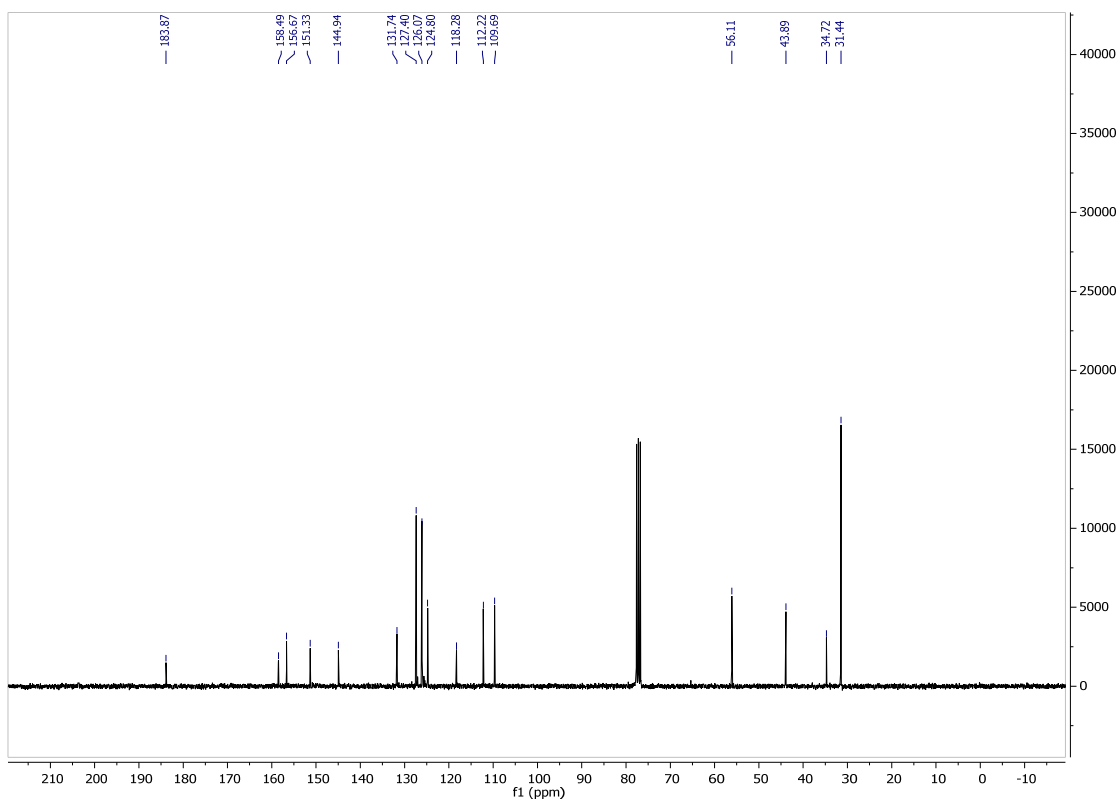
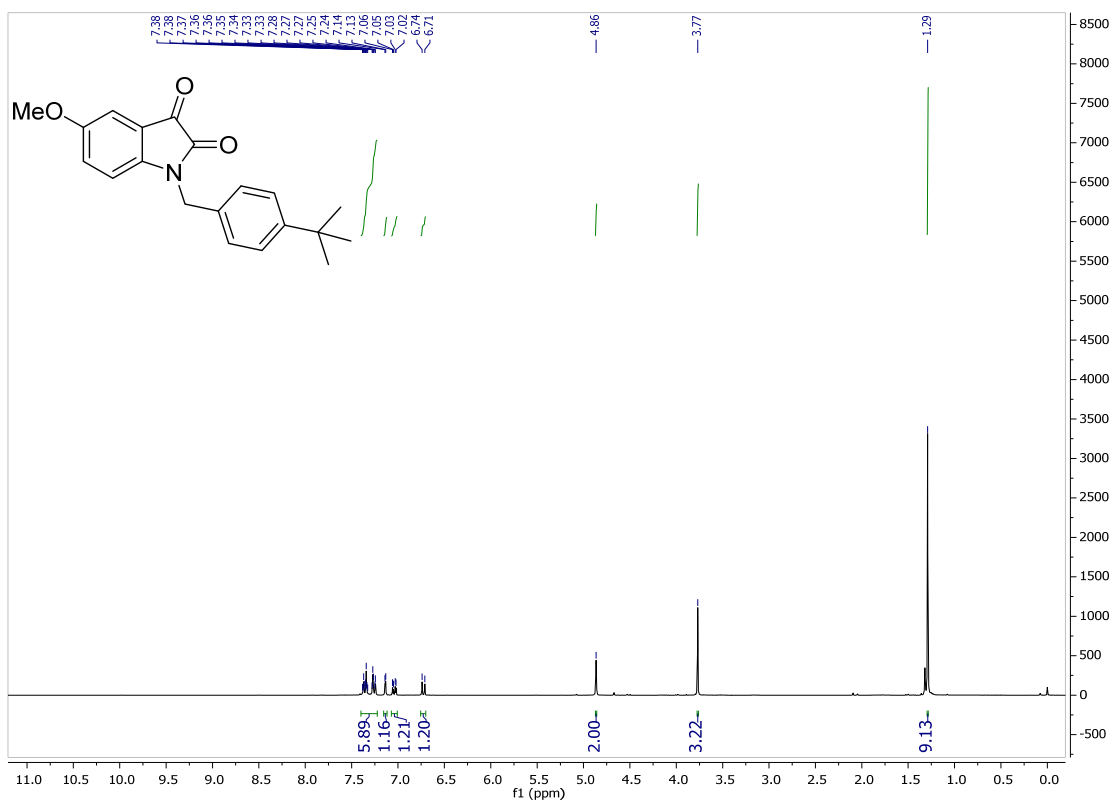
1-[4-(*tert*-Butyl)benzyl]-6-methoxyindoline-2,3-dione (1e)



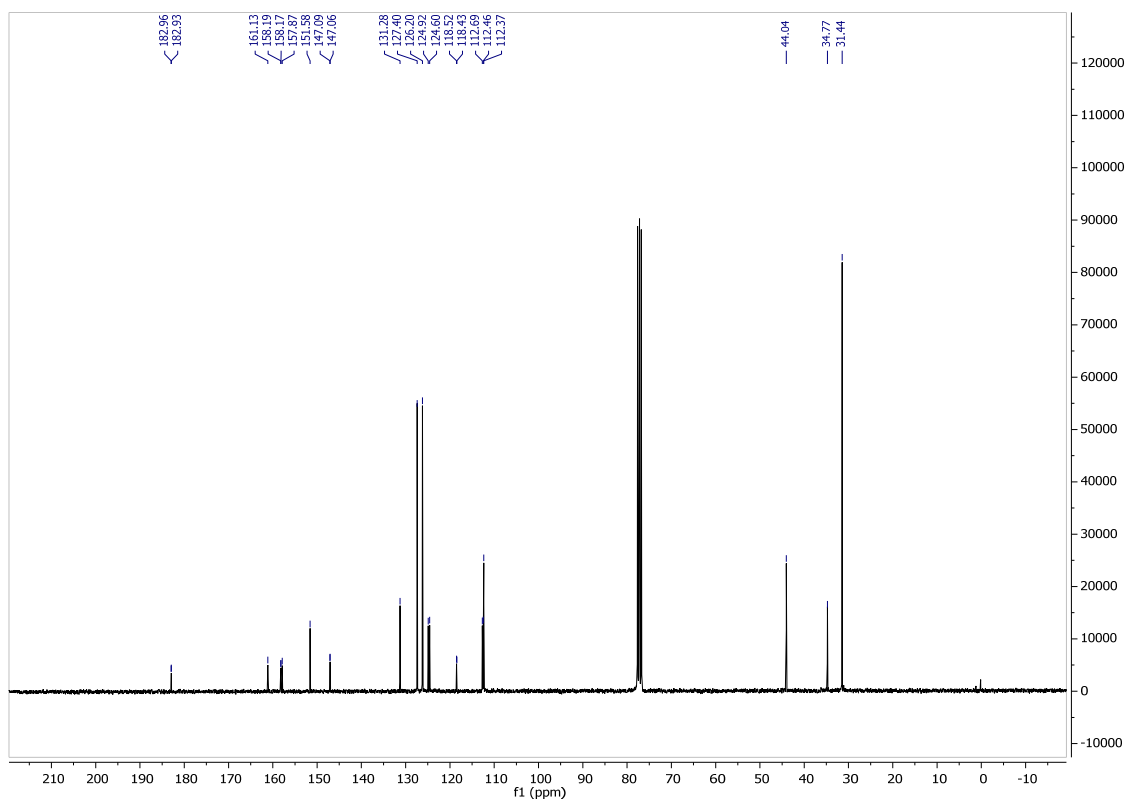
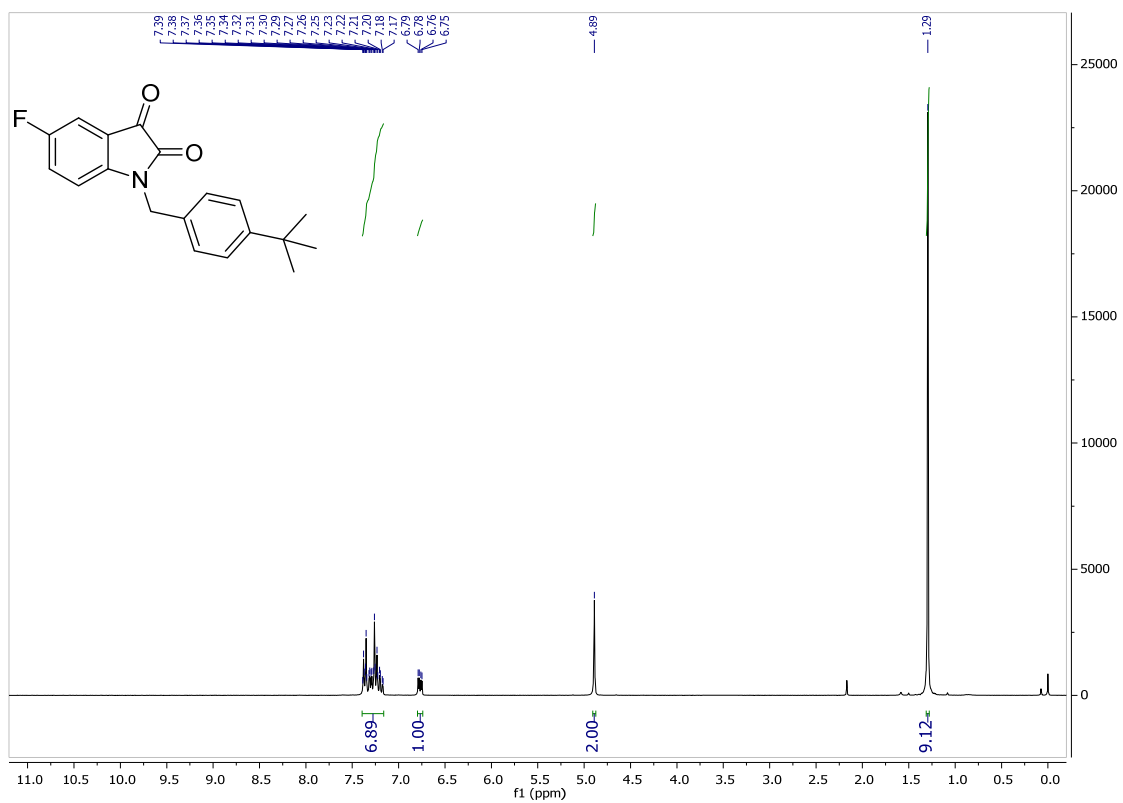
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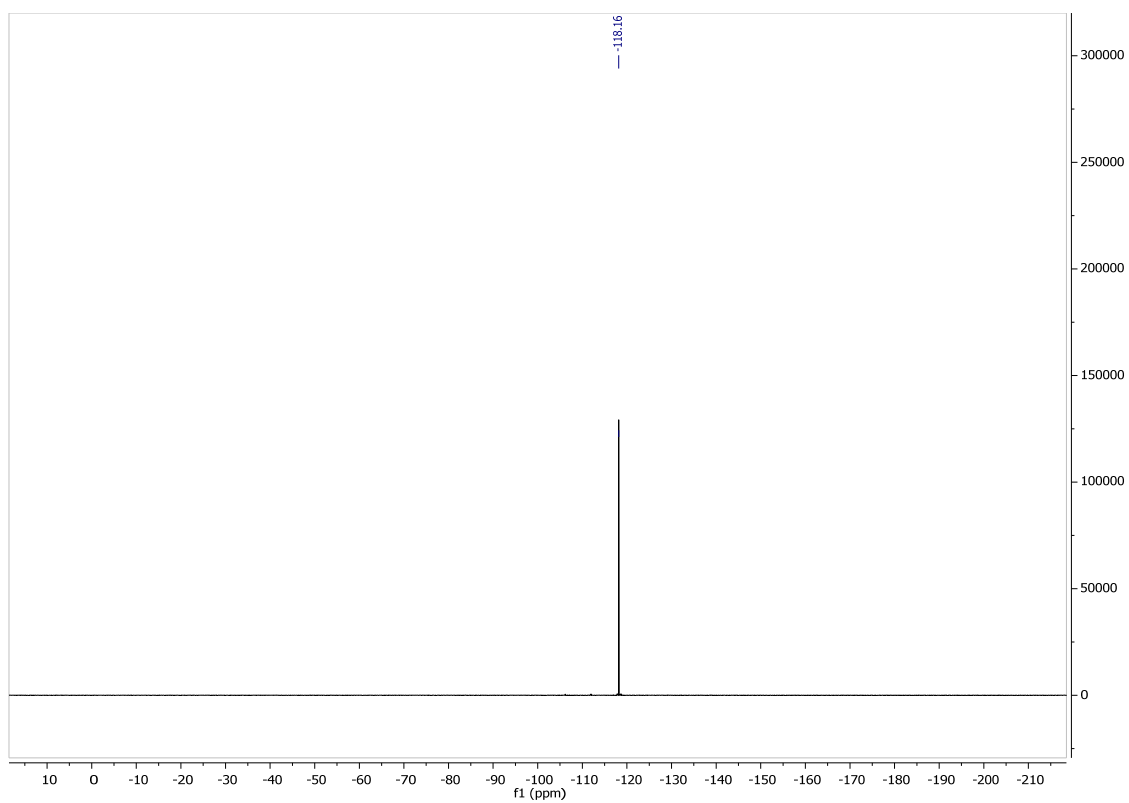


1-[4-(*tert*-Butyl)benzyl]-5-methoxyindoline-2,3-dione (1g)

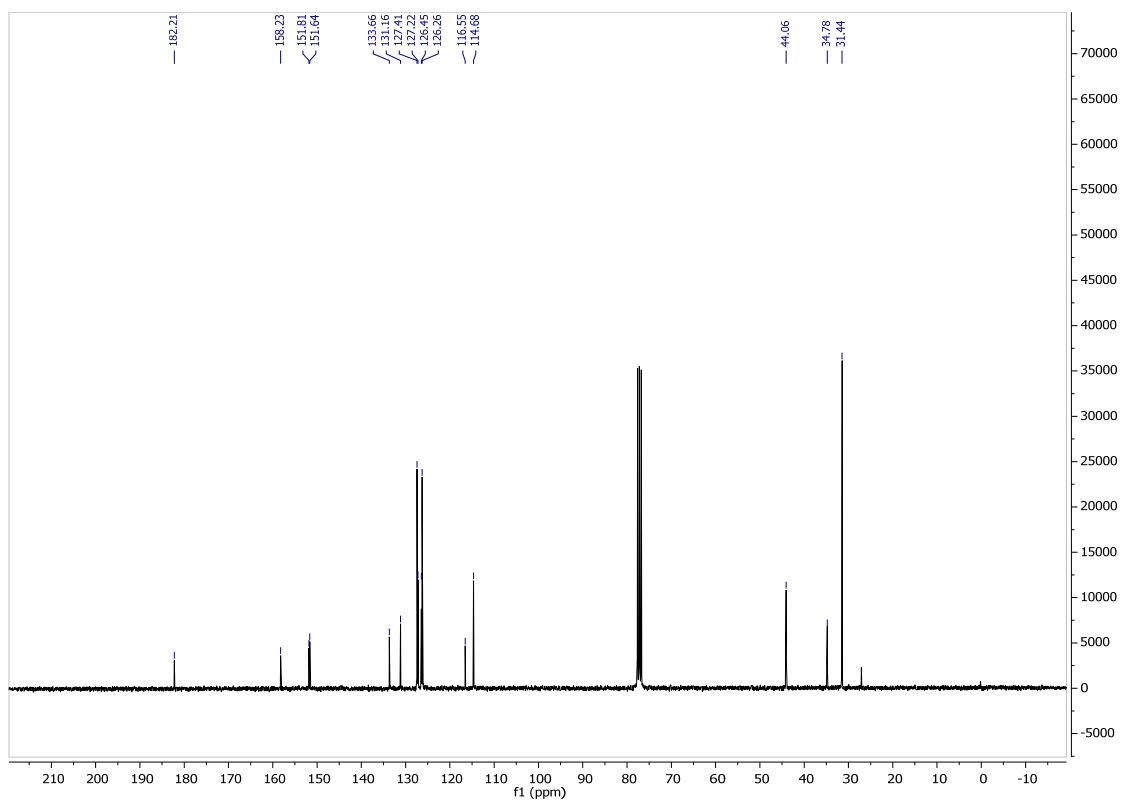
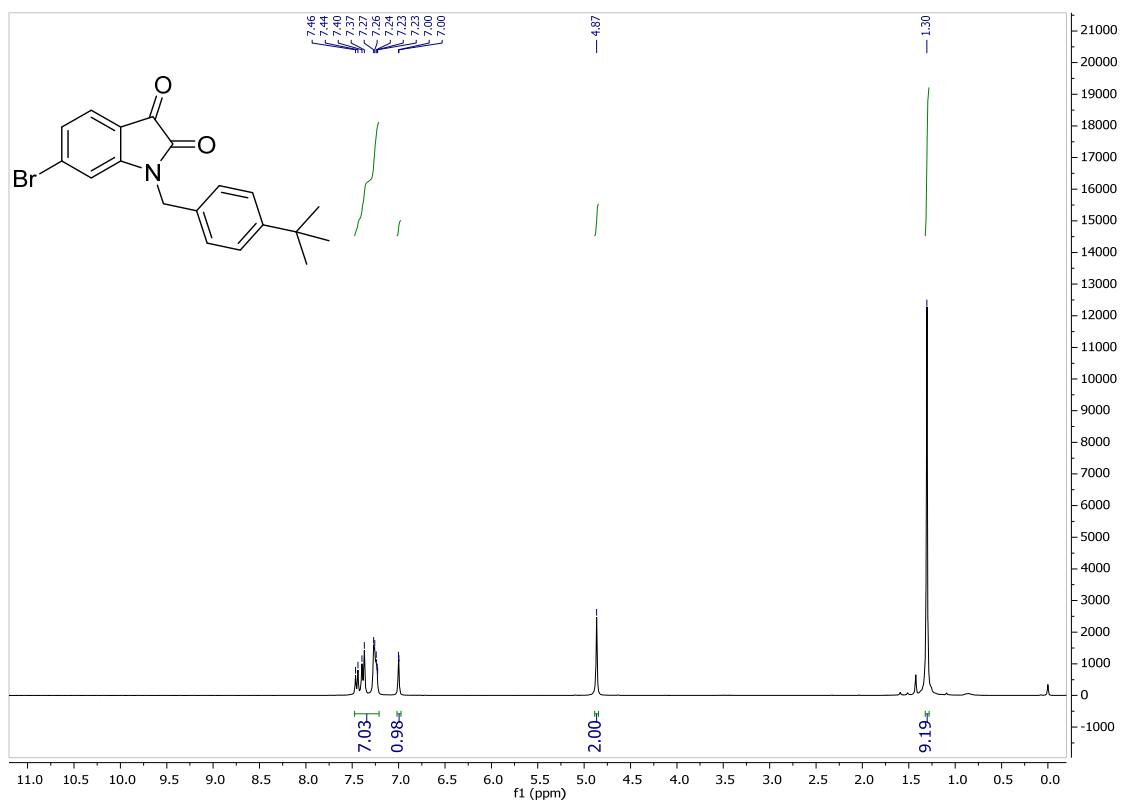


1-[4-(*tert*-Butyl)benzyl]-5-fluoroindoline-2,3-dione (1h)

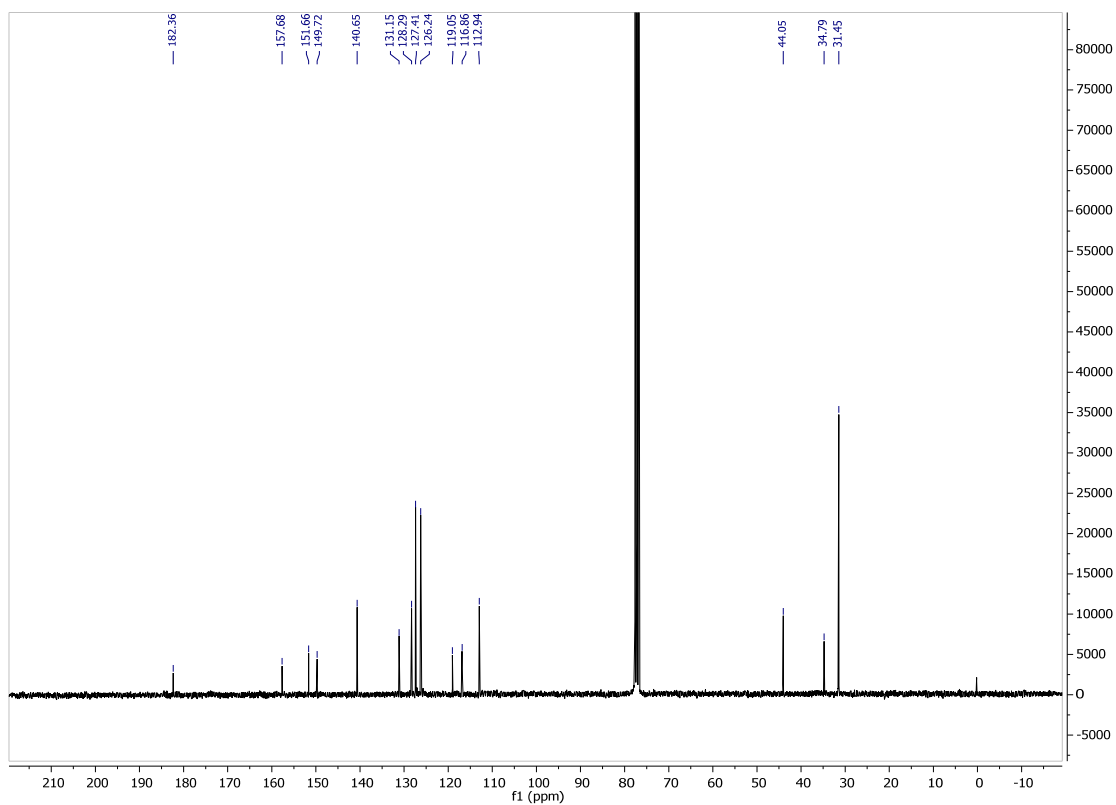
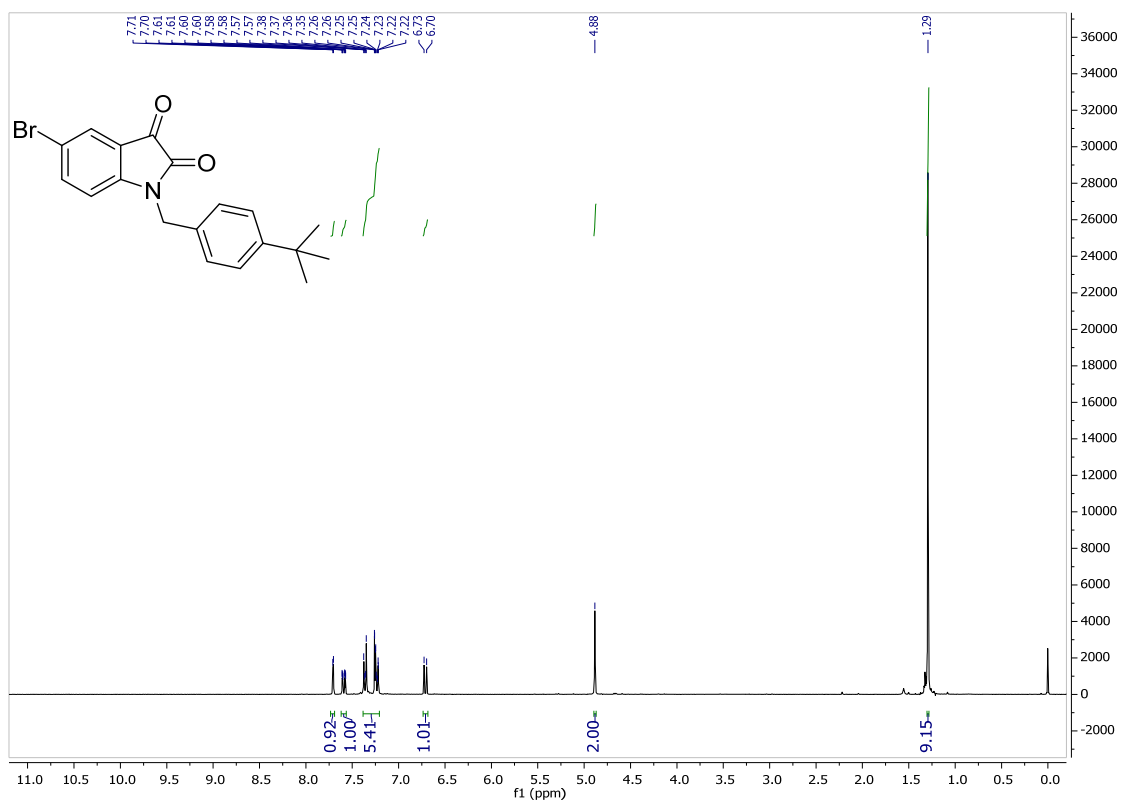




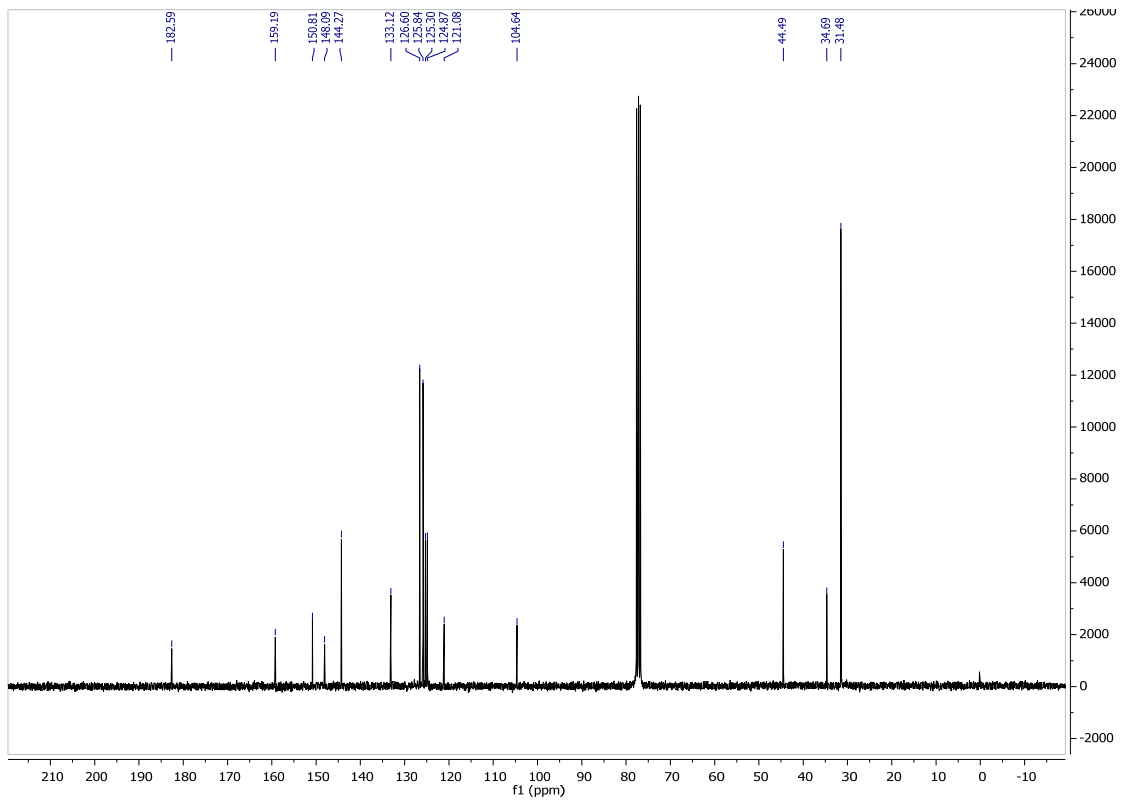
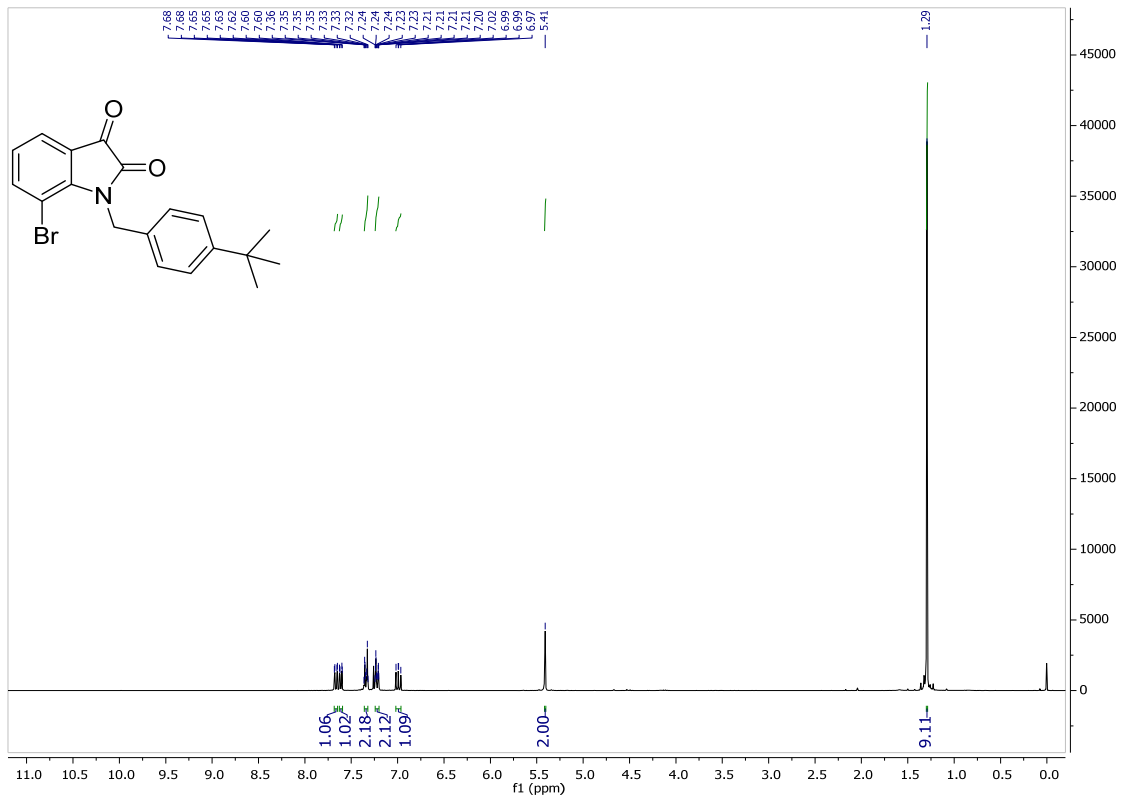
6-Bromo-1-[4-(*tert*-butyl)benzyl]indoline-2,3-dione (1i)



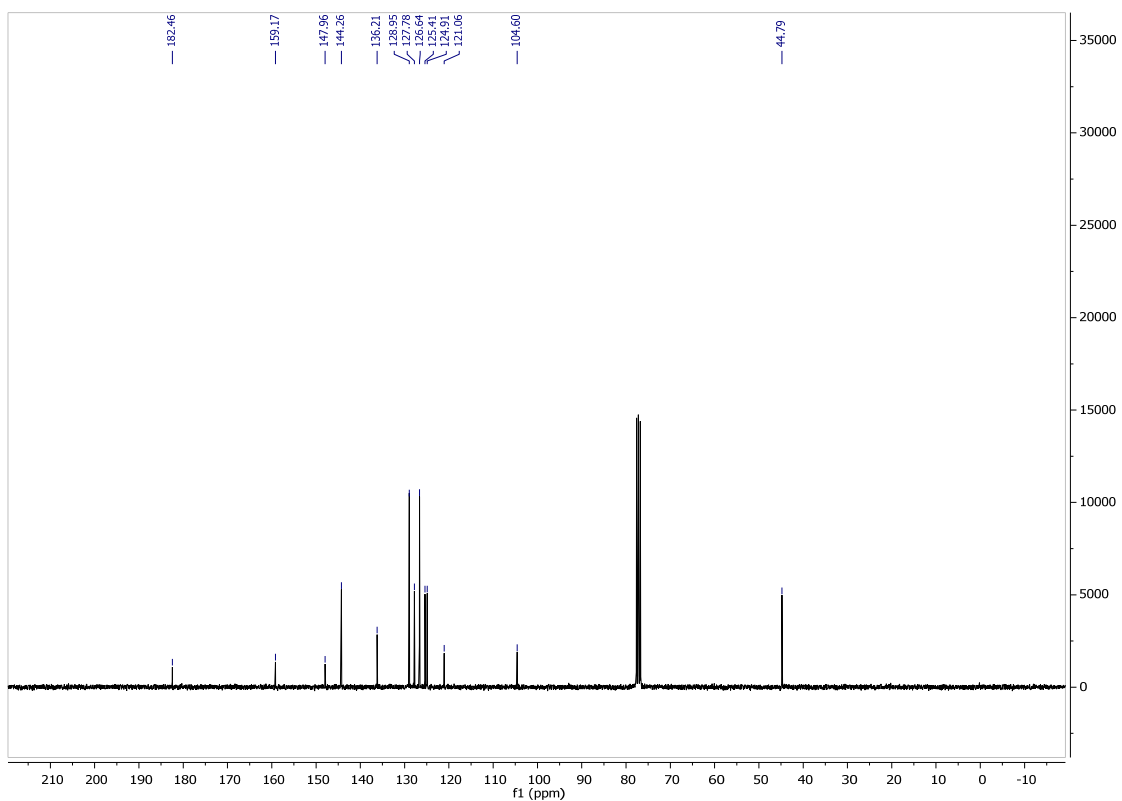
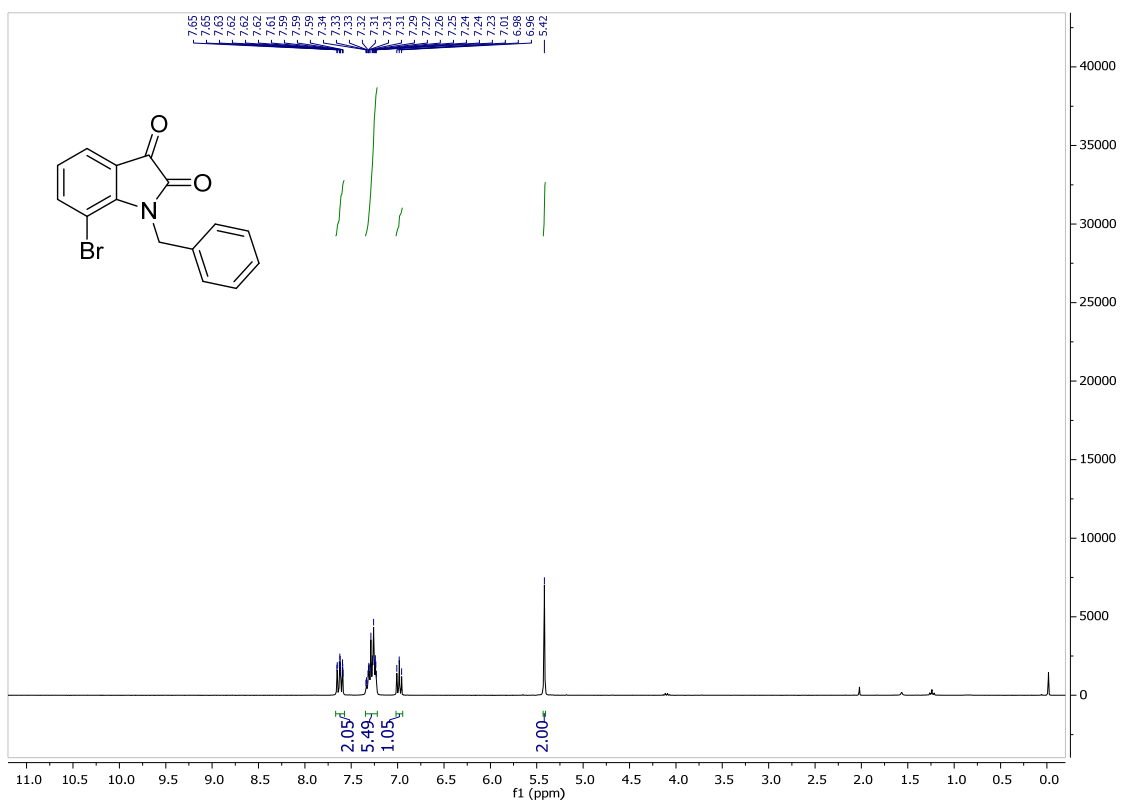
5-Bromo-1-[4-(*tert*-butyl)benzyl]indoline-2,3-dione (1j)



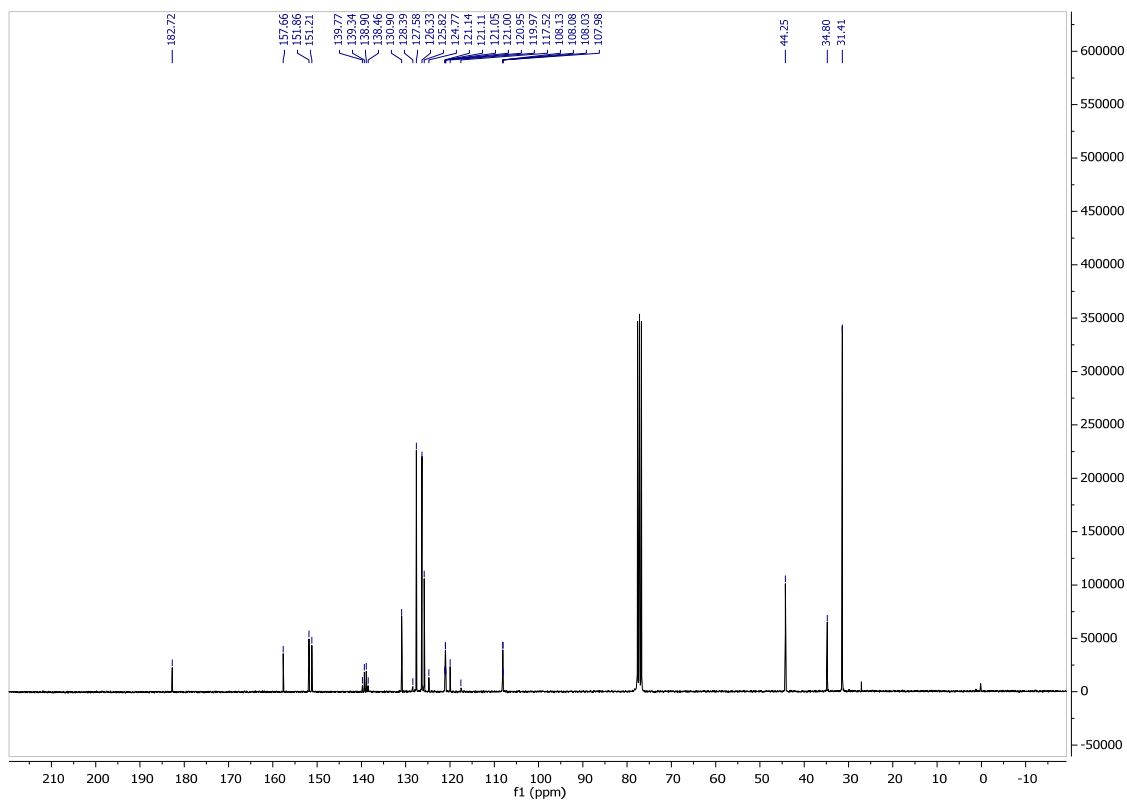
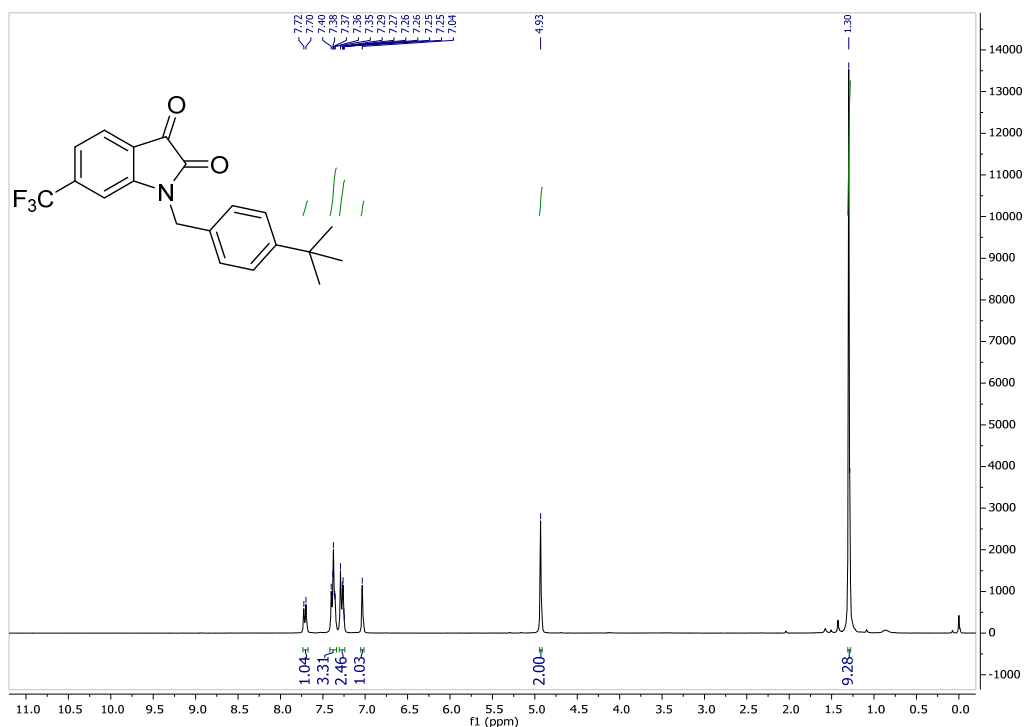
7-Bromo-1-[4-(*tert*-butyl)benzyl]indoline-2,3-dione (1k)

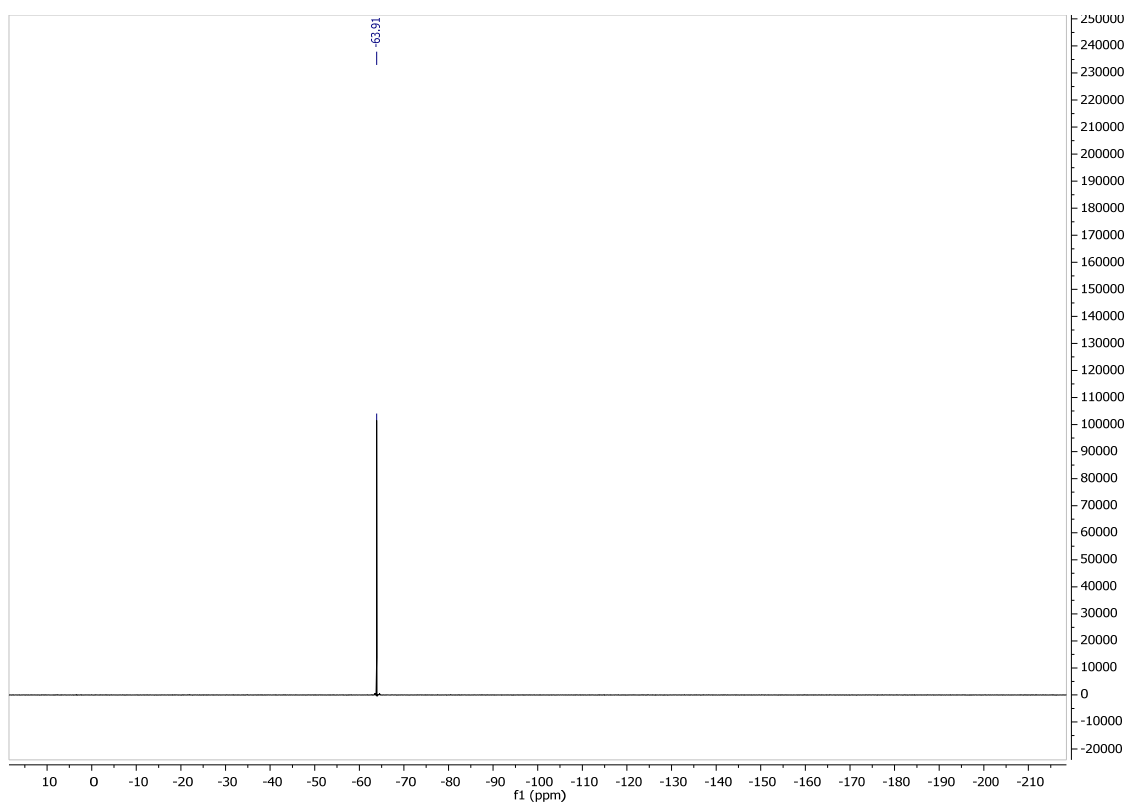


1-Benzyl-7-bromoindoline-2,3-dione (1I)

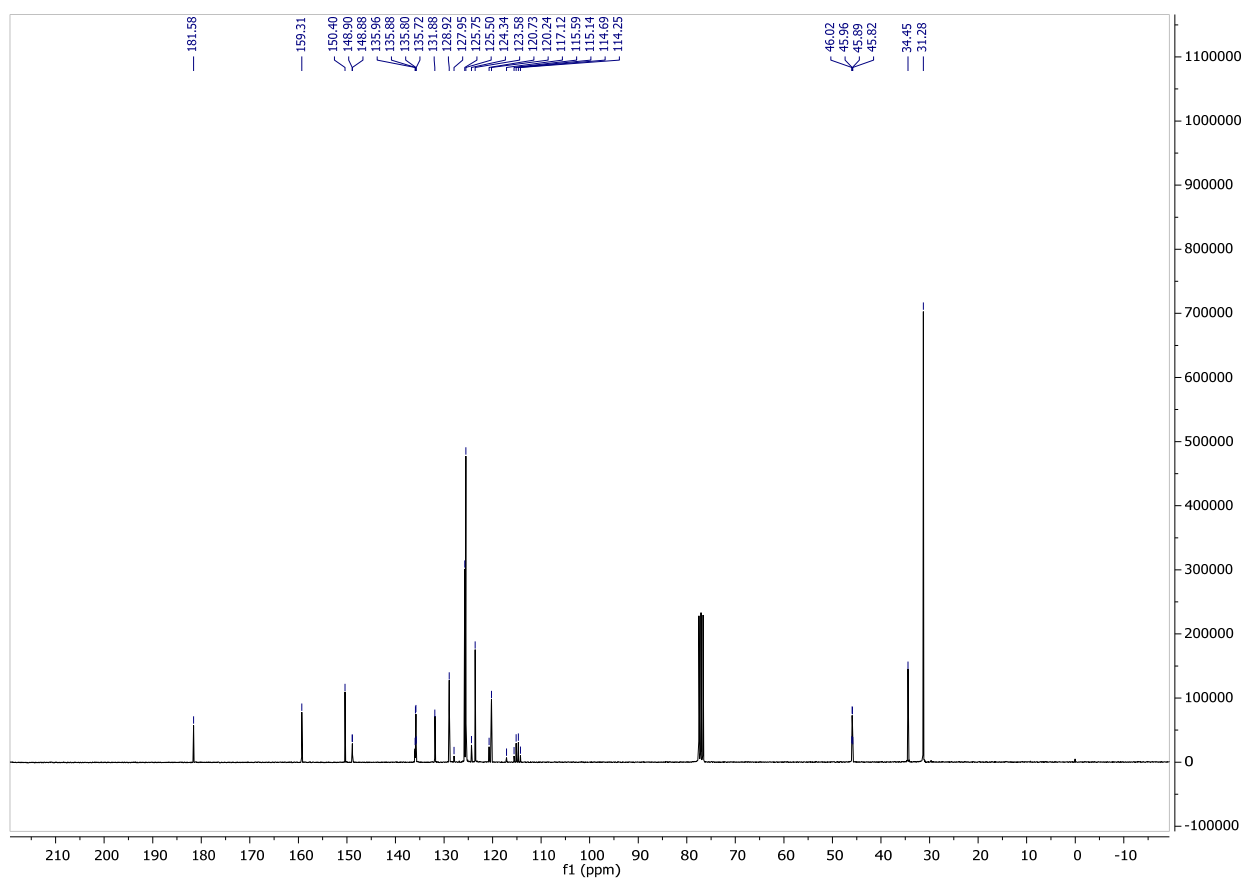
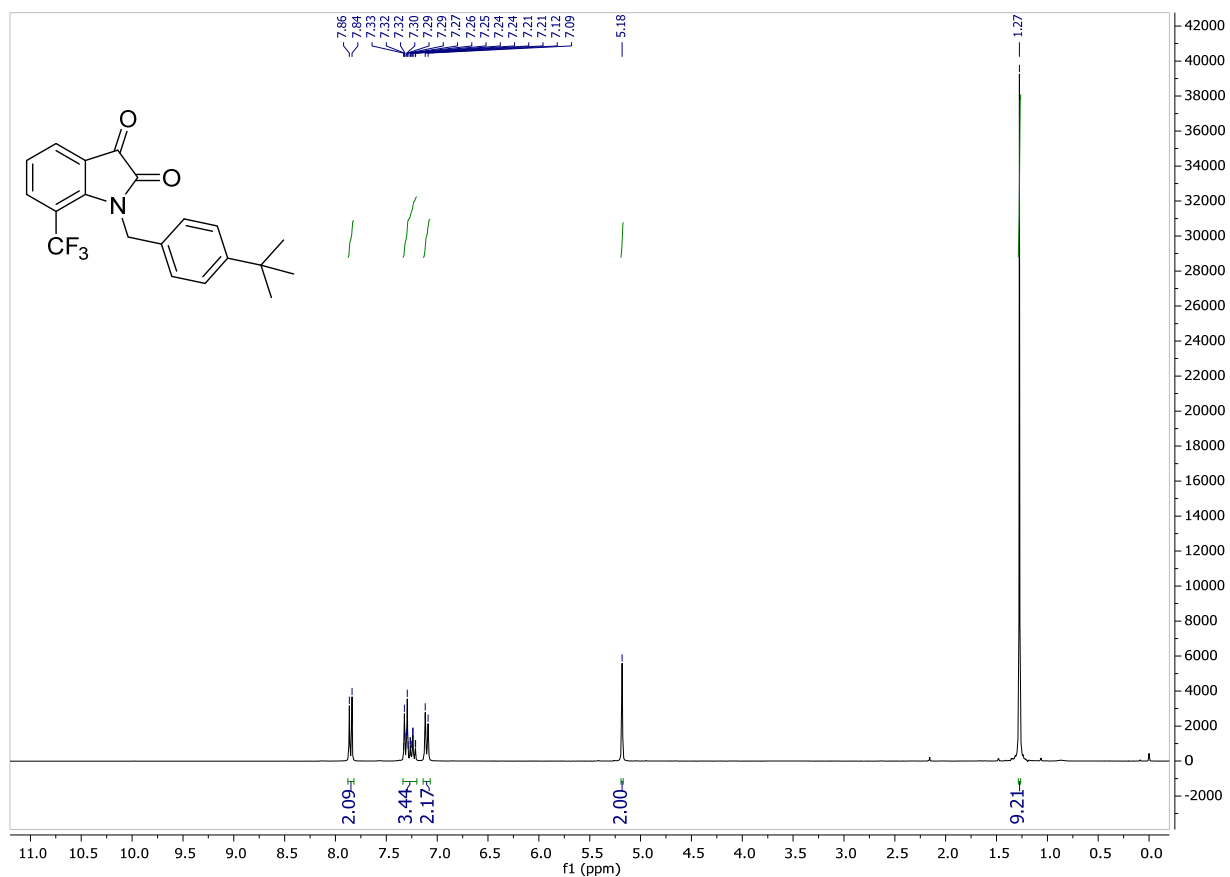


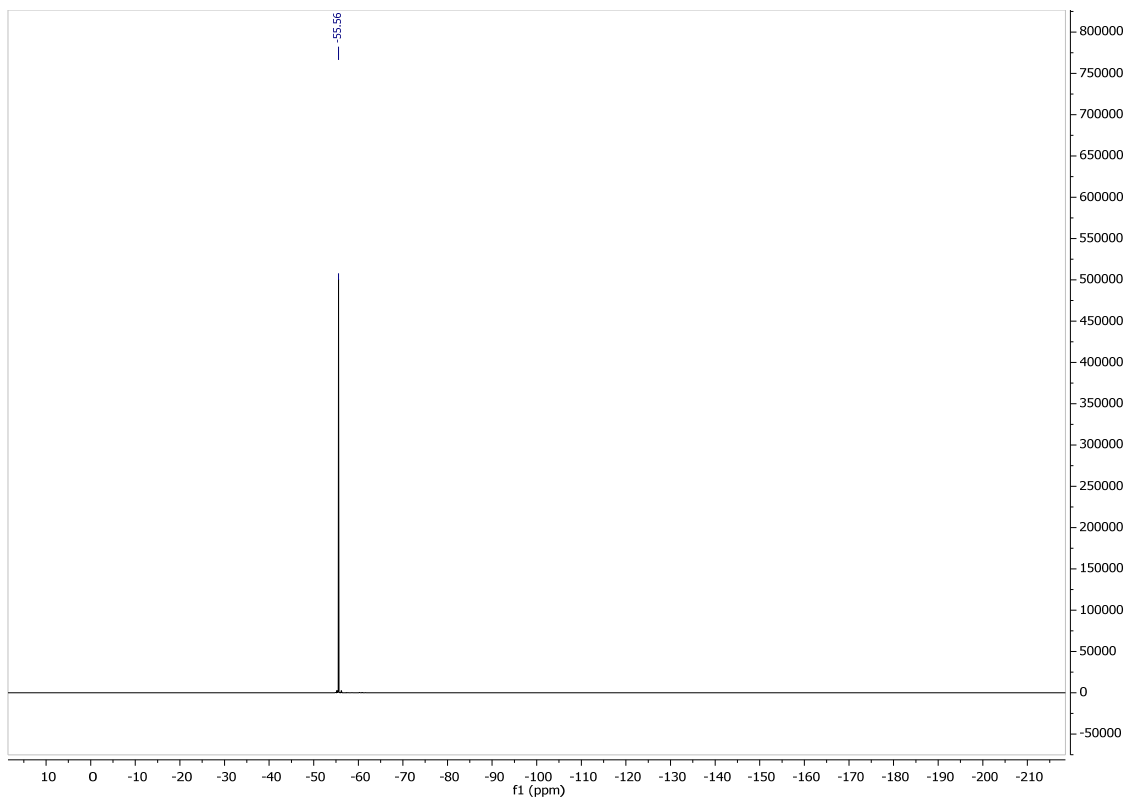
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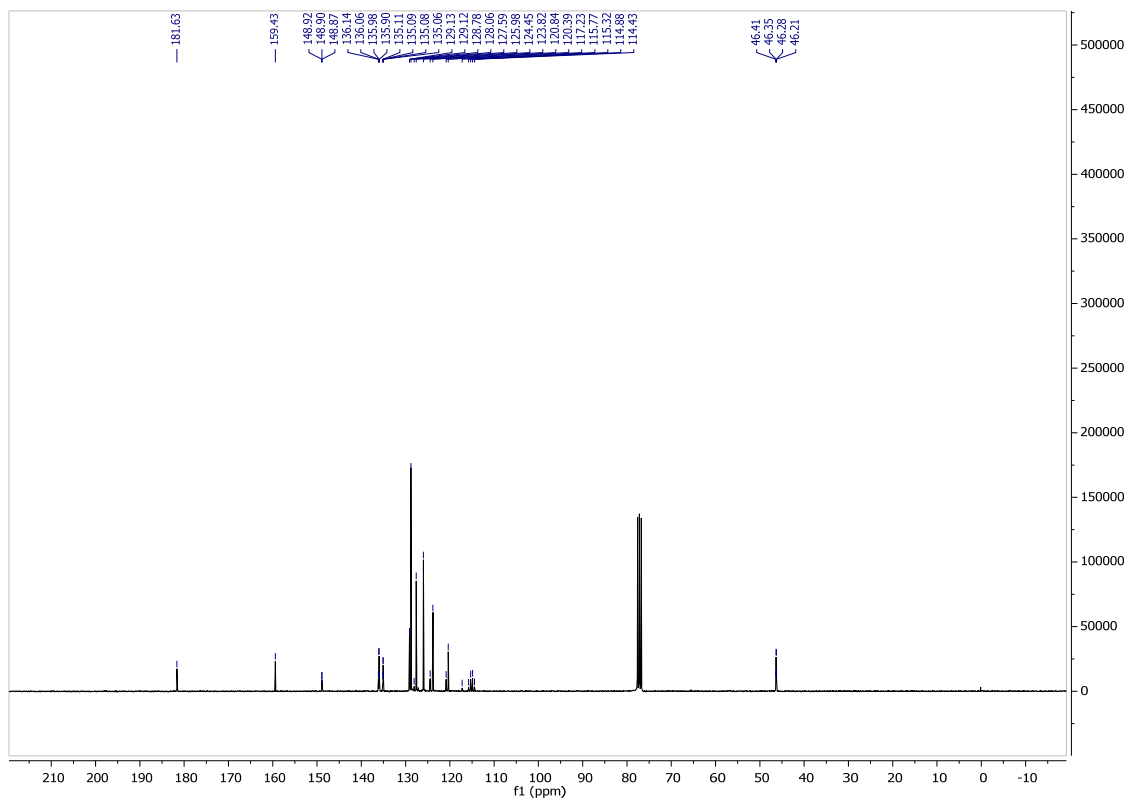
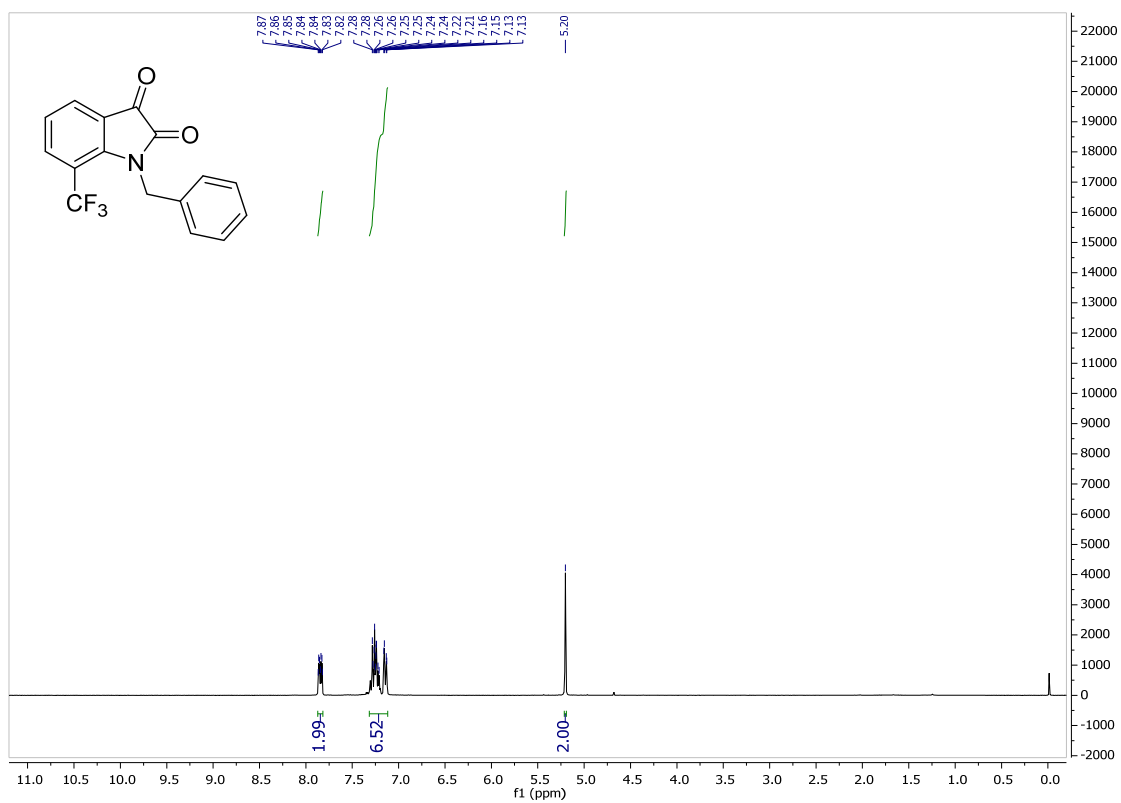


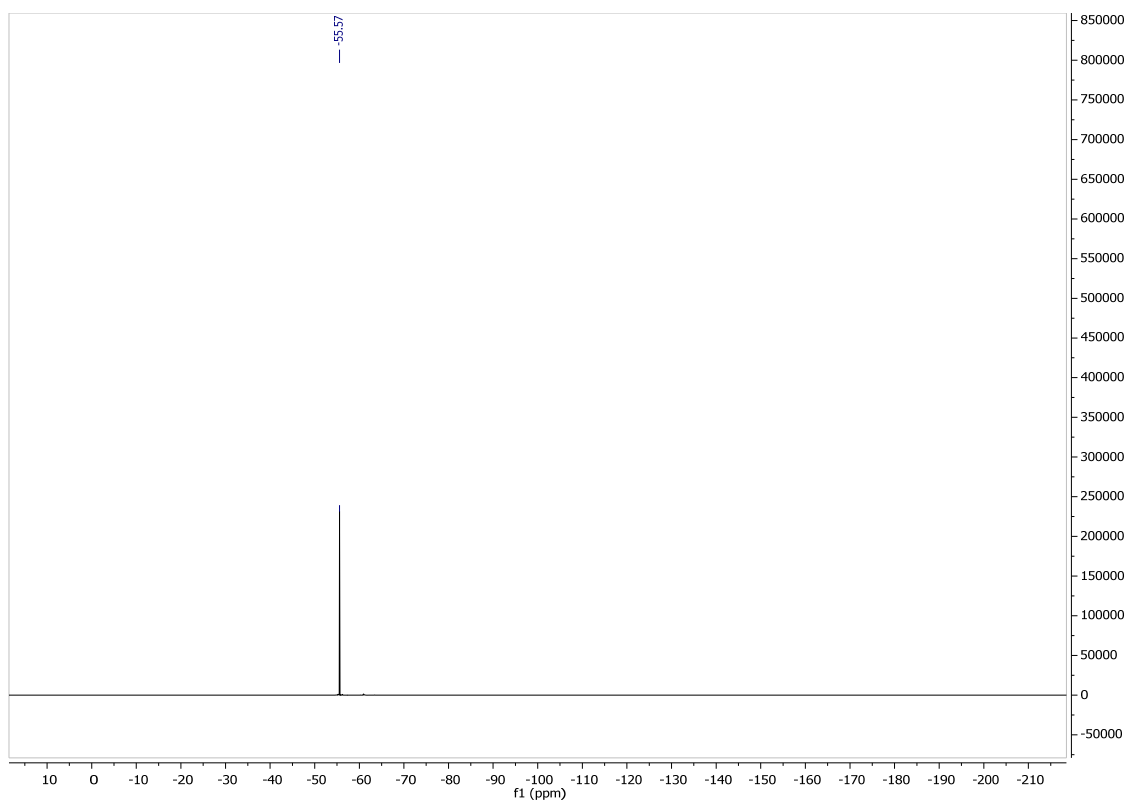
1-[4-(*tert*-Butyl)benzyl]-7-(trifluoromethyl)indoline-2,3-dione (1n)



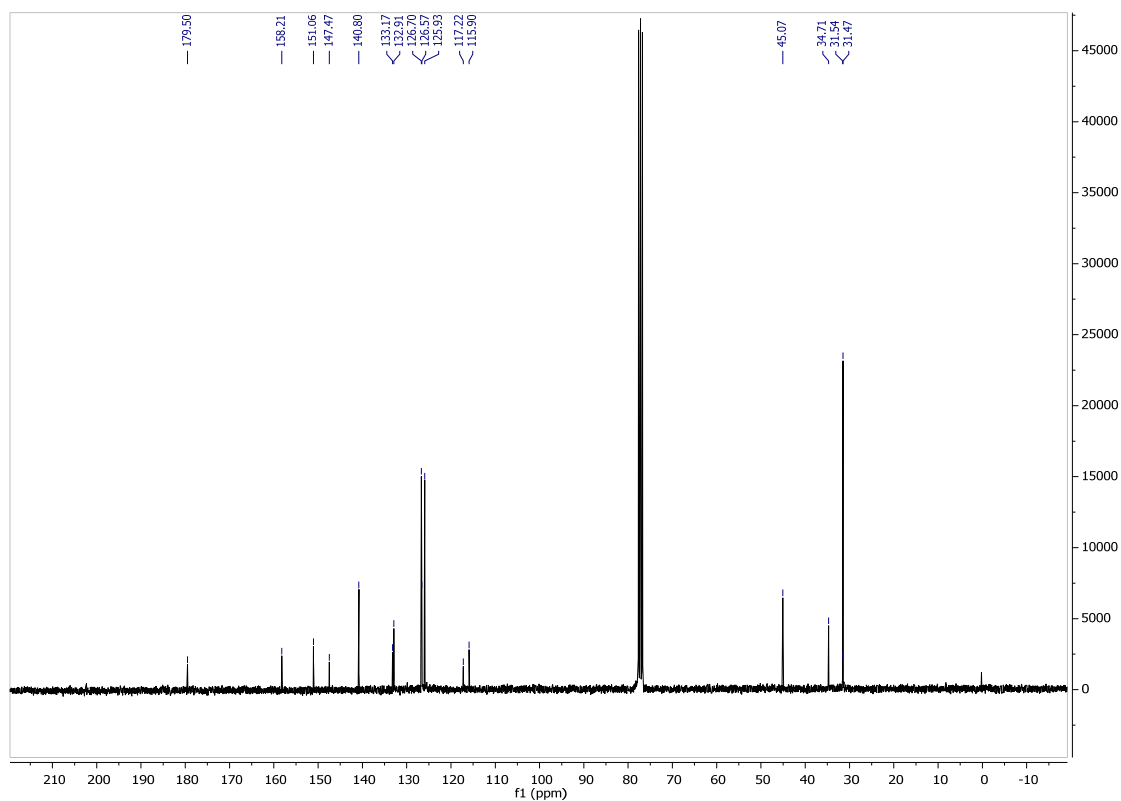
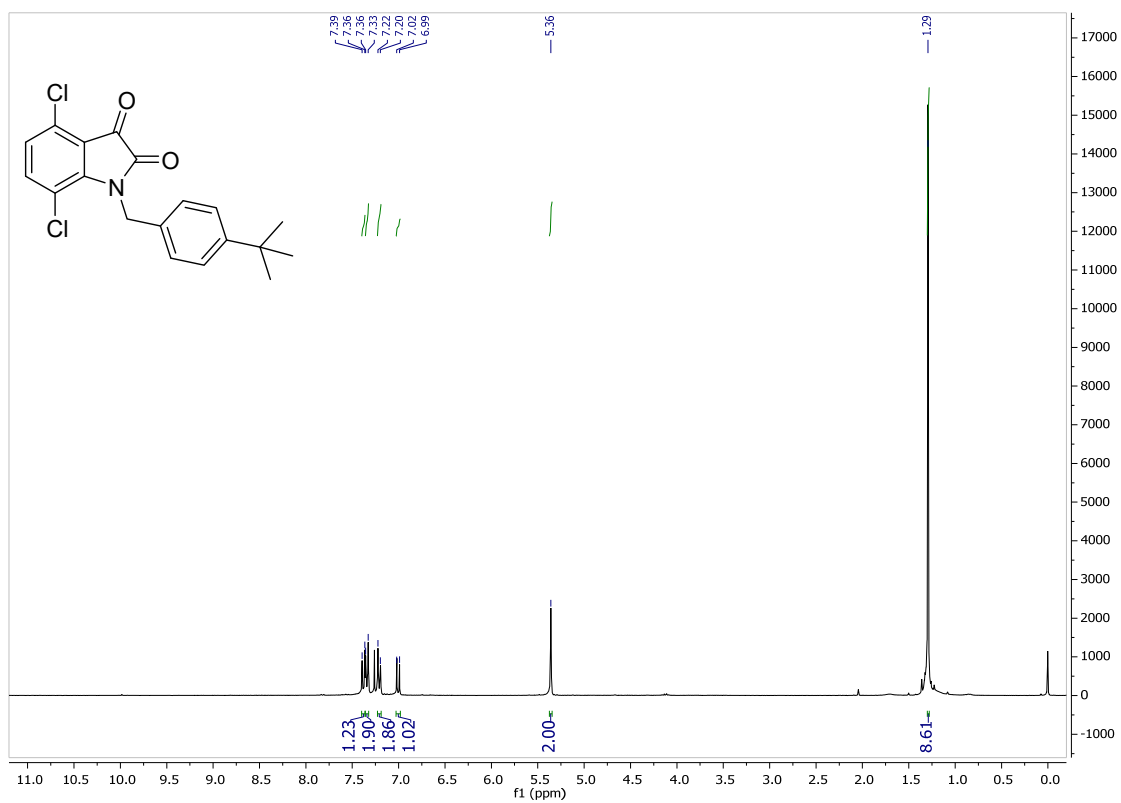


1-Benzyl-7-(trifluoromethyl)indoline-2,3-dione (1o)

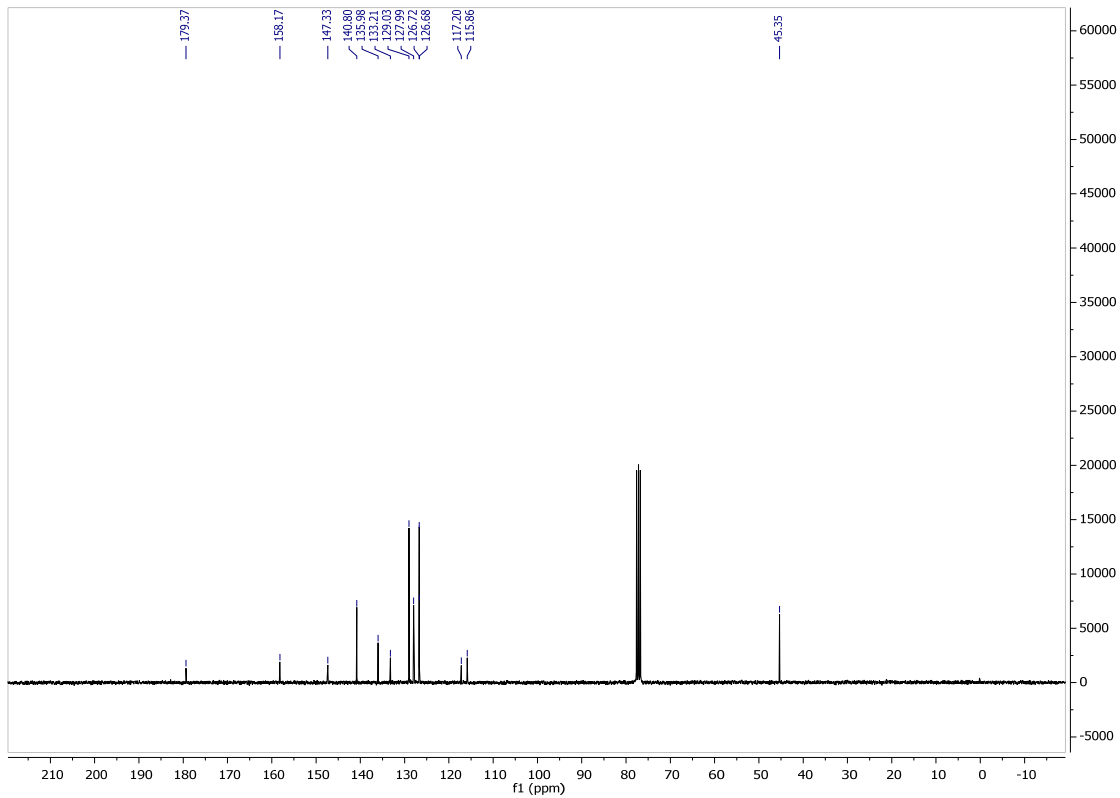
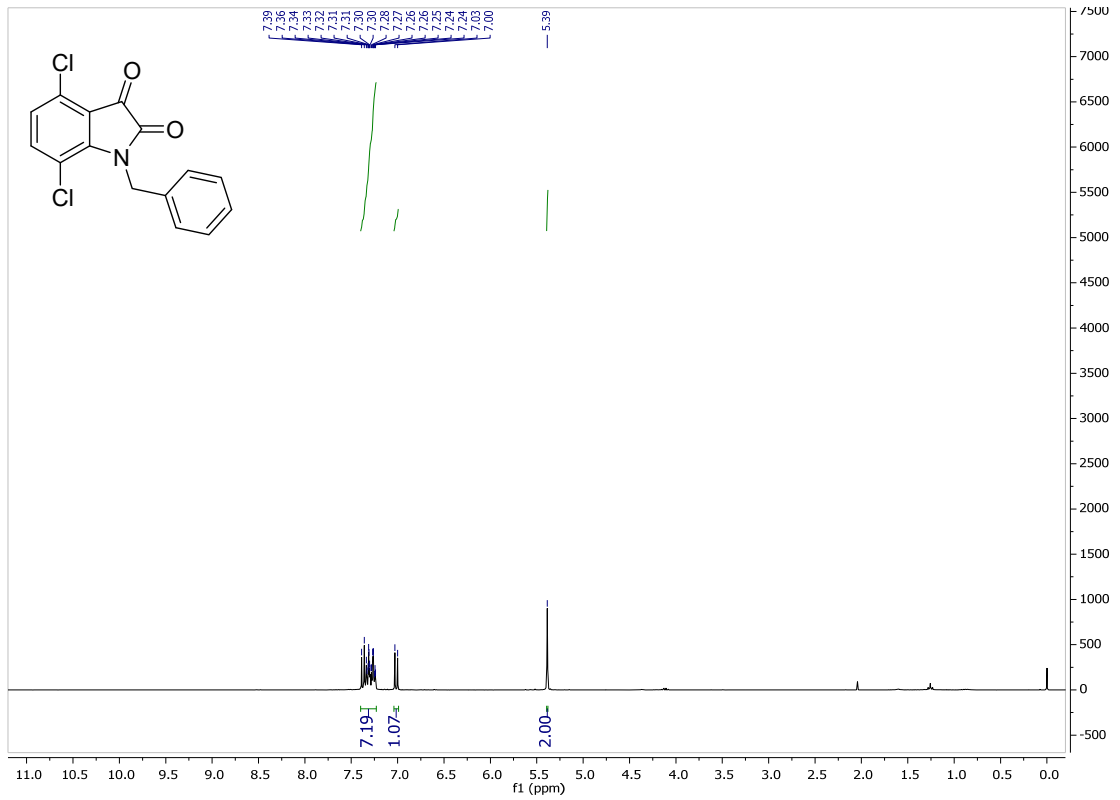




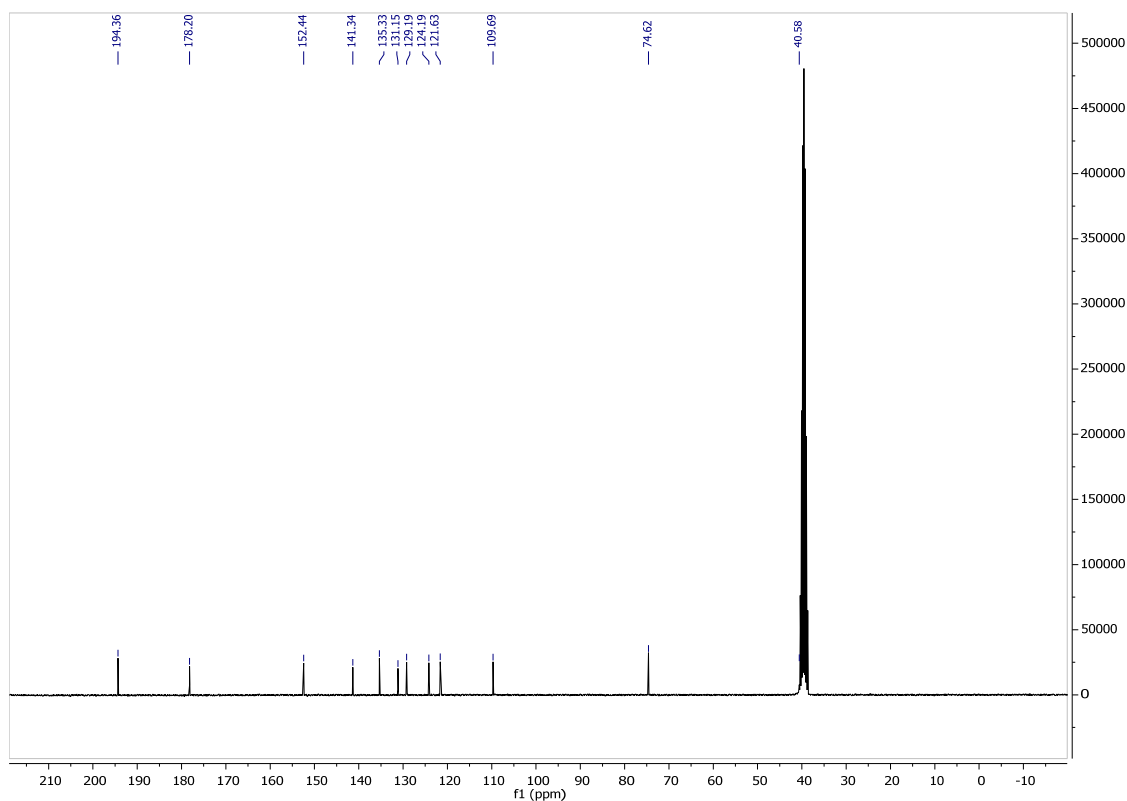
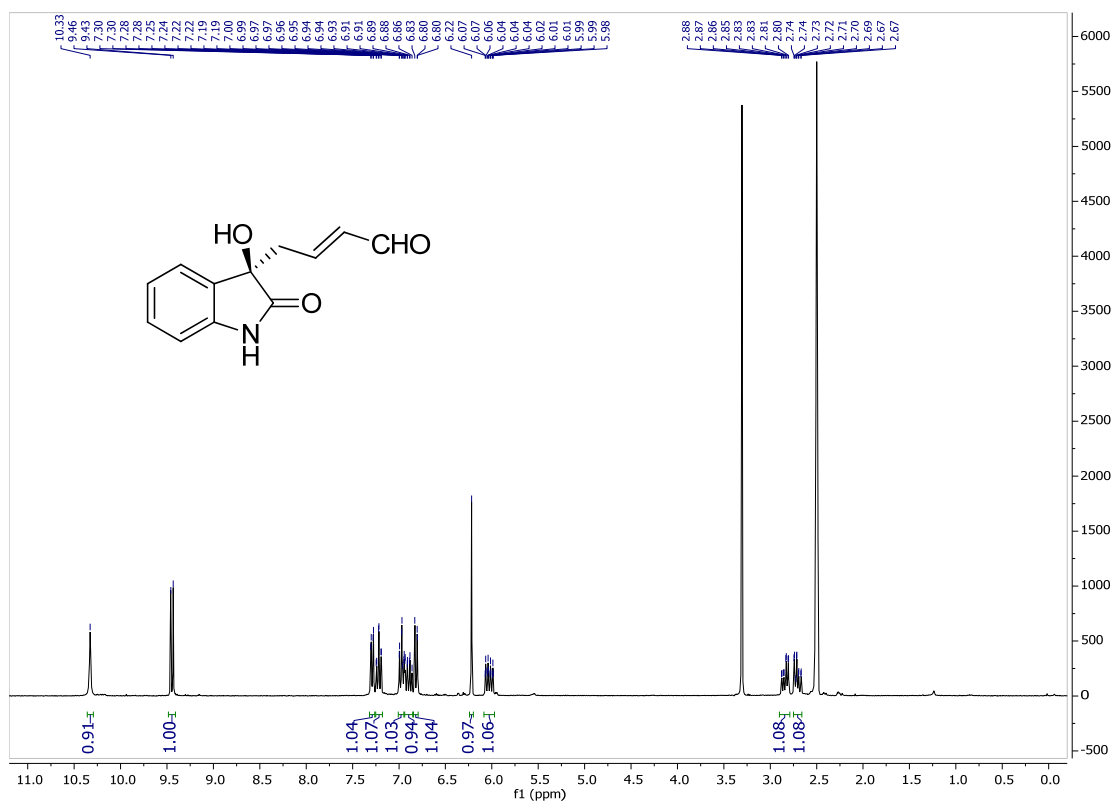
1-[4-(*tert*-Butyl)benzyl]-4,7-dichloroindoline-2,3-dione (1p)

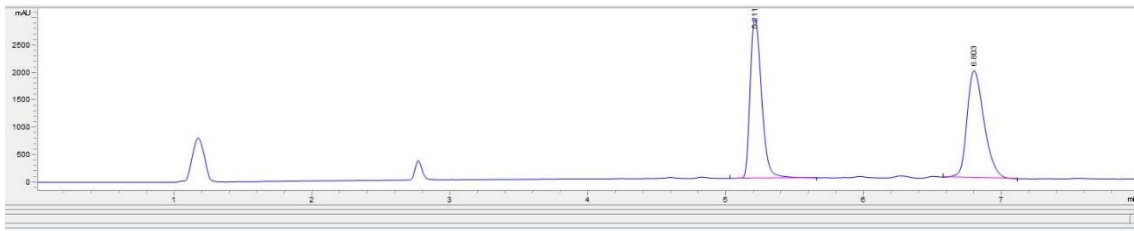


1-Benzyl-4,7-dichloroindoline-2,3-dione (1q)

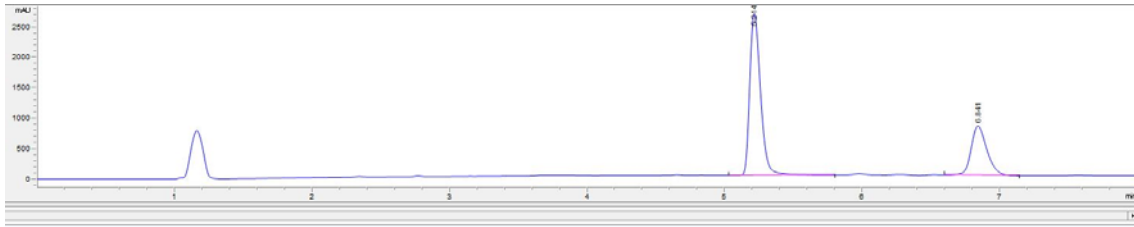


(R,E)-4-(3-Hydroxy-2-oxindolin-3-yl)but-2-enal (4a)



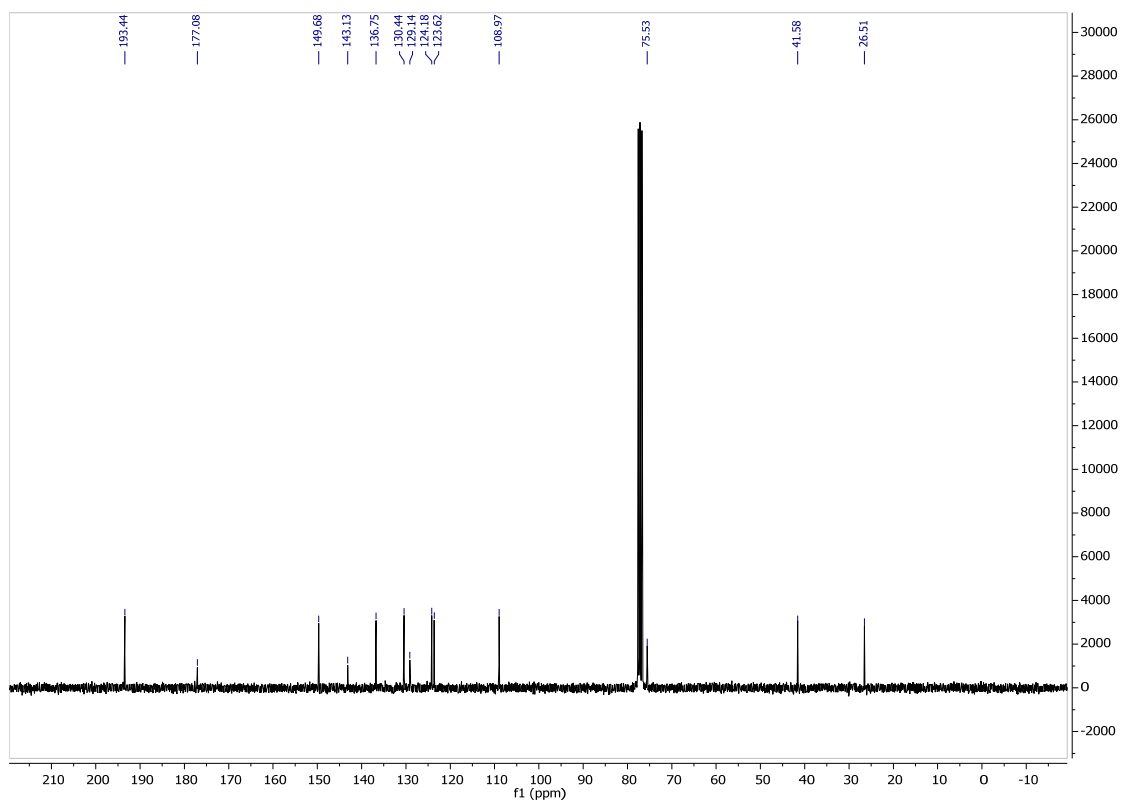
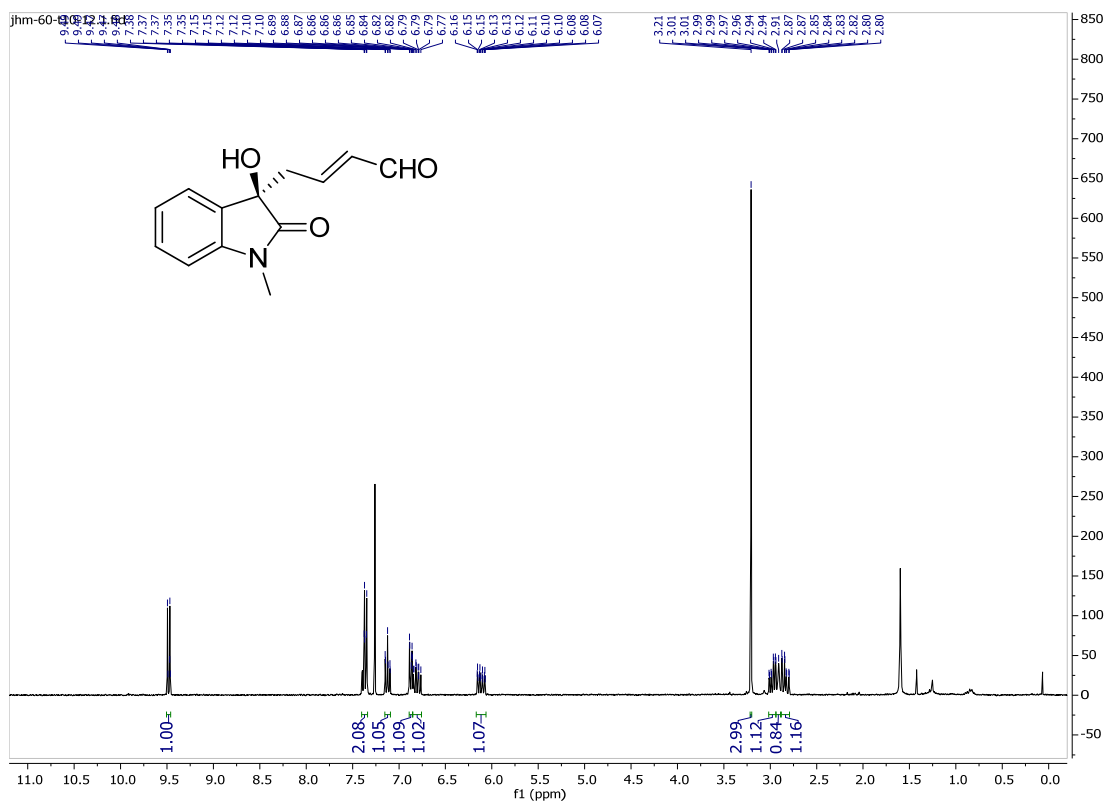


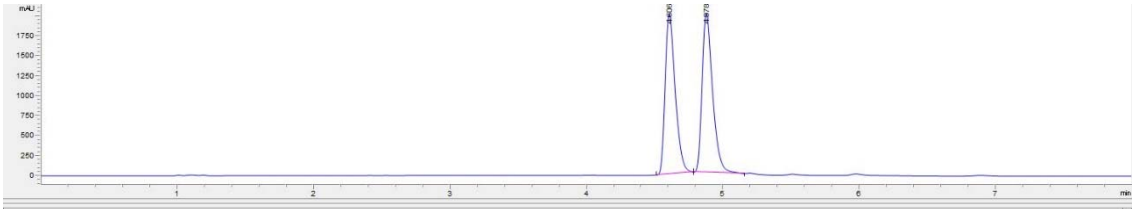
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.211	BB	16905.9	2939.1	0.0911	50.025	0.641
2	6.803	BB	16888.8	1968.4	0.1321	49.975	0.685



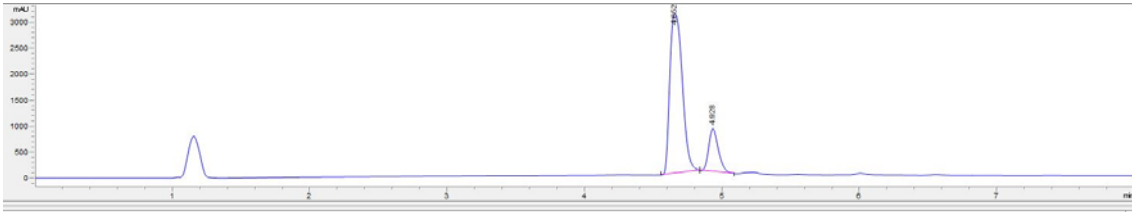
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.214	BB	14971.7	2646.7	0.0858	69.277	0.646
2	6.841	BB	6418.8	804.9	0.121	30.723	0.736

(R,E)-4-(3-Hydroxy-1-methyl-2-oxindolin-3-yl)but-2-enal (4b)



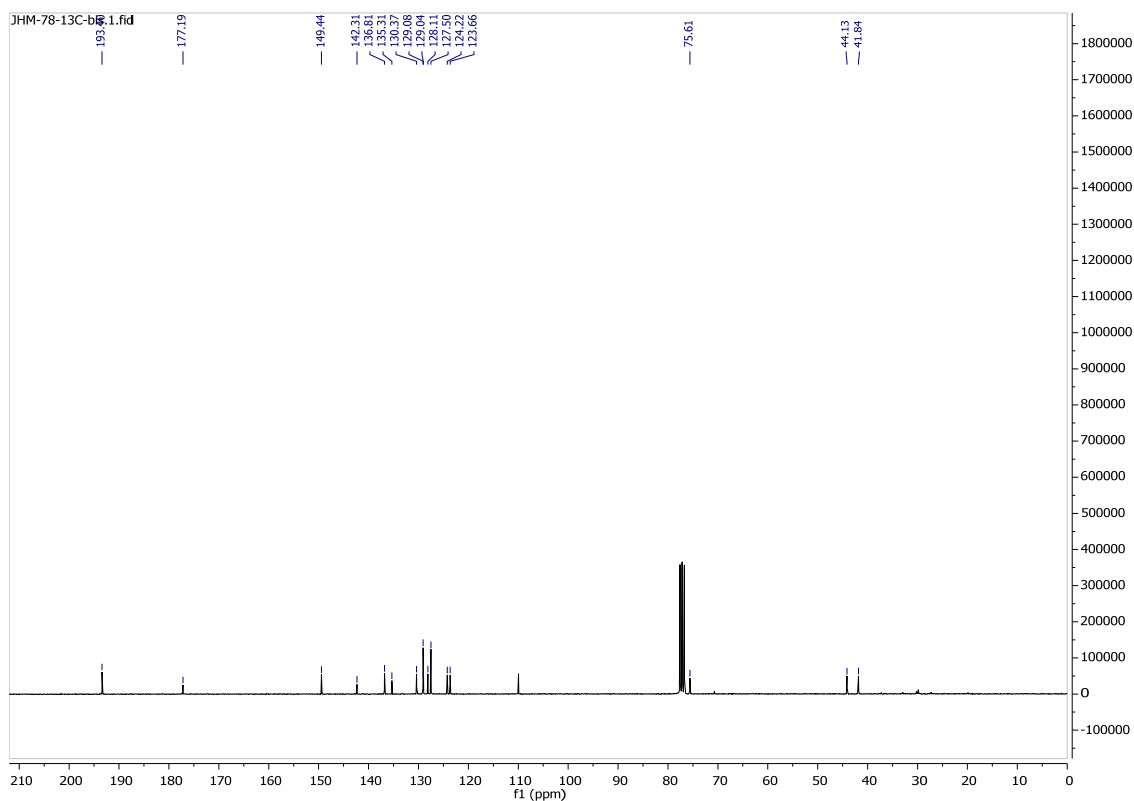
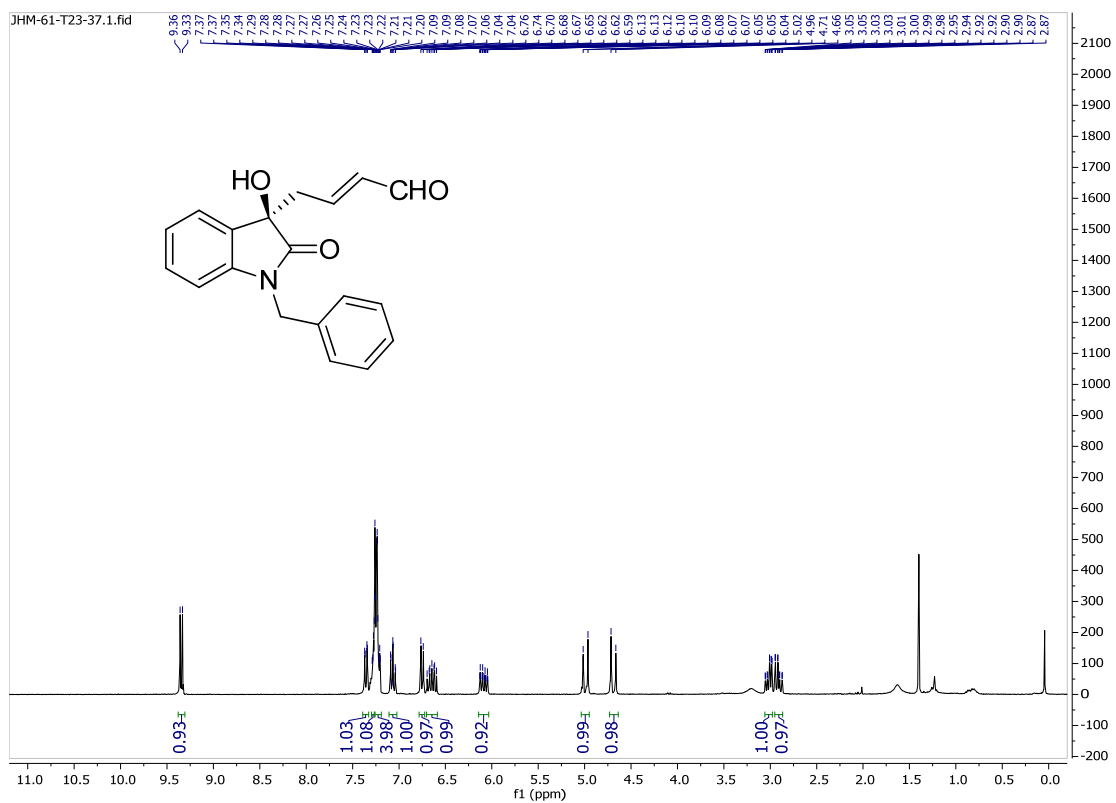


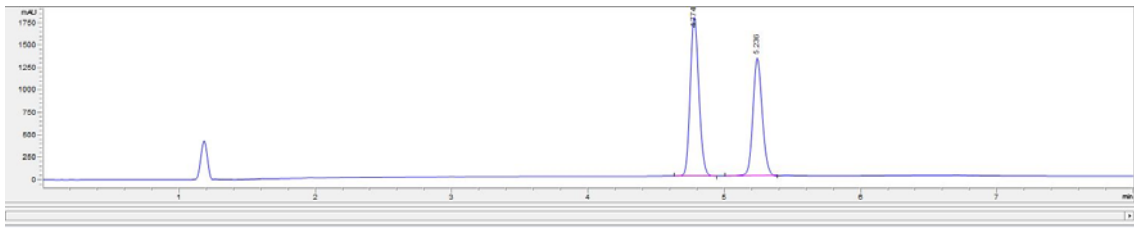
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.606	BB	10262.7	2015.2	0.0774	49.016	0.652
2	4.878	BB	10674.9	2003.8	0.0802	50.984	0.633



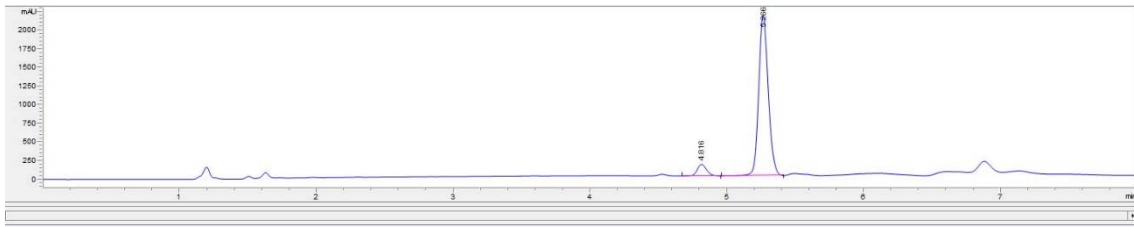
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.652	BB	19389.1	3074.1	0.1016	82.925	0.627
2	4.928	BB	3992.3	822.0	0.0746	17.075	0.712

(R,E)-4-(1-Benzyl-3-hydroxy-2-oxindolin-3-yl)but-2-enal (4c)



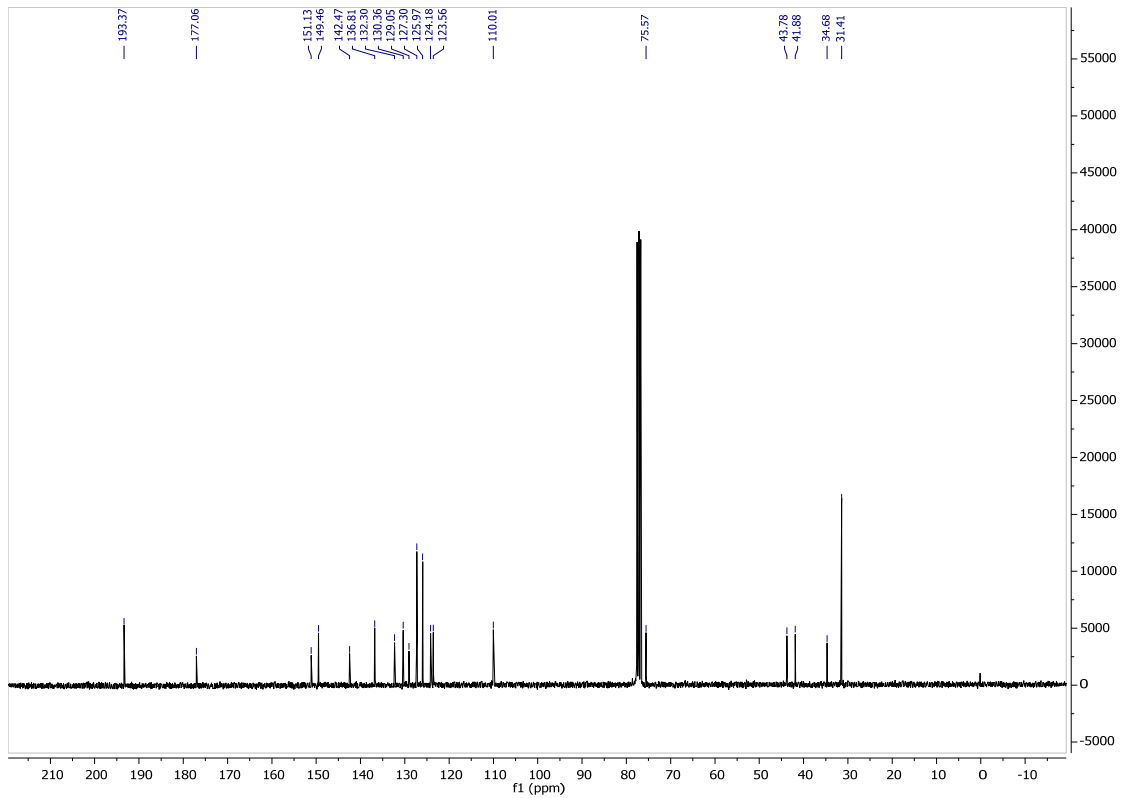
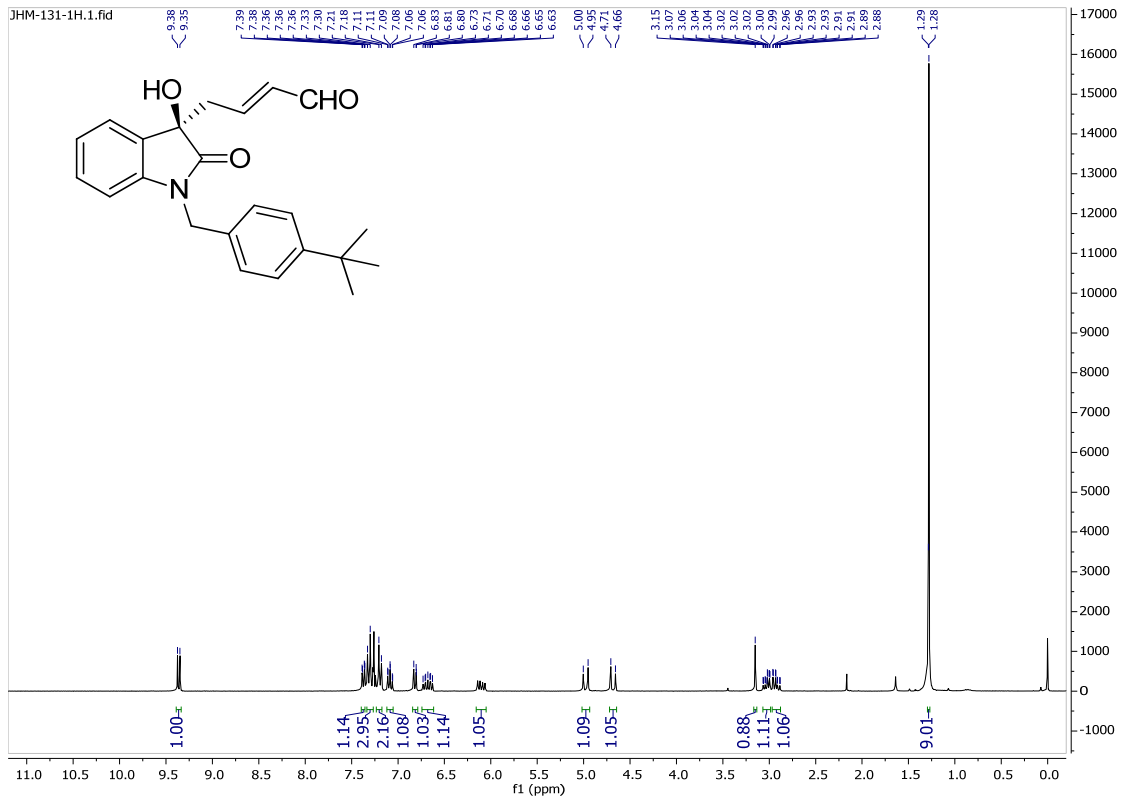


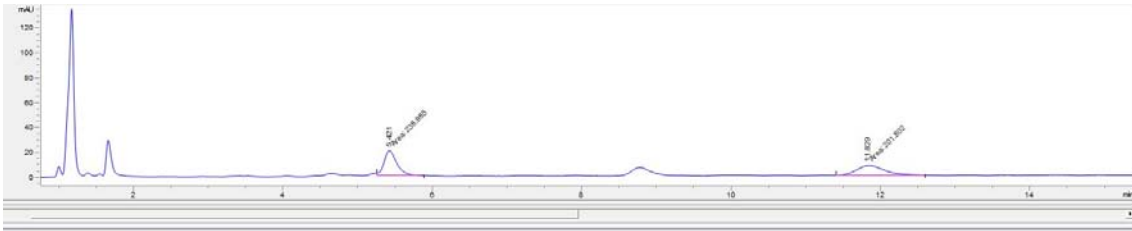
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.774	BB	7852.4	1761.3	0.0674	55.658	0.835
2	5.236	BB	6256	1314.8	0.0733	44.342	0.859



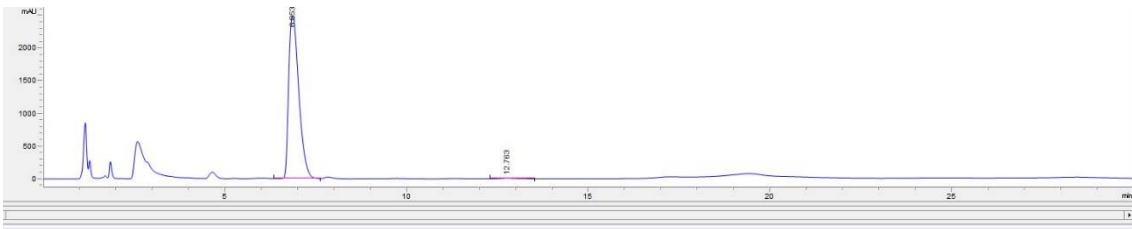
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.816	BB	723.5	154.7	0.0726	6.508	0.835

(R,E)-4-{1-[4-(tert-Butyl)benzyl]-3-hydroxy-2-oxindolin-3-yl}but-2-enal (4d)



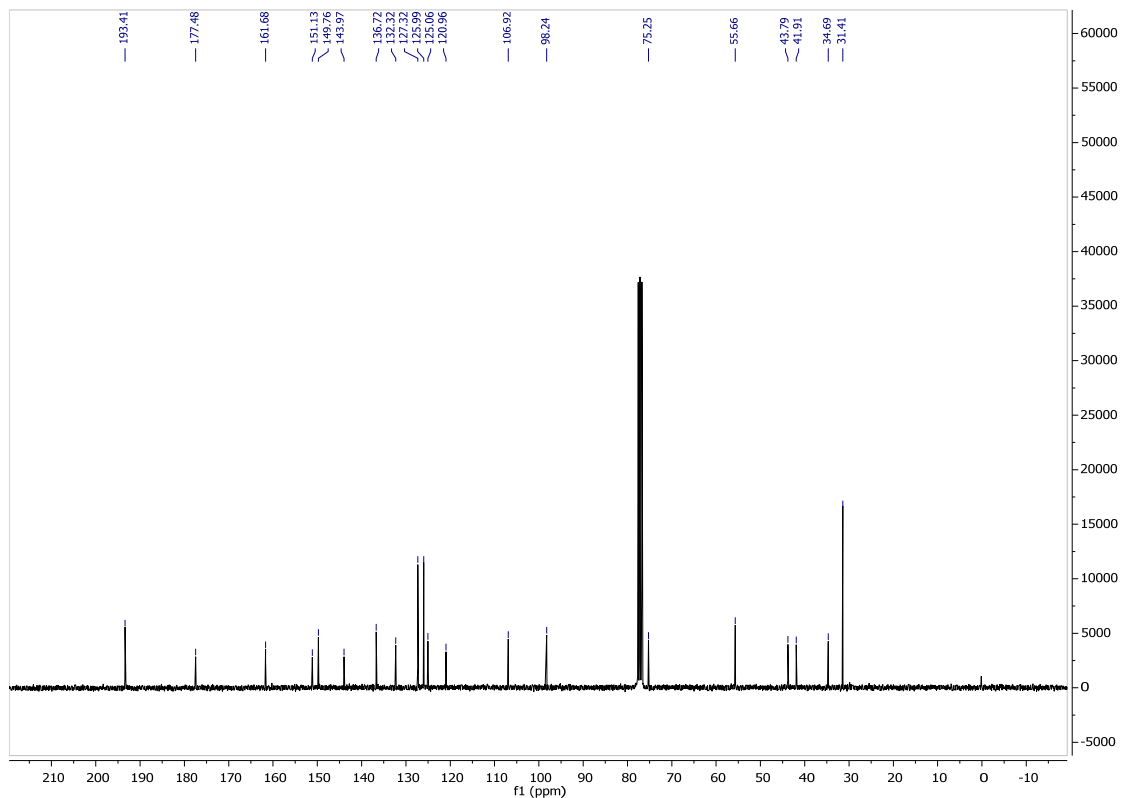
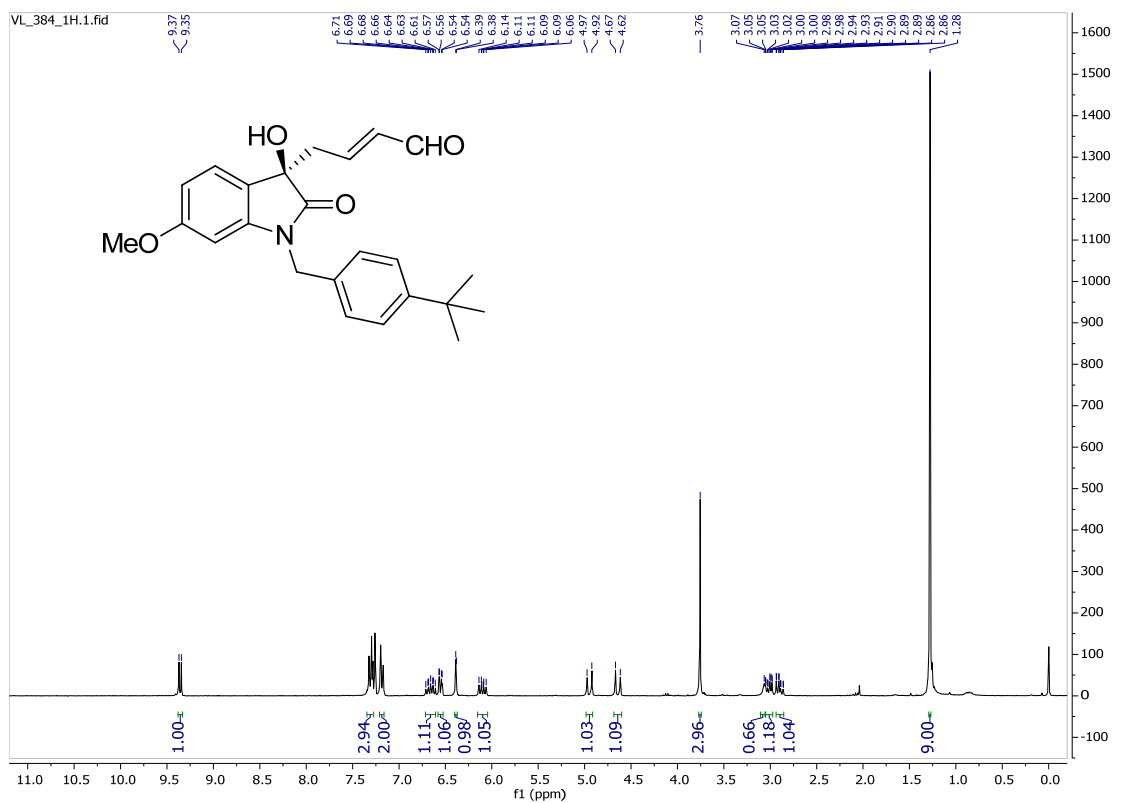


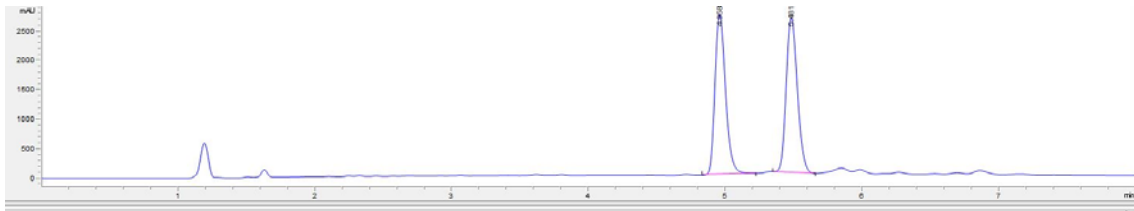
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.421	MM	239	20.2	0.1975	54.218	0.48
2	11.820	MM	201.8	7.7	0.436	45.782	0.697



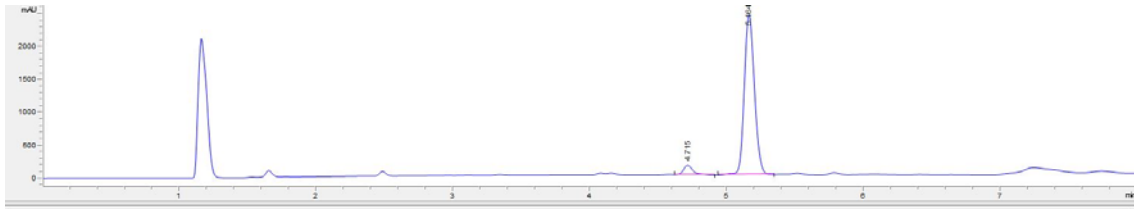
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	6.853	BB	46280.9	2494.2	0.3038	99.475	0.583
2	12.763	BB	254.6	8.6	0.5664	0.525	0.677

(R,E)-4-(1-(4-(tert-Butyl)benzyl)-3-hydroxy-6-methoxy-2-oxindolin-3-yl)but-2-enal (4e)



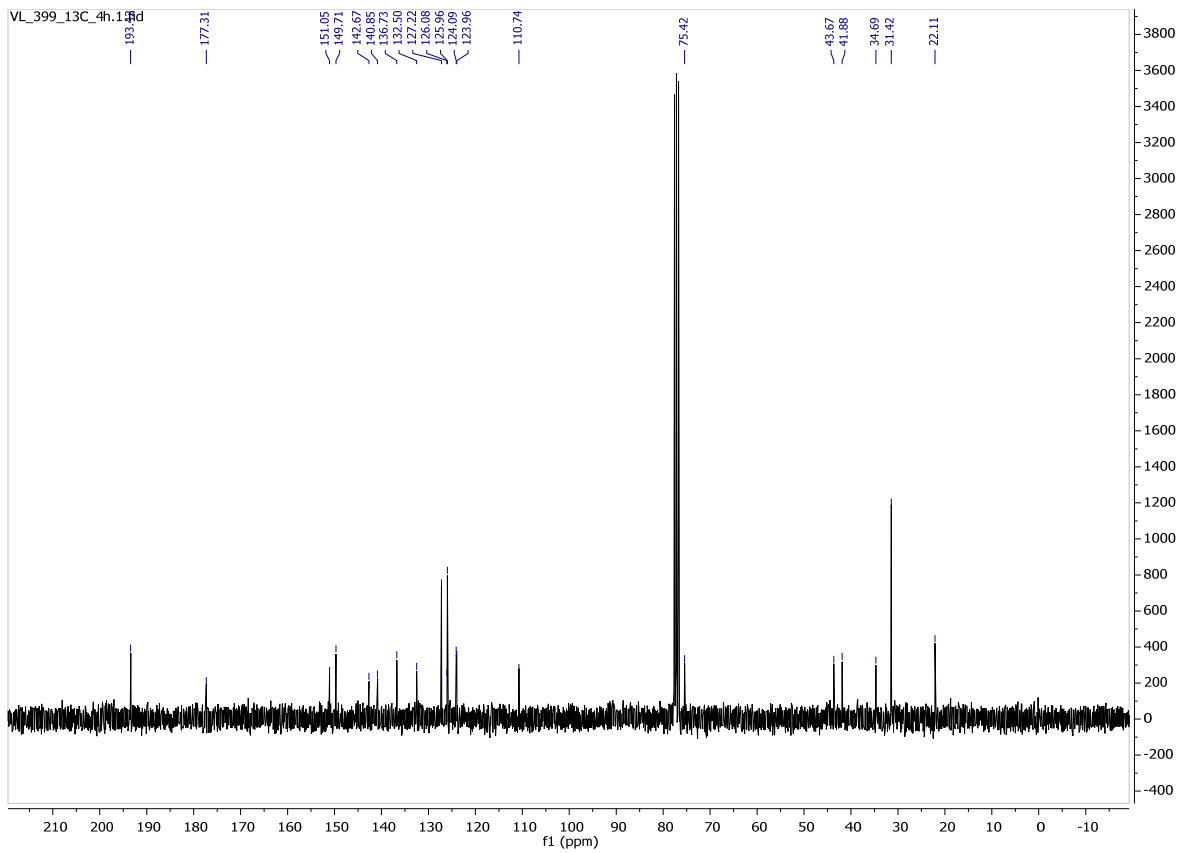
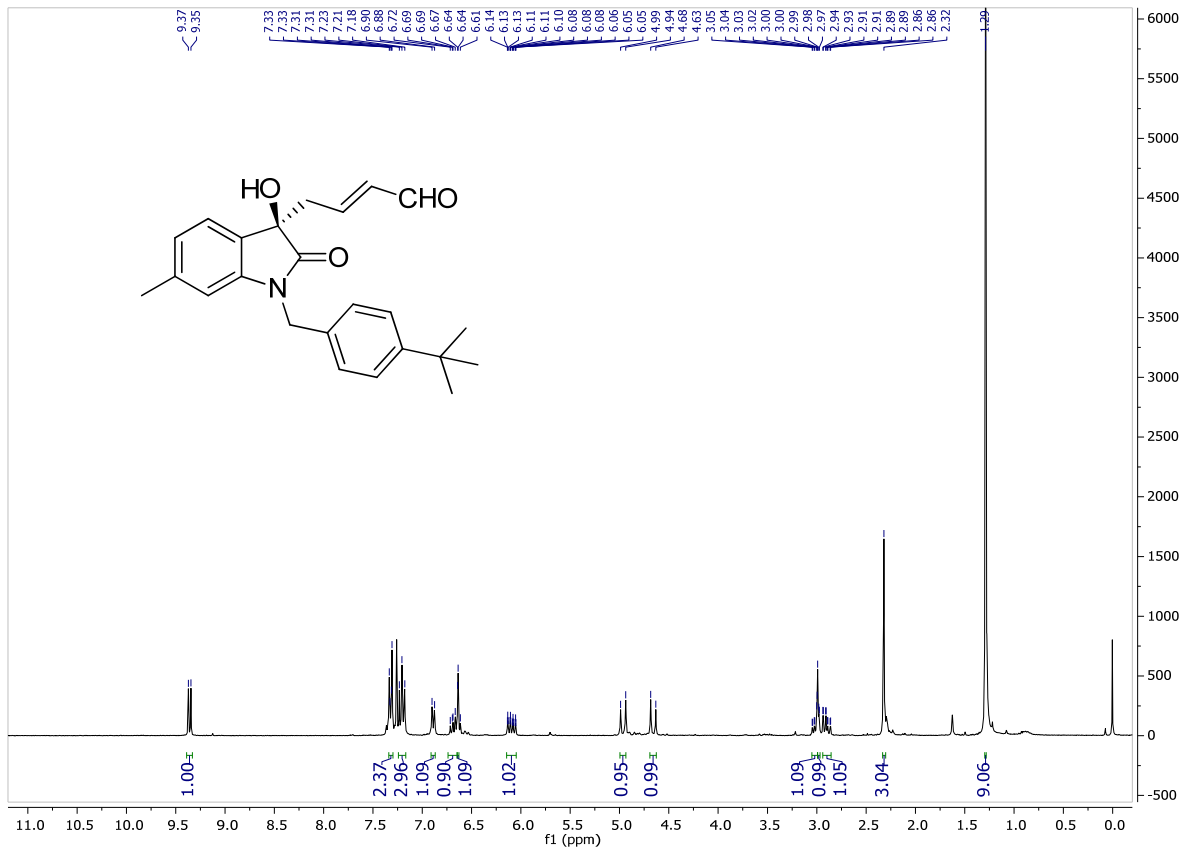


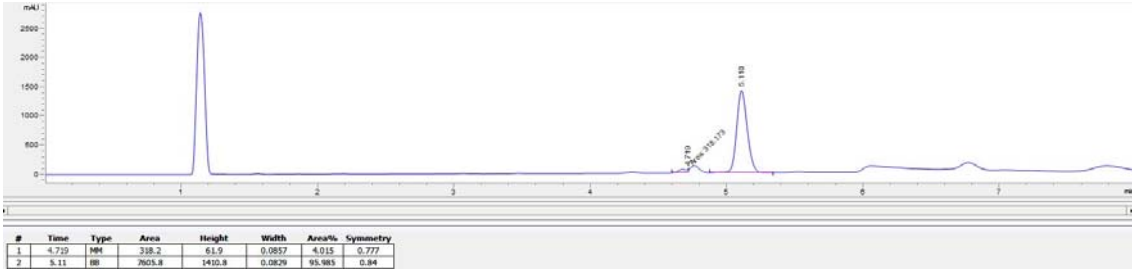
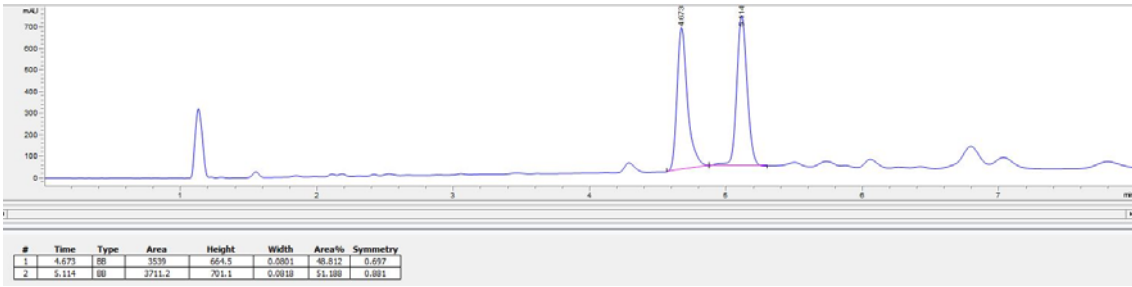
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.958	BB	14955.7	2710.5	0.0847	49.514	0.731
2	5.481	BB	14841.3	2620	0.0901	50.486	0.786



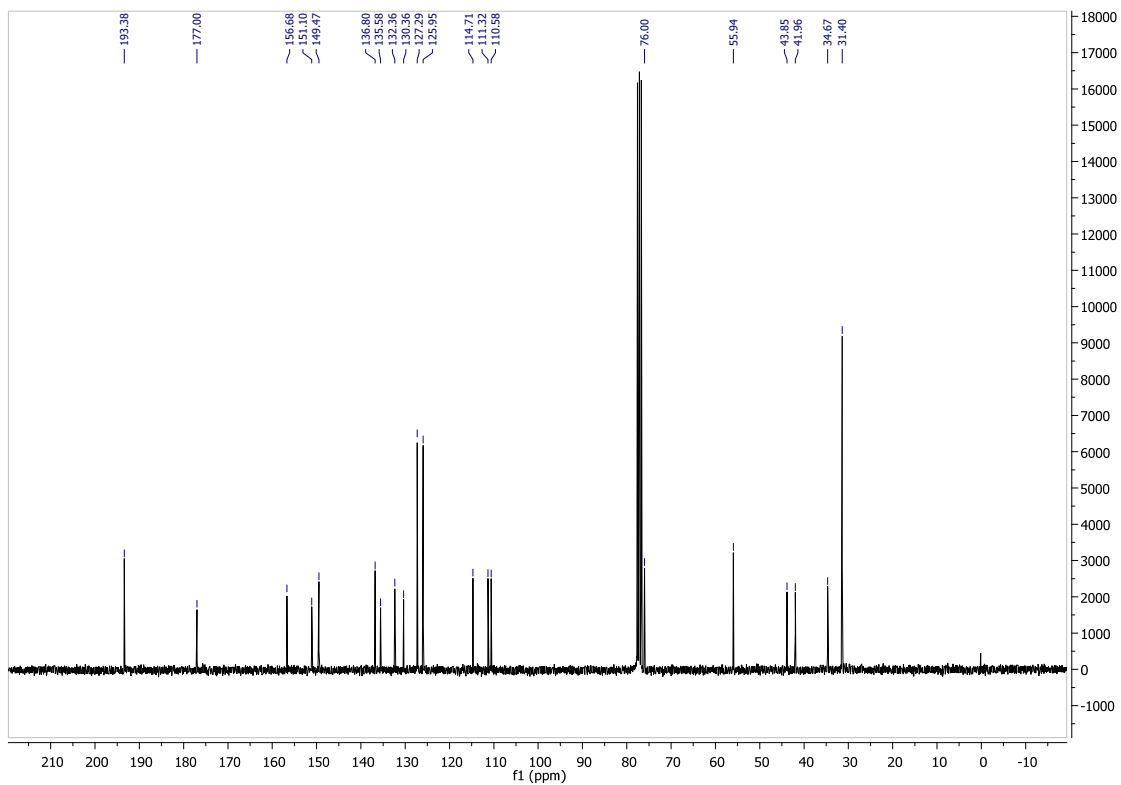
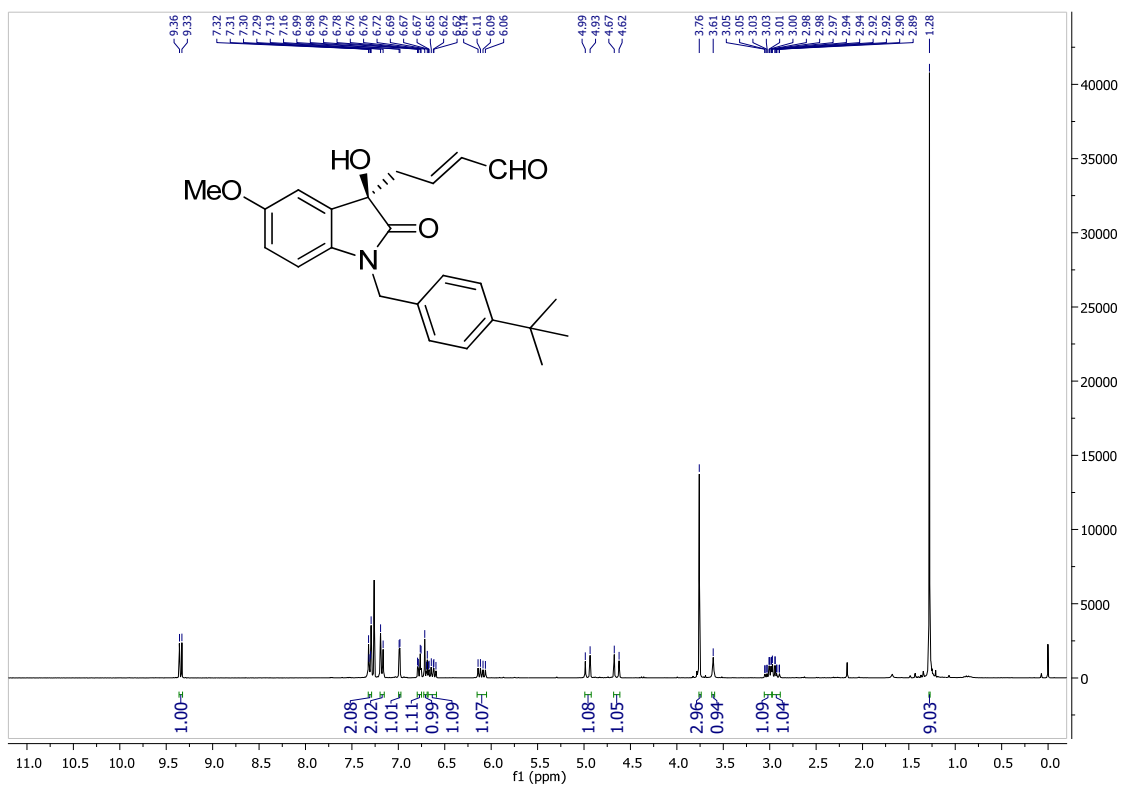
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.715	BB	692.7	146.2	0.0713	5.221	0.723
2	5.164	BB	12540.5	2443.1	0.0799	94.779	0.826

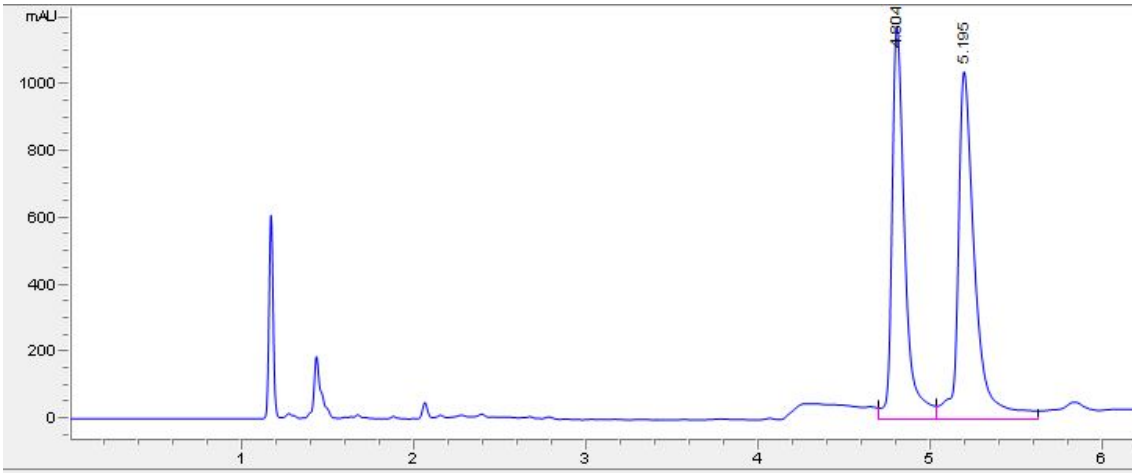
(R,E)-4-{1-[4-(tert-Butyl)benzyl]-3-hydroxy-2-oxo-6-methylindolin-3-yl}but-2-enal (4f)



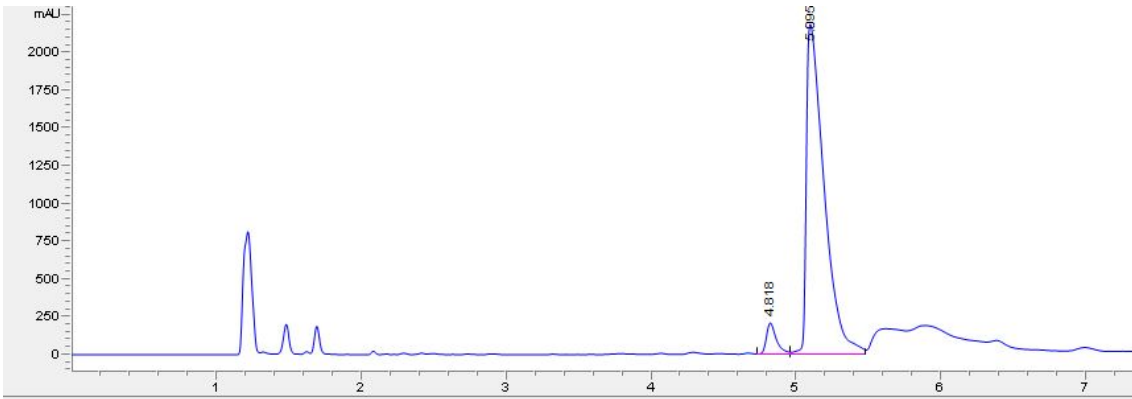


(R,E)-4-{1-[4-(tert-Butyl)benzyl]-3-hydroxy-5-methoxy-2-oxindolin-3-yl}but-2-enal (4g)



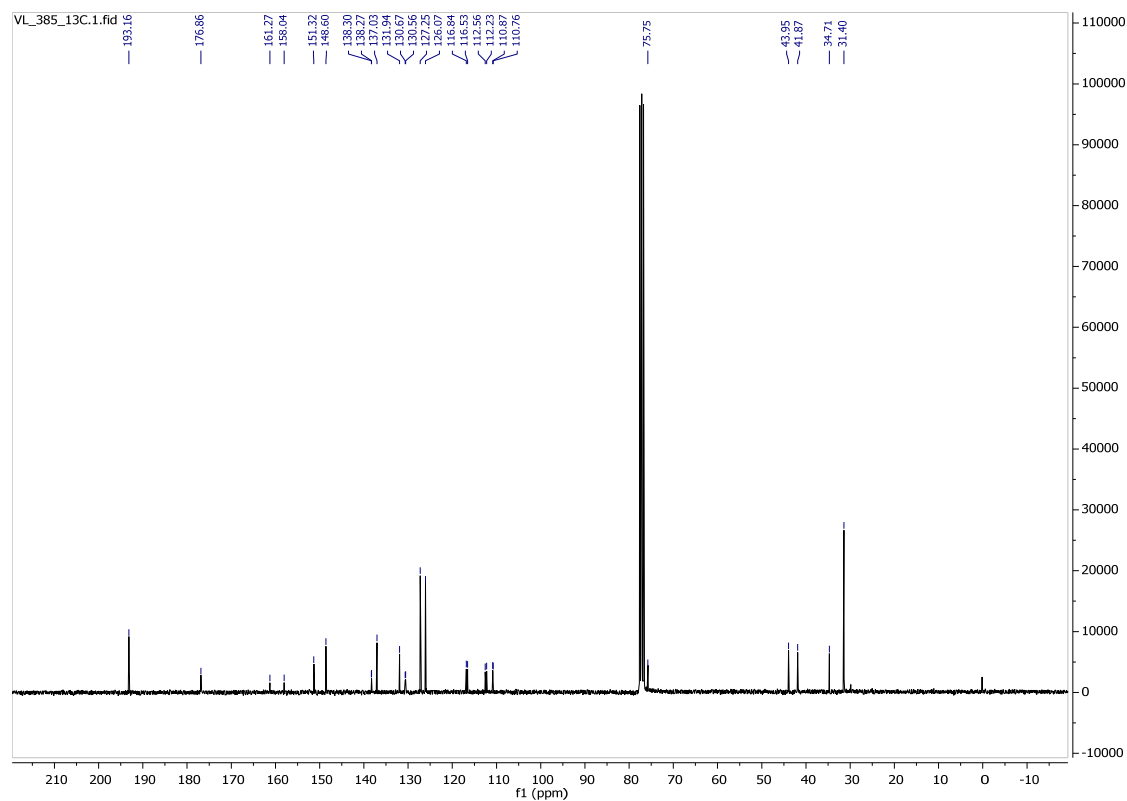
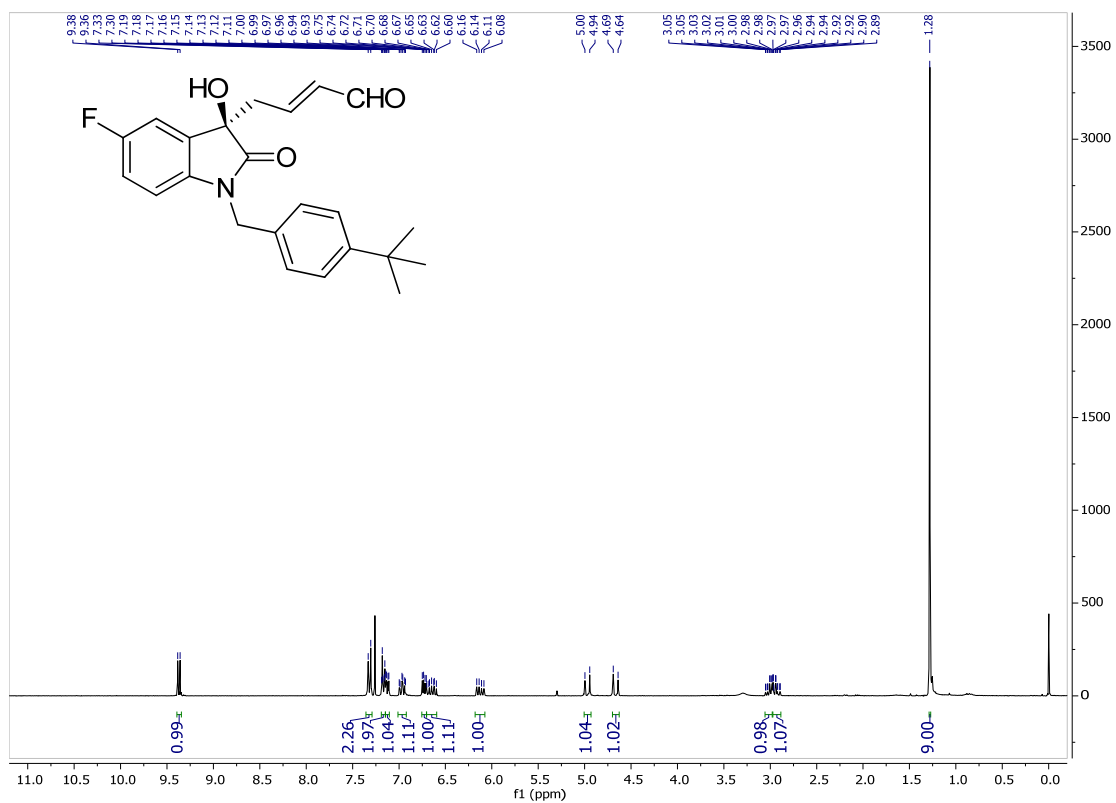


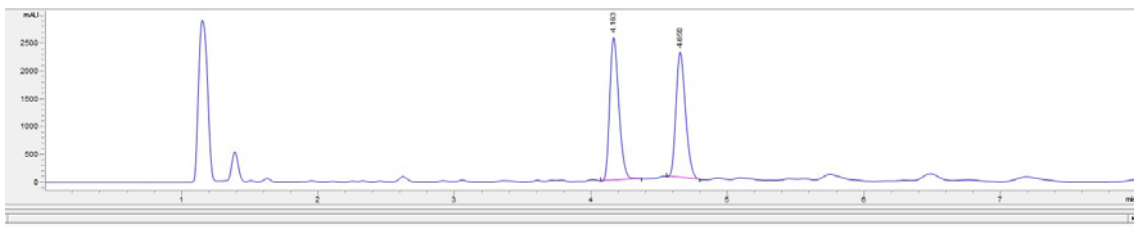
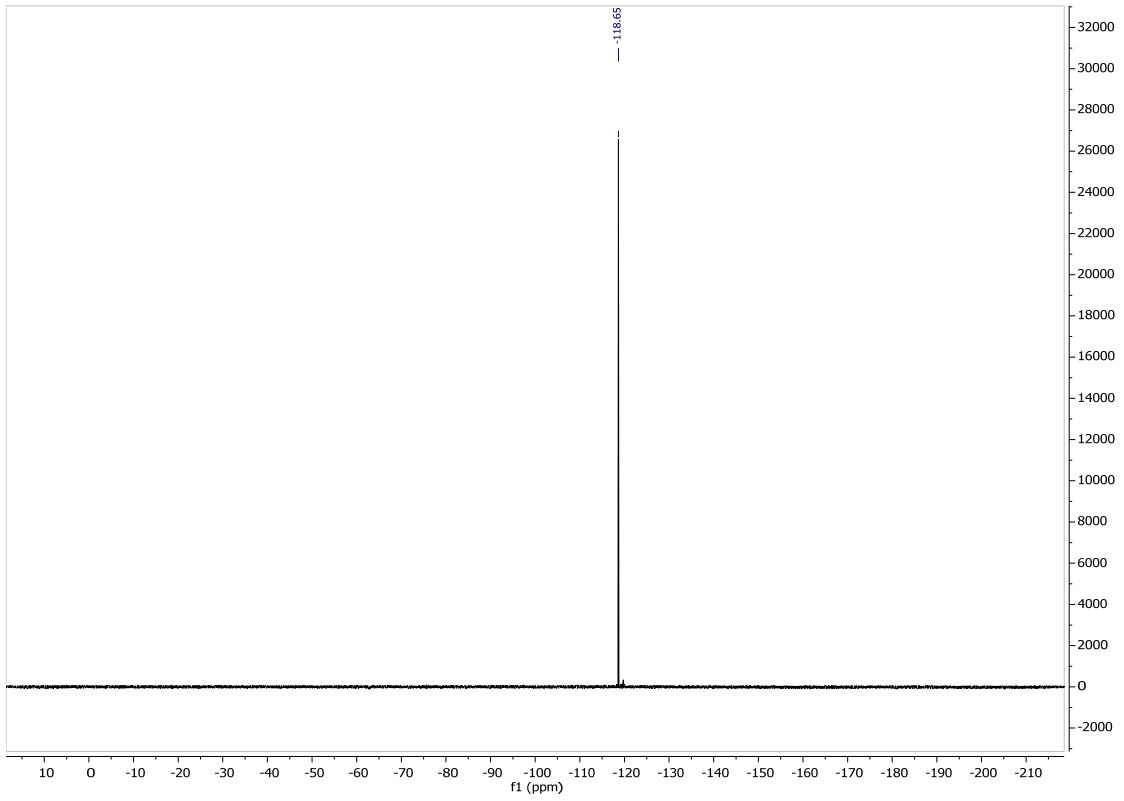
#	Time	Area	Height	Width	Area%	Symmetry
1	4.804	6085.6	1172.8	0.0785	46.095	0.571
2	5.195	7116.7	1039.9	0.0988	53.905	0.52



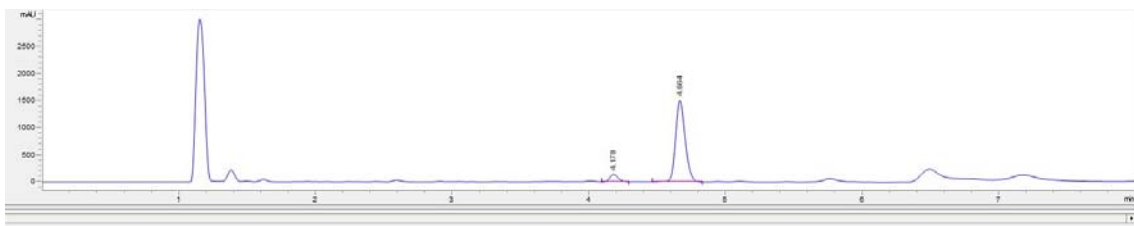
#	Time	Area	Height	Width	Area%	Symmetry
1	4.818	1040.5	209.7	0.0739	5.269	0.587
2	5.095	18707.9	2191.4	0.1326	94.731	0.273

(R,E)-4-{1-[4-(tert-Butyl)benzyl]-5-fluoro-3-hydroxy-2-oxoindolin-3-yl}but-2-enal (4h)



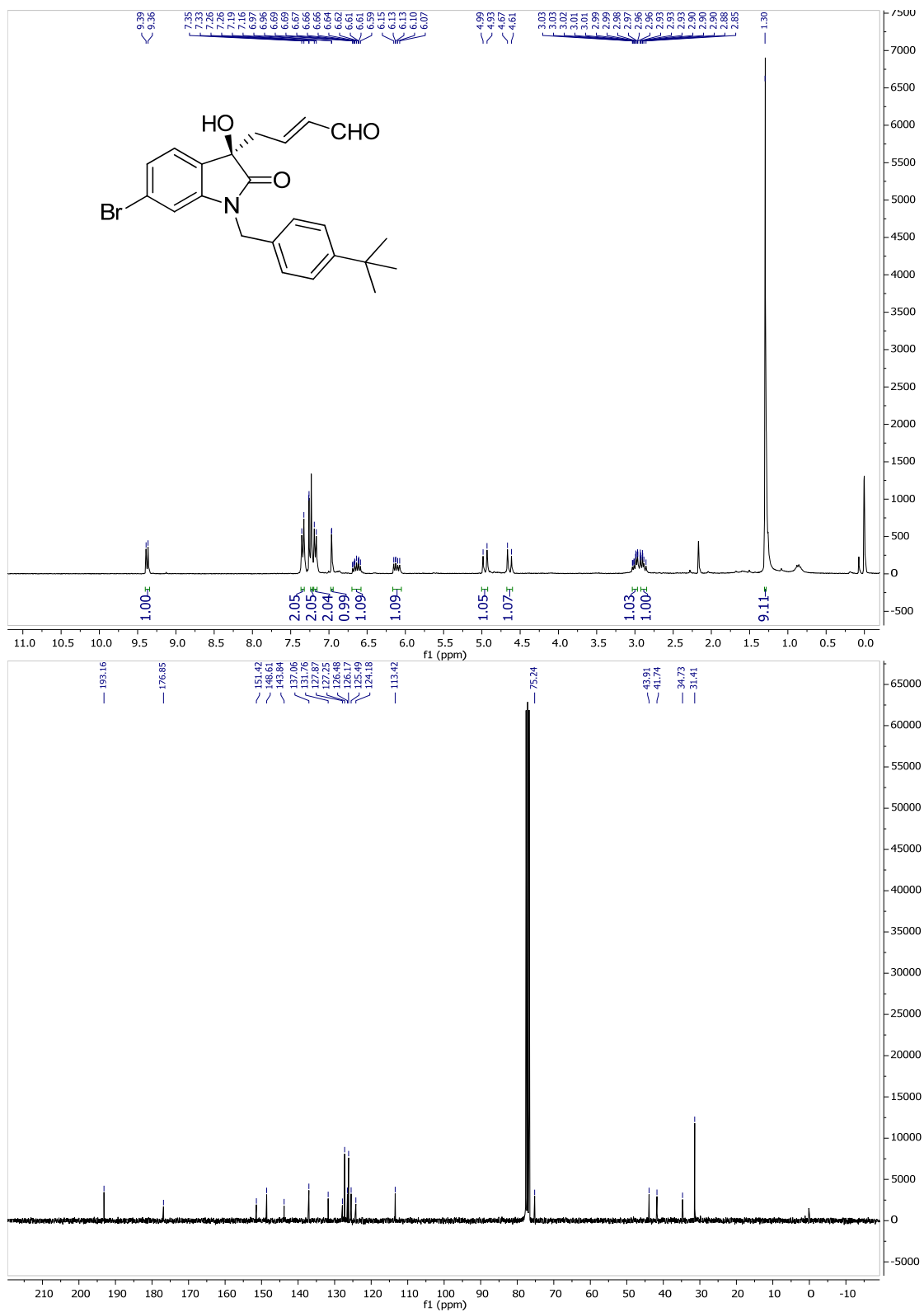


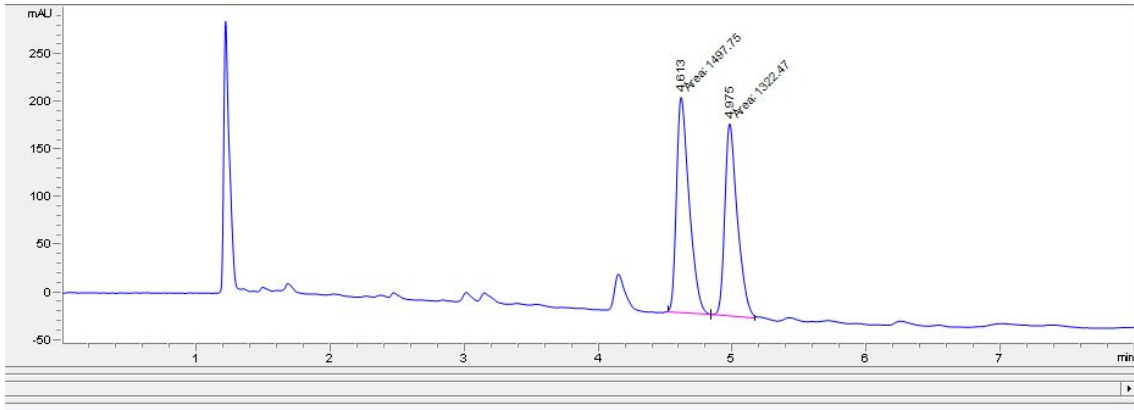
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.183	BB	12045.4	2593.2	0.0722	52.109	0.728
2	4.65	BB	11070.3	2278	0.0747	47.891	0.748



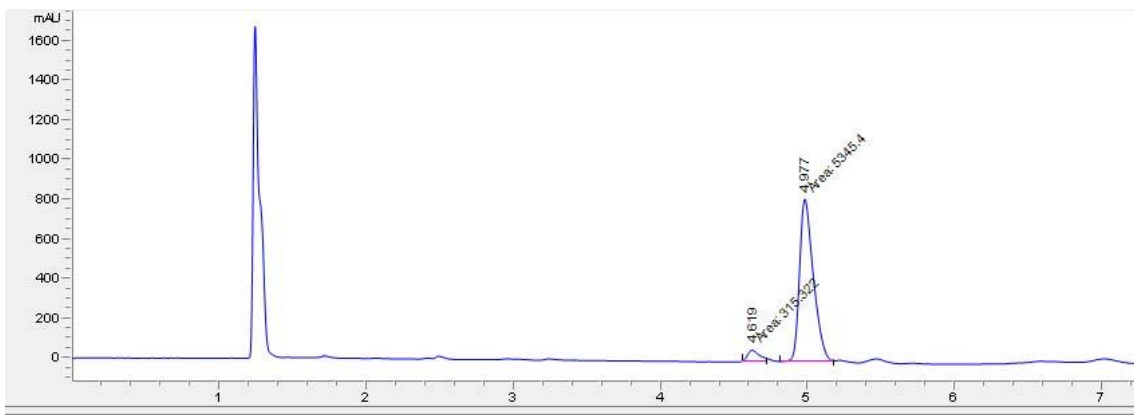
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.178	BB	602.9	138.9	0.0666	7.579	0.781
2	4.664	BB	7551.4	1515.7	0.0746	92.421	0.801

(R,E)-4-{6-Bromo-1-[4-(*tert*-butyl)benzyl]-3-hydroxy-2-oxindolin-3-yl}but-2-enal (4i)



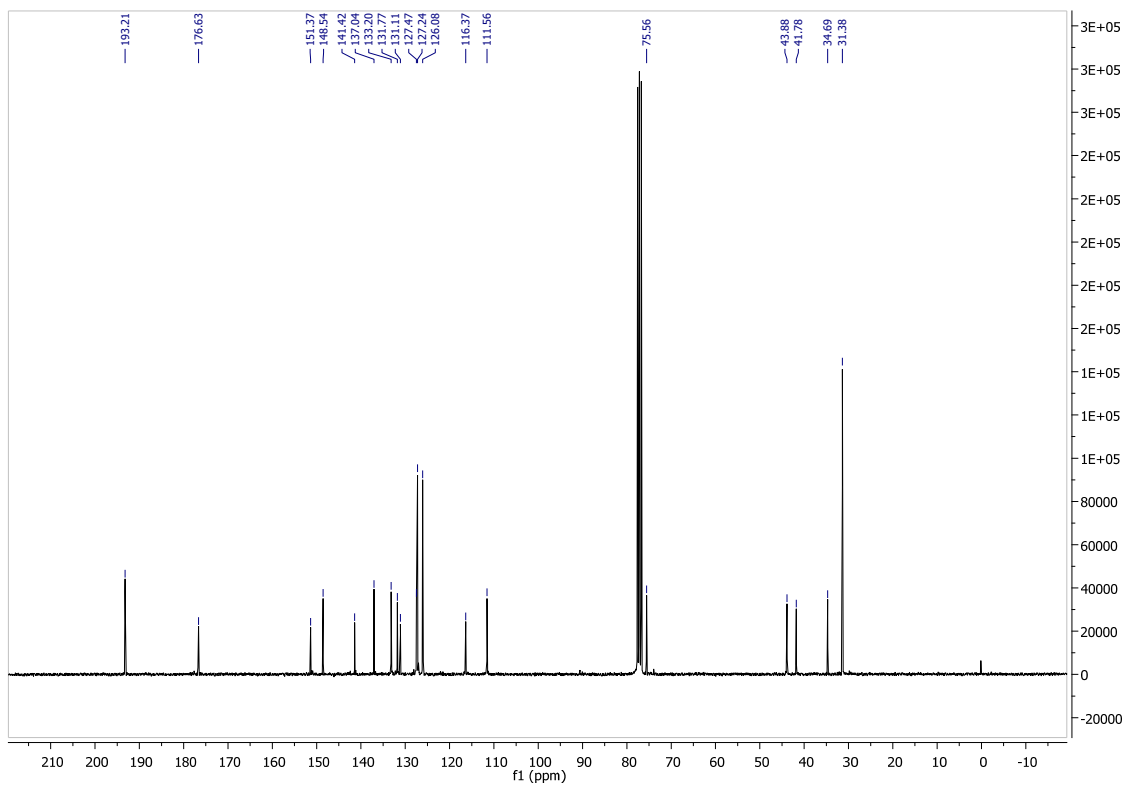
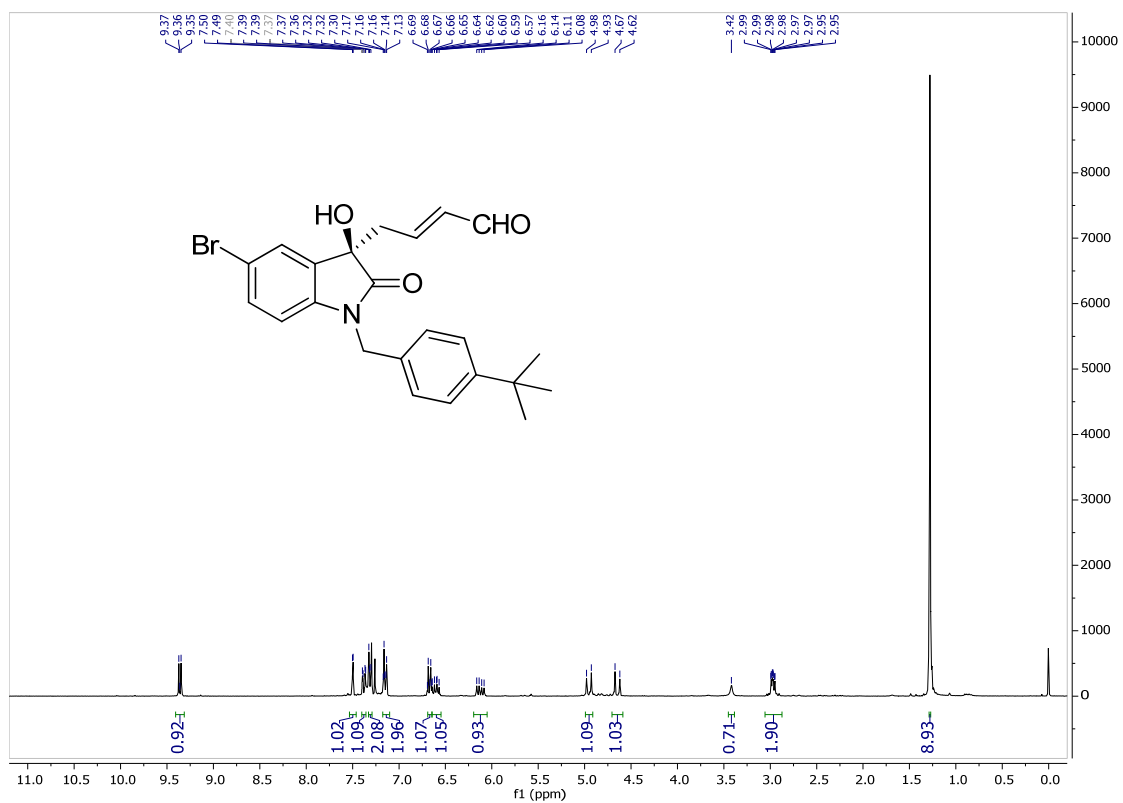


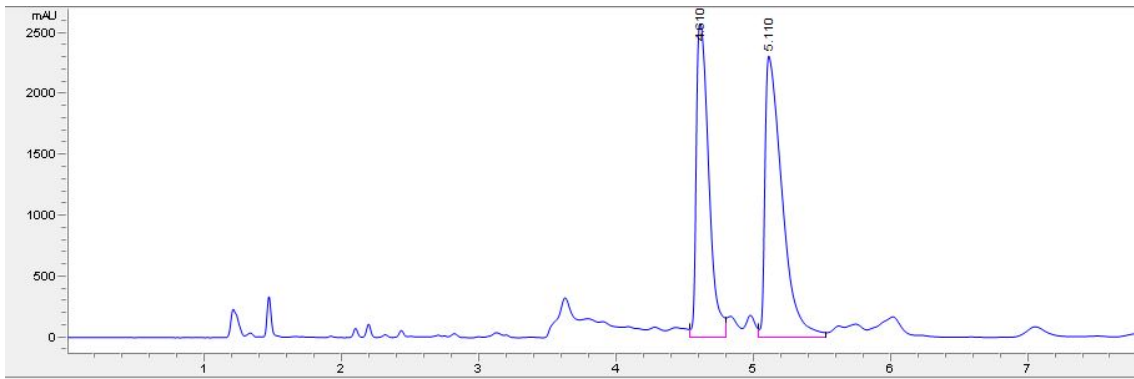
#	Time	Area	Height	Width	Area%	Symmetry
1	4.613	1497.8	226.4	0.1102	53.108	0.566
2	4.975	1322.5	201.7	0.1093	46.892	0.618



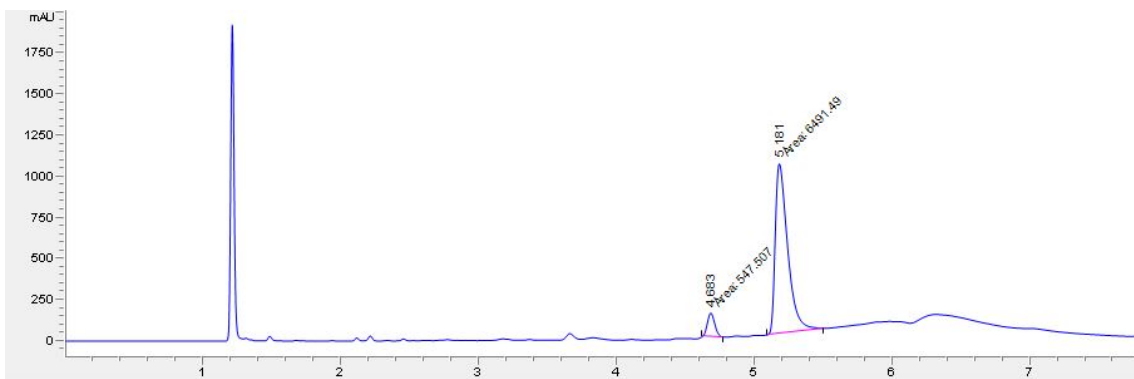
#	Time	Area	Height	Width	Area%	Symmetry
1	4.619	315.3	55	0.0956	5.570	0.561
2	4.977	5345.4	817.8	0.1089	94.430	0.617

(*R,E*)-4-{5-Bromo-1-[4-(*tert*-butyl)benzyl]-3-hydroxy-2-oxindolin-3-yl}but-2-enal (4j)



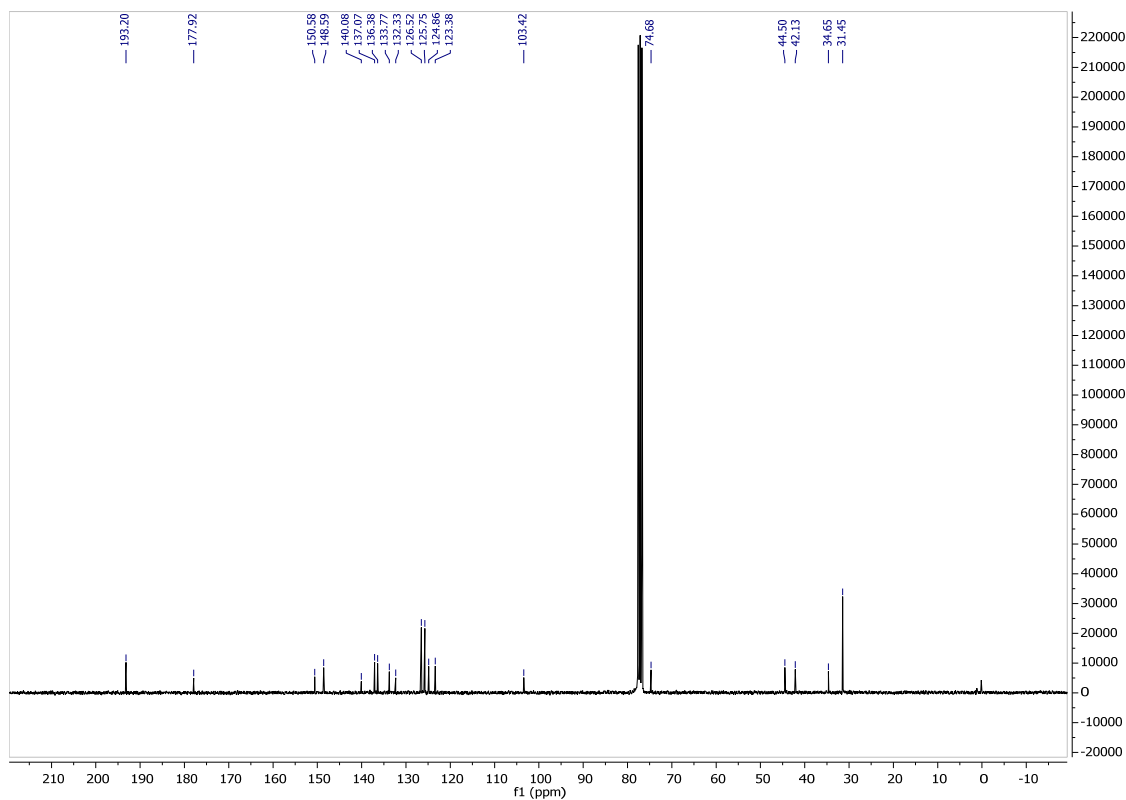
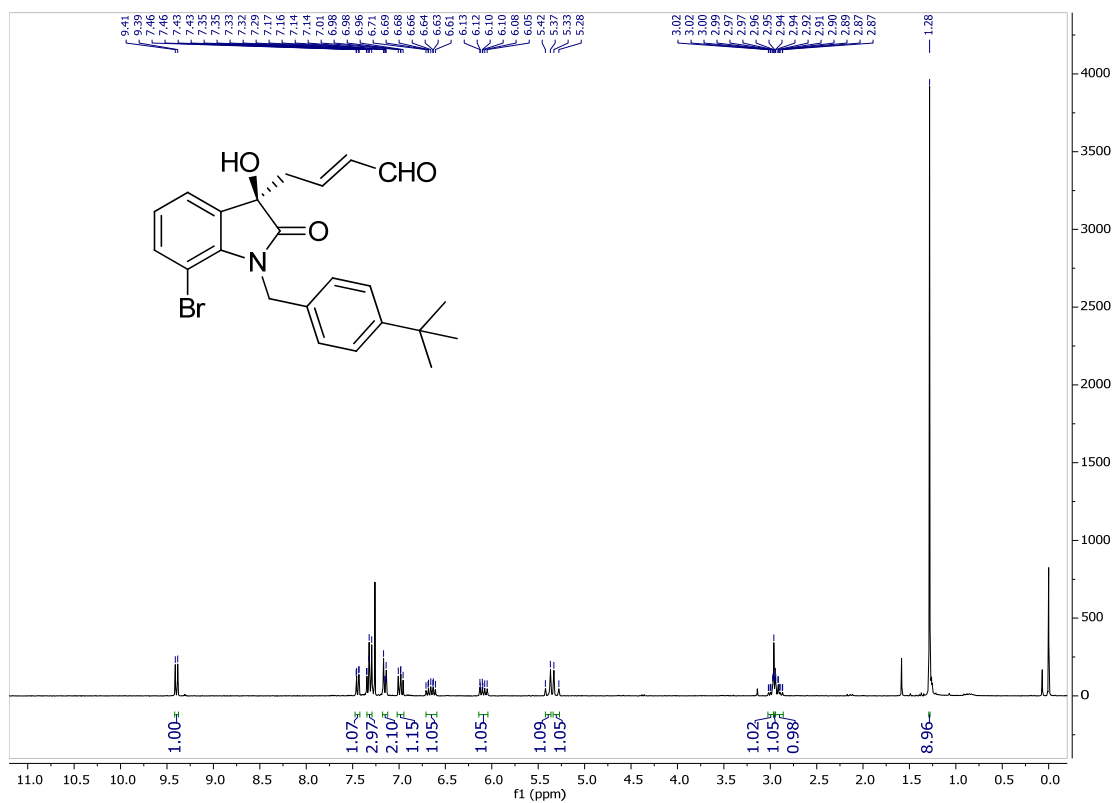


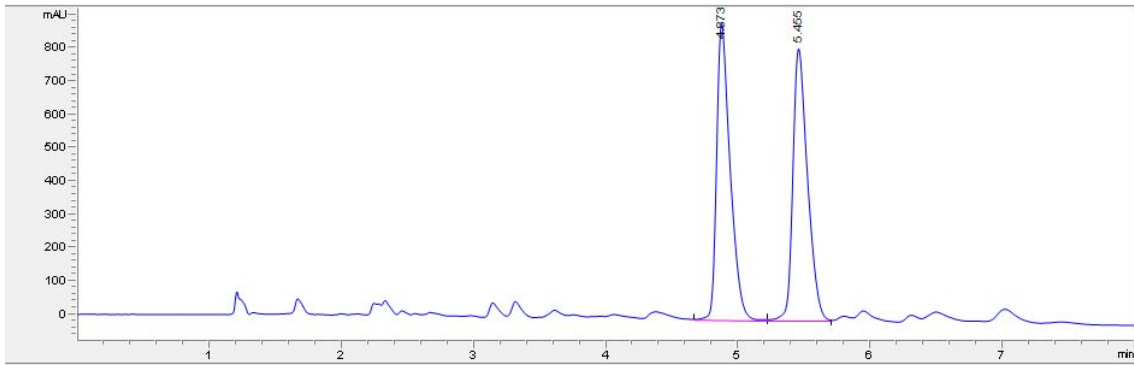
#	Time	Area	Height	Width	Area%	Symmetry
1	4.61	16313	2568.9	0.0991	44.825	0.445
2	5.11	20079.8	2303	0.1317	55.175	0.274



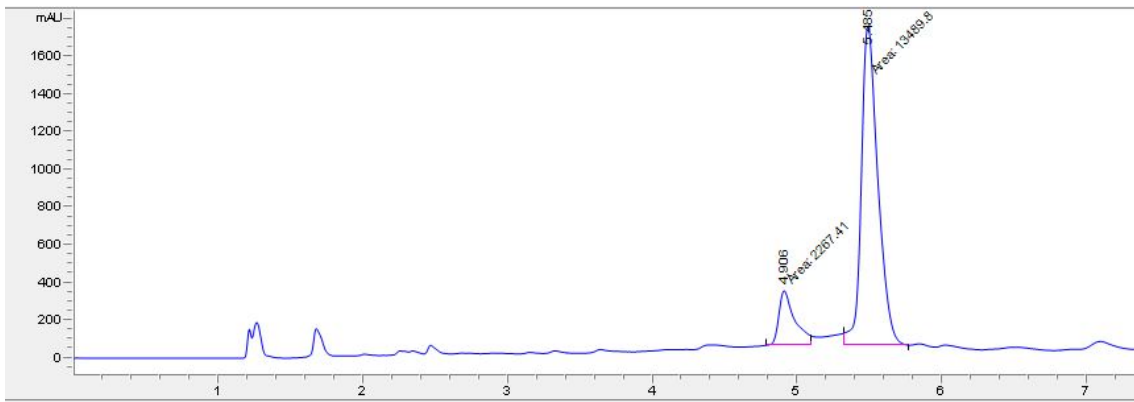
#	Time	Area	Height	Width	Area%	Symmetry
1	4.683	547.5	145.4	0.0628	7.778	0.837
2	5.181	6491.5	1032.6	0.1048	92.222	0.476

(*R,E*)-4-(7-Bromo-1-(4-(*tert*-butyl)benzyl)-3-hydroxy-2-oxindolin-3-yl)but-2-enal (4k)



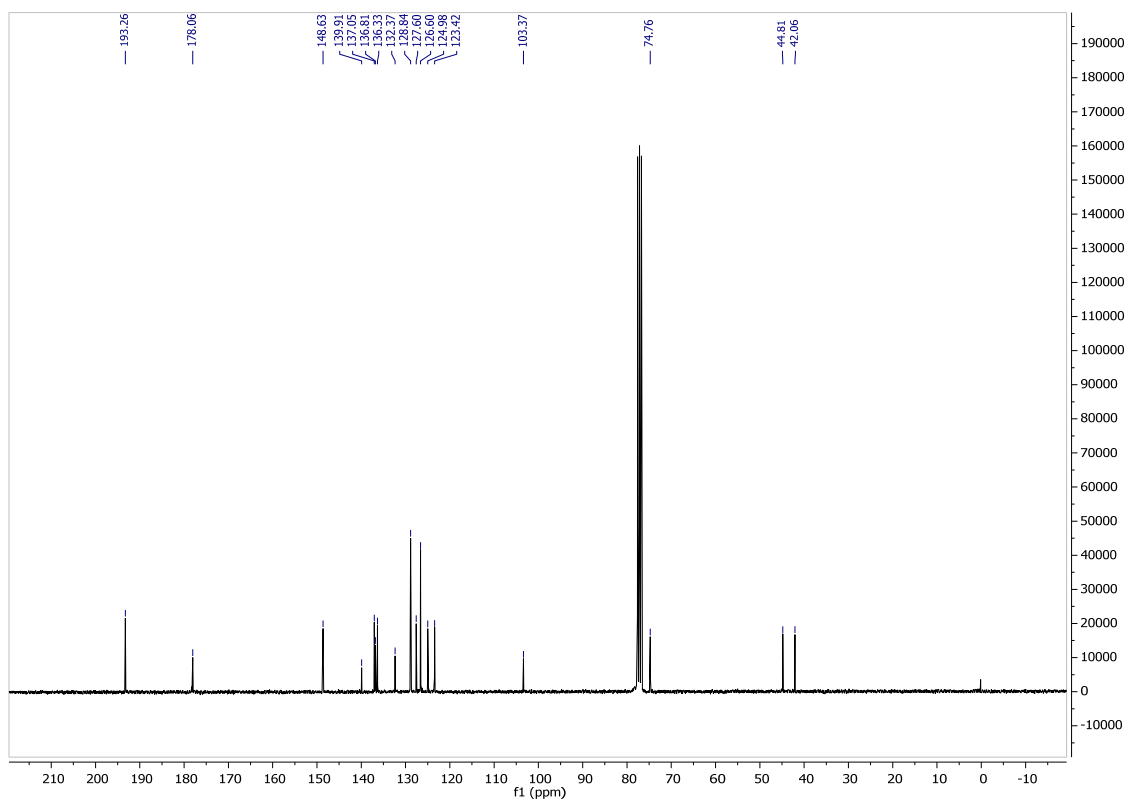
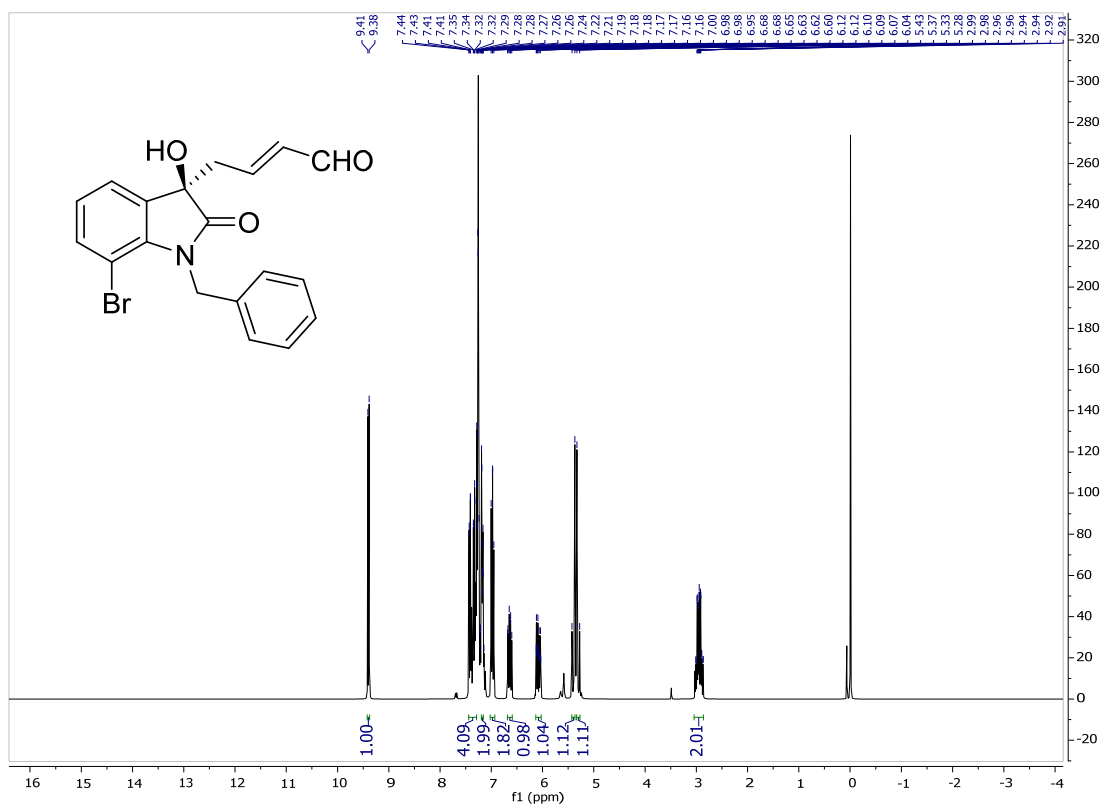


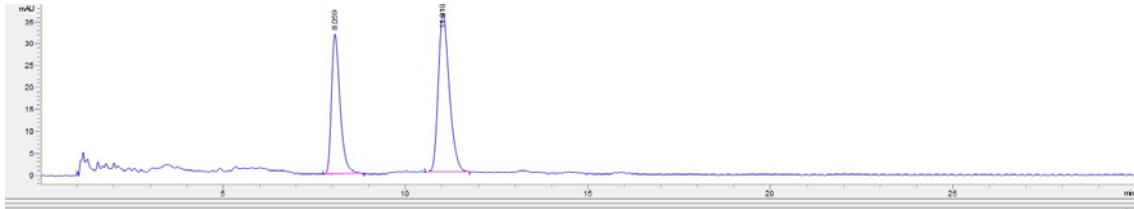
#	Time	Area	Height	Width	Area%	Symmetry
1	4.873	6446.5	894.7	0.1061	50.132	0.563
2	5.455	6412.6	822	0.116	49.868	0.632



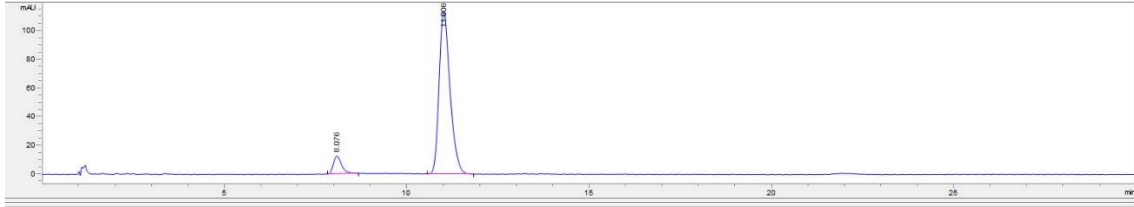
#	Time	Area	Height	Width	Area%	Symmetry
1	4.906	2267.4	289.1	0.1307	14.390	0.475
2	5.485	13489.8	1691.2	0.1329	85.610	0.656

(R,E)-4-(1-Benzyl-7-bromo-3-hydroxy-2-oxindolin-3-yl)but-2-enal (4l)





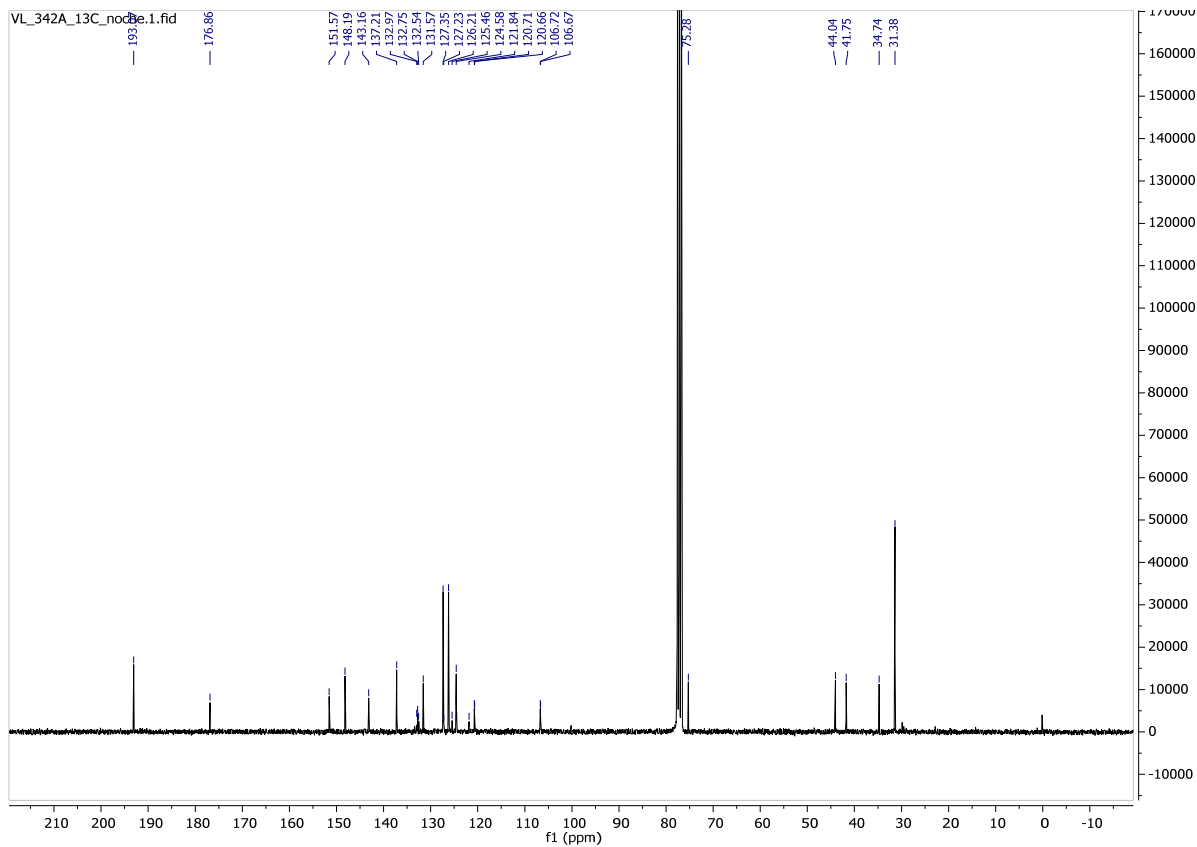
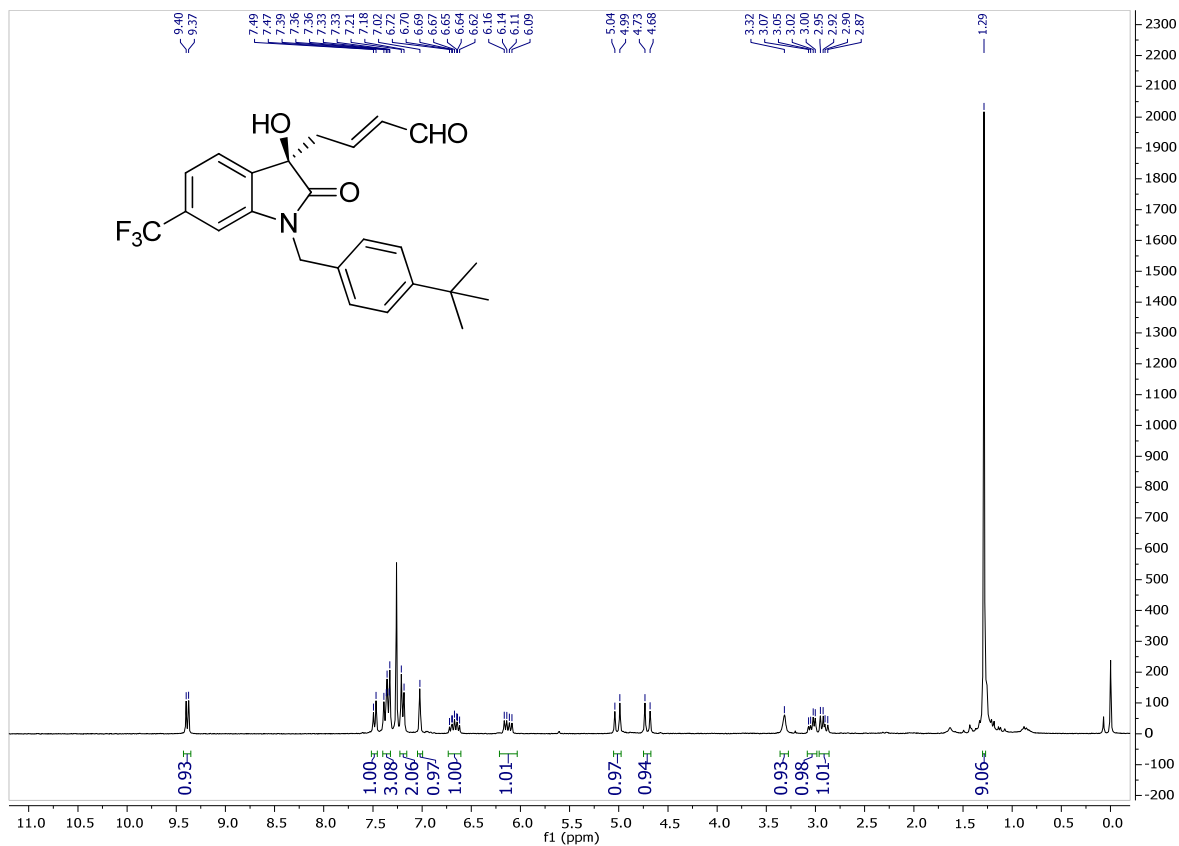
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	8.059	BB	525.3	32	0.2486	40.719	0.634
2	11.016	BB	764.7	36.3	0.3075	59.281	0.698

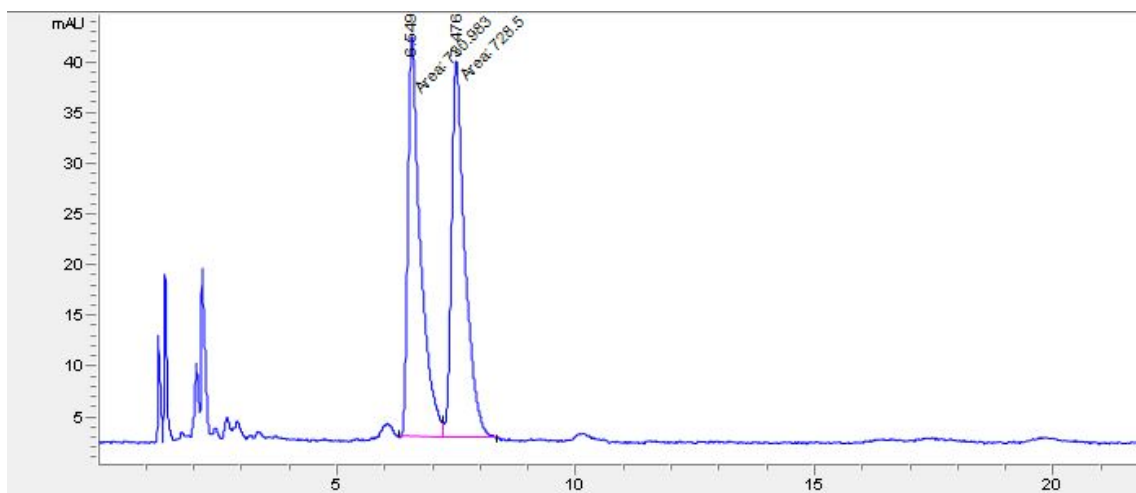
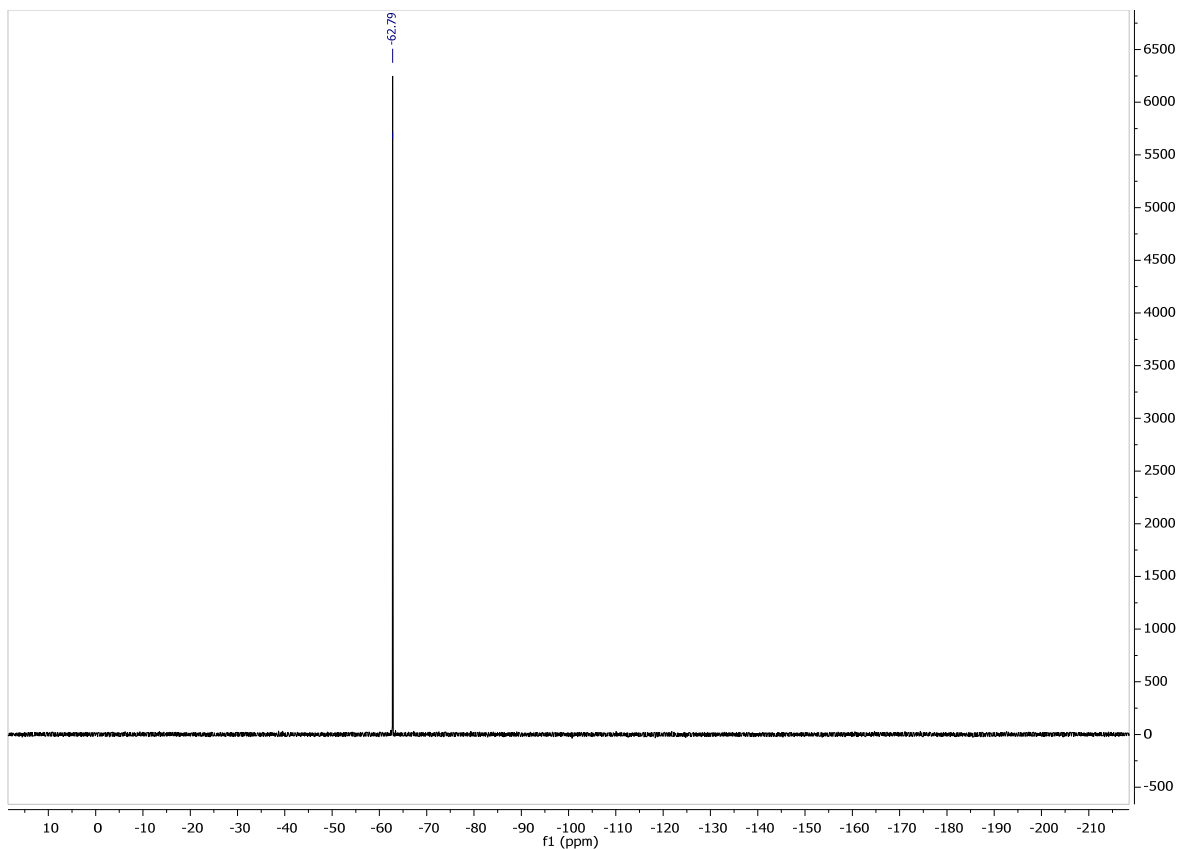


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	8.076	BB	202.3	12.5	0.2408	7.848	0.671
2	11.006	BB	2375.5	113.2	0.3209	92.152	0.702

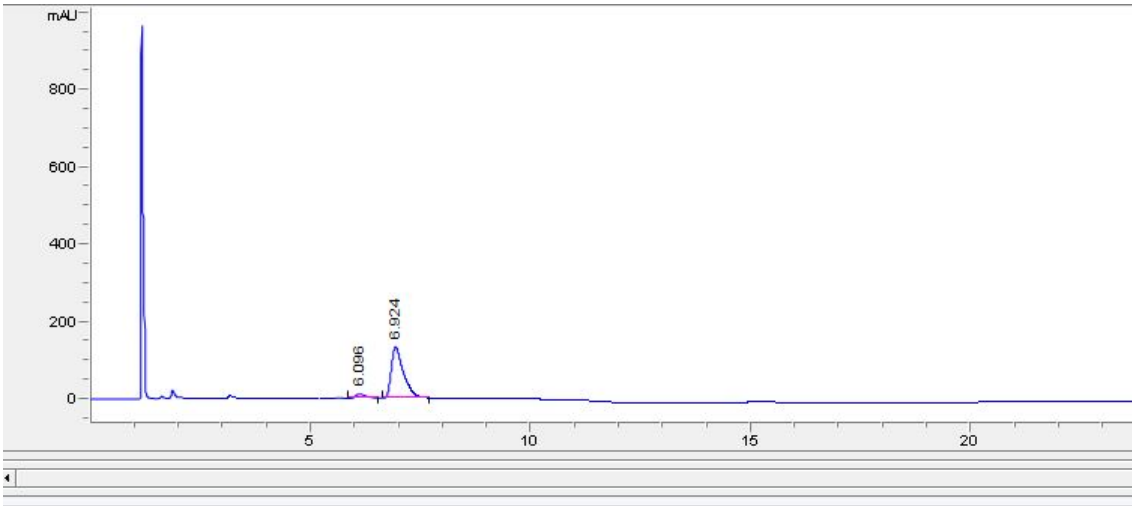
(*R,E*)-4-{1-[4-(*tert*-Butyl)benzyl]-3-hydroxy-2-oxo-6-(trifluoromethyl)indolin-3-yl}but-2-enal

(4m)





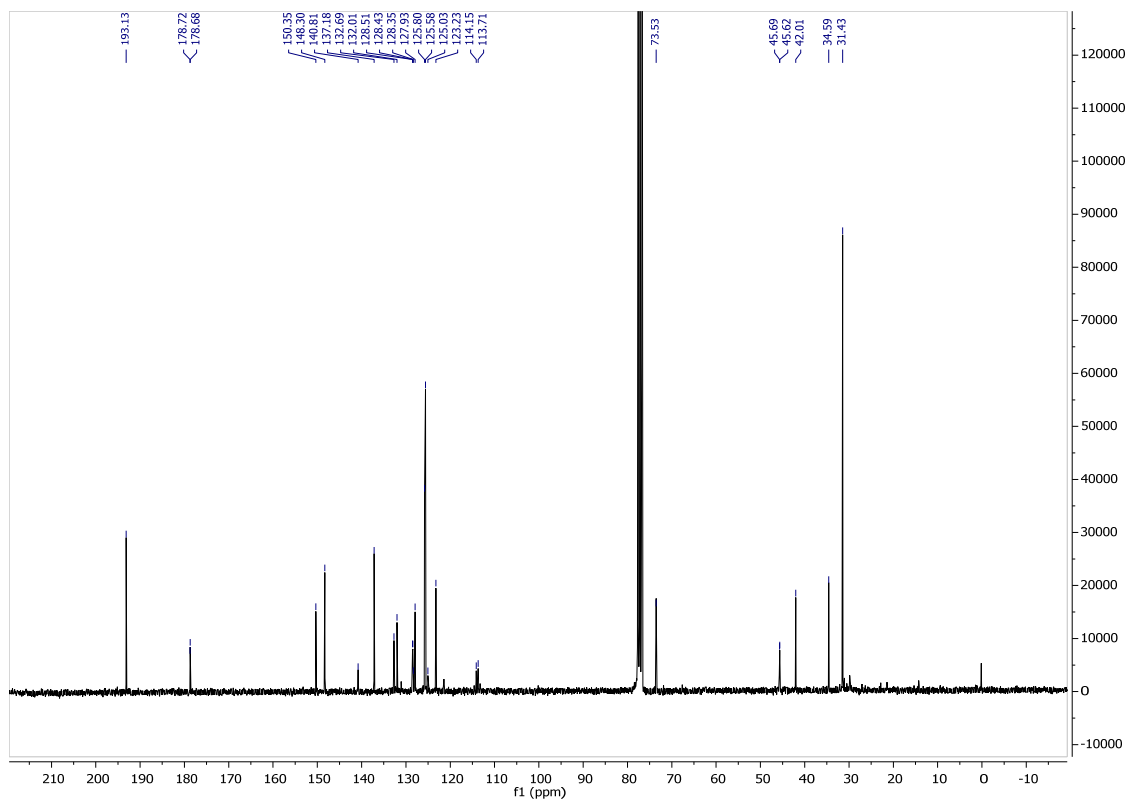
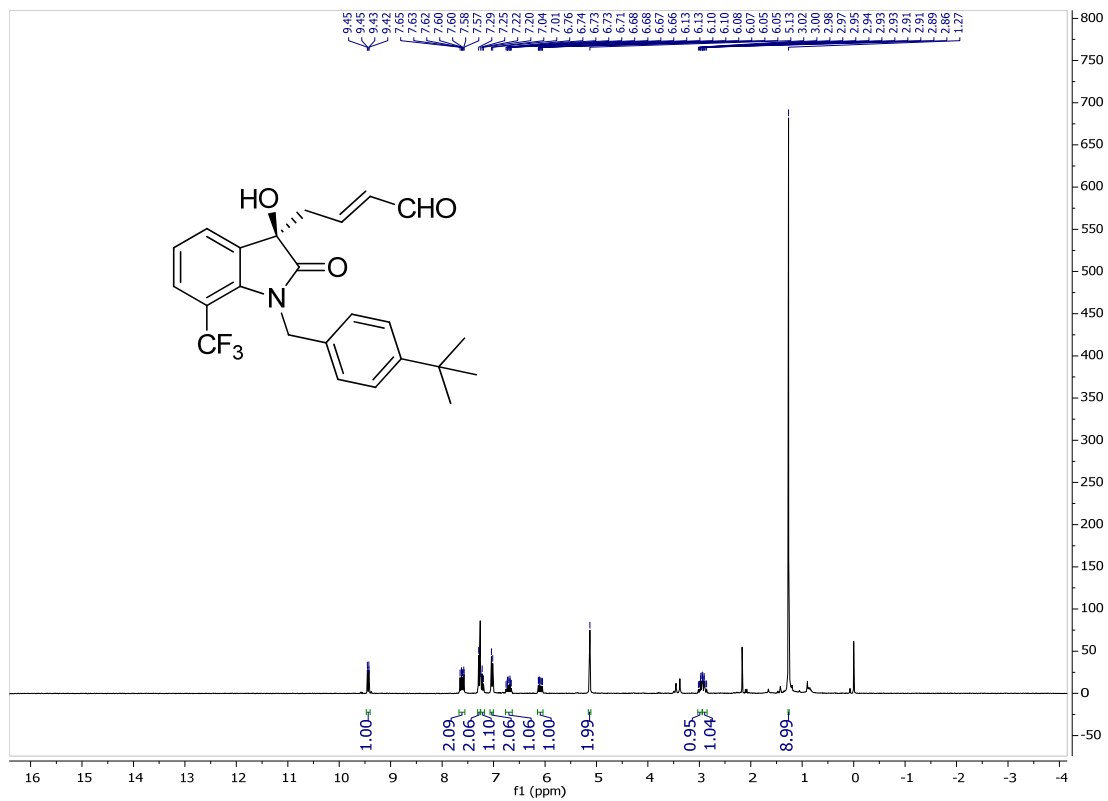
#	Time	Area	Height	Width	Area%	Symmetry
1	6.549	731	39.6	0.3077	50.085	0.439
2	7.476	728.5	37.3	0.3259	49.915	0.513

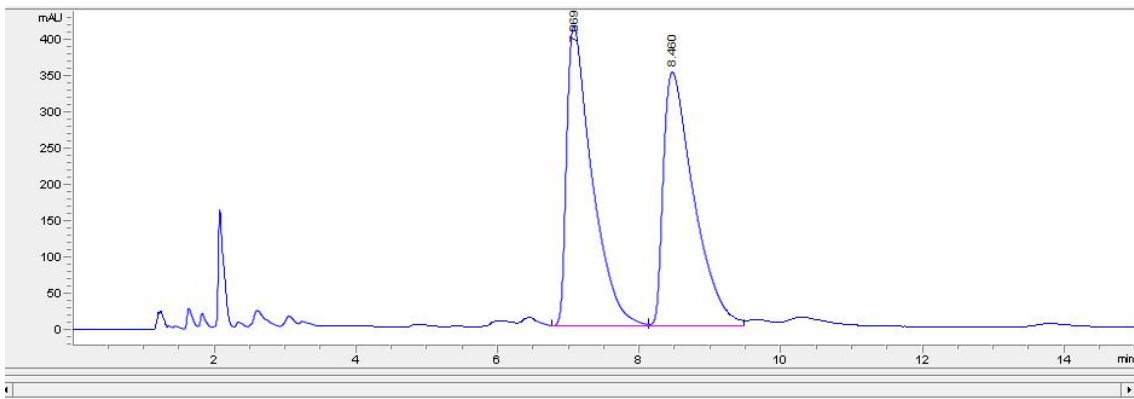
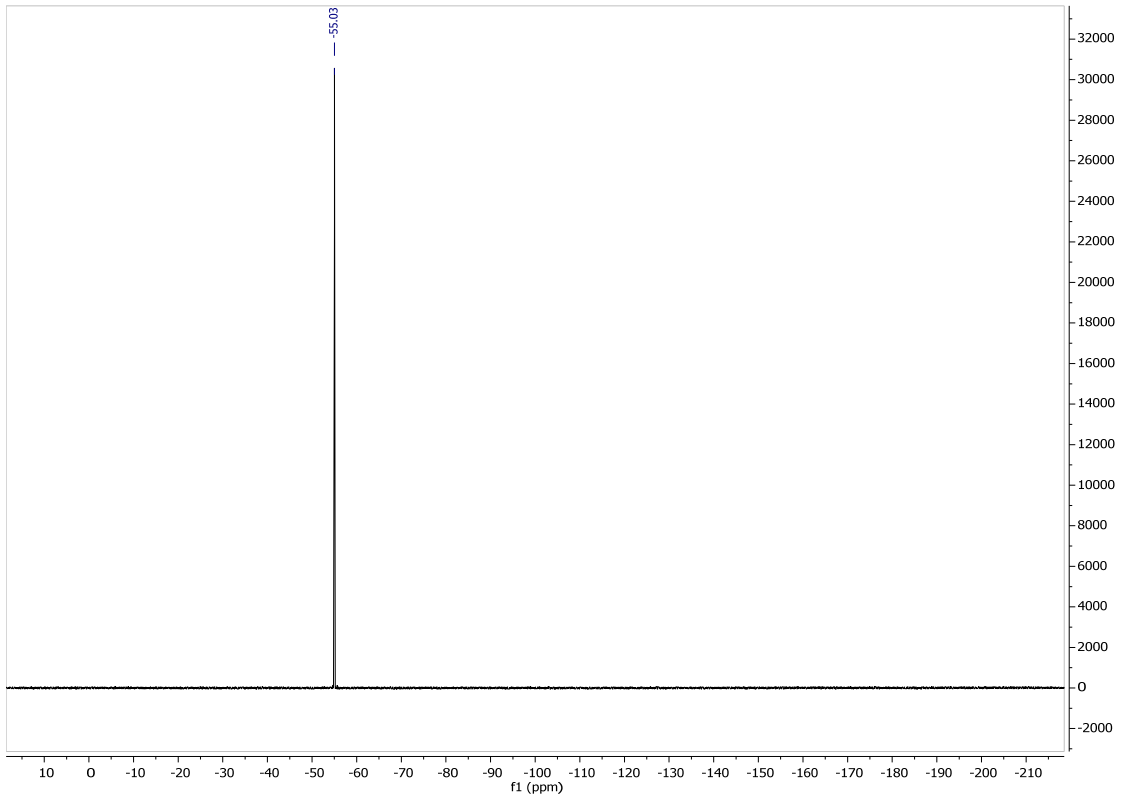


#	Time	Area	Height	Width	Area%	Symmetry
1	6.096	194.6	11.6	0.2134	7.070	0.534
2	6.924	2558.4	133.1	0.2812	92.930	0.52

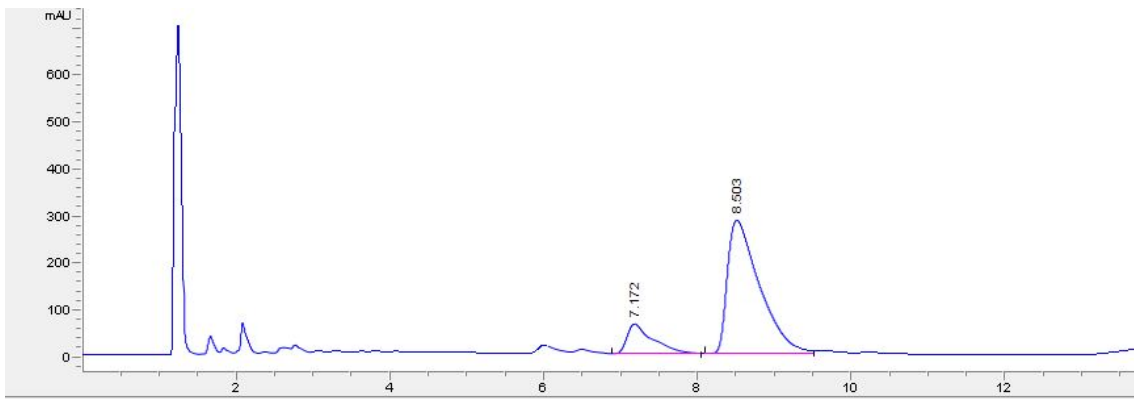
(*R,E*)-4-(1-(4-(*tert*-Butyl)benzyl)-3-hydroxy-2-oxo-7-(trifluoromethyl)indolin-3-yl)but-2-enal

(4n)



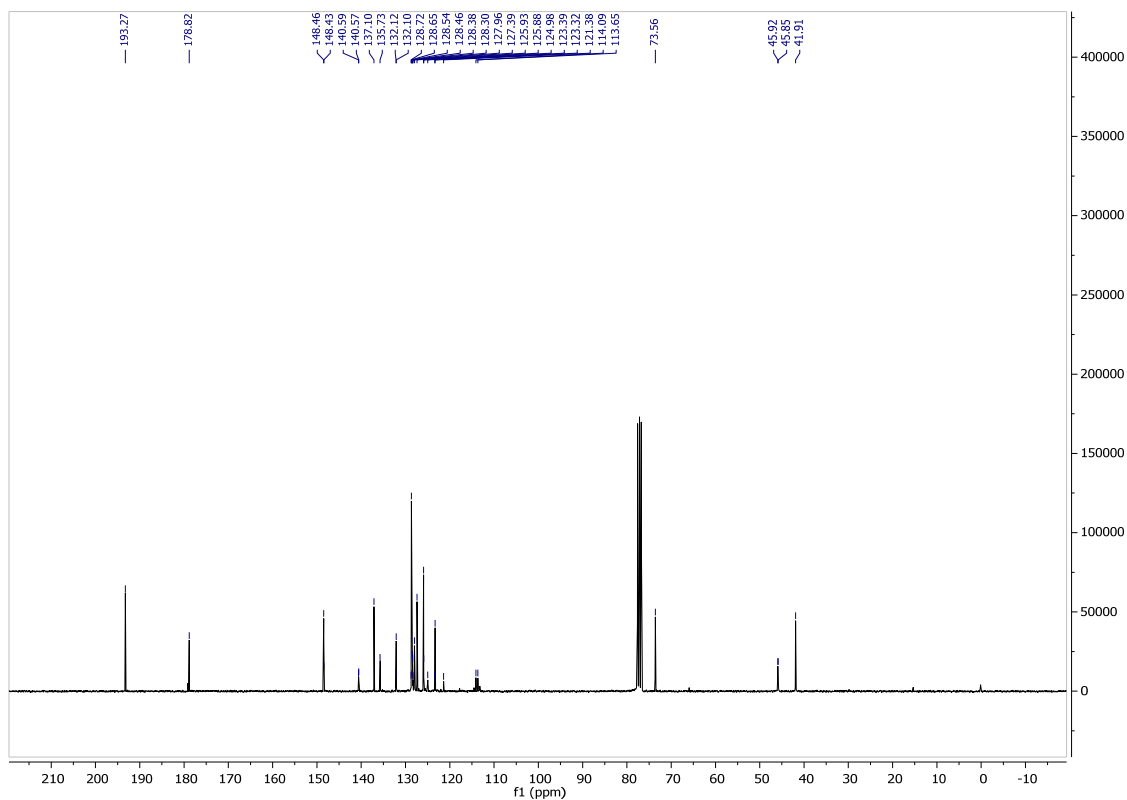
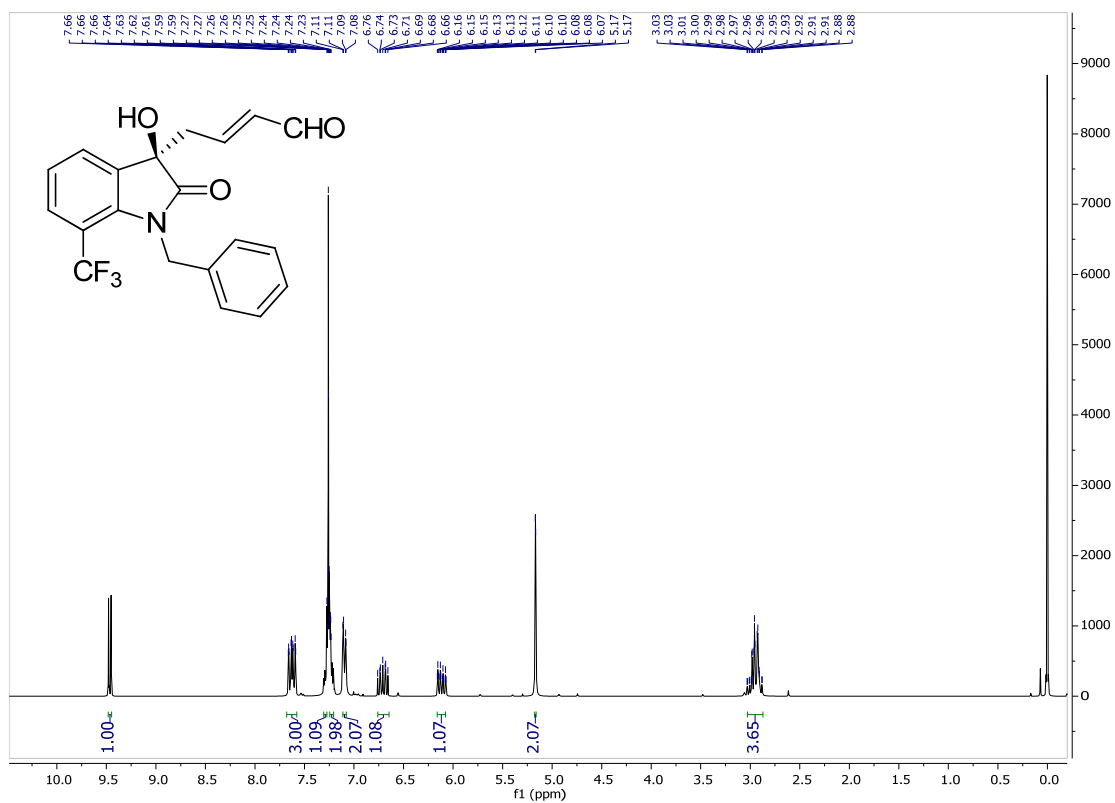


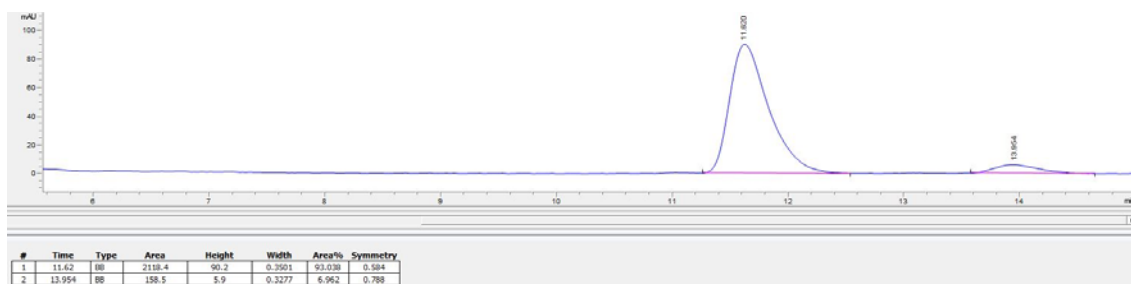
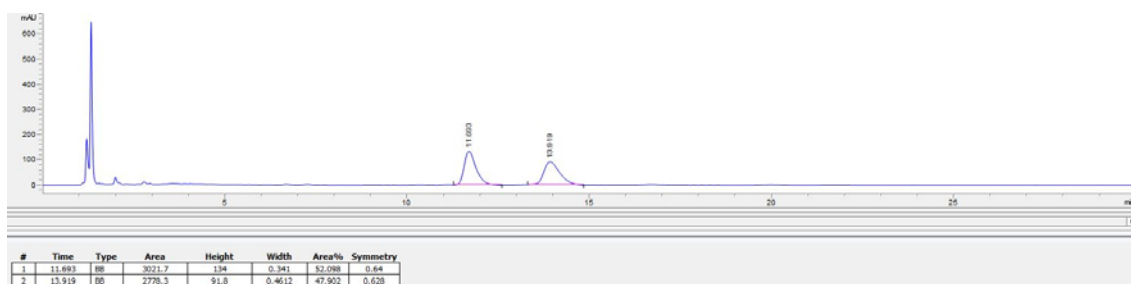
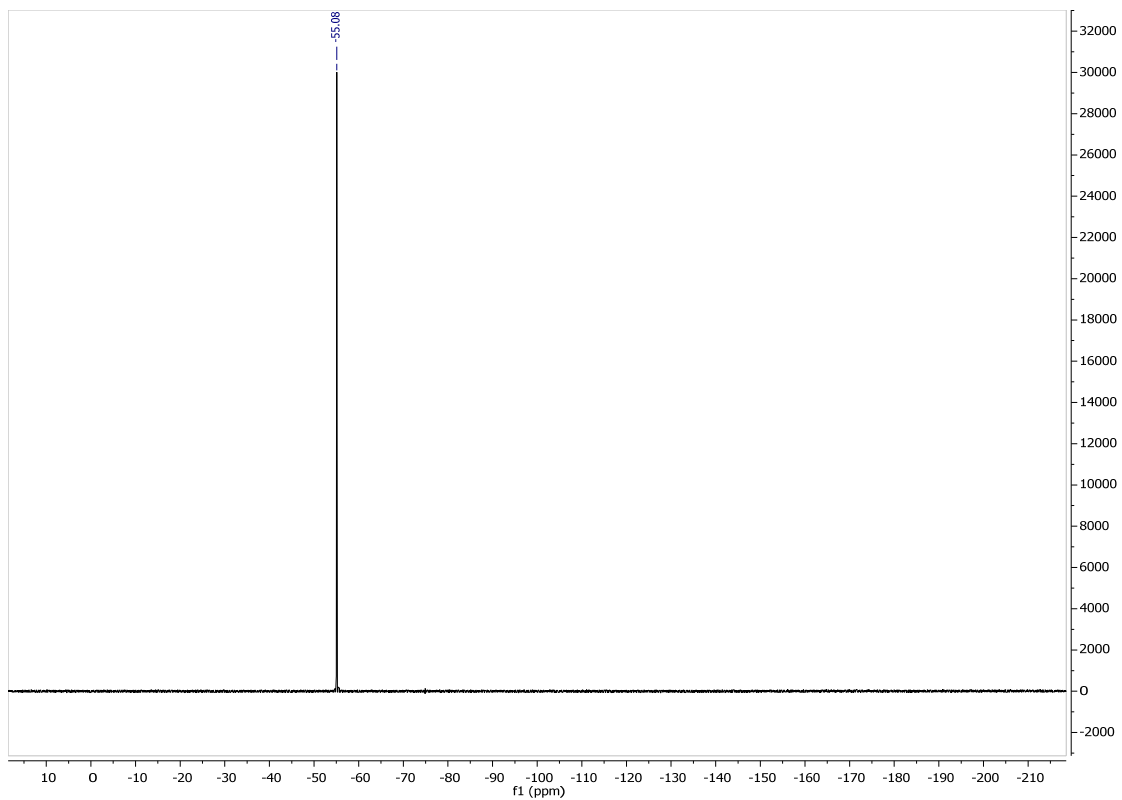
#	Time	Area	Height	Width	Area%	Symmetry
1	7.069	10383.8	414.3	0.3674	49.646	0.361
2	8.46	10531.9	351.4	0.4497	50.354	0.388



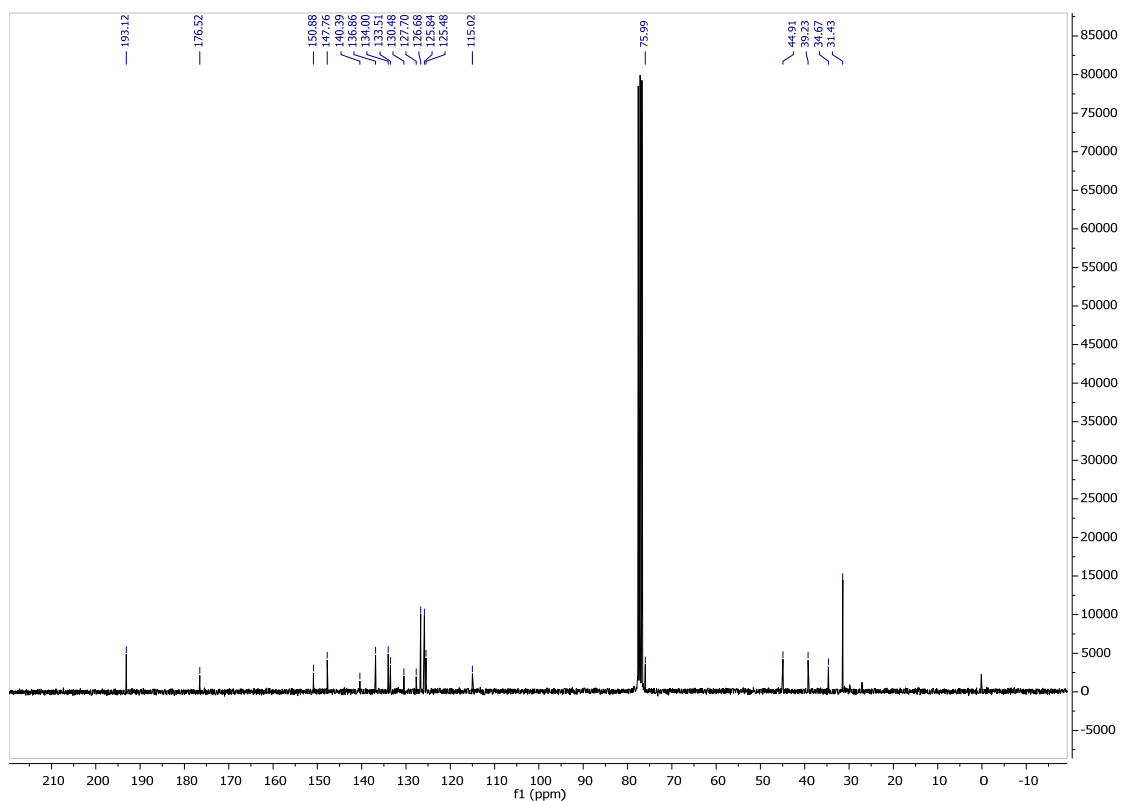
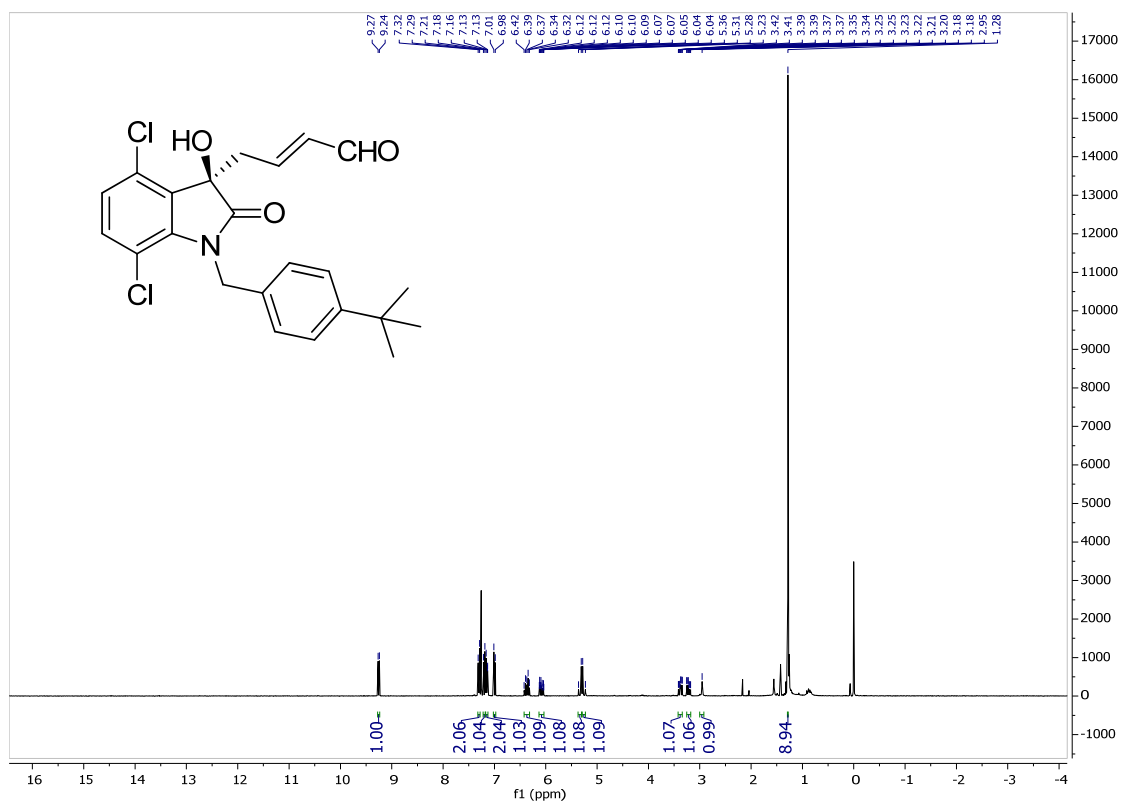
#	Time	Area	Height	Width	Area%	Symmetry
1	7.172	1496.8	63.8	0.3227	15.185	0.382
2	8.503	8360.5	285.8	0.4103	84.815	0.392

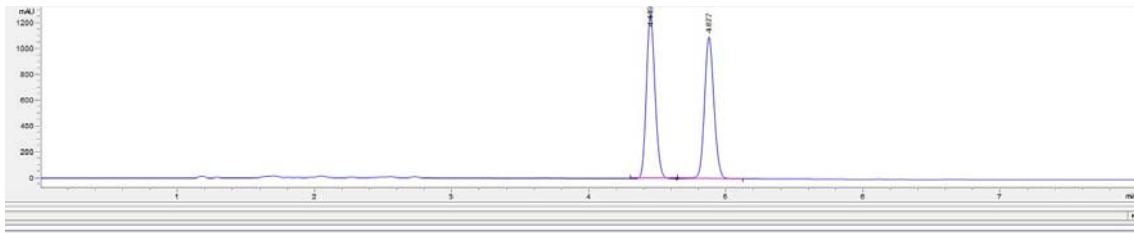
(*R,E*)-4-(1-Benzyl-3-hydroxy-2-oxo-7-(trifluoromethyl)indolin-3-yl)but-2-enal (4o)



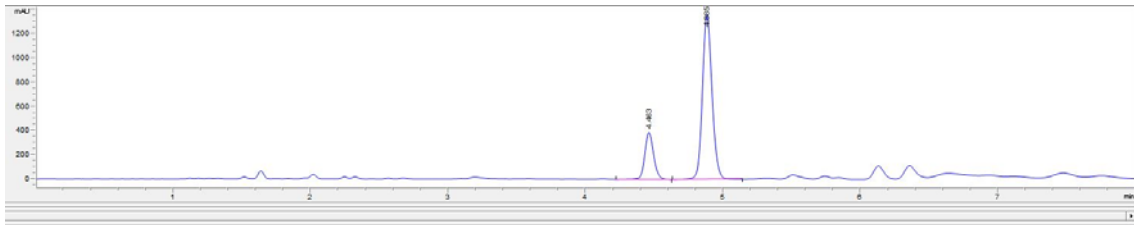


(R,E)-4-{1-[4-(tert-Butyl)benzyl]-4,7-dichloro-3-hydroxy-2-oxindolin-3-yl}but-2-enal (4p)



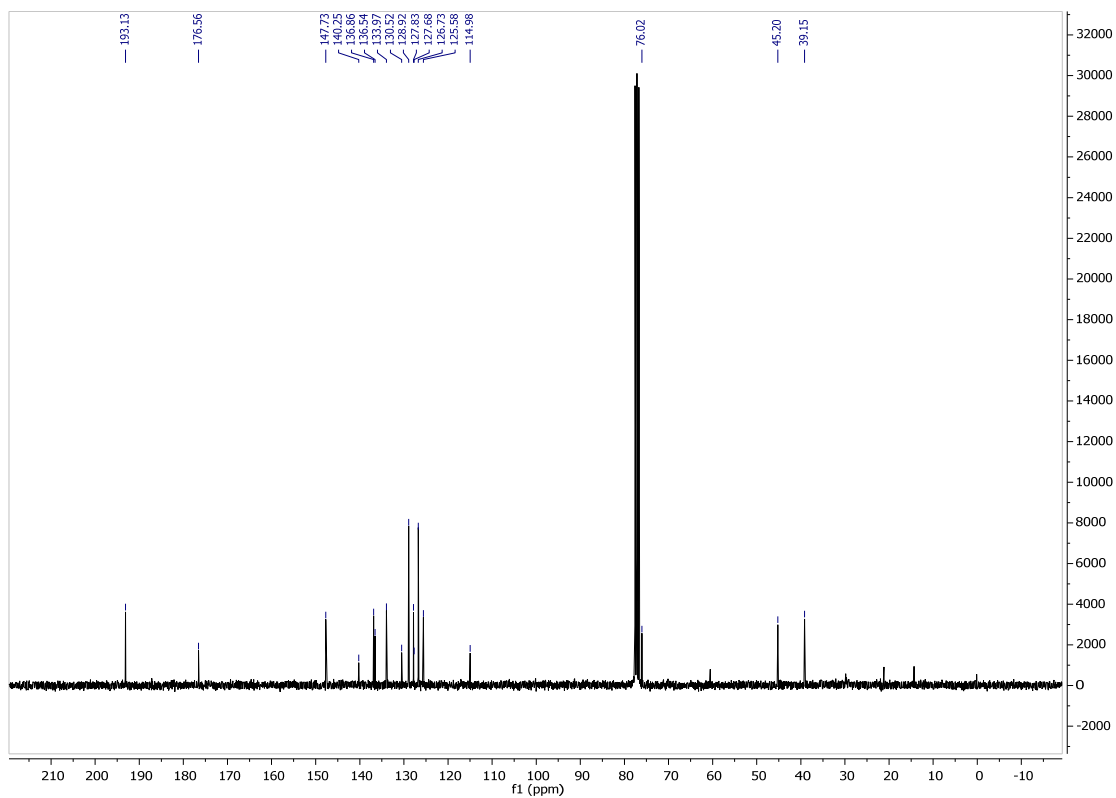
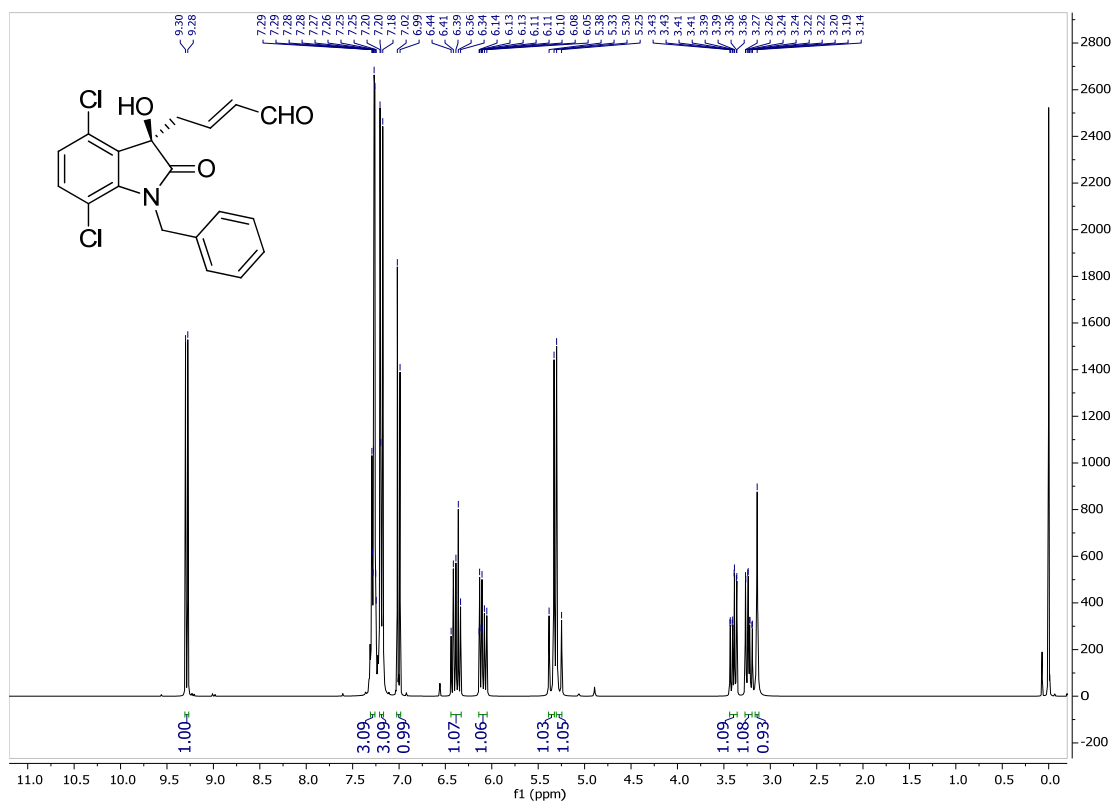


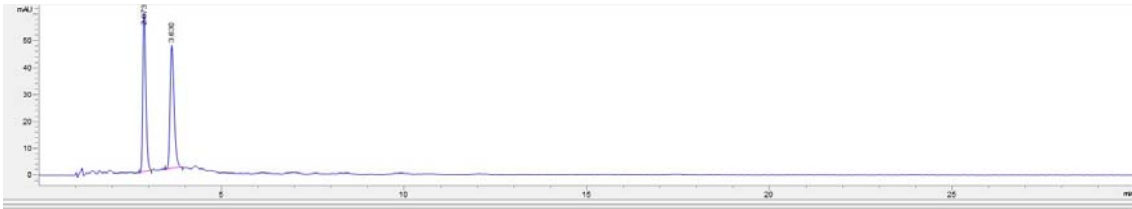
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.449	BB	5530.7	1264.9	0.0671	51.377	0.841
2	4.877	BB	5234.3	1097.8	0.0736	48.623	0.872



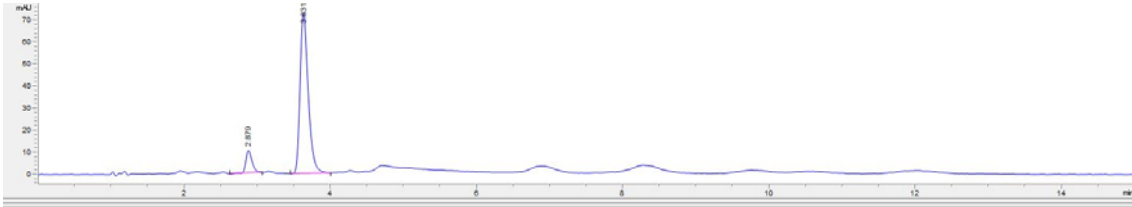
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.463	BB	1728.8	387.4	0.0581	20.838	0.862
2	4.855	BB	6567.6	1354.6	0.0746	79.162	0.84

(R,E)-4-(1-Benzyl-4,7-dichloro-3-hydroxy-2-oxindolin-3-yl)but-2-enal (4q)



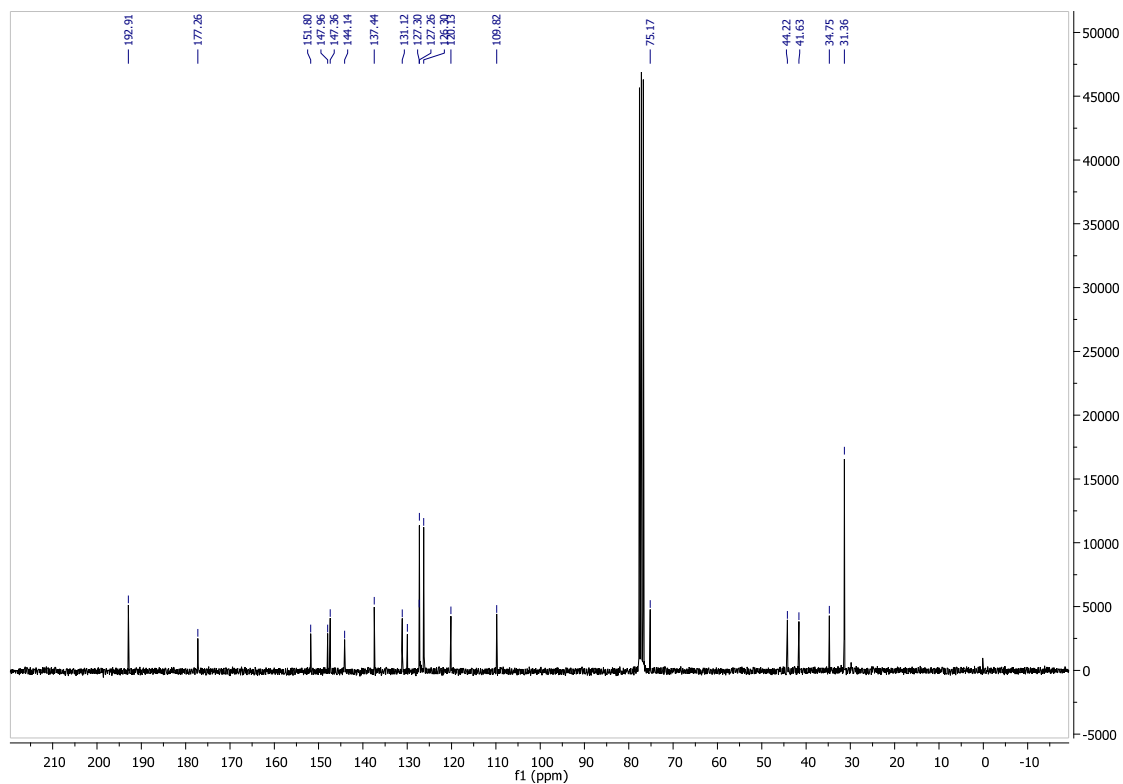
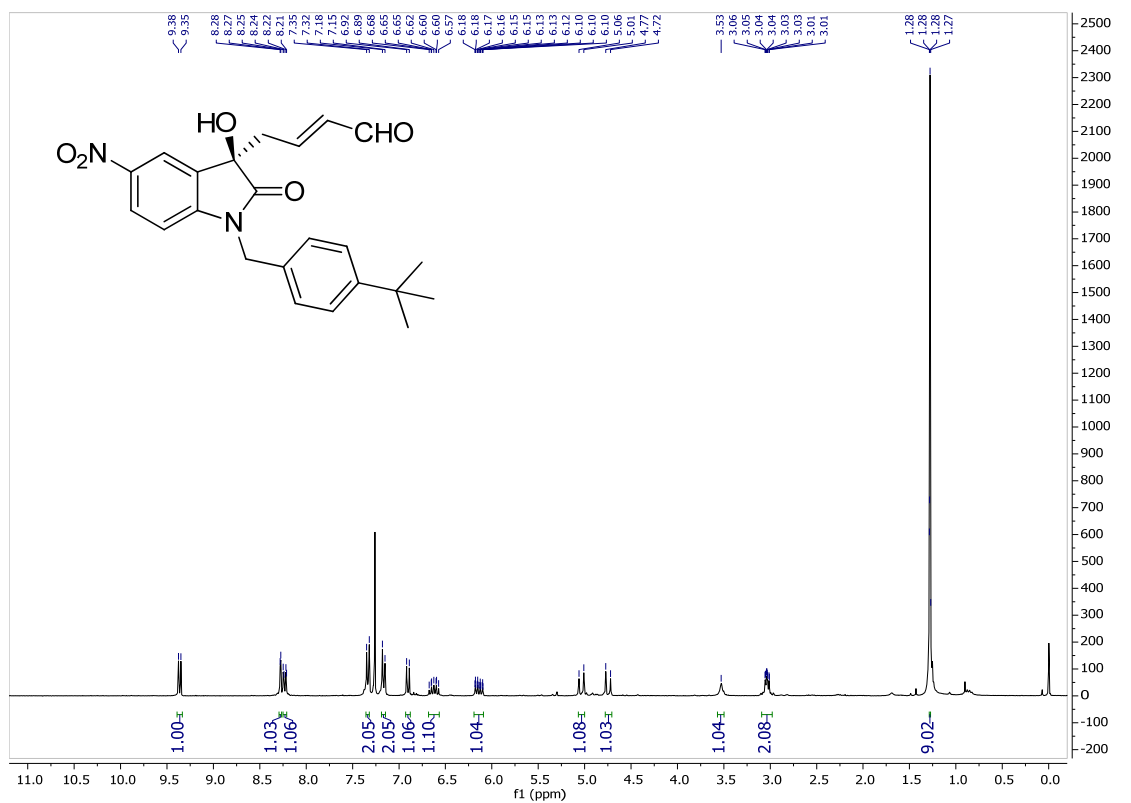


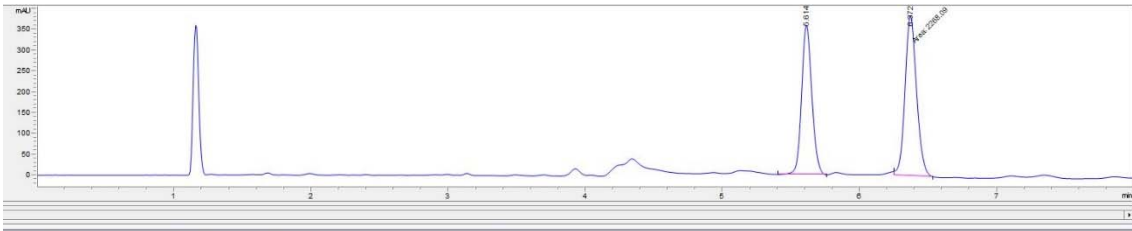
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	2.872	BD	241.1	58.8	0.0096	49.321	0.7
2	3.63	BD	350.4	45.7	0.1174	50.679	0.686



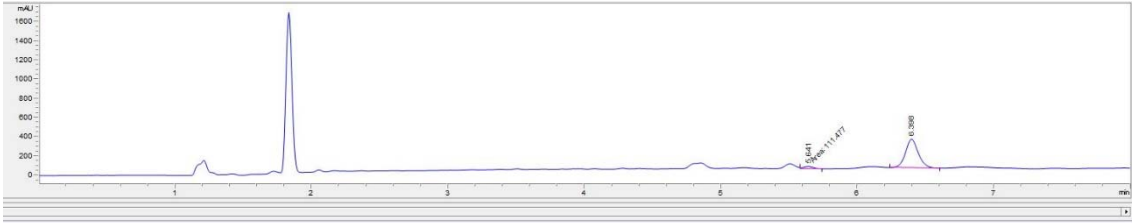
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	2.879	BD	62	20.3	0.092	9.862	0.737
2	3.631	BD	566.4	73.3	0.1162	90.138	0.667

(R,E)-4-{1-[4-(tert-Butyl)benzyl]-3-hydroxy-5-nitro-2-oxindolin-3-yl}but-2-enal (4r)



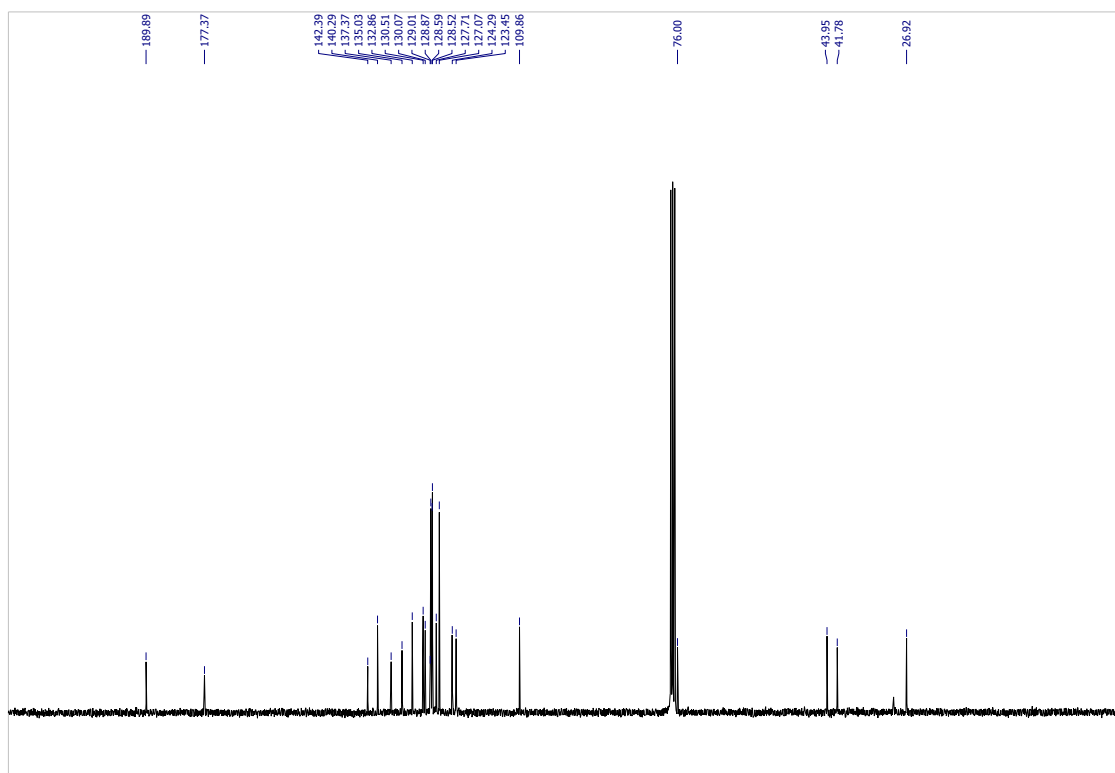
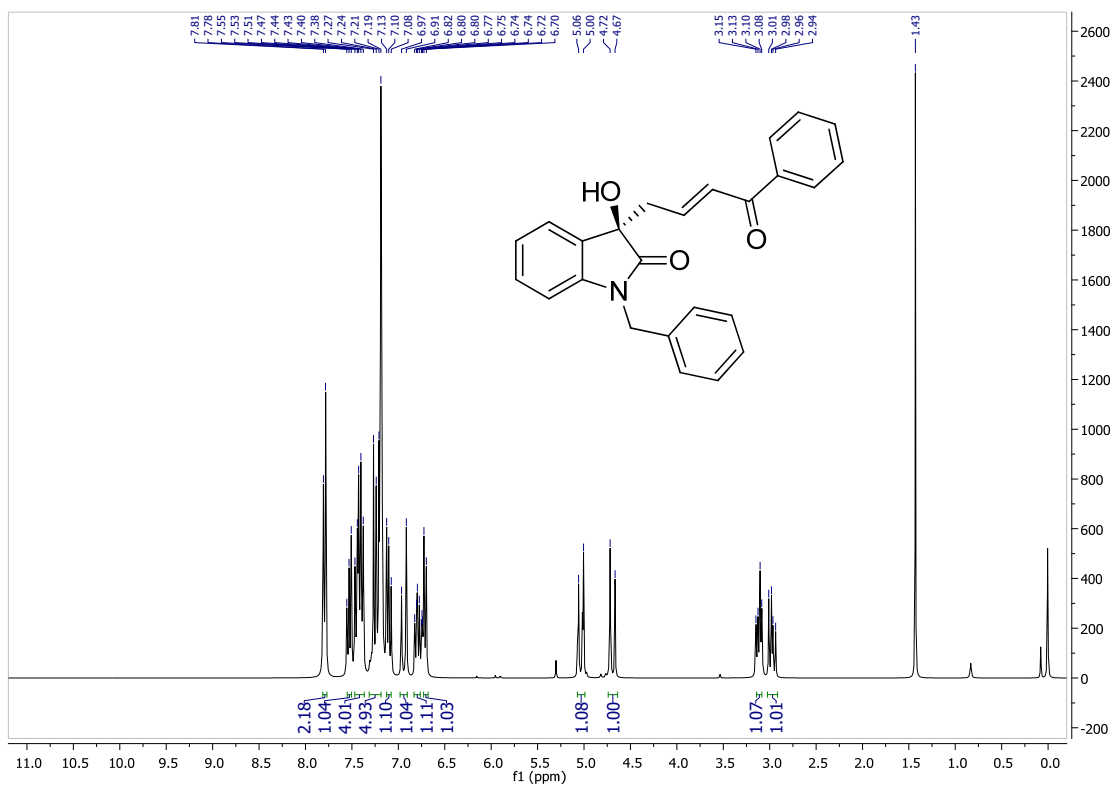


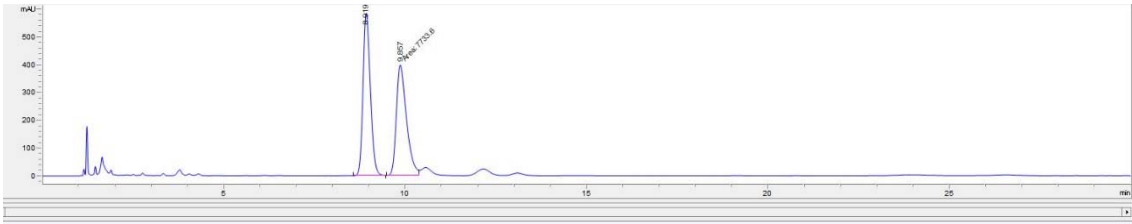
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.614	FM	1982.3	392.1	0.0206	45.352	0.867
2	6.372	FM	2268.1	387.7	0.0975	54.648	0.853



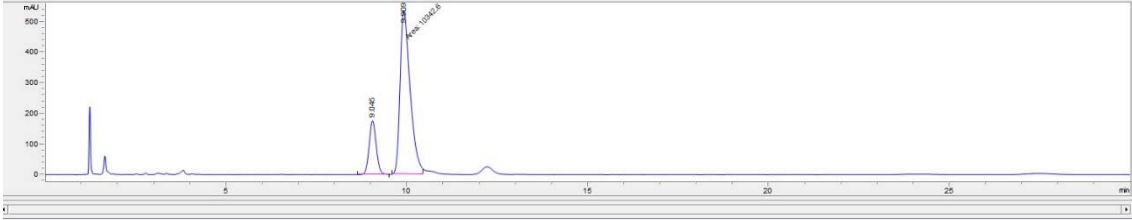
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.641	FM	111.5	22.9	0.0812	5.446	0.935
2	6.398	BB	1935.6	297.4	0.0979	94.554	0.857

(*R,E*)-1-Benzyl-3-hydroxy-3-(4-oxo-4-phenylbut-2-en-1-yl)indolin-2-one (4t)



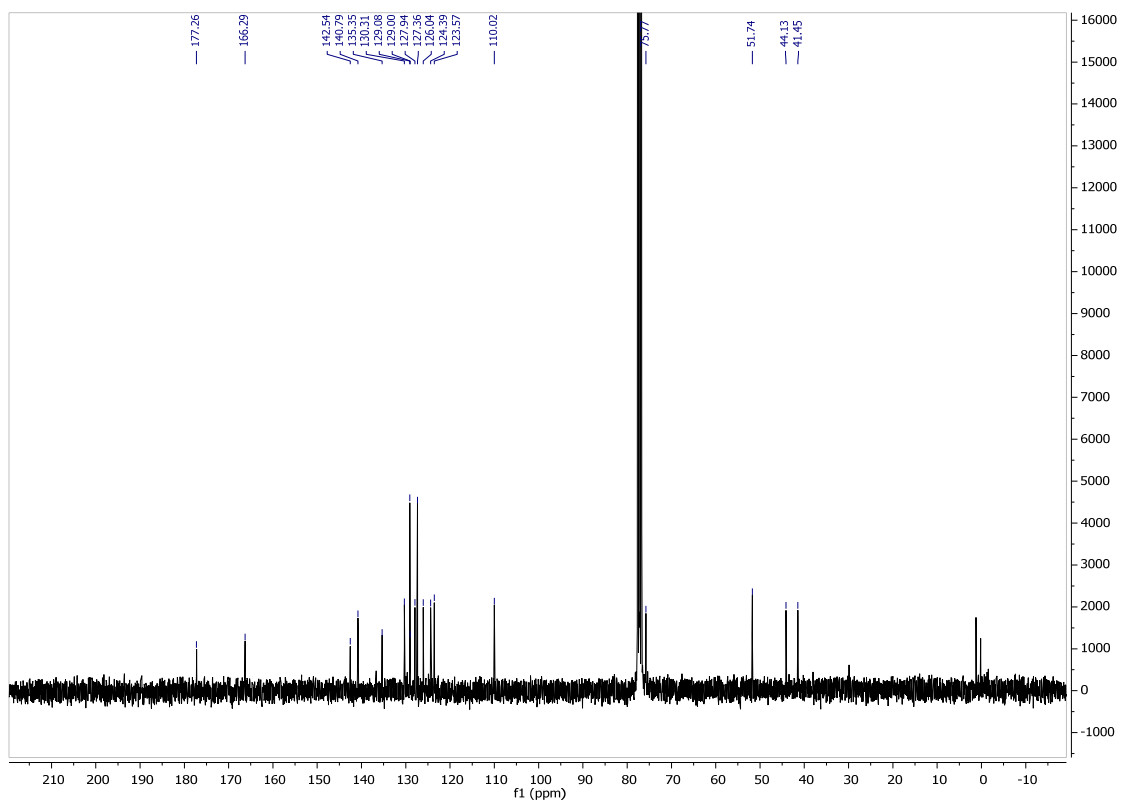
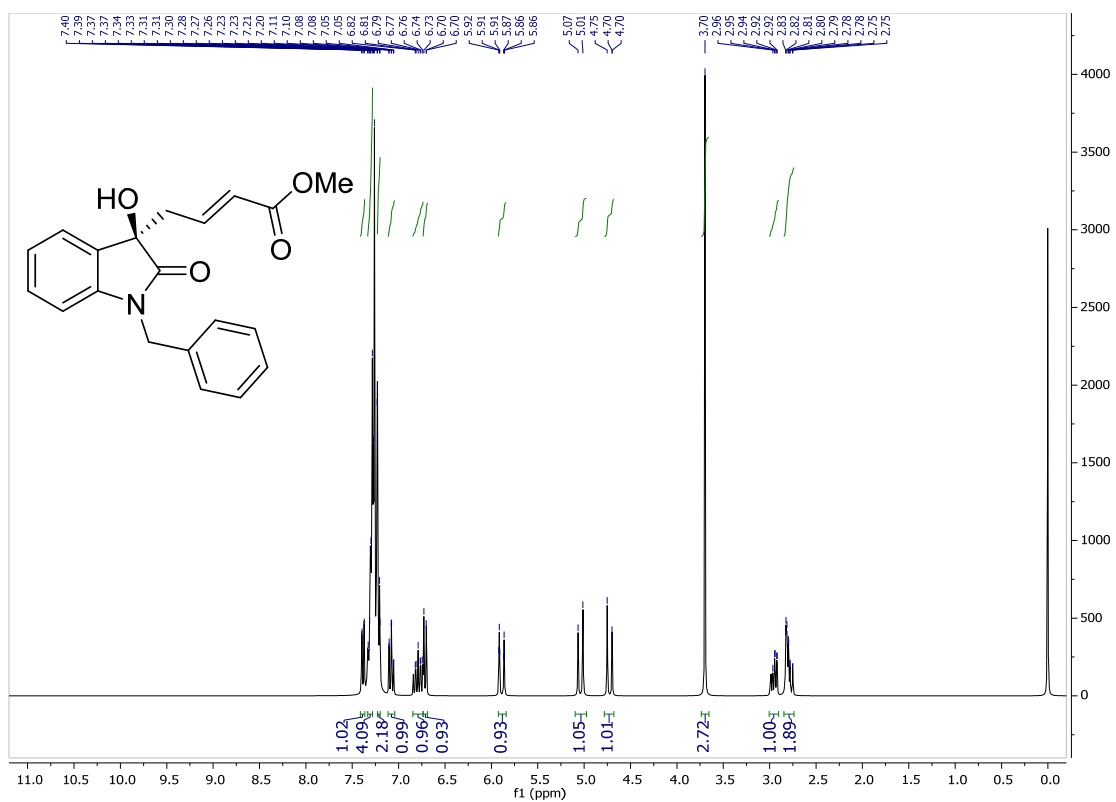


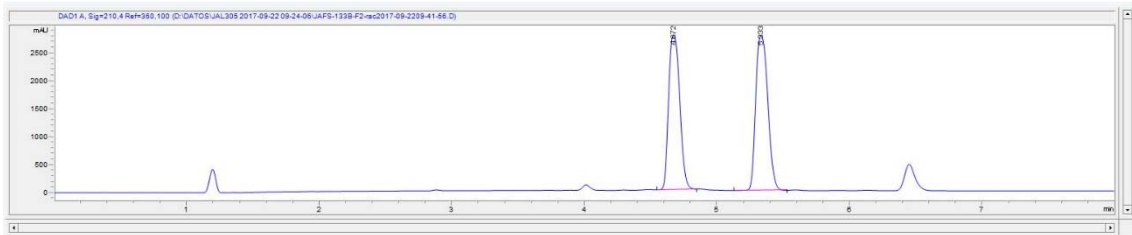
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	8.919	BB	8216.7	584	0.2161	51.514	0.744
2	9.857	MF	7733.6	397.7	0.3241	48.486	0.61



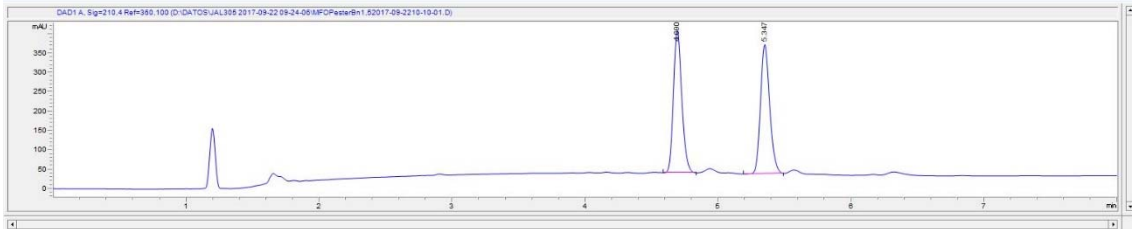
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	9.045	BB	2389.1	175.3	0.211	18.765	0.898
2	9.909	MF	10342.6	531.3	0.3245	81.235	0.564

Methyl (*R,E*)-4-(1-benzyl-3-hydroxy-2-oxindolin-3-yl)but-2-enoate (4u)



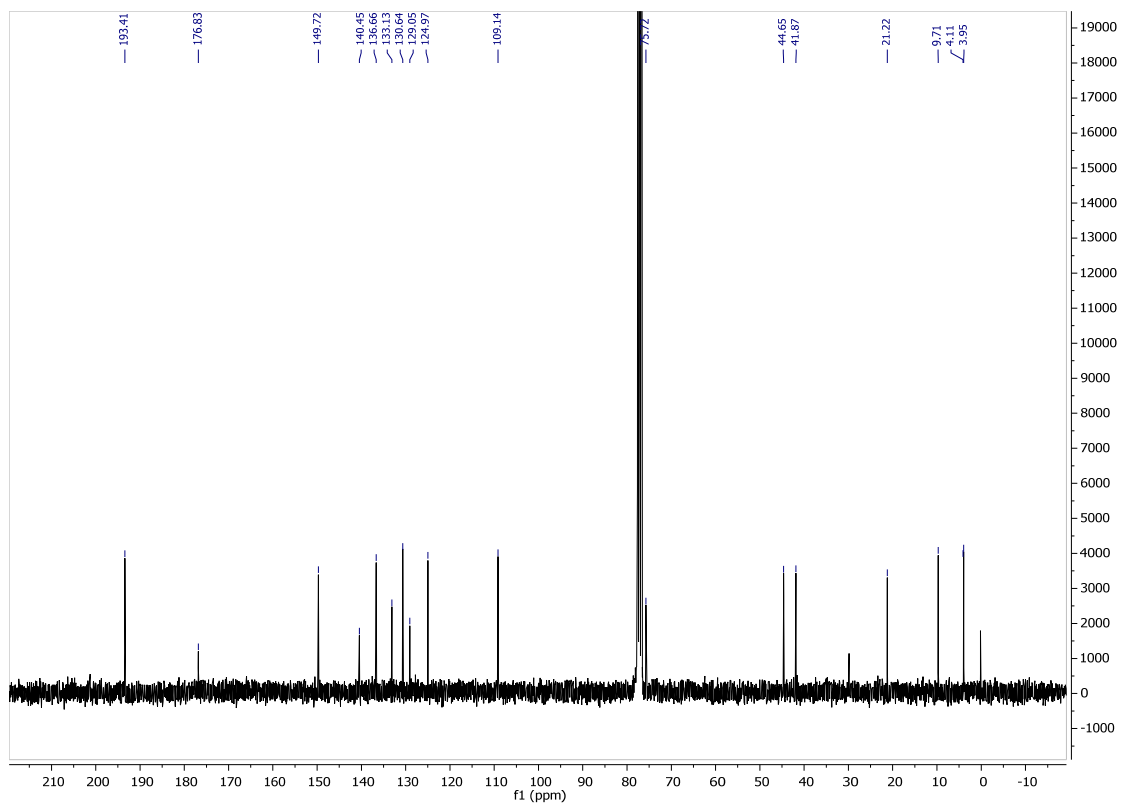
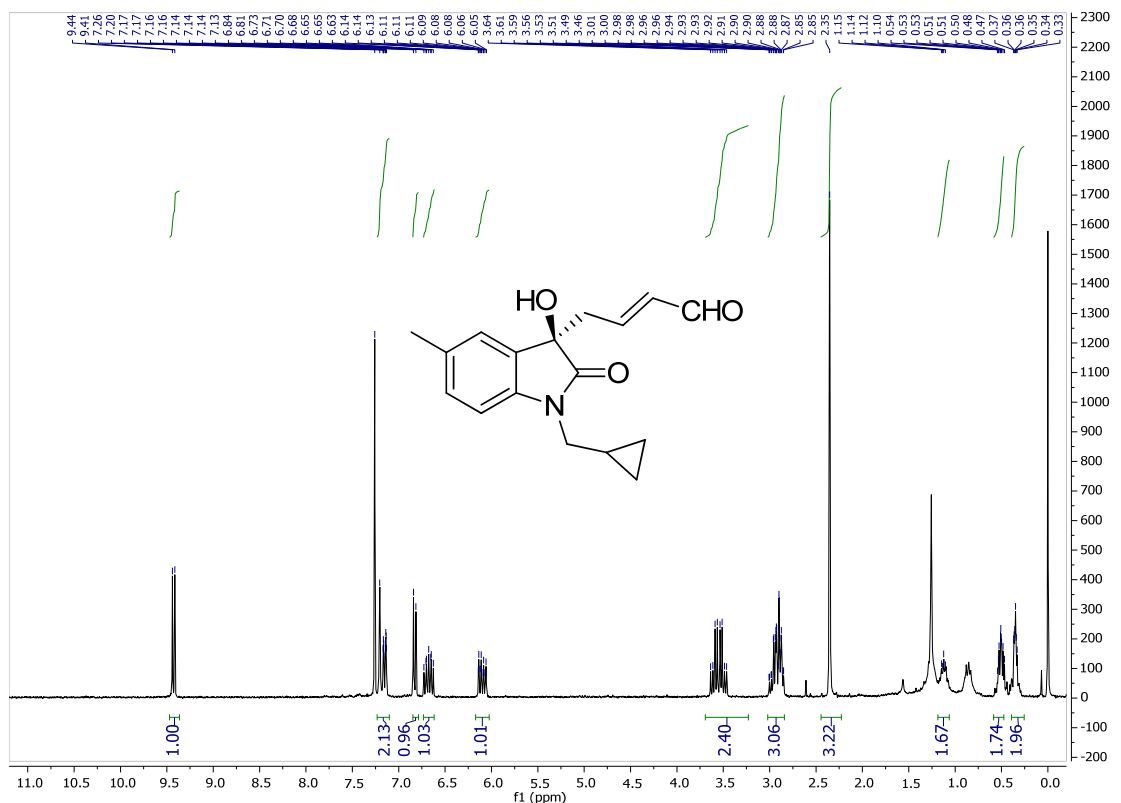


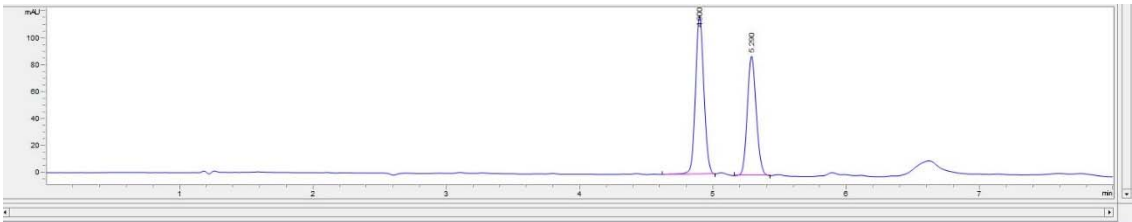
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.672	BB	16791.5	2774.1	0.0937	47.892	0.735
2	5.333	BB	17508.1	2766.8	0.1038	52.108	0.737



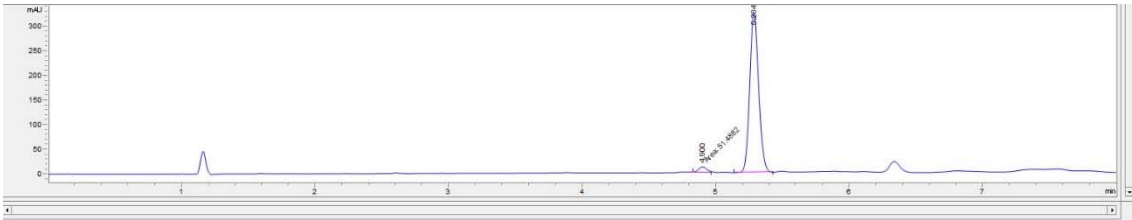
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.69	BB	1603.7	367.9	0.0669	50.106	0.795
2	5.347	BB	1596.9	332.6	0.074	49.894	0.809

(*R,E*)-4-[1-(Cyclopropylmethyl)-3-hydroxy-5-methyl-2-oxindolin-3-yl]but-2-enal (4v)



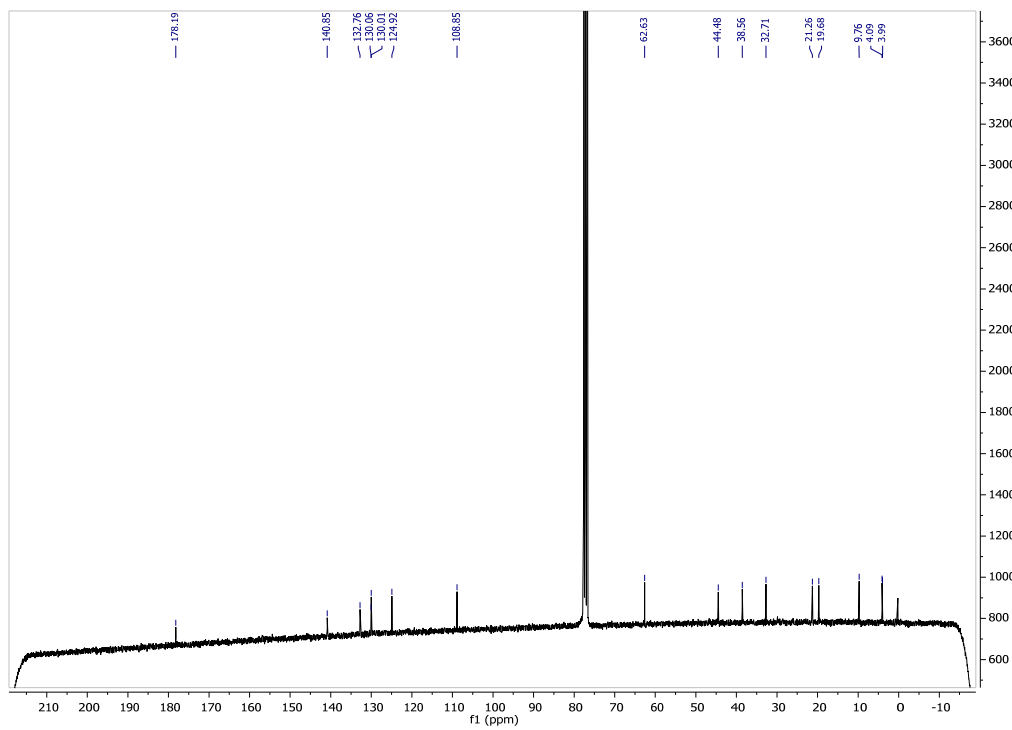
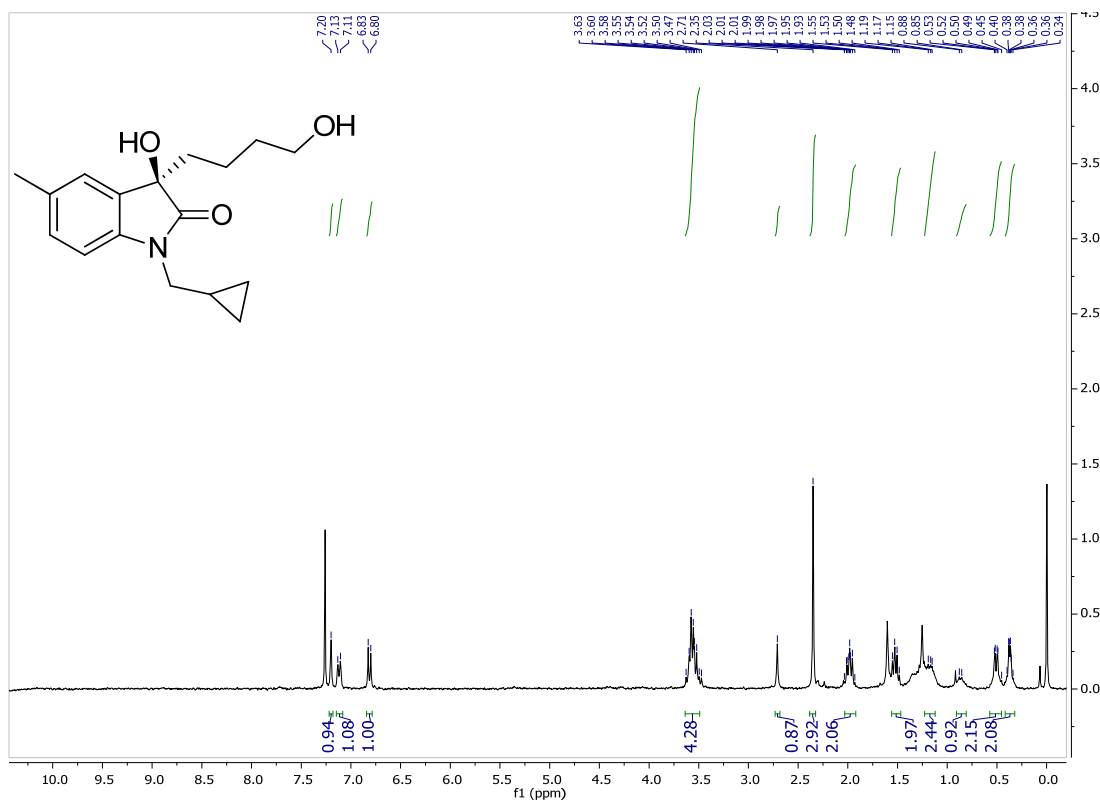


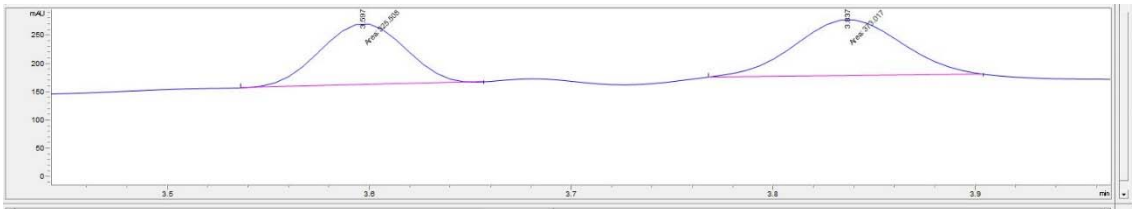
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.9	BB	513.1	117.3	0.069	55.414	0.905
2	5.29	BB	412.8	88.8	0.0722	44.586	0.863



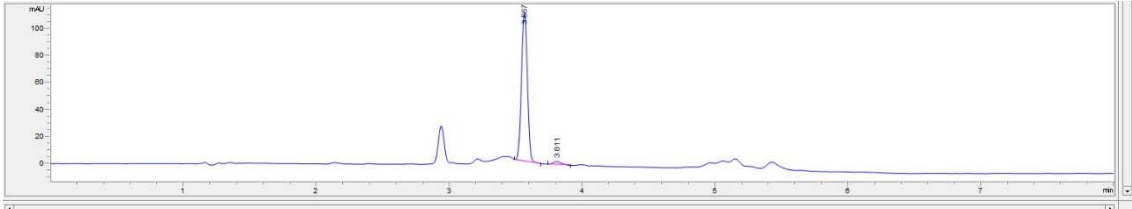
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.9	BB	51.5	11.6	0.0736	3.327	0.85
2	5.284	BB	1495.9	321.7	0.0722	96.673	0.851

(R,E)-1-(Cyclopropylmethyl)-3-hydroxy-3-(4-hydroxybutyl)-5-methylindolin-2-one (6)





#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.597	MM	325.5	110.6	0.049	46.599	1.036
2	3.837	MM	373	101.3	0.0614	53.401	0.982



#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.567	BB	330.6	109.6	0.05	97.121	0.959
2	3.811	BB	10	2.4	0.0644	2.879	0.753