

Supporting Information

**Palladium Catalyzed Asymmetric Allylic Alkylation of
Isoquinolinedione Derivatives in the Preparation of Quaternary
Carbon Stereocenter**

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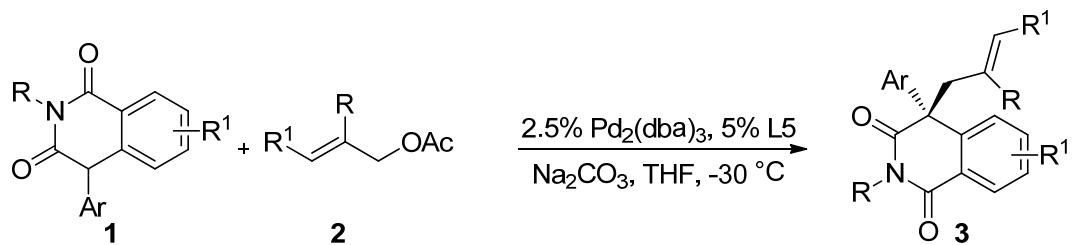
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General Information:

Proton nuclear magnetic resonance (^1H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on INOVA 400, 600MHz spectrometer (400, 600 MHz and 100, 150MHz). Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent (CDCl_3 : δ 7.26). Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent (CDCl_3 : δ 77.0). Data are represented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants in Hertz (Hz). All high resolution mass spectra were obtained on a Waters G2-XSQTof mass spectrometer. Melting points were determined on a Tektronix X-4 melting point apparatus. Analytical TLC was performed using EM separations percolated silica gel 0.2 mm layer UV 254 fluorescent sheets.

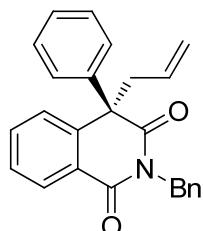
Starting Materials. All solvents and inorganic reagents were from commercial sources and used without purification unless otherwise noted. Starting material was prepared following the literature procedures.^{1,2}

General Procedure for Synthesis of 3a-3aj:



To a solution of **1** (0.05 mmol, 1 eq), $\text{Pd}_2(\text{dba})_3$ (1.1 mg, 0.000125mmol, 2.5%), Ligand (2.0 mg, 0.0025 mmol, 5%), Na_2CO_3 (11 mg, 0.1 mmol) in anhydrous THF (1 mL) was reacted at -30°C under N_2 atmosphere. After 10 minutes, **2** (2eq) was added ,and the mixture was stirred at the same temperature for 1-24 h until S1 was completely consumed (monitored by TLC).To the mixture, saturated aqueous NH_4Cl solution was added, and the mixture was extracted with EtOAc. The organic layers were combined, washed with brine, dried over anhydrous Na_2SO_4 , concentrated, Purification by flash column chromatography on SiO_2 (50:1 hexanes:EtOAc).

Spectroscopic Data for Products:



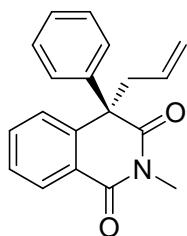
(R)-4-allyl-2-benzyl-4-phenylisoquinoline-1,3(2*H*,4*H*)-dione(3a):

White solid, 18 mg, 98% yield. mp: 97.1-98.8 °C;

Optical rotation: $[\alpha]_D^{25.9} = -47.23$ (c 10.70, CH_2Cl_2);

^1H NMR (600 MHz, CDCl_3) δ 8.30 (dd, $J = 7.9, 1.1$ Hz, 1H), 7.55 (td, $J = 7.9, 1.4$ Hz, 1H), 7.47 – 7.42 (m, 1H), 7.35 (d, $J = 6.8$ Hz, 2H), 7.30 – 7.26 (m, 2H), 7.25 (d, $J = 1.5$ Hz, 1H), 7.24 (d, $J = 3.1$ Hz, 1H), 7.23 – 7.20 (m, 2H), 7.15 – 7.11 (m, 2H), 7.10 (s, 1H), 5.22 (d, $J = 13.9$ Hz, 1H), 5.20 – 5.13 (m, 1H), 5.10 (d, $J = 13.9$ Hz, 1H), 4.88 (dd, $J = 17.0, 1.2$ Hz, 1H), 4.79 (dd, $J = 10.2, 0.7$ Hz, 1H), 3.66 (dd, $J = 13.0, 7.9$ Hz, 1H), 3.01 (dd, $J = 12.9, 6.6$ Hz, 1H). ^{13}C NMR (150 MHz, CDCl_3) δ 174.2, 164.2, 142.9, 142.4, 136.9, 134.0, 131.3, 128.8, 128.7, 128.6, 128.2, 127.9, 127.7, 127.6, 127.5, 127.3, 125.8, 120.2, 55.9, 44.2, 43.8. HRMS (ESI-TOF) m/z [M + H]⁺ calcd for $\text{C}_{25}\text{H}_{22}\text{NO}_2$ 368.1651, found 368.1655.

The enantiomeric excess was determined to be 92% by HPLC. [IC column, 230 nm, n-hexane:IPA = 97:3, 1.0mL/min]: 15.267 min (major), 11.113 min (minor);



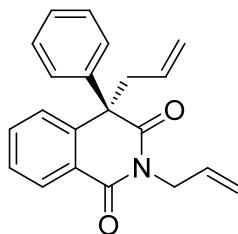
(R)-4-allyl-2-methyl-4-phenylisoquinoline-1,3(2H,4H)-dione(3b):

White solid, 12.9mg, 89% yield. mp: 82.3-83.4 °C;

Optical rotation: $[\alpha]_D^{25.7} = -20.34$ (c 21.50, CH₂Cl₂);

¹H NMR (600 MHz, CDCl₃) δ 8.29 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.59 – 7.53 (m, 1H), 7.45 (t, *J* = 7.3 Hz, 1H), 7.30 (t, *J* = 7.4 Hz, 2H), 7.26 – 7.22 (m, 1H), 7.19 – 7.15 (m, 2H), 7.13 – 7.09 (m, 1H), 5.40 – 5.17 (m, 1H), 5.01 (dd, *J* = 17.0, 1.0 Hz, 1H), 4.92 (d, *J* = 10.2 Hz, 1H), 3.66 (dd, *J* = 12.9, 7.9 Hz, 1H), 3.34 (d, *J* = 8.6 Hz, 3H), 3.02 (dd, *J* = 12.9, 6.5 Hz, 1H). ¹³C NMR (150 MHz, CDCl₃) δ 174.4, 164.5, 142.9, 142.4, 133.9, 131.7, 130.5, 129.0, 128.7, 128.4, 127.9, 127.6, 125.7, 120.0, 56.1, 44.4, 27.2. HRMS (ESI-TOF) m/z [M + H]⁺ calcd for C₁₉H₁₈NO₂ 292.1338, found 292.11340.

The enantiomeric excess was determined to be 90% by HPLC. [IC column, 230 nm, n-hexane:IPA = 95:5, 0.8mL/min]: 19.180 min (major), 14.627 min (minor);



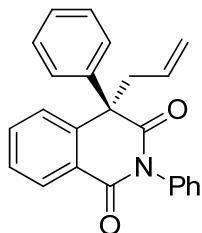
(R)-2,4-diallyl-4-phenylisoquinoline-1,3(2H,4H)-dione(3c)

White solid, 15.7 mg, 99% yield. Yellowish paste;

Optical rotation: $[\alpha]_D^{25.2} = -49.68$ (c 38.70, CH₂Cl₂);

¹H NMR (600 MHz, CDCl₃) δ 8.22 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.53 – 7.45 (m, 1H), 7.41 – 7.34 (m, 1H), 7.23 – 7.19 (m, 2H), 7.19 – 7.15 (m, 1H), 7.10 – 7.07 (m, 2H), 7.04 (dd, *J* = 7.9, 0.5 Hz, 1H), 5.74 (ddt, *J* = 17.1, 10.3, 5.8 Hz, 1H), 5.20 (dddd, *J* = 16.9, 10.2, 7.8, 6.6 Hz, 1H), 5.07 (ddq, *J* = 38.7, 10.3, 1.3 Hz, 2H), 4.96 – 4.82 (m, 2H), 4.58 – 4.42 (m, 2H), 3.62 (dd, *J* = 13.0, 7.8 Hz, 1H), 2.95 (dd, *J* = 13.0, 6.6 Hz, 1H). ¹³C NMR (150 MHz, CDCl₃) δ 174.0, 164.1, 143.1, 142.9, 134.2, 132.1, 131.8, 129.2, 128.9, 128.6, 128.5, 128.1, 127.8, 126.0, 120.4, 117.9, 56.1, 44.5, 42.9. HRMS (ESI-TOF) m/z [M + H]⁺ calcd for C₂₁H₂₀NO₂ 318.1494, found 318.1495.

The enantiomeric excess was determined to be 89% by HPLC. [IC column, 230 nm, n-hexane:IPA = 95:5, 0.8mL /min]: 12.733 min (major), 9.407 min (minor);



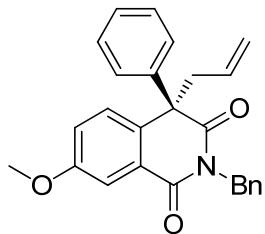
(R)-4-allyl-2,4-diphenylisoquinoline-1,3(2H,4H)-dione(3d)

White solid, 17.3mg, 98% yield. mp: 72.5-73.7 °C;

Optical rotation: $[\alpha]_{D}^{25.2} = -57.62$ (c 4.20, CH₂Cl₂);

¹H NMR (600 MHz, CDCl₃) δ 8.33 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.63 (td, *J* = 7.9, 1.4 Hz, 1H), 7.52 – 7.48 (m, 1H), 7.45 (t, *J* = 7.5 Hz, 2H), 7.40 (t, *J* = 7.4 Hz, 1H), 7.33 (dd, *J* = 10.2, 4.7 Hz, 2H), 7.31 – 7.27 (m, 1H), 7.26 – 7.23 (m, 2H), 7.22 (d, *J* = 7.8 Hz, 1H), 7.11 (dd, *J* = 13.8, 5.0 Hz, 2H), 5.44 (dddd, *J* = 16.7, 10.1, 8.1, 6.3 Hz, 1H), 5.19 – 5.12 (m, 1H), 5.11 – 5.02 (m, 1H), 3.72 (dd, *J* = 13.0, 8.2 Hz, 1H), 3.11 (dd, *J* = 13.0, 6.3 Hz, 1H). ¹³C NMR (150 MHz, CDCl₃) δ 174.1, 164.4, 142.8, 142.5, 135.4, 134.2, 131.6, 129.2, 128.8, 128.6, 128.3, 127.7, 127.6, 127.4, 127.0, 126.0, 122.7, 120.3, 56.5, 44.3. HRMS (ESI-TOF) m/z [M + H]⁺ calcd for C₂₄H₂₀NO₂ 354.1494, found 354.1492.

The enantiomeric excess was determined to be 95% by HPLC. [IC column, 230 nm, n-hexane:IPA = 90:10, 1.0mL/min]: 16.400 min (major), 13.160 min (minor);



(R)-4-allyl-2-benzyl-7-methoxy-4-phenylisoquinoline-1,3(2H,4H)-dione(3e):

White solid, 19mg, 96% yield. Yellowish paste;

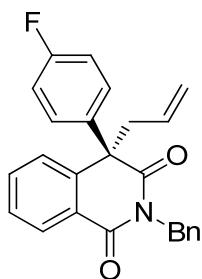
Optical rotation: $[\alpha]_{D}^{25.3} = -53.94$ (c 17.50, CH₂Cl₂);

¹H NMR (600 MHz, CDCl₃) δ 7.77 (d, *J* = 2.8 Hz, 1H), 7.65 (dd, *J* = 6.5, 2.9 Hz, 1H), 7.44 (dd, *J* = 5.0, 1.9 Hz, 1H), 7.37 – 7.34 (m, 2H), 7.30 – 7.27 (m, 2H), 7.25 – 7.23 (m, 2H), 7.18 – 7.12 (m, 3H), 7.03 (d, *J* = 8.7 Hz, 1H), 5.46 – 5.13 (m, 2H), 5.11 (d, *J* = 13.9 Hz, 1H), 4.91 (dd, *J* = 17.0, 1.2 Hz, 1H), 4.87 – 4.73 (m, 1H), 3.90 (s, 3H), 3.66 (dd, *J* = 13.0, 7.8 Hz, 1H), 2.99 (dd, *J* = 13.0, 6.6 Hz, 1H).

¹³C NMR (151 MHz, CDCl₃) δ 174.5, 164.3, 158.9, 143.5, 143.2, 137.1, 134.7, 131.7, 130.7, 129.3, 128.9, 128.8, 128.4, 127.7, 127.4, 122.8, 120.2, 110.4, 55.7, 55.6, 44.3, 44.1.

HRMS (ESI-TOF) m/z [M + H]⁺ C₂₆H₂₄NO₃ 398.1756, found 398.1753.

The enantiomeric excess was determined to be 90% by HPLC. [IC column, 230 nm, n-hexane:IPA = 97:3, 1.0mL/min]: 14.307 min (major), 10.713 min (minor);



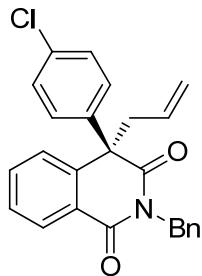
(R)-4-allyl-2-benzyl-4-(4-fluorophenyl)isoquinoline-1,3(2H,4H)-dione(3f):

White solid, 16.5mg, 86% yield. mp: 110.5–111.8 °C;

Optical rotation: $[\alpha]_D^{25.2} = -32.62$ (c 11.20, CH_2Cl_2);

^1H NMR (600 MHz, CDCl_3) δ 8.30 (dd, $J = 7.9, 1.0$ Hz, 1H), 7.57 (td, $J = 7.9, 1.3$ Hz, 1H), 7.48 – 7.44 (m, 1H), 7.33 (d, $J = 6.7$ Hz, 2H), 7.25 – 7.18 (m, 3H), 7.09 (dt, $J = 5.3, 4.0$ Hz, 3H), 6.98 – 6.91 (m, 2H), 5.23 – 5.07 (m, 3H), 4.90 – 4.84 (m, 1H), 4.79 (d, $J = 10.2$ Hz, 1H), 3.61 (dd, $J = 12.9, 7.9$ Hz, 1H), 2.97 (dd, $J = 12.9, 6.6$ Hz, 1H). ^{13}C NMR (150 MHz, CDCl_3) δ 174.0, 164.0, 162.8, 142.1, 138.7(d, $J = 3.4$ Hz, 0H), 136.8, 134.1, 131.1, 129.2, 128.9, 128.8, 128.3, 127.8, 127.7(d, $J = 3.4$ Hz, 1H), 127.4, 125.8, 120.4, 115.6, 55.4, 44.6, 43.8. HRMS (ESI-TOF) m/z [M + H]⁺ calcd for $\text{C}_{25}\text{H}_{21}\text{FNO}_2$ 386.1556, found 386.1562.

The enantiomeric excess was determined to be 92% by HPLC. [IC column, 230 nm, n-hexane:IPA = 97:3, 1.0mL/min]: 10.847 min (major), 9.273 min (minor);



(R)-4-allyl-2-benzyl-4-(4-chlorophenyl)isoquinoline-1,3(2H,4H)-dione(3g):

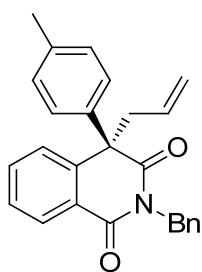
White solid, 16 mg, 80% yield. mp: 147.3–148.7 °C;

Optical rotation: $[\alpha]_D^{25.8} = -21.33$ (c 5.50, CH_2Cl_2);

^1H NMR (600 MHz, CDCl_3) δ 8.30 (dd, $J = 7.9, 1.0$ Hz, 1H), 7.57 (td, $J = 7.9, 1.4$ Hz, 1H), 7.51 – 7.40 (m, 1H), 7.34 (d, $J = 6.7$ Hz, 2H), 7.26 – 7.19 (m, 5H), 7.11 – 7.03 (m, 3H), 5.29 – 5.07 (m, 3H), 4.87 (dd, $J = 17.0, 1.0$ Hz, 1H), 4.79 (d, $J = 10.2$ Hz, 1H), 3.59 (dd, $J = 12.9, 7.9$ Hz, 1H), 2.96 (dd, $J = 12.9, 6.5$ Hz, 1H). ^{13}C NMR (150 MHz, CDCl_3) δ 173.8, 164.0, 141.9, 141.4, 136.8, 134.1, 133.7, 130.9, 129.1, 128.9, 128.8, 128.3, 127.8, 127.7, 127.4, 125.8, 120.4, 55.5, 44.4, 43.9.

HRMS (ESI-TOF) m/z [M + H]⁺ calcd for $\text{C}_{25}\text{H}_{21}\text{ClNO}_2$ 402.1261, found 402.1257.

The enantiomeric excess was determined to be 92% by HPLC. [IC column, 230 nm, n-hexane:IPA = 90:10, 1.0mL/min]: 9.080min (major), 6.880min (minor);



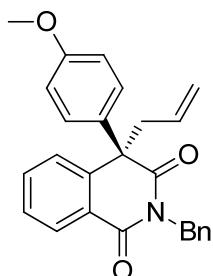
(R)-4-allyl-2-benzyl-4-(p-tolyl)isoquinoline-1,3(2H,4H)-dione (3h):

White solid, 18.1 mg, 95% yield. mp: 129.5–130.4 °C;

Optical rotation: $[\alpha]_D^{25.1} = -65.19$ (c 11.70, CH₂Cl₂);

¹H NMR (600 MHz, CDCl₃) δ 8.28 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.55 (td, *J* = 7.9, 1.4 Hz, 1H), 7.49 – 7.41 (m, 1H), 7.35 (d, *J* = 6.7 Hz, 2H), 7.25 – 7.21 (m, 2H), 7.22 – 7.19 (m, 1H), 7.11 (dd, *J* = 9.2, 5.1 Hz, 1H), 7.10 – 7.04 (m, 2H), 7.01 (d, *J* = 8.3 Hz, 2H), 5.42 – 4.93 (m, 3H), 4.87 (dd, *J* = 17.0, 1.2 Hz, 1H), 4.83 – 4.67 (m, 1H), 3.64 (dd, *J* = 13.0, 7.9 Hz, 1H), 2.99 (dd, *J* = 13.0, 6.6 Hz, 1H), 2.30 (s, 3H). ¹³C NMR (150 MHz, CDCl₃) δ 174.3, 164.2, 142.6, 140.0, 137.4, 137.0, 134.0, 131.4, 129.4, 129.0, 128.6, 128.2, 127.8, 127.5, 127.3, 127.2, 125.8, 120.1, 55.6, 44.3, 43.8, 20.9. HRMS (ESI-TOF) m/z [M + H]⁺ calcd for C₂₆H₂₄NO₂ 382.1807, found 382.1803.

The enantiomeric excess was determined to be 94% by HPLC. [IC column, 230 nm, n-hexane:IPA = 97:3, 1.0mL/min]: 19.073 min (major), 10.720 min (minor);



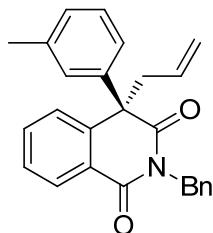
(R)-4-allyl-2-benzyl-4-(4-methoxyphenyl)isoquinoline-1,3(2H,4H)-dione (3i):

White solid, 19.7 mg, 99% yield. mp: 123.7–124.4 °C;

Optical rotation: $[\alpha]_D^{25.3} = -20.53$ (c 21.30, CH₂Cl₂);

¹H NMR (600 MHz, CDCl₃) δ 8.48 – 8.09 (m, 1H), 7.56 (td, *J* = 7.9, 1.4 Hz, 1H), 7.48 – 7.41 (m, 1H), 7.34 (d, *J* = 6.8 Hz, 2H), 7.22 (tdd, *J* = 6.9, 4.6, 2.3 Hz, 3H), 7.13 (d, *J* = 8.1 Hz, 1H), 7.07 – 7.01 (m, 2H), 6.84 – 6.74 (m, 2H), 5.23 – 5.19 (m, 1H), 5.19 – 5.12 (m, 1H), 5.09 (d, *J* = 13.9 Hz, 1H), 4.88 (dd, *J* = 17.0, 1.2 Hz, 1H), 4.78 (d, *J* = 10.1 Hz, 1H), 3.77 (s, 3H), 3.64 (dd, *J* = 13.0, 7.9 Hz, 1H), 2.97 (dd, *J* = 13.0, 6.6 Hz, 1H). ¹³C NMR (150 MHz, CDCl₃) δ 174.4, 164.2, 158.8, 142.6, 137.0, 135.0, 133.9, 131.5, 128.8, 128.6, 128.5, 128.2, 127.8, 127.5, 127.3, 125.8, 120.1, 114.0, 55.3, 55.3, 44.4, 43.80. HRMS (ESI-TOF) m/z [M + H]⁺ calcd for C₂₆H₂₄NO₃ 398.1756, found 398.1768.

The enantiomeric excess was determined to be 93% by HPLC. [IC column, 230 nm, n-hexane:IPA = 97:3, 1.0mL/min]: 34.560 min (major), 18.800min (minor);



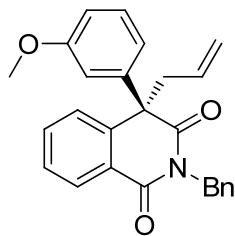
(R)-4-allyl-2-benzyl-4-(m-tolyl)isoquinoline-1,3(2H,4H)-dione (3j):

White solid, 18.1 mg, 95% yield. mp: 104.1–105.5 °C;

Optical rotation: $[\alpha]_D^{25.8} = -75.56$ (c 15.00, CH_2Cl_2);

^1H NMR (600 MHz, CDCl_3) δ 8.29 (dd, $J = 7.9, 1.0$ Hz, 1H), 7.63 – 7.48 (m, 1H), 7.43 (t, $J = 7.2$ Hz, 1H), 7.36 (d, $J = 6.9$ Hz, 2H), 7.26 – 7.21 (m, 2H), 7.22 – 7.18 (m, 1H), 7.15 (t, $J = 8.0$ Hz, 1H), 7.10 (t, $J = 6.6$ Hz, 1H), 7.05 (d, $J = 7.5$ Hz, 1H), 6.91 (d, $J = 6.5$ Hz, 2H), 5.37 – 4.95 (m, 3H), 4.87 (d, $J = 17.0$ Hz, 1H), 4.78 (d, $J = 10.2$ Hz, 1H), 3.63 (dd, $J = 12.9, 7.9$ Hz, 1H), 3.01 (dd, $J = 12.9, 6.6$ Hz, 1H), 2.25 (s, 3H). ^{13}C NMR (150 MHz, CDCl_3) δ 174.3, 164.2, 142.8, 142.6, 138.4, 137.0, 134.0, 131.4, 128.9, 128.6, 128.5, 128.4, 128.2, 127.9, 127.8, 127.5, 127.3, 125.6, 124.2, 120.1, 55.8, 44.2, 43.8, 21.5. HRMS (ESI-TOF) m/z [M + H] $^+$ calcd for $\text{C}_{26}\text{H}_{24}\text{NO}_2$ 382.1807, found 382.1811.

The enantiomeric excess was determined to be 95% by HPLC. [IC column, 230 nm, n-hexane:IPA = 97:3, 1.0 mL/min]: 13.160 min (major), 10.093 min (minor);



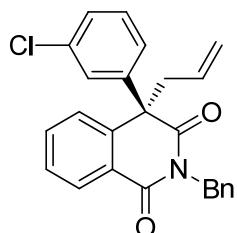
(R)-4-allyl-2-benzyl-4-(3-methoxyphenyl)isoquinoline-1,3(2H,4H)-dione (3k):

White solid, 19.1 mg, 96% yield. mp: 107.7–108.9 °C;

Optical rotation: $[\alpha]_D^{25.6} = -70.34$ (c 11.60, CH_2Cl_2);

^1H NMR (600 MHz, CDCl_3) δ 8.26 (dd, $J = 7.9, 1.1$ Hz, 1H), 7.58 – 7.49 (m, 1H), 7.46 – 7.38 (m, 1H), 7.34 (d, $J = 6.9$ Hz, 2H), 7.23 – 7.19 (m, 2H), 7.19 – 7.16 (m, 1H), 7.16 (t, $J = 8.0$ Hz, 1H), 7.10 (d, $J = 7.9$ Hz, 1H), 6.76 (dd, $J = 8.2, 2.3$ Hz, 1H), 6.71 – 6.62 (m, 2H), 5.61 – 4.90 (m, 3H), 4.86 (dd, $J = 17.0, 1.2$ Hz, 1H), 4.77 (d, $J = 10.2$ Hz, 1H), 3.66 (s, 3H), 3.59 (dd, $J = 12.9, 7.9$ Hz, 1H), 2.99 (dd, $J = 12.9, 6.6$ Hz, 1H). ^{13}C NMR (150 MHz, CDCl_3) δ 174.2, 164.4, 159.9, 144.6, 142.6, 137.2, 134.2, 131.5, 129.8, 129.1, 128.8, 128.5, 128.0, 127.8, 127.5, 125.9, 120.4, 119.9, 113.9, 112.8, 56.1, 55.4, 44.4, 44.0. HRMS (ESI-TOF) m/z [M + H] $^+$ calcd for $\text{C}_{26}\text{H}_{24}\text{NO}_3$ 398.1756, found 398.1756.

The enantiomeric excess was determined to be 89% by HPLC. [IC column, 230 nm, n-hexane:IPA = 97:3, 1.0 mL/min]: 22.900 min (major), 15.020 min (minor);



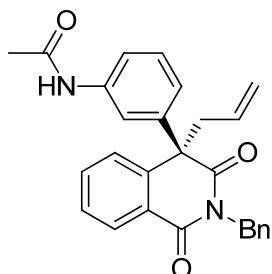
(R)-4-allyl-2-benzyl-4-(3-chlorophenyl)isoquinoline-1,3(2H,4H)-dione (3l):

White solid, 18.2 mg, 81% yield. mp: 155.3–156.6 °C;

Optical rotation: $[\alpha]_D^{25.9} = -275.46$ (c 9.10, CH₂Cl₂);

¹H NMR (600 MHz, CDCl₃) δ 8.30 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.57 (td, *J* = 7.8, 1.4 Hz, 1H), 7.49 – 7.44 (m, 1H), 7.36 (d, *J* = 6.9 Hz, 2H), 7.26 – 7.23 (m, 2H), 7.23 – 7.21 (m, 2H), 7.19 (t, *J* = 7.9 Hz, 1H), 7.16 (t, *J* = 1.8 Hz, 1H), 7.08 (d, *J* = 7.8 Hz, 1H), 6.96 (ddd, *J* = 7.8, 1.6, 1.1 Hz, 1H), 5.49 – 4.99 (m, 3H), 4.86 (dd, *J* = 17.0, 1.1 Hz, 1H), 4.78 (d, *J* = 10.1 Hz, 1H), 3.58 (dd, *J* = 12.8, 7.9 Hz, 1H), 2.97 (dd, *J* = 12.8, 6.5 Hz, 1H). ¹³C NMR (150 MHz, CDCl₃) δ 173.6, 164.0, 144.8, 141.7, 136.8, 134.7, 134.2, 130.8, 129.9, 128.9, 128.8, 128.3, 127.9, 127.9, 127.7, 127.6, 127.5, 125.7, 120.5, 55.7, 44.4, 43.9. HRMS (ESI-TOF) m/z [M + H]⁺ calcd for C₂₅H₂₁ClNO₂ 402.1261, found 402.1260.

The enantiomeric excess was determined to be 86% by HPLC. [IC column, 230 nm, n-hexane:IPA = 97:3, 0.5mL/min]: 21.887 min (major), 18.200 min (minor);



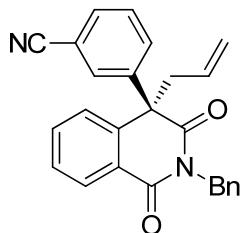
(R)-N-(3-(4-allyl-2-benzyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl)acetamide (3m):

White solid, 19.1 mg, 90% yield. mp: 68.1–69.8 °C;

Optical rotation: $[\alpha]_D^{25.3} = -5.55$ (c 10.50, CH₂Cl₂);

¹H NMR (600 MHz, CDCl₃) δ 8.46 – 8.11 (m, 1H), 7.59 – 7.53 (m, 1H), 7.53 – 7.46 (m, 1H), 7.46 – 7.42 (m, 1H), 7.41 – 7.32 (m, 2H), 7.26 – 7.23 (m, 1H), 7.23 – 7.22 (m, 1H), 7.22 – 7.20 (m, 1H), 7.20 – 7.16 (m, 1H), 7.17 – 7.09 (m, 3H), 6.92 – 6.67 (m, 1H), 5.22 – 5.17 (m, 1H), 5.17 – 5.14 (m, 1H), 5.14 – 5.10 (m, 1H), 4.91 – 4.84 (m, 1H), 4.85 – 4.73 (m, 1H), 3.63 – 3.53 (m, 1H), 3.09 – 2.94 (m, 1H), 2.15 – 2.05 (m, 3H). ¹³C NMR (150 MHz, CDCl₃) δ 174.1, 168.3, 164.1, 143.6, 142.1, 138.3, 136.9, 134.1, 131.2, 129.4, 128.9, 128.7, 128.2, 127.8, 127.7, 127.4, 125.6, 123.0, 120.3, 119.2, 118.5, 55.8, 44.1, 43.8, 24.5. HRMS (ESI-TOF) m/z [M + H]⁺ calcd for C₂₇H₂₅N₂O₃ 425.1865, found 425.1863.

The enantiomeric excess was determined to be 92% by HPLC. [IC column, 230 nm, n-hexane:IPA = 80:10, 1.0mL/min]: 35.760min (major), 17.093 min (minor);



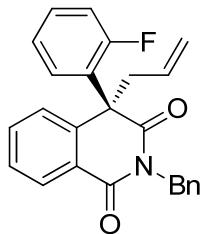
(R)-3-(4-allyl-2-benzyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)benzonitrile(3n):

White solid, 18.6 mg, 95% yield. mp: 161.5–162.3 °C;

Optical rotation: $[\alpha]_{\text{D}}^{25.2} = -40.00$ (c 20.00, CH_2Cl_2);

^1H NMR (600 MHz, CDCl_3) δ 8.33 (dd, $J = 7.9, 1.1$ Hz, 1H), 7.60 (td, $J = 7.8, 1.4$ Hz, 1H), 7.55 (d, $J = 7.5$ Hz, 1H), 7.52 – 7.47 (m, 1H), 7.45 (s, 1H), 7.38 (t, $J = 7.8$ Hz, 1H), 7.36 – 7.31 (m, 3H), 7.24 (ddd, $J = 9.1, 6.6, 2.3$ Hz, 3H), 7.04 (d, $J = 7.8$ Hz, 1H), 5.34 – 4.94 (m, 3H), 4.87 (dd, $J = 17.0, 0.9$ Hz, 1H), 4.80 (d, $J = 10.2$ Hz, 1H), 3.59 (dd, $J = 12.8, 7.9$ Hz, 1H), 2.97 (dd, $J = 12.8, 6.5$ Hz, 1H). ^{13}C NMR (150 MHz, CDCl_3) δ 173.2, 163.7, 144.3, 140.9, 136.6, 134.4, 132.1, 131.3, 131.1, 130.3, 129.5, 129.1, 128.9, 128.3, 128.2, 127.6, 125.8, 120.9, 118.3, 112.9, 55.7, 44.5, 43.9. HRMS (ESI-TOF) m/z [M + H] $^+$ calcd for $\text{C}_{26}\text{H}_{21}\text{N}_2\text{O}_2$ 393.1603, found 393.1600.

The enantiomeric excess was determined to be 88% by HPLC. [IC column, 230 nm, n-hexane:IPA = 80:10, 1.0 mL/min]: 28.360 min (major), 17.113 min (minor);



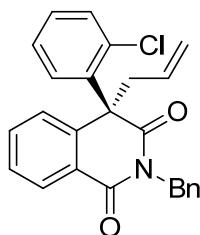
(R)-4-allyl-2-benzyl-4-(2-fluorophenyl)isoquinoline-1,3(2H,4H)-dione(3o):

White solid, 16.4 mg, 85% yield. mp: 90.5–91.3 °C;

Optical rotation: $[\alpha]_{\text{D}}^{25.8} = -229.33$ (c 10.00, CH_2Cl_2);

^1H NMR (600 MHz, CDCl_3) δ 8.26 (dd, $J = 7.9, 1.0$ Hz, 1H), 7.75 – 7.69 (m, 1H), 7.48 – 7.45 (m, 3H), 7.43 – 7.38 (m, 2H), 7.35 – 7.30 (m, 1H), 7.29 – 7.27 (m, 2H), 7.23 (t, $J = 7.3$ Hz, 1H), 6.92 (ddt, $J = 14.4, 7.4, 3.7$ Hz, 1H), 6.89 (s, 1H), 5.37 – 5.00 (m, 3H), 4.73 (dd, $J = 13.5, 7.7$ Hz, 2H), 3.31 – 3.18 (m, 1H), 2.96 (dd, $J = 12.4, 6.5$ Hz, 1H). ^{13}C NMR (150 MHz, CDCl_3) δ 174.2, 164.3, 160.8, 143.3, 141.9, 136.9, 133.8, 130.8 (d, $J = 13.3$ Hz, 1H), 129.7 (d, $J = 8.6$ Hz), 129.5, 129.1, 128.9, 128.5 (d, $J = 10.5$ Hz), 128.2, 127.4 (d, $J = 3.5$ Hz), 127.3 (d, $J = 17.0$ Hz), 126.3, 124.2 (d, $J = 3.4$ Hz), 120.9, 116.2 (d, $J = 21.9$ Hz), 52.4, 45.8, 43.8. HRMS (ESI-TOF) m/z [M + H] $^+$ calcd for $\text{C}_{25}\text{H}_{21}\text{FNO}_2$ 386.1556, found 386.1551.

The enantiomeric excess was determined to be 91% by HPLC. [IC column, 230 nm, n-hexane:IPA = 97:3, 0.5 mL/min]: 43.920 min (major), 34.227 min (minor);



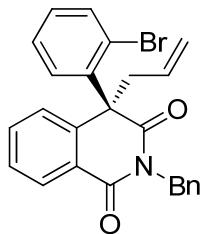
(R)-4-allyl-2-benzyl-4-(2-chlorophenyl)isoquinoline-1,3(2H,4H)-dione(3p):

White solid, 18 mg, 90% yield. mp: 96.3-97.6 °C;

Optical rotation: $[\alpha]_D^{25.2} = -25.00$ (c 3.20, CH_2Cl_2);

^1H NMR (600 MHz, CDCl_3) δ 8.27 (dd, $J = 7.8, 1.2$ Hz, 1H), 7.79 (d, $J = 7.8$ Hz, 1H), 7.52 (d, $J = 7.3$ Hz, 2H), 7.48 – 7.34 (m, 4H), 7.33 – 7.29 (m, 1H), 7.29 – 7.27 (m, 2H), 7.23 (dd, $J = 8.3, 6.2$ Hz, 1H), 6.72 (d, $J = 7.7$ Hz, 1H), 5.30 – 5.06 (m, 3H), 4.76 (d, $J = 10.1$ Hz, 1H), 4.68 (d, $J = 17.0$ Hz, 1H), 3.22 (dd, $J = 12.2, 8.2$ Hz, 1H), 2.91 (dd, $J = 12.2, 6.6$ Hz, 1H). ^{13}C NMR (150 MHz, CDCl_3) δ 174.0, 164.6, 142.0, 140.2, 136.7, 134.3, 133.8, 131.1, 129.8, 129.6, 129.3, 128.9, 128.6, 128.4, 128.1, 127.4, 126.8, 126.4, 125.8, 120.9, 55.7, 47.6, 43.8. HRMS (ESI-TOF) m/z [M + H]⁺ calcd for $\text{C}_{25}\text{H}_{21}\text{ClNO}_2$ 402.1261, found 402.1268.

The enantiomeric excess was determined to be 94% by HPLC. [IC column, 230 nm, n-hexane:IPA = 97:3, 0.5 mL/min]: 43.707 min (major), 27.427 min (minor);



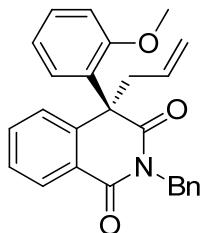
(R)-4-allyl-2-benzyl-4-(2-bromophenyl)isoquinoline-1,3(2H,4H)-dione(3q):

White solid, 21.6 mg, 97% yield. mp: 117.5-118.4 °C;

Optical rotation: $[\alpha]_D^{25.1} = -43.86$ (c 7.60, CH_2Cl_2);

^1H NMR (400 MHz, CDCl_3) δ 8.39 – 8.01 (m, 1H), 7.71 (dd, $J = 8.0, 1.4$ Hz, 1H), 7.51 – 7.45 (m, 2H), 7.42 (dd, $J = 7.9, 1.3$ Hz, 1H), 7.38 (dd, $J = 7.4, 1.6$ Hz, 1H), 7.36 – 7.34 (m, 1H), 7.34 – 7.30 (m, 1H), 7.23 – 7.18 (m, 2H), 7.16 (dt, $J = 3.0, 1.6$ Hz, 1H), 7.14 (dd, $J = 5.5, 3.9$ Hz, 1H), 6.65 – 6.58 (m, 1H), 5.18 – 5.05 (m, 2H), 5.07 – 4.99 (m, 1H), 4.78 – 4.50 (m, 2H), 3.14 (dd, $J = 12.3, 8.1$ Hz, 1H), 2.81 (dd, $J = 12.3, 6.6$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 173.8, 164.6, 142.1, 141.5, 136.6, 134.8, 133.8, 130.0, 129.8, 129.5, 129.3, 128.3, 128.1, 127.4, 127.3, 126.9, 125.8, 125.0, 120.8, 57.3, 48.1, 43.8. HRMS (ESI-TOF) m/z [M + H]⁺ calcd for $\text{C}_{25}\text{H}_{21}\text{BrNO}$ 446.0756, found 446.0756.

The enantiomeric excess was determined to be 92% by HPLC. [IC column, 230 nm, n-hexane:IPA = 95:5, 1.0 mL/min]: 13.880 min (major), 10.260 min (minor);



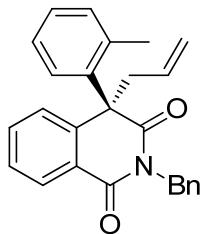
(R)-4-allyl-2-benzyl-4-(2-methoxyphenyl)isoquinoline-1,3(2H,4H)-dione (3r):

White solid, 17.9 mg, 90% yield. mp: 145.7–146.8 °C;

Optical rotation: $[\alpha]_D^{26} = -37.73$ (c 17.60, CH_2Cl_2);

^1H NMR (600 MHz, CDCl_3) δ 8.23 (dd, $J = 7.8, 1.1$ Hz, 1H), 7.66 (dd, $J = 7.7, 1.2$ Hz, 1H), 7.55 (d, $J = 7.3$ Hz, 2H), 7.39 (td, $J = 7.7, 1.4$ Hz, 1H), 7.36 – 7.31 (m, 1H), 7.30 – 7.27 (m, 1H), 7.26 – 7.23 (m, 2H), 7.21 (t, $J = 7.3$ Hz, 1H), 7.07 (td, $J = 7.6, 0.9$ Hz, 1H), 6.85 (d, $J = 7.8$ Hz, 1H), 6.67 (d, $J = 8.1$ Hz, 1H), 5.43 – 4.98 (m, 3H), 4.91 – 4.60 (m, 2H), 3.20 (dd, $J = 12.3, 8.3$ Hz, 1H), 3.00 (s, 3H), 2.96 (dd, $J = 12.3, 6.5$ Hz, 1H). ^{13}C NMR (150 MHz, CDCl_3) δ 175.3, 165.0, 156.0, 143.3, 137.7, 133.5, 132.3, 130.5, 130.0, 129.2, 128.0, 127.4, 126.9, 126.7, 126.1, 125.9, 120.7, 120.4, 111.6, 54.8, 53.1, 46.2, 43.6. HRMS (ESI-TOF) m/z [M + H]⁺ calcd for $\text{C}_{26}\text{H}_{24}\text{NO}_3$ 398.1756, found 398.1751.

The enantiomeric excess was determined to be 92% by HPLC. [IC column, 230 nm, n-hexane:IPA = 97:3, 1.0 mL/min]: 18.980 min (major), 15.887 min (minor);



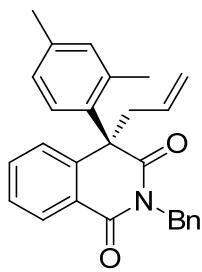
(R)-4-allyl-2-benzyl-4-(o-tolyl)isoquinoline-1,3(2H,4H)-dione (3s):

White solid, 16.8 mg, 88% yield. mp: 88.6–89.7 °C;

Optical rotation: $[\alpha]_D^{25,6} = -55.71$ (c 5.60, CH_2Cl_2);

^1H NMR (600 MHz, CDCl_3) δ 8.40 – 8.24 (m, 1H), 7.76 – 7.72 (m, 1H), 7.58 – 7.54 (m, 2H), 7.48 – 7.45 (m, 1H), 7.44 – 7.40 (m, 1H), 7.39 – 7.33 (m, 1H), 7.32 – 7.23 (m, 4H), 7.10 – 7.02 (m, 1H), 6.85 – 6.79 (m, 1H), 5.26 – 5.19 (m, 2H), 5.19 – 5.11 (m, 1H), 4.75 (dd, $J = 46.4, 13.5$ Hz, 2H), 3.32 – 3.24 (m, 1H), 3.04 – 2.90 (m, 1H), 1.52 (s, 3H). ^{13}C NMR (150 MHz, CDCl_3) δ 174.8, 164.7, 143.0, 140.8, 136.9, 136.7, 134.2, 132.4, 130.3, 130.1, 129.1, 128.4, 128.3, 128.1, 127.7, 127.5, 126.9, 126.6, 126.1, 120.8, 55.8, 48.4, 43.8, 20.3. HRMS (ESI-TOF) m/z [M + H]⁺ calcd for $\text{C}_{26}\text{H}_{24}\text{NO}_2$ 382.1807, found 382.1812.

The enantiomeric excess was determined to be 97% by HPLC. [IC column, 230 nm, n-hexane:IPA = 97:3, 1.0 mL/min]: 14.873 min (major), 9.987 min (minor);



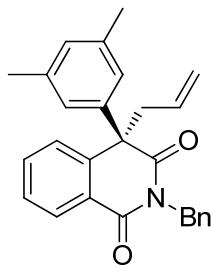
(R)-4-allyl-2-benzyl-4-(2,4-dimethylphenyl)isoquinoline-1,3(2H,4H)-dione (3t):

White solid, 18.6 mg, 94% yield. mp: 155.7–156.6 °C;

Optical rotation: $[\alpha]_D^{25.4} = -47.58$ (c 10.20, CH₂Cl₂);

¹H NMR (600 MHz, CDCl₃) δ 8.26 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.52 (d, *J* = 7.1 Hz, 2H), 7.44 (td, *J* = 7.6, 1.4 Hz, 1H), 7.41 – 7.35 (m, 1H), 7.29 – 7.26 (m, 1H), 7.26 – 7.21 (m, 2H), 7.13 (d, *J* = 7.8 Hz, 1H), 6.85 (s, 1H), 6.81 (d, *J* = 7.7 Hz, 1H), 5.39 – 4.99 (m, 3H), 4.76 (d, *J* = 10.1 Hz, 1H), 4.68 (d, *J* = 17.0 Hz, 1H), 3.24 (dd, *J* = 12.2, 8.2 Hz, 1H), 2.90 (dd, *J* = 12.2, 6.7 Hz, 1H), 2.30 (s, 3H), 1.44 (s, 3H). ¹³C NMR (150 MHz, CDCl₃) δ 175.0, 164.8, 143.4, 138.0, 137.8, 137.0, 136.4, 134.3, 133.4, 130.5, 130.2, 128.4, 127.8, 127.5, 127.0, 126.7, 126.7, 126.1, 120.8, 55.6, 48.5, 43.9, 21.0, 20.2. HRMS (ESI-TOF) m/z [M + H]⁺ calcd for C₂₇H₂₆NO₂ 396.1964, found 396.1958.

The enantiomeric excess was determined to be 91% by HPLC. [IC column, 230 nm, n-hexane:IPA = 97:3, 1.0 mL/min]: 21.520 min (major), 11.593 min (minor);



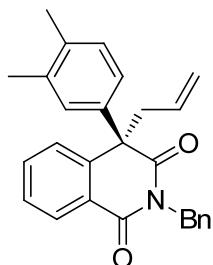
(R)-4-allyl-2-benzyl-4-(3,5-dimethylphenyl)isoquinoline-1,3(2H,4H)-dione (3u):

White solid, 18.8 mg, 95% yield. mp: 144.1–145.2 °C;

Optical rotation: $[\alpha]_D^{26} = -78.33$ (c 16.00, CH₂Cl₂);

¹H NMR (600 MHz, CDCl₃) δ 8.29 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.54 (td, *J* = 7.8, 1.4 Hz, 1H), 7.46 – 7.39 (m, 1H), 7.37 (d, *J* = 6.9 Hz, 2H), 7.26 – 7.18 (m, 3H), 7.11 (d, *J* = 7.8 Hz, 1H), 6.87 (s, 1H), 6.70 (s, 2H), 5.40 – 4.99 (m, 3H), 4.86 (dd, *J* = 17.0, 1.1 Hz, 1H), 4.77 (d, *J* = 10.1 Hz, 1H), 3.60 (dd, *J* = 12.9, 7.9 Hz, 1H), 3.01 (dd, *J* = 12.9, 6.6 Hz, 1H), 2.20 (s, 6H). ¹³C NMR (150 MHz, CDCl₃) δ 174.3, 164.3, 142.8, 142.8, 138.2, 137.0, 134.0, 131.4, 129.3, 128.9, 128.5, 128.2, 127.8, 127.4, 127.3, 125.5, 124.9, 120.0, 55.7, 44.1, 43.7, 21.4. HRMS (ESI-TOF) m/z [M + H]⁺ calcd for C₂₇H₂₆NO₂ 396.1964, found 396.1961.

The enantiomeric excess was determined to be 95% by HPLC. [IC column, 230 nm, n-hexane:IPA = 95:5, 0.8 mL/min]: 11.713 min (major), 9.587 min (minor);



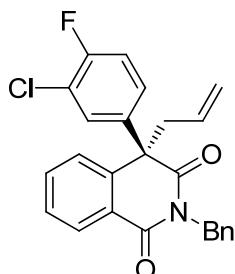
(R)-4-allyl-2-benzyl-4-(3,4-dimethylphenyl)isoquinoline-1,3(2H,4H)-dione (3v):

White solid, 18.6 mg, 94% yield. mp: 122.8–124.2 °C;

Optical rotation: $[\alpha]_D^{25.9} = -50.71$ (c 18.30, CH₂Cl₂);

¹H NMR (600 MHz, CDCl₃) δ 8.28 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.56 – 7.50 (m, 1H), 7.42 (dd, *J* = 11.1, 4.0 Hz, 1H), 7.36 (d, *J* = 6.9 Hz, 2H), 7.25 – 7.18 (m, 3H), 7.12 (d, *J* = 7.8 Hz, 1H), 7.03 (d, *J* = 8.6 Hz, 1H), 6.85 (d, *J* = 5.9 Hz, 2H), 5.35 – 5.02 (m, 3H), 4.86 (d, *J* = 17.0 Hz, 1H), 4.77 (d, *J* = 10.1 Hz, 1H), 3.62 (dd, *J* = 13.0, 7.9 Hz, 1H), 2.99 (dd, *J* = 12.9, 6.6 Hz, 1H), 2.20 (s, 3H), 2.14 (s, 3H). ¹³C NMR (150 MHz, CDCl₃) δ 174.4, 164.3, 142.8, 140.4, 137.0, 137.0, 136.1, 134.0, 131.5, 129.9, 128.9, 128.5, 128.4, 128.2, 127.8, 127.4, 127.3, 125.7, 124.5, 120.0, 55.6, 44.2, 43.8, 19.9, 19.3. HRMS (ESI-TOF) m/z [M + H]⁺ calcd for C₂₇H₂₆NO₂ 396.1964, found 396.1964.

The enantiomeric excess was determined to be 96% by HPLC. [IC column, 230 nm, n-hexane:IPA = 97:3, 0.5 mL/min]: 63.673 min (major), 49.113 min (minor);



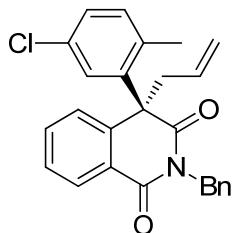
(R)-4-allyl-2-benzyl-4-(3-chloro-4-fluorophenyl)isoquinoline-1,3(2H,4H)-dione (3w):

White solid, 19.9 mg, 95% yield. mp: 87.3–88.6 °C;

Optical rotation: $[\alpha]_D^{25.3} = -30.44$ (c 12.00, CH₂Cl₂);

¹H NMR (600 MHz, CDCl₃) δ 8.31 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.59 (td, *J* = 7.8, 1.3 Hz, 1H), 7.53 – 7.44 (m, 1H), 7.35 (d, *J* = 6.8 Hz, 2H), 7.26 – 7.23 (m, 2H), 7.23 – 7.17 (m, 2H), 7.09 (t, *J* = 12.4 Hz, 1H), 7.02 (t, *J* = 8.6 Hz, 1H), 6.94 (ddd, *J* = 8.7, 4.3, 2.5 Hz, 1H), 5.25 – 5.02 (m, 3H), 4.86 (dd, *J* = 17.0, 0.9 Hz, 1H), 4.79 (d, *J* = 10.2 Hz, 1H), 3.55 (dd, *J* = 12.8, 7.9 Hz, 1H), 2.94 (dd, *J* = 12.8, 6.5 Hz, 1H). ¹³C NMR (150 MHz, CDCl₃) δ 173.5, 163.8, 158.2, 156.6, 141.4, 139.9, 136.7, 134.3, 130.6, 129.8, 128.9, 128.4, 128.3, 128.0, 127.7, 121.3, 120.7, 116.7, 116.6, 55.2, 44.7, 43.9. HRMS (ESI-TOF) m/z [M + H]⁺ calcd for C₂₅H₂₀ClFNO₂ 420.1167, found 420.1167.

The enantiomeric excess was determined to be 92% by HPLC. [IC column, 230 nm, n-hexane:IPA = 97:3, 1.0 mL/min]: 10.587 min (major), 9.113 min (minor);



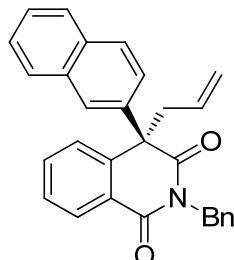
(R)-4-allyl-2-benzyl-4-(5-chloro-2-methylphenyl)isoquinoline-1,3(2H,4H)-dione (3x):

White solid, 19.1 mg, 92% yield. mp: 153.4–154.6 °C;

Optical rotation: $[\alpha]_D^{25.4} = -56.22$ (c 12.00, CH_2Cl_2);

^1H NMR (600 MHz, CDCl_3) δ 8.28 (dd, $J = 7.9, 1.1$ Hz, 1H), 7.77 – 7.62 (m, 1H), 7.56 – 7.49 (m, 2H), 7.47 (td, $J = 7.6, 1.4$ Hz, 1H), 7.41 (tt, $J = 11.1, 5.5$ Hz, 1H), 7.28 (t, $J = 1.5$ Hz, 1H), 7.27 (s, 1H), 7.25 – 7.20 (m, 2H), 7.11 – 6.86 (m, 1H), 6.93 – 6.64 (m, 1H), 5.43 – 5.00 (m, 3H), 4.79 (t, $J = 19.6$ Hz, 1H), 4.76 – 4.52 (m, 1H), 3.22 (dd, $J = 12.1, 8.2$ Hz, 1H), 2.88 (dd, $J = 12.1, 6.6$ Hz, 1H), 1.44 (s, 3H). ^{13}C NMR (150 MHz, CDCl_3) δ 174.34, 164.5, 142.7, 142.2, 136.8, 135.3, 134.4, 133.6, 132.1, 130.2, 129.8, 128.6, 128.5, 128.1, 127.9, 127.8, 127.6, 126.5, 126.1, 121.3, 55.7, 48.4, 44.0, 19.8. HRMS (ESI-TOF) m/z [M + H]⁺ calcd for $\text{C}_{26}\text{H}_{23}\text{ClNO}_2$ 416.1417, found 416.1409.

The enantiomeric excess was determined to be 93% by HPLC. [IC column, 230 nm, n-hexane:IPA = 99:1, 0.5 mL/min]: 32.353 min (major), 27.593 min (minor);



(R)-4-allyl-2-benzyl-4-(naphthalen-2-yl)isoquinoline-1,3(2H,4H)-dione (3y):

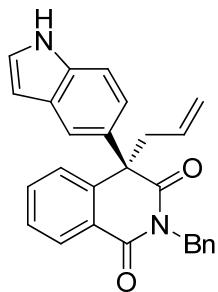
White solid, 20.4 mg, 98% yield. mp: 173.1–174.8 °C;

Optical rotation: $[\alpha]_D^{25.2} = -74.90$ (c 16.20, CH_2Cl_2);

^1H NMR (600 MHz, CDCl_3) δ 8.33 (dd, $J = 7.9, 1.1$ Hz, 1H), 7.83 – 7.75 (m, 3H), 7.69 (d, $J = 8.7$ Hz, 1H), 7.53 (td, $J = 7.8, 1.4$ Hz, 1H), 7.51 – 7.47 (m, 2H), 7.47 – 7.43 (m, 1H), 7.39 (dd, $J = 7.7, 1.5$ Hz, 2H), 7.26 – 7.18 (m, 3H), 7.11 (d, $J = 7.8$ Hz, 1H), 7.05 (dd, $J = 8.7, 1.9$ Hz, 1H), 5.25 (dd, $J = 11.9, 5.4$ Hz, 1H), 5.21 (ddd, $J = 10.1, 9.0, 4.6$ Hz, 1H), 5.13 (d, $J = 13.9$ Hz, 1H), 4.91 (dd, $J = 17.0, 1.1$ Hz, 1H), 4.82 (d, $J = 10.2$ Hz, 1H), 3.76 (dd, $J = 12.8, 7.9$ Hz, 1H), 3.14 (dd, $J = 12.7, 6.5$ Hz, 1H).

^{13}C NMR (150 MHz, CDCl_3) δ 174.2, 164.2, 142.4, 140.1, 136.9, 134.0, 133.1, 132.5, 131.2, 129.0, 128.7, 128.7, 128.3, 127.9, 127.6, 127.5, 127.4, 126.5, 126.4, 125.9, 125.8, 125.5, 120.3, 56.1, 44.5, 43.8. HRMS (ESI-TOF) m/z [M + H]⁺ calcd for $\text{C}_{29}\text{H}_{24}\text{NO}_2$ 418.1807, found 418.1803.

The enantiomeric excess was determined to be 92% by HPLC. [IC column, 230 nm, n-hexane:IPA = 97:3, 1.0 mL/min]: 24.393 min (major), 14.673 min (minor);



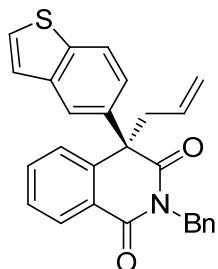
(R)-4-allyl-2-benzyl-4-(1H-indol-5-yl)isoquinoline-1,3(2H,4H)-dione(3z):

White solid, 20.1mg, 99% yield. mp: 163.5–164.2 °C;

Optical rotation: $[\alpha]_D^{25.2} = -74.11$ (c 15.40, CH_2Cl_2);

^1H NMR (600 MHz, CDCl_3) δ 8.30 (dd, $J = 8.0, 1.1$ Hz, 1H), 8.20 (s, 1H), 7.58 – 7.47 (m, 2H), 7.45 – 7.40 (m, 1H), 7.36 (d, $J = 6.4$ Hz, 2H), 7.24 – 7.18 (m, 4H), 7.16 (dt, $J = 12.3, 6.3$ Hz, 2H), 6.81 (dd, $J = 8.6, 1.8$ Hz, 1H), 6.51 – 6.44 (m, 1H), 5.41 – 5.02 (m, 3H), 4.90 (d, $J = 17.1$ Hz, 1H), 4.85 – 4.68 (m, 1H), 3.75 (dd, $J = 12.9, 7.9$ Hz, 1H), 3.10 (dd, $J = 12.9, 6.6$ Hz, 1H). ^{13}C NMR (150 MHz, CDCl_3) δ 174.9, 164.4, 143.5, 137.1, 134.8, 134.5, 133.9, 131.8, 128.8, 128.4, 128.2, 128.1, 127.8, 127.3, 127.2, 125.6, 125.0, 121.6, 119.9, 119.2, 111.3, 103.0, 55.9, 44.6, 43.8. HRMS (ESI-TOF) m/z [M + H] $^+$ calcd for $\text{C}_{27}\text{H}_{23}\text{N}_2\text{O}_2$ 407.1760, found 407.1763.

The enantiomeric excess was determined to be 90% by HPLC. [IC column, 230 nm, n-hexane:IPA = 80:10, 1.0 mL/min]: 24.400 min (major), 8.680 min (minor);



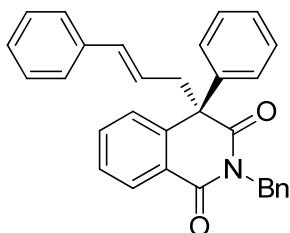
(R)-4-allyl-4-(benzo[b]thiophen-5-yl)-2-benzylisoquinoline-1,3(2H,4H)-dione(3aa):

White solid, 20.3 mg, 96% yield. mp: 113.2–114.5 °C;

Optical rotation: $[\alpha]_D^{25.3} = -56.37$ (c 21.50, CH_2Cl_2);

^1H NMR (600 MHz, CDCl_3) δ 8.32 (dd, $J = 8.0, 1.1$ Hz, 1H), 7.76 – 7.72 (m, 1H), 7.68 (d, $J = 1.7$ Hz, 1H), 7.63 (dd, $J = 6.5, 2.9$ Hz, 1H), 7.54 (td, $J = 7.8, 1.4$ Hz, 1H), 7.45 – 7.42 (m, 2H), 7.36 (dd, $J = 7.5, 1.5$ Hz, 2H), 7.25 (d, $J = 5.4$ Hz, 1H), 7.22 – 7.20 (m, 2H), 7.12 (dd, $J = 7.1, 2.9$ Hz, 1H), 6.99 (dd, $J = 8.6, 1.8$ Hz, 1H), 5.36 – 5.02 (m, 3H), 4.90 (d, $J = 17.0$ Hz, 1H), 4.81 (d, $J = 10.2$ Hz, 1H), 3.73 – 3.70 (m, 1H), 3.09 (dd, $J = 12.8, 6.5$ Hz, 1H). ^{13}C NMR (150 MHz, CDCl_3) δ 174.3, 164.2, 143.3, 142.6, 139.8, 139.2, 136.9, 134.0, 131.3, 130.5, 129.0, 128.9, 128.7, 128.4, 127.9, 127.6, 125.4, 124.0, 123.8, 122.8, 122.1, 120.3, 55.9, 44.5, 43.8. HRMS (ESI-TOF) m/z [M + H] $^+$ calcd for $\text{C}_{27}\text{H}_{22}\text{NO}_2\text{S}$ 424.1371, found 424.1374.

The enantiomeric excess was determined to be 93% by HPLC. [IA column, 230 nm, n-hexane:IPA = 94:6, 0.8 mL/min]: 41.233 min (major), 30.827 min (minor);



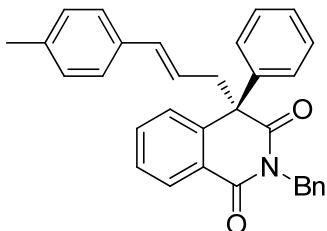
(R)-2-benzyl-4-cinnamyl-4-phenylisoquinoline-1,3(2H,4H)-dione(3ab):

White solid, 21.9 mg, 99% yield. Yellowish paste;

Optical rotation: $[\alpha]_D^{25.1} = -51.73$ (c 10.00, CH_2Cl_2);

^1H NMR (400 MHz, CDCl_3) δ 8.29 (dd, $J = 7.9, 1.3$ Hz, 1H), 7.59 (td, $J = 7.7, 1.4$ Hz, 1H), 7.51 – 7.42 (m, 1H), 7.34 – 7.30 (m, 2H), 7.30 – 7.28 (m, 2H), 7.27 (s, 1H), 7.20 (d, $J = 2.0$ Hz, 2H), 7.18 (d, $J = 1.5$ Hz, 2H), 7.17 (t, $J = 2.2$ Hz, 2H), 7.15 – 7.10 (m, 1H), 7.10 – 7.04 (m, 2H), 7.01 – 6.88 (m, 2H), 6.24 (d, $J = 15.8$ Hz, 1H), 5.75 – 5.40 (m, 1H), 5.30 – 5.08 (m, 2H), 3.85 (dd, $J = 13.0, 8.0$ Hz, 1H), 3.18 (ddd, $J = 13.0, 6.9, 1.1$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 174.2, 164.0, 142.8, 142.5, 136.8, 136.5, 135.0, 134.1, 129.0, 128.7, 128.4, 128.4, 128.3, 128.3, 127.8, 127.7, 127.5, 127.4, 127.2, 126.2, 125.7, 122.6, 56.4, 43.8, 43.6. HRMS (ESI-TOF) m/z [M + H] $^+$ calcd for $\text{C}_{31}\text{H}_{26}\text{NO}_2$ 444.1964, found 444.1966.

The enantiomeric excess was determined to be 97% by HPLC. [IA column, 230 nm, n-hexane:IPA = 85:15, 1.0 mL/min]: 10.800 min (major), 27.867 min (minor);



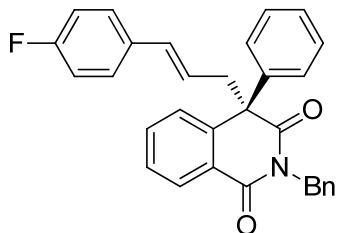
(R,E)-2-benzyl-4-phenyl-4-(3-(p-tolyl)allyl)isoquinoline-1,3(2H,4H)-dione(3ac):

White solid, 22.6 mg, 99% yield. mp: 103.4–104.5 °C;

Optical rotation: $[\alpha]_D^{25.3} = -40.40$ (c 13.20, CH_2Cl_2);

^1H NMR (400 MHz, CDCl_3) δ 8.27 (dd, $J = 7.9, 1.2$ Hz, 1H), 7.62 – 7.55 (m, 1H), 7.48 – 7.41 (m, 1H), 7.33 – 7.29 (m, 2H), 7.29 (d, $J = 4.2$ Hz, 2H), 7.27 (d, $J = 1.6$ Hz, 1H), 7.21 – 7.16 (m, 2H), 7.16 (d, $J = 2.8$ Hz, 1H), 7.15 – 7.11 (m, 1H), 7.13 – 7.07 (m, 2H), 6.98 (d, $J = 7.9$ Hz, 2H), 6.83 (d, $J = 8.1$ Hz, 2H), 6.19 (d, $J = 15.7$ Hz, 1H), 5.62 – 5.39 (m, 1H), 5.14 (dd, $J = 32.2, 13.9$ Hz, 2H), 3.82 (ddd, $J = 13.0, 7.8, 0.8$ Hz, 1H), 3.15 (ddd, $J = 13.0, 7.0, 1.1$ Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 174.2, 164.1, 142.9, 142.6, 137.3, 136.9, 134.9, 134.0, 133.8, 129.0, 128.7, 128.7, 128.5, 128.3, 127.9, 127.7, 127.6, 127.4, 127.2, 126.1, 125.8, 121.5, 56.4, 43.8, 43.7, 21.1. HRMS (ESI-TOF) m/z [M + H] $^+$ calcd for $\text{C}_{32}\text{H}_{28}\text{NO}_2$ 458.2120, found 458.2117.

The enantiomeric excess was determined to be 92% by HPLC. [IA column, 230 nm, n-hexane:IPA = 85:15, 1.0 mL /min]: 8.807 min (major), 26.893 min (minor);



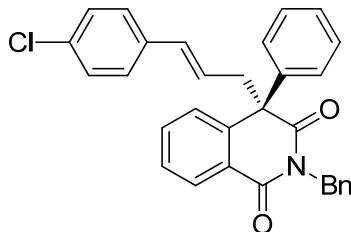
(R,E)-2-benzyl-4-(3-(4-fluorophenyl)allyl)-4-phenylisoquinoline-1,3(2H,4H)-dione (3ad):

White solid, 22.6 mg, 98% yield. mp: 113.2–114.7 °C;

Optical rotation: $[\alpha]_D^{26.1} = -44.30$ (c 21.70, CH_2Cl_2);

^1H NMR (400 MHz, CDCl_3) δ 8.29 (dd, $J = 7.9, 1.2$ Hz, 1H), 7.63 – 7.55 (m, 1H), 7.45 (dt, $J = 11.2, 2.0$ Hz, 1H), 7.33 – 7.27 (m, 5H), 7.18 (ddd, $J = 10.2, 6.2, 2.7$ Hz, 3H), 7.14 – 7.05 (m, 3H), 6.86 (d, $J = 7.0$ Hz, 4H), 6.16 (d, $J = 15.8$ Hz, 1H), 5.50 – 5.36 (m, 1H), 5.14 (dd, $J = 31.1, 13.8$ Hz, 2H), 3.81 (ddd, $J = 13.0, 8.0, 0.7$ Hz, 1H), 3.15 (ddd, $J = 13.0, 6.8, 1.1$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 174.2, 164.0, 163.4, 161.0, 142.8, 142.5, 136.8, 134.1, 133.8, 132.7 (d, $J = 3.4$ Hz), 128.8, 128.7, 128.6, 128.3, 127.8, 127.7, 127.6, 127.4, 127.3, 125.7, 122.3 (d, $J = 2.1$ Hz), 115.3, 56.4, 43.8, 43.6. HRMS (ESI-TOF) m/z [M + H] $^+$ calcd for $\text{C}_{31}\text{H}_{25}\text{FNO}_2$ 462.1869, found 462.1876

The enantiomeric excess was determined to be 90% by HPLC. [IA column, 230 nm, n-hexane:IPA = 85:15, 1.0 mL/min]: 9.740 min (major), 27.660 min (minor);



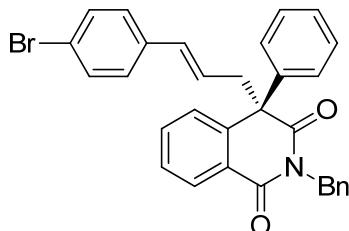
(R,E)-2-benzyl-4-(3-(4-chlorophenyl)allyl)-4-phenylisoquinoline-1,3(2H,4H)-dione (3ae):

White solid, 22.9 mg, 96% yield. mp: 142.2–143.5 °C;

Optical rotation: $[\alpha]_D^{25.3} = -69.45$ (c 17.70, CH_2Cl_2);

^1H NMR (400 MHz, CDCl_3) δ 8.29 (dd, $J = 7.9, 1.2$ Hz, 1H), 7.59 (td, $J = 7.6, 1.5$ Hz, 1H), 7.50 – 7.42 (m, 1H), 7.32 (dd, $J = 5.0, 3.7$ Hz, 2H), 7.30 (dd, $J = 3.3, 1.7$ Hz, 2H), 7.28 (dd, $J = 3.8, 1.2$ Hz, 1H), 7.21 – 7.16 (m, 3H), 7.16 – 7.14 (m, 1H), 7.14 – 7.12 (m, 2H), 7.12 – 7.07 (m, 2H), 6.92 – 6.72 (m, 2H), 6.14 (d, $J = 15.8$ Hz, 1H), 5.70 – 5.37 (m, 1H), 5.14 (dd, $J = 35.7, 13.8$ Hz, 2H), 3.82 (ddd, $J = 13.0, 7.9, 0.9$ Hz, 1H), 3.14 (ddd, $J = 13.0, 7.0, 1.2$ Hz, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ 174.1, 164.0, 142.7, 142.4, 136.8, 135.0, 134.1, 133.8, 133.1, 129.0, 128.8, 128.7, 128.7, 128.5, 128.4, 128.3, 127.8, 127.7, 127.4, 127.3, 125.7, 123.3, 56.3, 43.8, 43.6. HRMS (ESI-TOF) m/z [M + H] $^+$ calcd for $\text{C}_{31}\text{H}_{25}\text{ClNO}_2$ 478.1574, found 478.1576

The enantiomeric excess was determined to be 95% by HPLC. [IA column, 230 nm, n-hexane:IPA = 85:15, 1.0 mL/min]: 9.653 min (major), 34.707 min (minor);



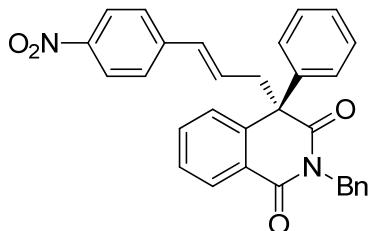
(*R,E*)-2-benzyl-4-(3-(4-bromophenyl)allyl)-4-phenylisoquinoline-1,3(2*H*,4*H*)-dione(3af):

White solid, 25.8 mg, 99% yield. mp: 142.6–143.5 °C;

Optical rotation: $[\alpha]_D^{26.1} = -12.95$ (c 19.30, CH_2Cl_2);

^1H NMR (400 MHz, CDCl_3) δ 8.29 (dd, $J = 7.9, 1.2$ Hz, 1H), 7.59 (td, $J = 7.7, 1.4$ Hz, 1H), 7.52 – 7.38 (m, 1H), 7.32 (d, $J = 5.2$ Hz, 2H), 7.32 – 7.30 (m, 2H), 7.29 (s, 2H), 7.27 (d, $J = 1.7$ Hz, 1H), 7.21 – 7.15 (m, 3H), 7.14 (dd, $J = 3.7, 2.3$ Hz, 1H), 7.12 – 7.07 (m, 2H), 6.74 (d, $J = 8.4$ Hz, 2H), 6.12 (d, $J = 15.8$ Hz, 1H), 5.71 – 5.42 (m, 1H), 5.14 (dd, $J = 37.0, 13.8$ Hz, 2H), 3.81 (dd, $J = 13.0, 7.9$ Hz, 1H), 3.13 (ddd, $J = 13.0, 7.0, 1.0$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 174.1, 164.0, 142.7, 142.4, 136.8, 135.4, 134.1, 133.8, 131.4, 128.8, 128.7, 128.7, 128.3, 127.8, 127.7, 127.7, 127.3, 127.3, 125.7, 123.5, 121.2, 56.3, 43.8, 43.6. HRMS (ESI-TOF) m/z [M + H]⁺ calcd for $\text{C}_{31}\text{H}_{25}\text{BrNO}_2$ 522.1069, found 522.1069.

The enantiomeric excess was determined to be 96% by HPLC. [IA column, 230 nm, n-hexane:IPA = 80:20, 1.0 mL/min]: 8.733 min (major), 34.093 min (minor);



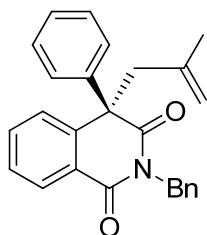
(*R,E*)-2-benzyl-4-(3-(4-nitrophenyl)allyl)-4-phenylisoquinoline-1,3(2*H*,4*H*)-dione(3ag):

White solid, 23.9 mg, 98% yield. mp: 151.8–152.7 °C;

Optical rotation: $[\alpha]_D^{25.9} = -51.79$ (c 19.00, CH_2Cl_2);

^1H NMR (400 MHz, CDCl_3) δ 8.30 (dd, $J = 7.9, 1.2$ Hz, 1H), 8.10 – 7.95 (m, 2H), 7.61 (td, $J = 7.7, 1.5$ Hz, 1H), 7.55 – 7.43 (m, 1H), 7.34 (d, $J = 3.6$ Hz, 1H), 7.33 – 7.31 (m, 2H), 7.31 – 7.27 (m, 2H), 7.21 – 7.16 (m, 3H), 7.14 (dt, $J = 3.3, 2.8$ Hz, 1H), 7.10 (ddd, $J = 8.7, 3.8, 2.2$ Hz, 2H), 6.96 (dd, $J = 9.0, 2.0$ Hz, 2H), 6.22 (d, $J = 15.8$ Hz, 1H), 5.90 – 5.59 (m, 1H), 5.14 (dd, $J = 43.0, 13.7$ Hz, 2H), 3.87 (ddd, $J = 13.0, 7.8, 0.8$ Hz, 1H), 3.18 (ddd, $J = 13.0, 7.1, 1.2$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 173.9, 163.9, 146.8, 142.7, 142.4, 142.1, 136.8, 134.2, 133.0, 128.9, 128.8, 128.3, 128.0, 127.9, 127.8, 127.7, 127.4, 127.3, 126.6, 125.7, 123.7, 56.1, 43.8, 43.6. HRMS (ESI-TOF) m/z [M + H]⁺ calcd for $\text{C}_{31}\text{H}_{25}\text{N}_2\text{O}_4$ 488.1814, found 488.1811.

The enantiomeric excess was determined to be 94% by HPLC. [IA column, 230 nm, n-hexane:IPA = 80:20, 1.0 mL/min]: 14.213 min (major), 65.413 min (minor);



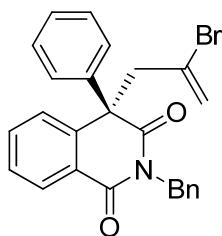
(R)-2-benzyl-4-(2-methylallyl)-4-phenylisoquinoline-1,3(2H,4H)-dione (3ah):

White solid, 18.1 mg, 95% yield. mp: 106.5–107.4 °C;

Optical rotation: $[\alpha]_D^{25.7} = -28.53$ (c 10.00, CH₂Cl₂);

¹H NMR (400 MHz, CDCl₃) δ 8.42 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.66 (td, *J* = 7.6, 1.5 Hz, 1H), 7.60 – 7.53 (m, 1H), 7.51 – 7.44 (m, 2H), 7.43 – 7.34 (m, 4H), 7.35 – 7.29 (m, 3H), 7.25 – 7.20 (m, 2H), 5.36 (d, *J* = 13.8 Hz, 1H), 5.18 (d, *J* = 13.8 Hz, 1H), 4.53 (d, *J* = 97.9 Hz, 2H), 3.91 (d, *J* = 13.5 Hz, 1H), 3.09 (d, *J* = 13.4 Hz, 1H), 1.28 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 174.2, 164.3, 143.7, 142.5, 140.0, 136.8, 133.7, 128.9, 128.7, 128.7, 128.4, 128.2, 127.6, 127.5, 127.3, 127.2, 125.8, 115.9, 55.6, 46.9, 43.9, 23.5. HRMS (ESI-TOF) m/z [M + H]⁺ calcd for C₂₆H₂₄NO₂ 382.807, found 382.1810.

The enantiomeric excess was determined to be 95% by HPLC. [IC column, 230 nm, n-hexane:IPA = 95:5, 1.0 mL/min]: 8.307 min (major), 7.273 min (minor);



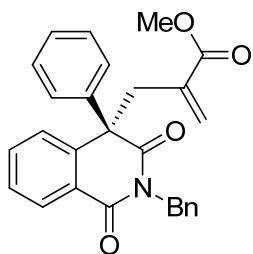
(R)-2-benzyl-4-(2-bromoallyl)-4-phenylisoquinoline-1,3(2H,4H)-dione (3ai):

White solid, 21.1 mg, 95% yield. Yellowish paste;

Optical rotation: $[\alpha]_D^{25.1} = -14.00$ (c 8.00, CH₂Cl₂);

¹H NMR (400 MHz, CDCl₃) δ 8.36 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.59 (td, *J* = 7.6, 1.5 Hz, 1H), 7.50 (td, *J* = 7.8, 1.2 Hz, 1H), 7.44 (dd, *J* = 5.0, 1.8 Hz, 1H), 7.39 – 7.33 (m, 2H), 7.29 – 7.26 (m, 2H), 7.25 – 7.18 (m, 3H), 7.17 – 7.12 (m, 1H), 7.10 – 7.06 (m, 2H), 5.29 (d, *J* = 13.8 Hz, 1H), 5.25 – 5.19 (m, 2H), 5.08 (d, *J* = 13.8 Hz, 1H), 4.31 (d, *J* = 14.5 Hz, 1H), 3.45 (d, *J* = 14.5 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 173.4, 164.0, 143.3, 142.8, 140.7, 136.6, 133.7, 129.0, 128.9, 128.8, 128.4, 128.2, 128.0, 127.8, 127.3, 127.0, 126.8, 121.9, 55.3, 49.5, 44.1. HRMS (ESI-TOF) m/z [M + H]⁺ calcd for C₂₅H₂₁BrNO₂ 446.0756, found 446.0756.

The enantiomeric excess was determined to be 93% by HPLC. [IA column, 254 nm, n-hexane:IPA = 70:30, 0.5 mL/min]: 17.100 min (major), 15.353 min (minor);



(*R*)-methyl 2-((2-benzyl-1,3-dioxo-4-phenyl-1,2,3,4-tetrahydroisoquinolin-4-yl)methyl)acrylate (3aj):

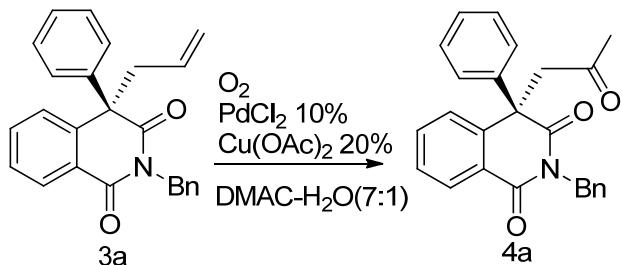
White solid, 19.6 mg, 92% yield. mp: 179.9–108.6 °C;

Optical rotation: $[\alpha]_D^{25.1} = -3.01$ (c 12.40, CH₂Cl₂);

¹H NMR (400 MHz, CDCl₃) δ 8.26 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.52 (td, *J* = 7.6, 1.5 Hz, 1H), 7.47 – 7.41 (m, 1H), 7.42 – 7.36 (m, 2H), 7.32 – 7.27 (m, 3H), 7.26 – 7.18 (m, 3H), 7.17 – 7.13 (m, 2H), 7.12 (d, *J* = 0.6 Hz, 1H), 5.72 (s, 1H), 5.29 (d, *J* = 13.6 Hz, 1H), 5.15 – 4.89 (m, 2H), 3.81 (t, *J* = 10.1 Hz, 1H), 3.59 (d, *J* = 13.5 Hz, 1H), 3.39 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 174.1, 167.0, 164.0, 143.0, 141.3, 136.8, 135.3, 133.5, 129.2, 129.1, 128.7, 128.5, 128.4, 128.2, 127.7, 127.7, 127.4, 127.3, 125.7, 56.1, 51.7, 43.9, 40.2. HRMS (ESI-TOF) m/z [M + H]⁺ calcd for C₂₇H₂₄NO₄ 426.1705, found 426.1707.

The enantiomeric excess was determined to be 87% by HPLC. [IC column, 254 nm, n-hexane:IPA = 90:10, 1.0 mL/min]: 18.133 min (major), 13.760 min (minor);

General Procedure for Synthesis of 4a:



(R)-2-benzyl-4-(2-oxopropyl)-4-phenylisoquinoline-1,3(2H,4H)-dione(4a):

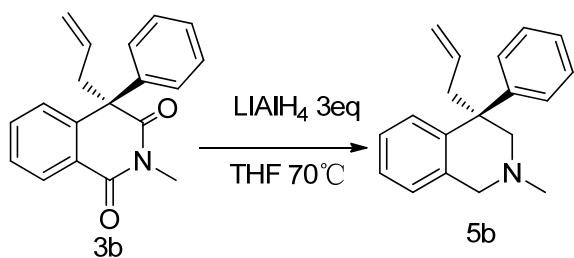
To a solution of 3a (36.7 mg, 0.1 mmol), PdCl_2 (1.8 mg, 0.01 mmol), $\text{Cu}(\text{OAc})_2$ (3.6 mg, 0.02 mmol) in DMAC-H₂O (7:1, 1 mL) stay at room temperature under O₂ atmosphere, and the mixture was stirred at the same temperature for 20 h until 3a was completely consumed (monitored by TLC). To the mixture, saturated aqueous NH₄Cl solution was added, and the mixture was extracted with EtOAc. The organic layers were combined, washed with brine, dried over anhydrous Na₂SO₄, concentrated, Purification by flash column chromatography on SiO₂ (10:1 hexanes:EtOAc) afforded 34 mg (0.1 mmol, 89% yield) of the Coupling product as a white solid (m.p.135.3-136.6 °C).

Optical rotation: $[\alpha]_{D}^{25.5} = -92.21$ (c 20.10, CH₂Cl₂);

¹H NMR (600 MHz, CDCl₃) δ 8.33 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.56 (td, *J* = 7.7, 1.4 Hz, 1H), 7.50 – 7.41 (m, 1H), 7.20 (dd, *J* = 7.1, 1.4 Hz, 2H), 7.19 – 7.17 (m, 4H), 7.17 – 7.15 (m, 1H), 7.14 (s, 1H), 7.13 (s, 1H), 6.98 (dt, *J* = 3.8, 2.5 Hz, 2H), 5.16 (s, 2H), 4.31 (d, *J* = 18.1 Hz, 1H), 3.72 (dd, *J* = 16.1, 9.3 Hz, 1H), 2.11 (s, 3H). ¹³C NMR (150 MHz, CDCl₃) δ 204.5, 174.3, 164.4, 141.9, 141.1, 136.9, 134.0, 129.6, 128.9, 128.3, 128.0, 127.8, 127.1, 126.9, 126.6, 125.3, 52.8, 52.2, 44.1, 30.0. HRMS (ESI-TOF) m/z [M + H]⁺ calcd for C₂₅H₂₂NO₃ 384.1600, found 384.1598.

The enantiomeric excess was determined to be 91% by HPLC. [IA column, 230 nm, n-hexane:IPA = 80:20, 1.0mL/min]: 16.247 min (major), 49.493min (minor);

General Procedure for Synthesis of 5b:



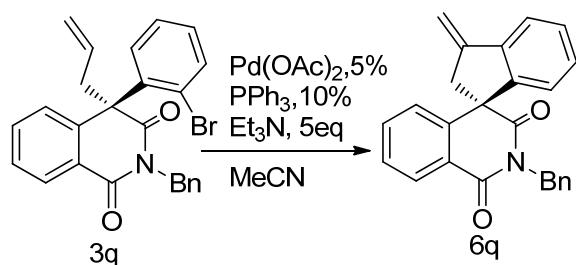
(R)-2'-benzyl-3-methylene-2,3-dihydro-1'H-spiro[indene-1,4'-isoquinoline]-1',3'(2'H)-dione(5b):

To a solution of 3b (29 mg, 0.1 mmol) in anhydrous THF (3 mL) at room temperature under N₂ atmosphere, LiAlH₄ (11 mg, 0.3 mmol) was added within half an hour, heat to 70 °C and the mixture was stirred at the same temperature for 5 h until 3b was completely consumed (monitored by TLC). To the mixture, 4ml H₂O was added slowly, and the mixture was extracted with EtOAc. The organic layers were combined, washed with brine, dried over anhydrous Na₂SO₄, concentrated and purified by flash column chromatography on SiO₂ (4:1 hexanes:EtOAc) to give 5b (19.8 mg, 75%) as a colorless oil . Optical rotation: $[\alpha]_{D}^{25.4} = -34.87$ (c 10.40, CH₂Cl₂)

¹H NMR (600 MHz, CDCl₃) δ 7.29 – 7.26 (m, 2H), 7.24 (dd, *J* = 6.7, 1.6 Hz, 2H), 7.18 – 7.14 (m, 1H), 7.13 (dd, *J* = 7.3, 1.5 Hz, 1H), 7.10 (td, *J* = 7.5, 1.7 Hz, 1H), 7.09 – 7.06 (m, 1H), 7.00 (dd, *J* = 7.7, 1.2 Hz, 1H), 5.71 (ddt, *J* = 17.2, 10.2, 7.0 Hz, 1H), 5.24 – 4.87 (m, 2H), 3.61 (dd, *J* = 47.6, 14.7 Hz, 2H), 3.02 – 2.90 (m, 2H), 2.80 – 2.69 (m, 2H), 2.32 (s, 3H). ¹³C NMR (150 MHz, CDCl₃) δ 148.5, 139.9, 135.8, 135.7, 129.5, 128.1, 128.0, 126.5, 126.2, 126.1, 126.1, 117.7, 66.6, 59.2, 47.2, 46.4, 44.5. HRMS (ESI-TOF) m/z [M + H]⁺ calcd for C₁₉H₂₂N 264.1752, found 264.1752.

The enantiomeric excess was determined to be 86% by HPLC. [OD-H column, 230 nm, n-hexane:IPA = 98:2, 1.0mL/min]: 36.800 min (major), 28.380 min (minor);

General Procedure for Synthesis of 6q:



(R)-4-allyl-2-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline(6q):

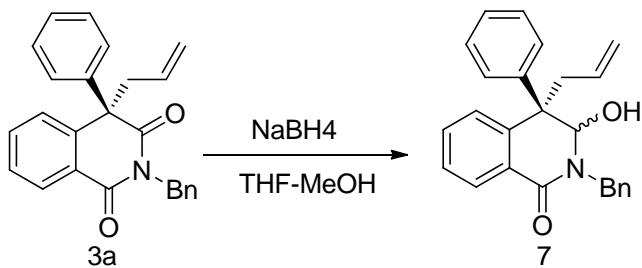
To a solution of 3q (44.5 mg, 0.1 mmol), Pd(OAc)₂ (1.1 mg, 0.005 mmol), PPh₃ (2.62 mg, 0.01 mmol), Et₃N (70 ul, 0.5 mmol) in anhydrous MeCN (2 mL) stay at 90 °C under N₂ atmosphere, and the mixture was stirred at the same temperature for 15 h until 3q was completely consumed (monitored by TLC). To the mixture, saturated aqueous NH₄Cl solution was added, and the mixture was extracted with EtOAc. The organic layers were combined, washed with brine, dried over anhydrous Na₂SO₄, concentrated and purified by flash column chromatography on SiO₂ (10:1 hexanes:EtOAc) afforded 32mg (0.1mmol, 89% yield) of the Coupling product as a white solid (m.p.70.5–71.2 °C)..

Optical rotation: [α]_D^{25,6} = -42.22 (c 8.40, CH₂Cl₂);

¹H NMR (400 MHz, CDCl₃) δ 8.18 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.53 (d, *J* = 7.7 Hz, 1H), 7.43 – 7.35 (m, 3H), 7.34 – 7.28 (m, 1H), 7.21 (dt, *J* = 2.0, 1.5 Hz, 2H), 7.19 – 7.17 (m, 2H), 7.07 – 7.00 (m, 1H), 6.97 (dd, *J* = 7.9, 0.7 Hz, 1H), 6.62 (d, *J* = 7.7 Hz, 1H), 5.59 (t, *J* = 2.4 Hz, 1H), 5.22 – 5.06 (m, 3H), 3.68 (dt, *J* = 16.7, 2.3 Hz, 1H), 3.09 (dt, *J* = 16.7, 2.1 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 174.7, 164.4, 148.4, 147.0, 143.8, 140.6, 137.1, 134.4, 129.4, 129.1, 128.8, 128.7, 128.4, 127.7, 127.6, 126.5, 124.2, 124.0, 121.4, 104.8, 57.4, 48.1, 44.0. HRMS (ESI-TOF) m/z [M + H]⁺ calcd for C₂₅H₂₀NO₂ 366.1494, found 366.1494.

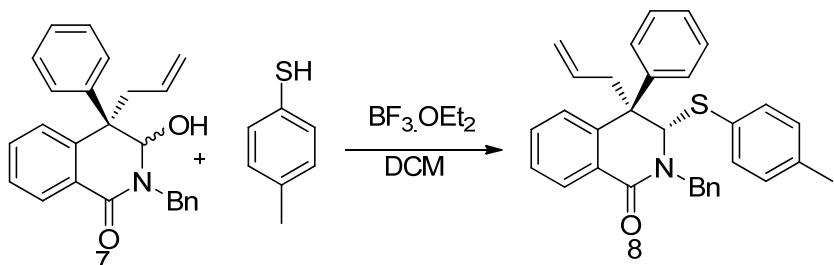
The enantiomeric excess was determined to be 91% by HPLC. [OD-H column, 254nm, n-hexane:IPA = 95:5, 0.5mL/min]: 50.920min (major), 39.027 min (minor);

General Procedure for Synthesis of 7a-10a:



(3S,4R)-4-allyl-2-benzyl-3-hydroxy-4-phenyl-3,4-dihydroisoquinolin-1(2H)-one(7a):

To a solution of **3a** (0.367 g, 1 mmol) in anhydrous THF-MeOH (2:1, 5 mL) was added NaBH₄ (0.302 g, 8 mmol) portionwise at -5 °C under N₂ atmosphere, and the mixture was stirred at the same temperature for 4 h until **3a** was completely consumed (monitored by TLC). To the mixture, saturated aqueous NH₄Cl solution was added, and the mixture was extracted with EtOAc. The organic layers were combined, washed with brine, dried over anhydrous Na₂SO₄, concentrated, Purification by flash column chromatography on SiO₂ (4:1 hexanes:EtOAc) to give **7** (0.307 g, 83%) as mixture of diastereoisomers as a colorless oil.



(3S,4R)-4-allyl-2-benzyl-4-phenyl-3-(p-tolylthio)-3,4-dihydroisoquinolin-1(2H)-one(8a):

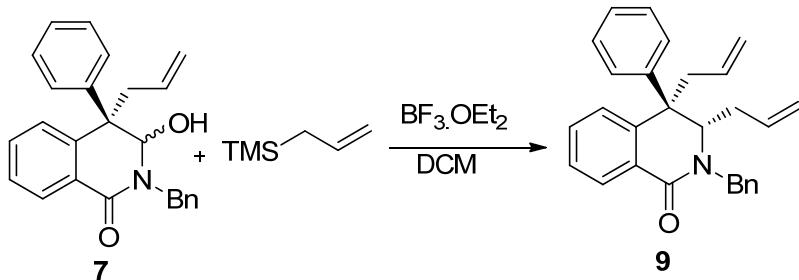
The **7** (37 mg, 0.1 mmol) was dissolved in dichloromethane (1 mL) and cooled to -78 °C. 4-methylbenzenethiol (37.2 mg, 0.3 mmol) was added, and the reaction was allowed to stir for 5 min under N₂. 1 M solution of BF₃OEt₂ (0.9 mL, 0.9 mmol) in dichloromethane was added over 75 minutes via syringe pump, and the reaction was subsequently allowed to gradually warm to 0 °C. The reaction was quenched with aqueous NaHCO₃, diluted with EtOAc, and partitioned in a separatory funnel. The aqueous layer was extracted twice with ethyl acetate, and the combined organic layers were washed with brine, dried over MgSO₄, and concentrated. ¹H NMR analysis of the unpurified reaction mixture in CDCl₃ revealed a >20:1 ratio of trans:cis diastereomers. Purification by flash column chromatography on SiO₂ (10:1 hexanes:EtOAc) afforded 45.6 mg (0.1 mmol, 96% yield) of both diastereomers of the product as a white solid (m.p. 97.1–98.4 °C).

Optical rotation: $[\alpha]_D^{26.1} = -180.51$ (c 11.80, CH_2Cl_2);

¹H NMR (400 MHz, CDCl₃) δ 7.84 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.73 – 7.61 (m, 1H), 7.57 – 7.50 (m, 1H), 7.36 (td, *J* = 7.6, 1.1 Hz, 1H), 7.23 – 7.14 (m, 3H), 7.06 – 7.00 (m, 2H), 7.01 – 6.95 (m, 3H), 6.87 – 6.79 (m, 2H), 6.70 (d, *J* = 7.3 Hz, 2H), 6.37 (dd, *J* = 8.4, 1.0 Hz, 2H), 5.53 – 5.42 (m, 2H), 5.21 (dd, *J* = 17.2, 1.5 Hz, 1H), 5.13 – 5.00 (m, 2H), 3.83 (d, *J* = 14.6 Hz, 1H), 3.35 (dd, *J* = 15.1, 7.5 Hz, 1H), 3.09 (ddt, *J* = 15.1, 5.8, 1.7 Hz, 1H), 2.32 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 164.2, 143.0, 141.3, 138.7, 135.9, 135.4, 134.8, 132.1, 129.7, 129.2, 128.9, 128.4, 128.3, 127.9, 127.7, 127.5, 127.1, 126.8, 126.3, 126.0, 118.4, 75.3, 50.4, 48.6, 43.3, 21.1.

HRMS (ESI-TOF) m/z [M + H]⁺ calcd for C₃₂H₃₀NOS 476.2048, found 476.2051.

The enantiomeric excess was determined to be 92% by HPLC. [IA column, 230 nm, n-hexane:IPA = 94:6, 0.8 mL/min]: 28.487 min (major), 37.640 min (minor);



(3*S*,4*R*)-3,4-diallyl-2-benzyl-4-phenyl-3,4-dihydroisoquinolin-1(2*H*)-one(9a):

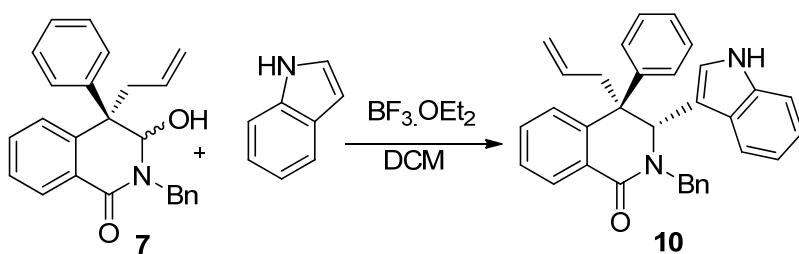
The 7 (37 mg, 0.1 mmol) was dissolved in dichloromethane (1 mL) and cooled to -78 °C. Allyltrimethylsilane (48 µL, 0.3 mmol) was added, and the reaction was allowed to stir for 5 min under N₂. A 1 M solution of BF₃OEt₂ (0.9 mL, 0.9 mmol) in dichloromethane was added over 75 minutes via syringe pump, and the reaction was subsequently allowed to gradually warm to 0 °C. The reaction was quenched with aqueous NaHCO₃, diluted with EtOAc, and partitioned in a separatory funnel. The aqueous layer was extracted twice with ethyl acetate, and the combined organic layers were washed with brine, dried over MgSO₄, and concentrated. ¹H NMR analysis of the unpurified reaction mixture in CDCl₃ revealed a 5:1 ratio of trans:cis diastereomers. Purification by flash column chromatography on SiO₂ (10:1 hexanes:EtOAc) afforded 31mg (80% yield) of both diastereomers of the allylated product as a white solid (m.p.105.7-106.8 °C).

Optical rotation: [α]_D^{25.5} = -43.19 (c 14.20, CH₂Cl₂);

¹H NMR (400 MHz, CDCl₃) δ 8.18 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.60 (dt, *J* = 7.1, 3.6 Hz, 1H), 7.58 – 7.53 (m, 1H), 7.47 (td, *J* = 7.5, 1.4 Hz, 1H), 7.14 (t, *J* = 7.4 Hz, 1H), 7.03 (dd, *J* = 10.3, 4.7 Hz, 2H), 7.01 – 6.95 (m, 1H), 6.86 (dd, *J* = 10.1, 3.6 Hz, 2H), 6.84 – 6.78 (m, 2H), 6.56 – 6.50 (m, 2H), 5.81 – 5.64 (m, 1H), 5.61 – 5.43 (m, 1H), 5.28 (d, *J* = 14.7 Hz, 1H), 5.12 (dd, *J* = 17.1, 1.6 Hz, 1H), 5.07 – 4.92 (m, 3H), 3.95 (dd, *J* = 7.9, 4.3 Hz, 1H), 3.89 (d, *J* = 14.7 Hz, 1H), 2.95 (dd, *J* = 15.0, 7.2 Hz, 1H), 2.80 (ddt, *J* = 15.0, 6.1, 1.6 Hz, 1H), 2.64 – 2.50 (m, 1H), 2.31 (dq, *J* = 14.4, 7.7 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 164.1, 143.5, 142.4, 136.7, 134.8, 134.7, 132.0, 130.2, 128.7, 128.6, 128.3, 127.8, 127.6, 127.0, 126.9, 126.3, 126.2, 118.0, 64.6, 51.1, 49.1, 41.9, 35.3.

HRMS (ESI-TOF) m/z [M + H]⁺ calcd for C₂₈H₂₈NO 394.2171, found 394.2172.

The enantiomeric excess was determined to be 92% by HPLC. [IA column, 230 nm, n-hexane:IPA = 94:6, 0.8mL/min]: 52.907 min (major), 41.000 min (minor);



(3*S*,4*R*)-4-allyl-2-benzyl-3-(1*H*-indol-3-yl)-4-phenyl-3,4-dihydroisoquinolin-1(2*H*)-one(10a):

The 7 (37 mg, 0.1 mmol) was dissolved in dichloromethane (1 mL) and cooled to -78 °C. 1*H*-indole

(36mg, 0.3 mmol) was added, and the reaction was allowed to stir for 5 min under N₂. A 1 M solution of BF₃·OEt₂ (0.9mL, 0.9 mmol) in dichloromethane was added over 75 minutes via syringe pump, and the reaction was subsequently allowed to gradually warm to 0 °C. The reaction was quenched with aqueous NaHCO₃, diluted with EtOAc, and partitioned in a separatory funnel. The aqueous layer was extracted twice with ethyl acetate, and the combined organic layers were washed with brine, dried over MgSO₄, and concentrated. ¹H NMR analysis of the unpurified reaction mixture in CDCl₃ revealed a 5:1 ratio of trans:cis diastereomers. Purification by flash column chromatography on SiO₂ (10:1 hexanes:EtOAc) afforded 35mg (75% yield) of both diastereomers of the product as a white solid (m.p. 79-79.6 °C).

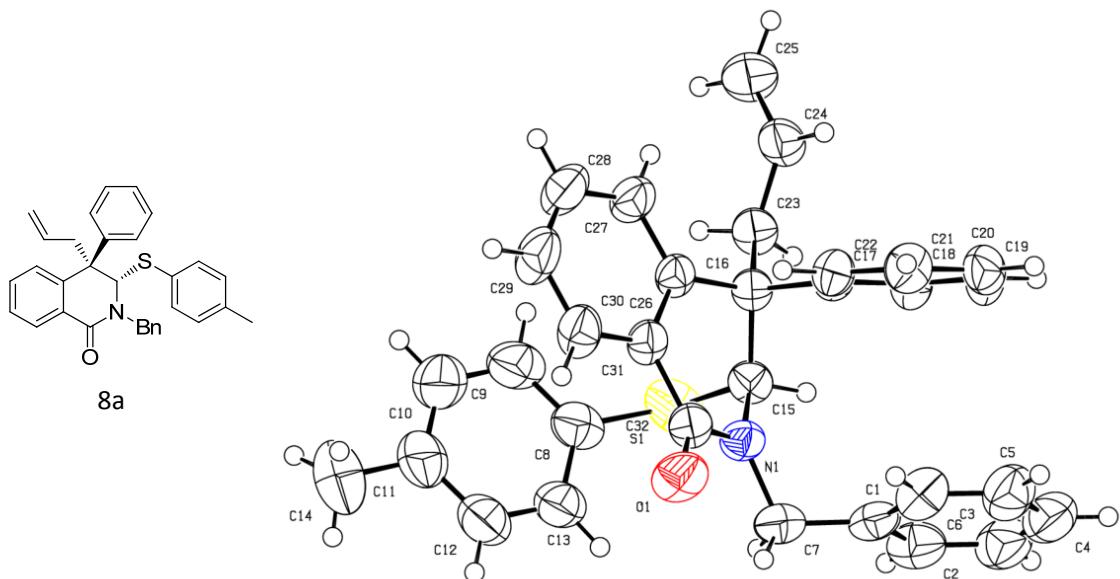
Optical rotation: [α]_D^{25.2} = -118.81 (c 10.10, CH₂Cl₂);

¹H NMR (400 MHz,) δ 8.44 (s, 1H), 8.30 (d, J = 7.1 Hz, 1H), 7.67 (d, J = 7.2 Hz, 1H), 7.61 – 7.51 (m, 2H), 7.38 (d, J = 6.4 Hz, 1H), 7.23 (d, J = 5.1 Hz, 2H), 7.18 (d, J = 7.3 Hz, 1H), 7.14 – 7.03 (m, 3H), 6.99 (t, J = 7.5 Hz, 2H), 6.74 (d, J = 7.0 Hz, 2H), 6.68 (d, J = 7.2 Hz, 2H), 6.29 (s, 1H), 5.39 (d, J = 14.8 Hz, 1H), 5.30 (s, 2H), 5.15 (s, 1H), 4.85 – 4.71 (m, 2H), 3.43 (d, J = 14.8 Hz, 1H), 2.76 (d, J = 15.7 Hz, 1H), 2.57 (dd, J = 15.4, 8.2 Hz, 1H). ¹³C NMR (100 MHz,) δ 164.2, 144.2, 142.4, 136.3, 135.4, 135.0, 132.2, 130.6, 128.6, 128.3, 128.2, 128.1, 127.8, 127.3, 127.1, 126.9, 126.3, 122.6, 122.2, 120.1, 117.9, 117.2, 112.6, 111.5, 53.4, 49.9, 48.3, 42.1.

HRMS (ESI-TOF) m/z [M + H]⁺ calcd for C₃₃H₂₉N₂O 469.2280, found 469.2282.

The enantiomeric excess was determined to be 92% by HPLC. [IC column, 230 nm, n-hexane:IPA = 85:15, 1.0mL/min]: 10.413 min (major), 8.627 min (minor);

Single X-ray structure date of 8a:



Bond precision: C-C = 0.0043 Å Wavelength=1.54184

Cell: a=9.25182(19) b=14.2225(3) c=10.38203(19)

alpha=90 beta=106.464(2) gamma=90

Temperature: 293 K

Calculated Reported

Volume 1310.10(5) 1310.09(4)

Space group P 21 P 1 21 1

Hall group P 2yb P 2yb

Moiety formula C32 H29 N O S C32 H29 N O S

Sum formula C32 H29 N O S C32 H29 N O S

Mr 475.62 475.62

D_x,g cm⁻³ 1.206 1.206

Z 2 2

μ (mm⁻¹) 1.274 1.274

F000 504.0 504.0

F000' 505.92

h,k,lmax 11,17,12 11,17,12

Nref 5278[2751] 3578

Tmin,Tmax 0.858,0.903 0.805,1.000

Tmin' 0.858

Correction method= # Reported T Limits: Tmin=0.805 Tmax=1.000

AbsCorr = MULTI-SCAN

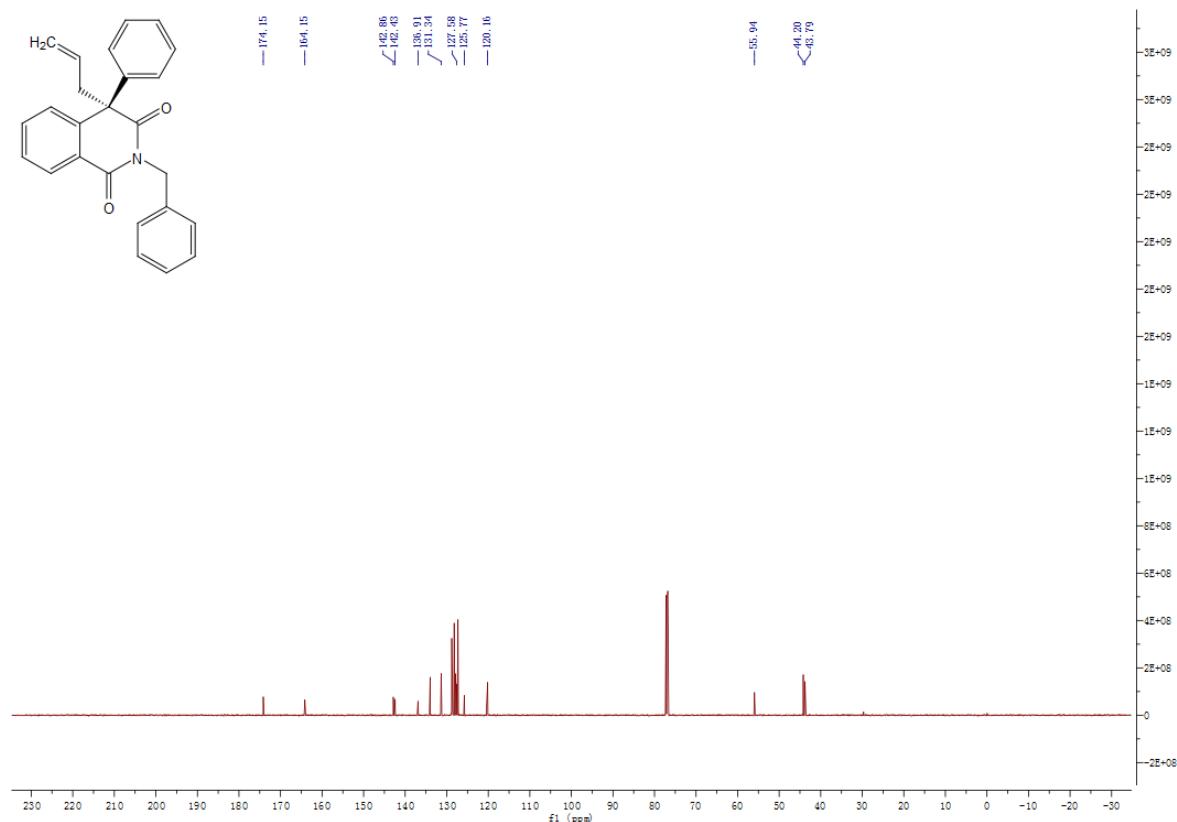
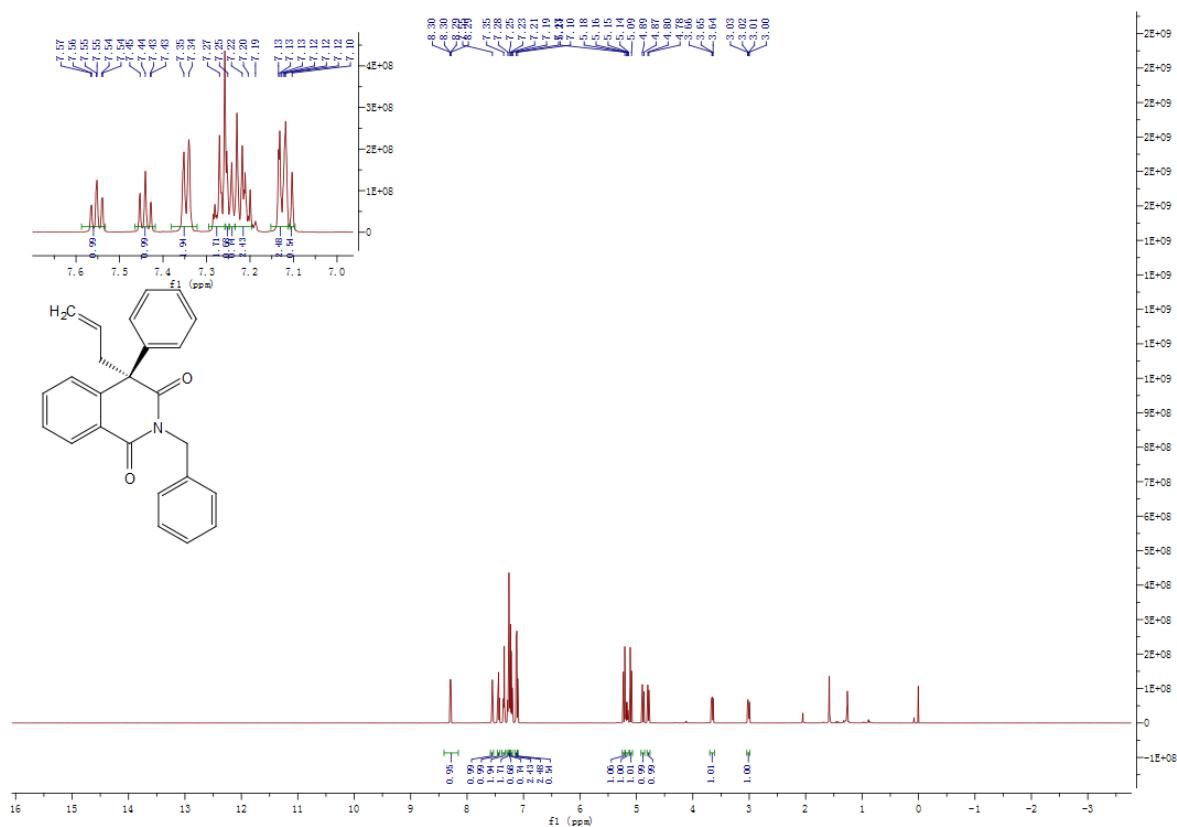
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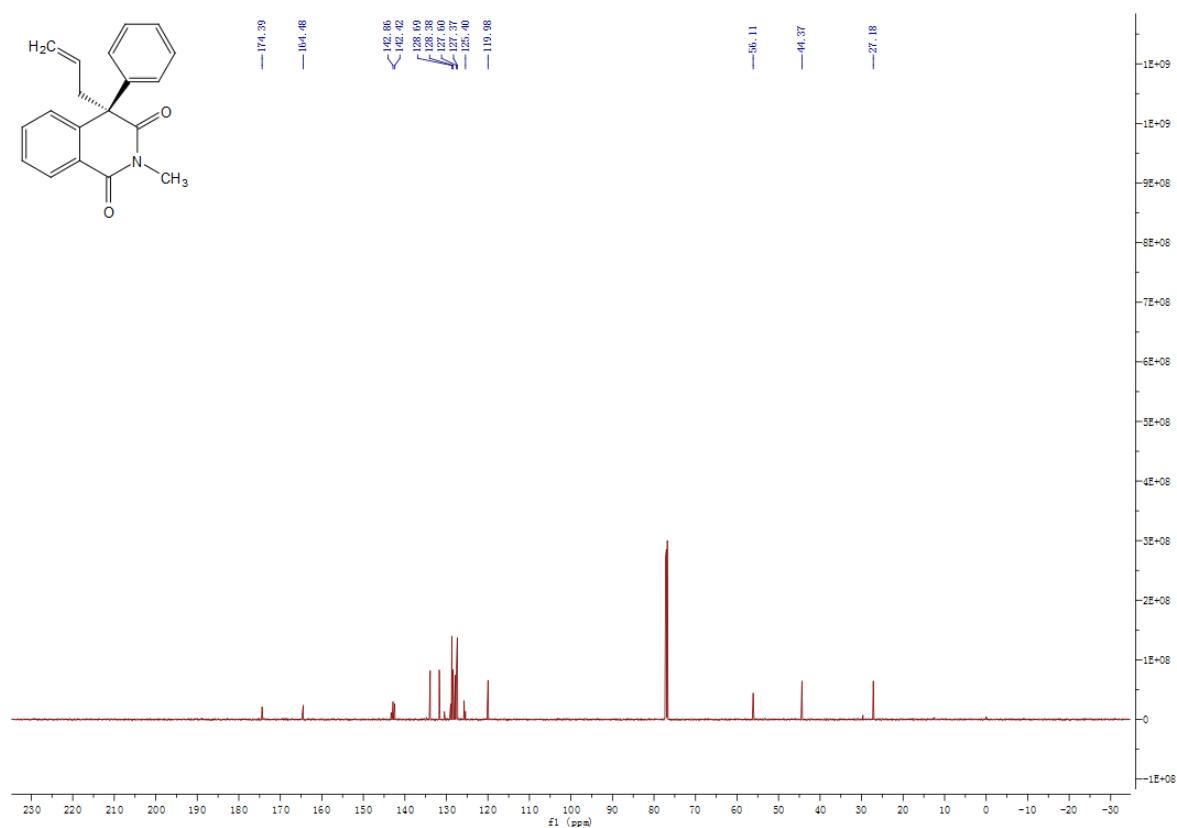
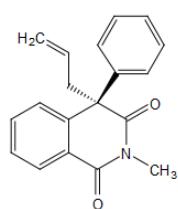
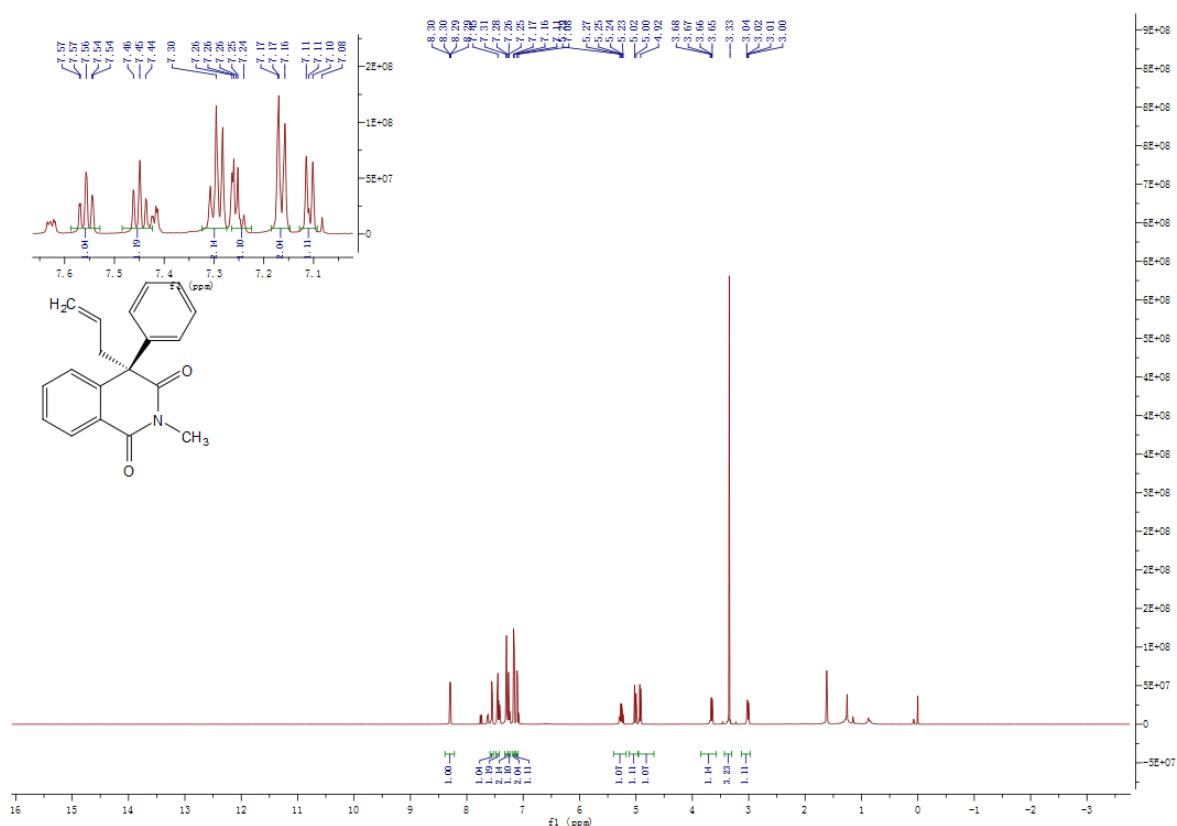
S = 1.056 Npar= 326

^1H and ^{13}C NMR Spectra:

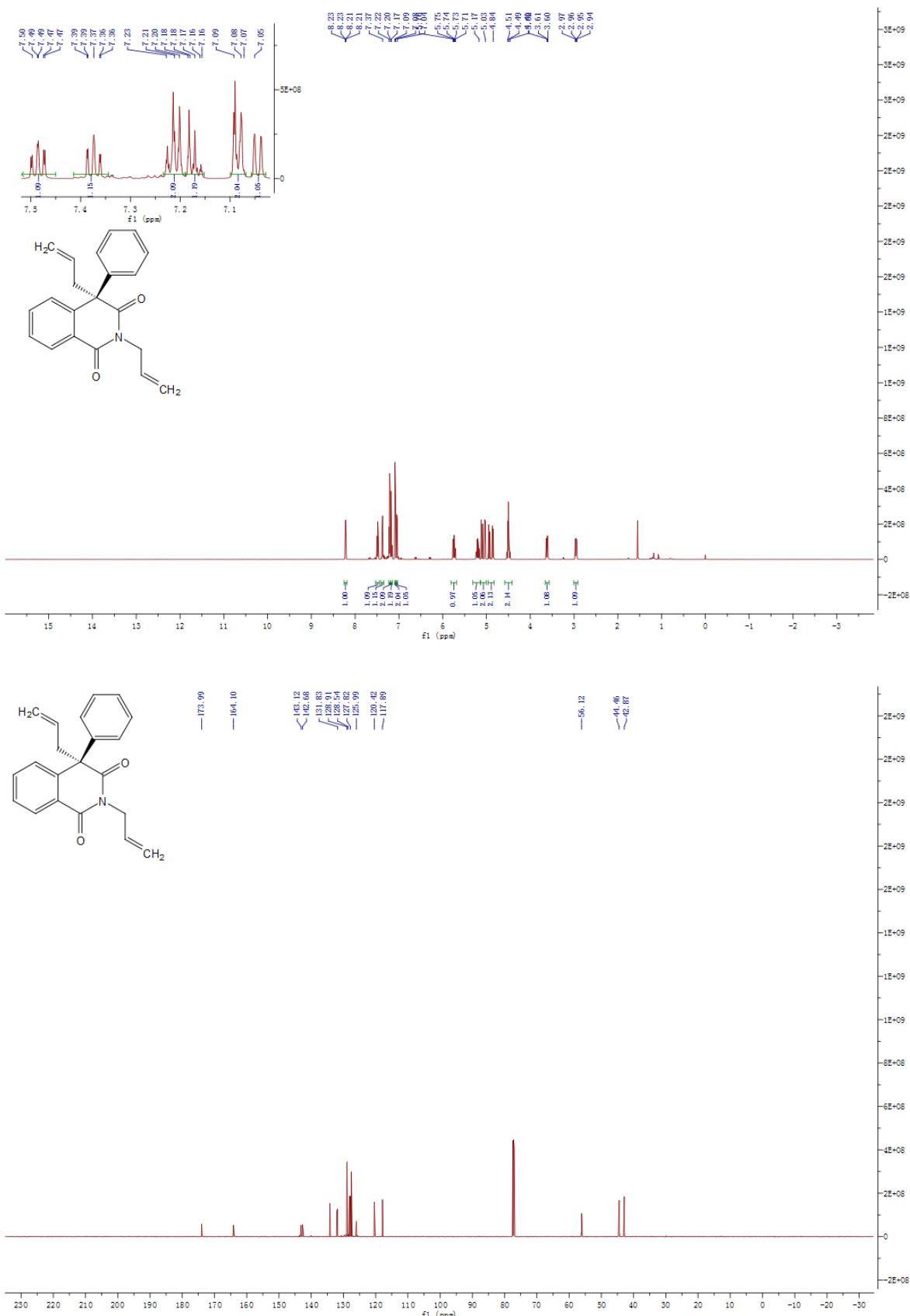
(R)-4-allyl-2-benzyl-4-phenylisoquinoline-1,3(2*H*,4*H*)-dione(3a):



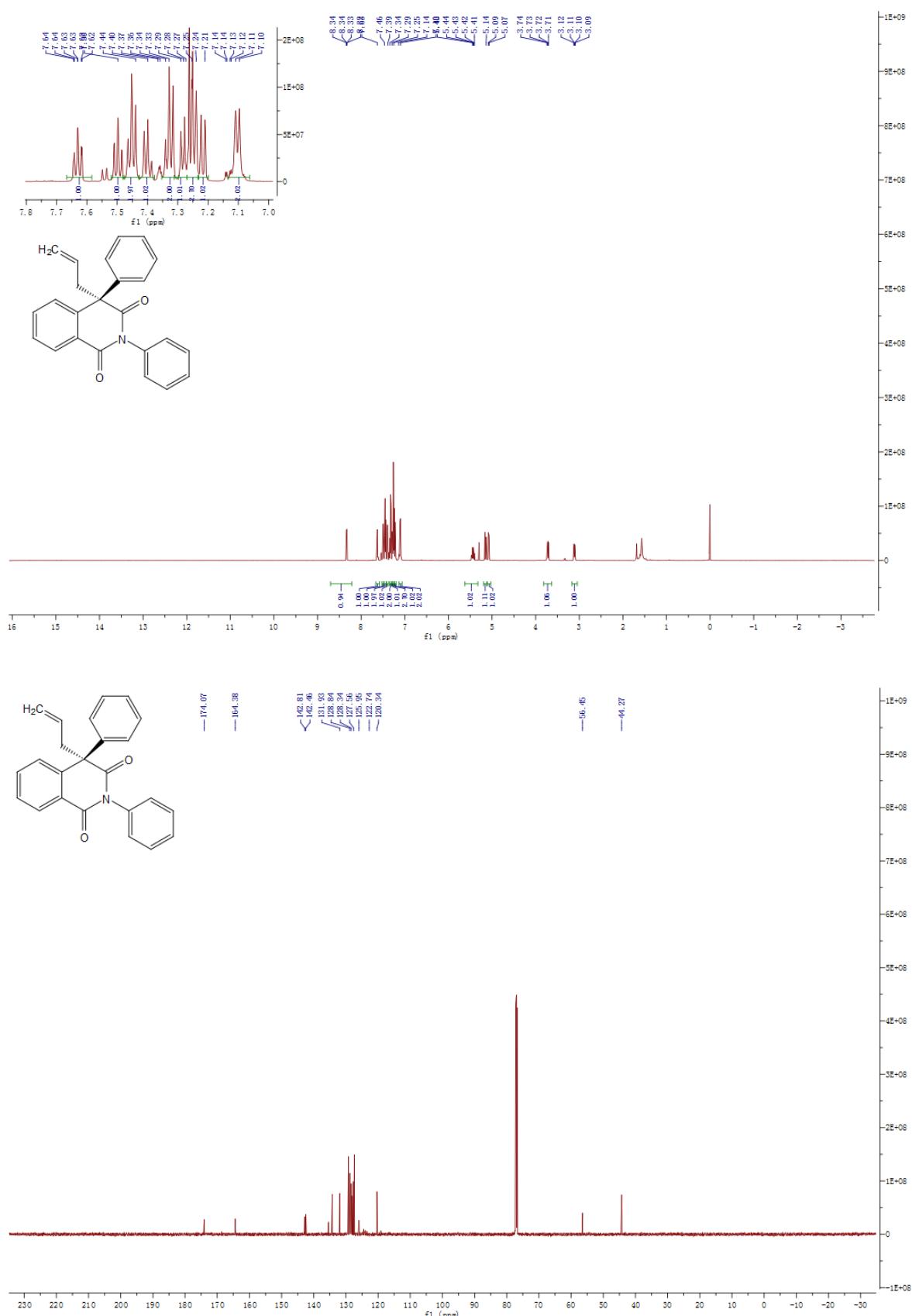
(R)-4-allyl-2-methyl-4-phenylisoquinoline-1,3(2H,4H)-dione(3b):



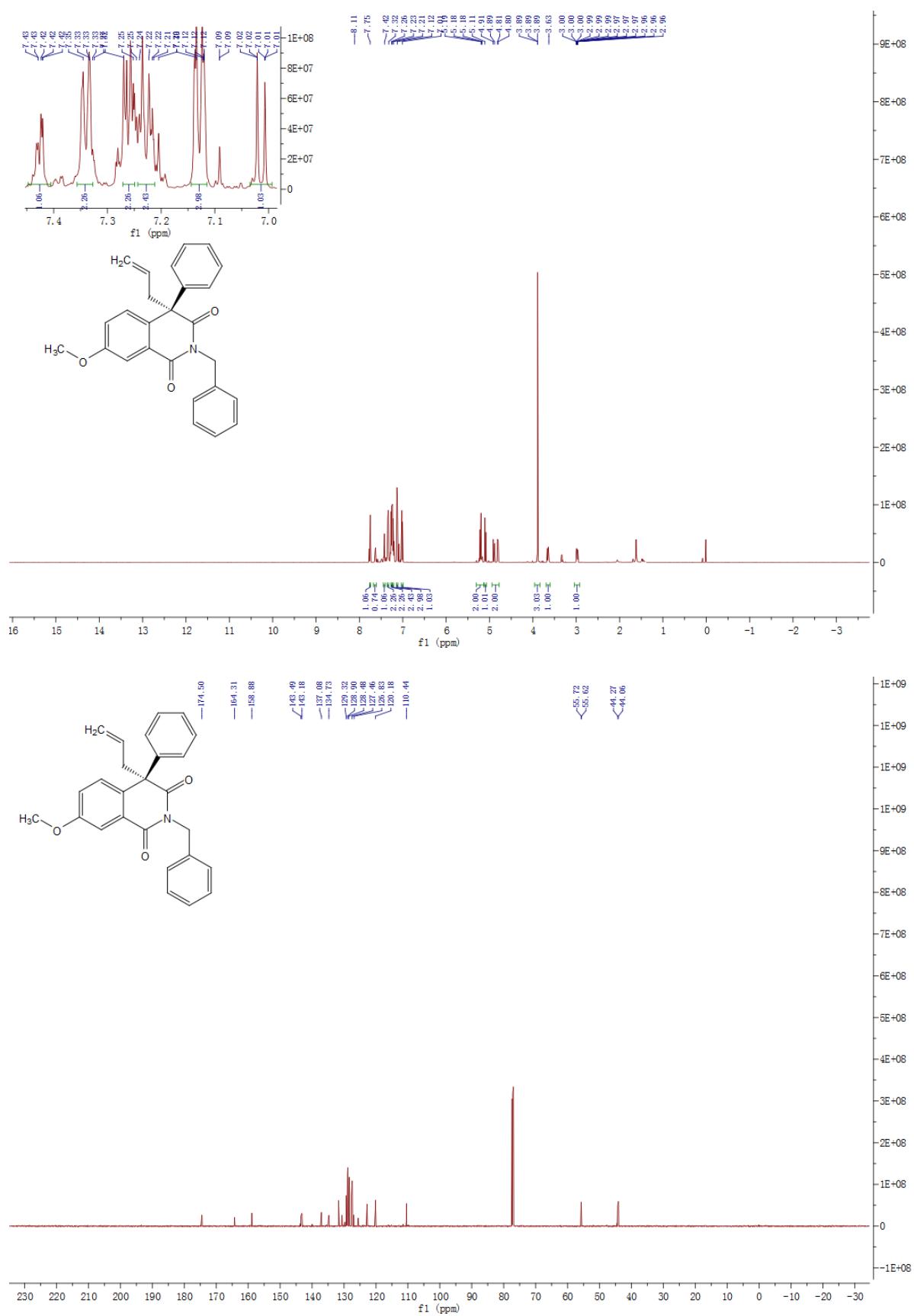
(R)-2,4-diallyl-4-phenylisoquinoline-1,3(2H,4H)-dione(3c):



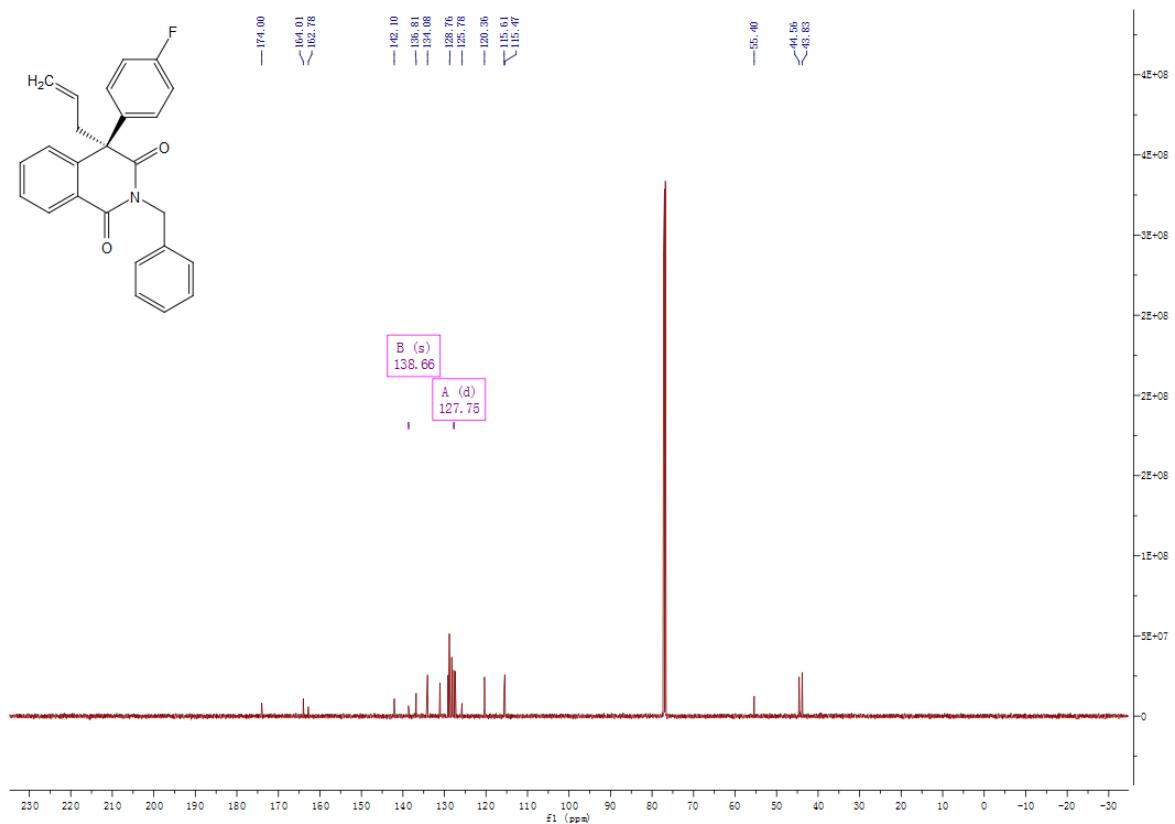
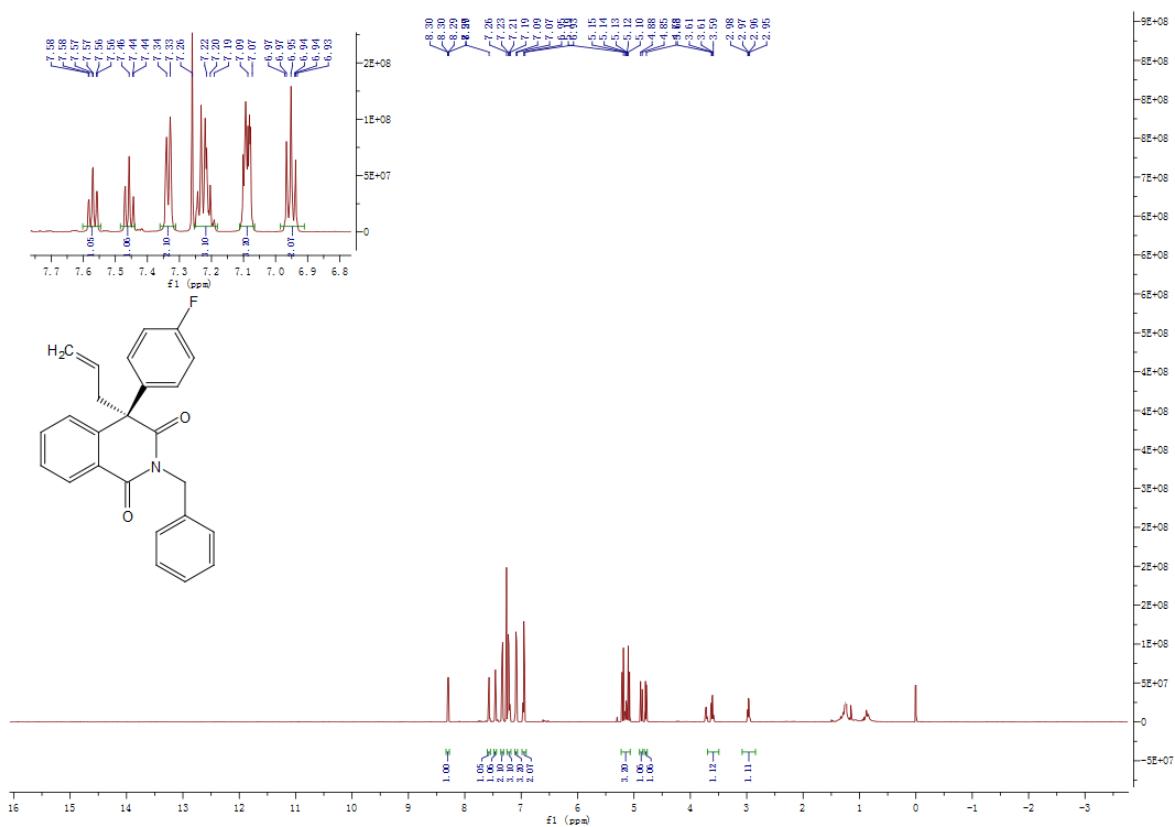
(R)-4-allyl-2,4-diphenylisoquinoline-1,3(2*H*,4*H*)-dione(3d):



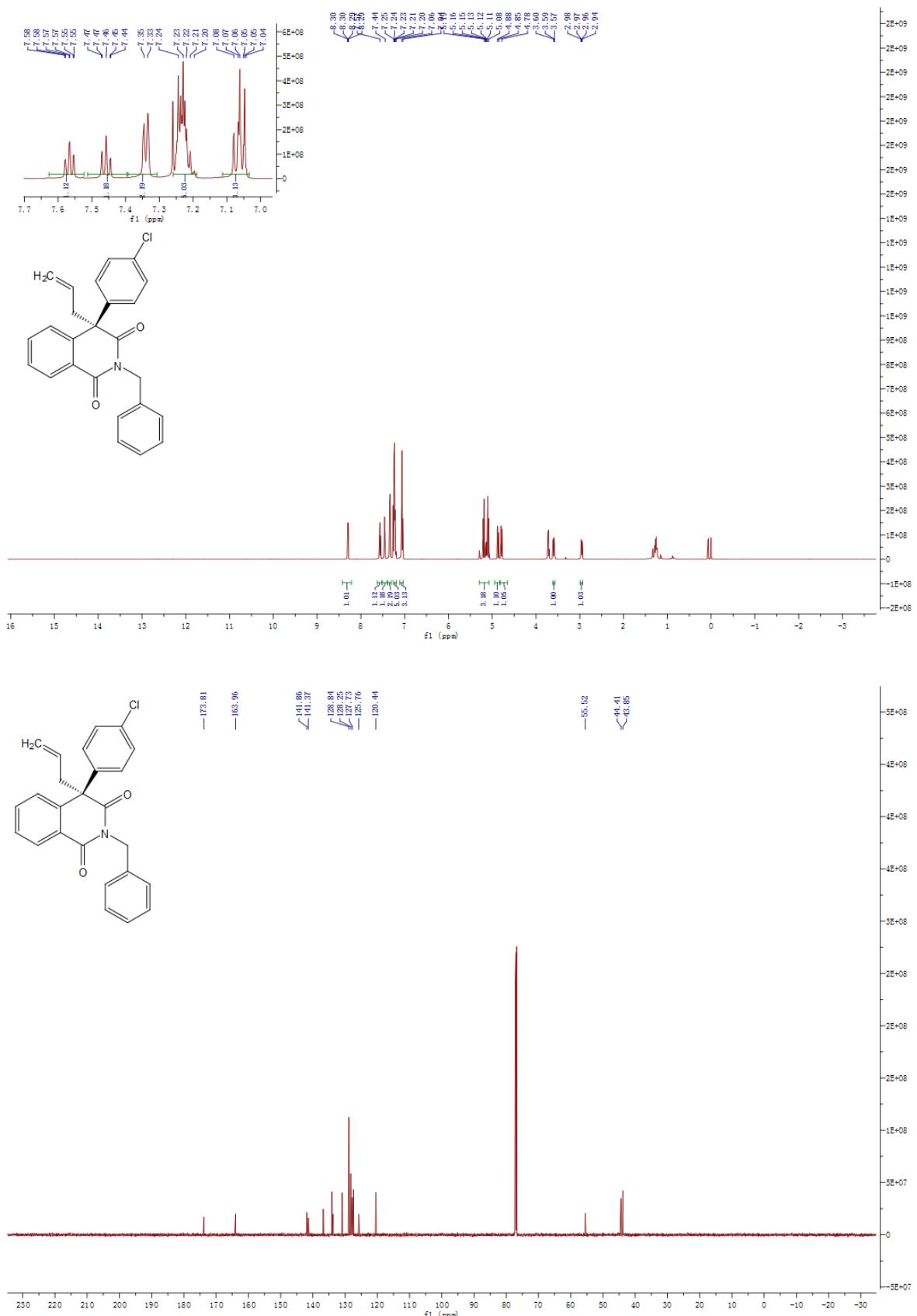
(R)-4-allyl-2-benzyl-7-methoxy-4-phenylisoquinoline-1(2H),3(4H)-dione(3e):



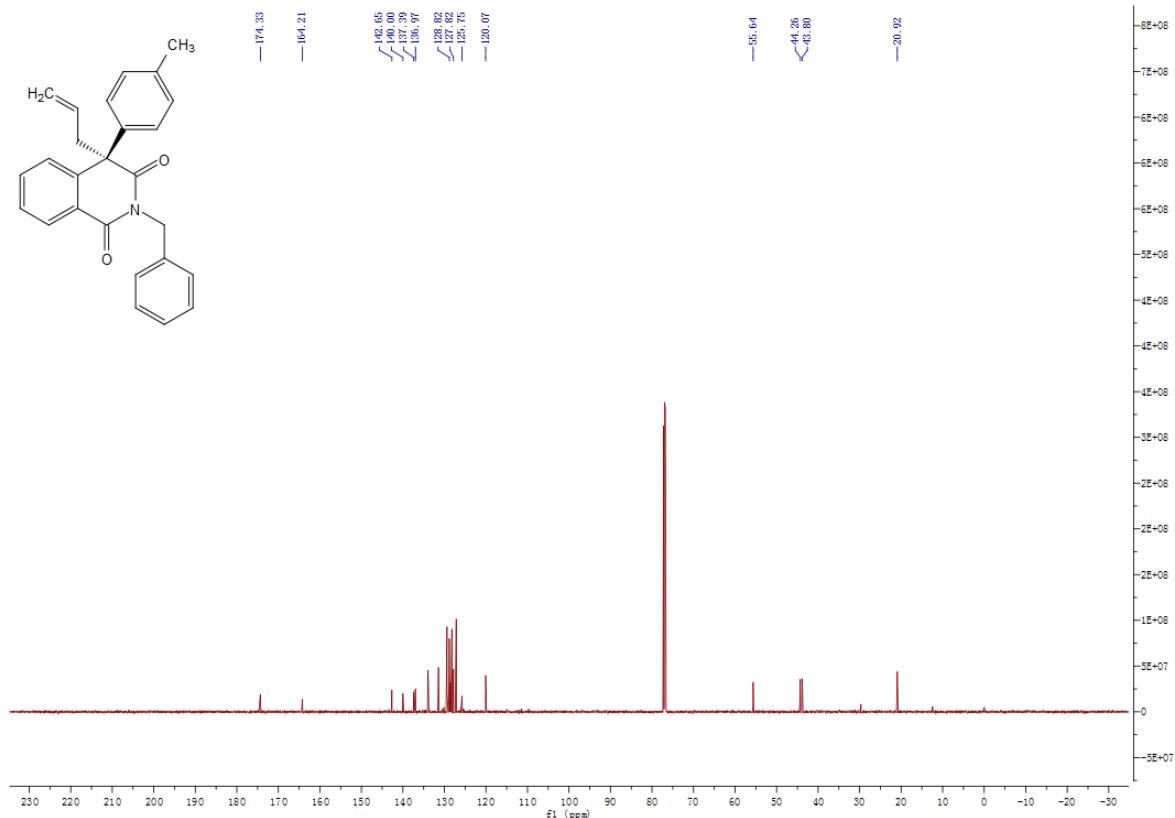
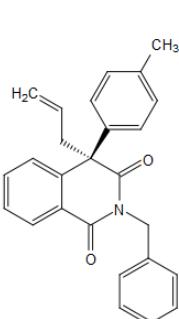
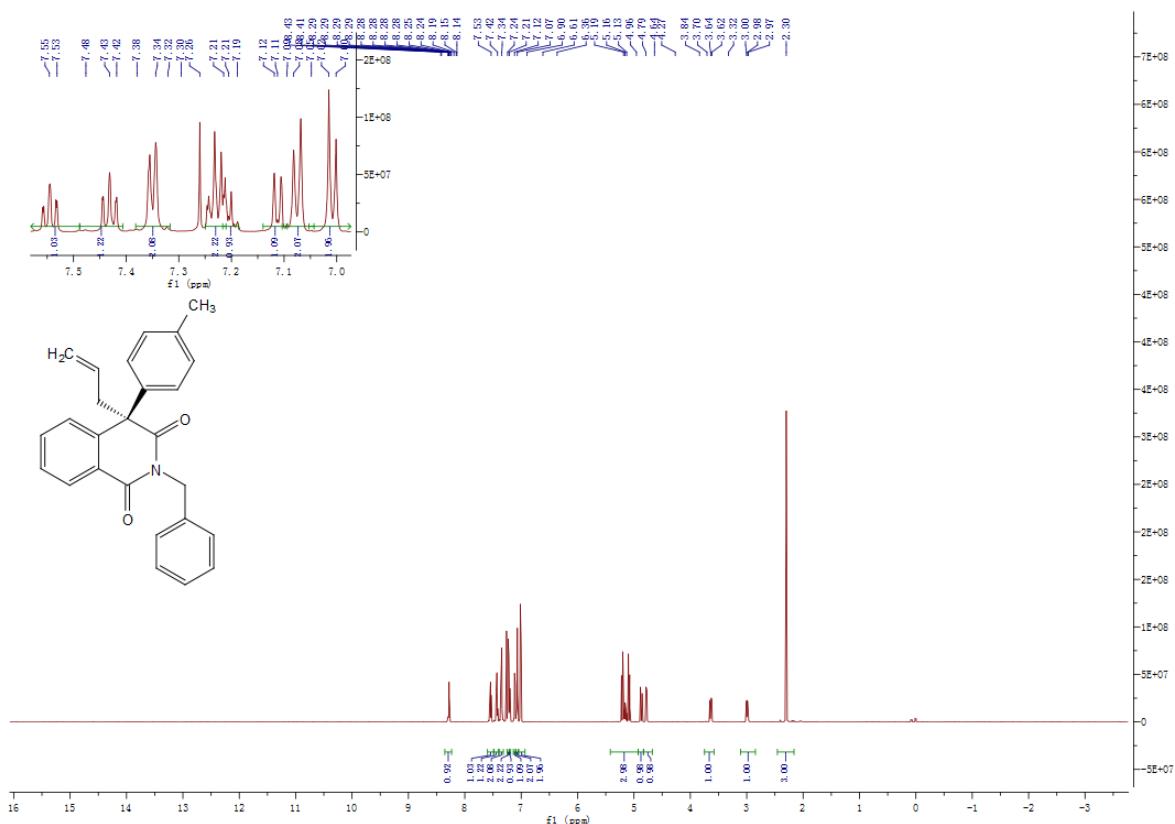
(R)-4-allyl-2-benzyl-4-(4-fluorophenyl)isoquinoline-1,3(2H,4H)-dione(3f):



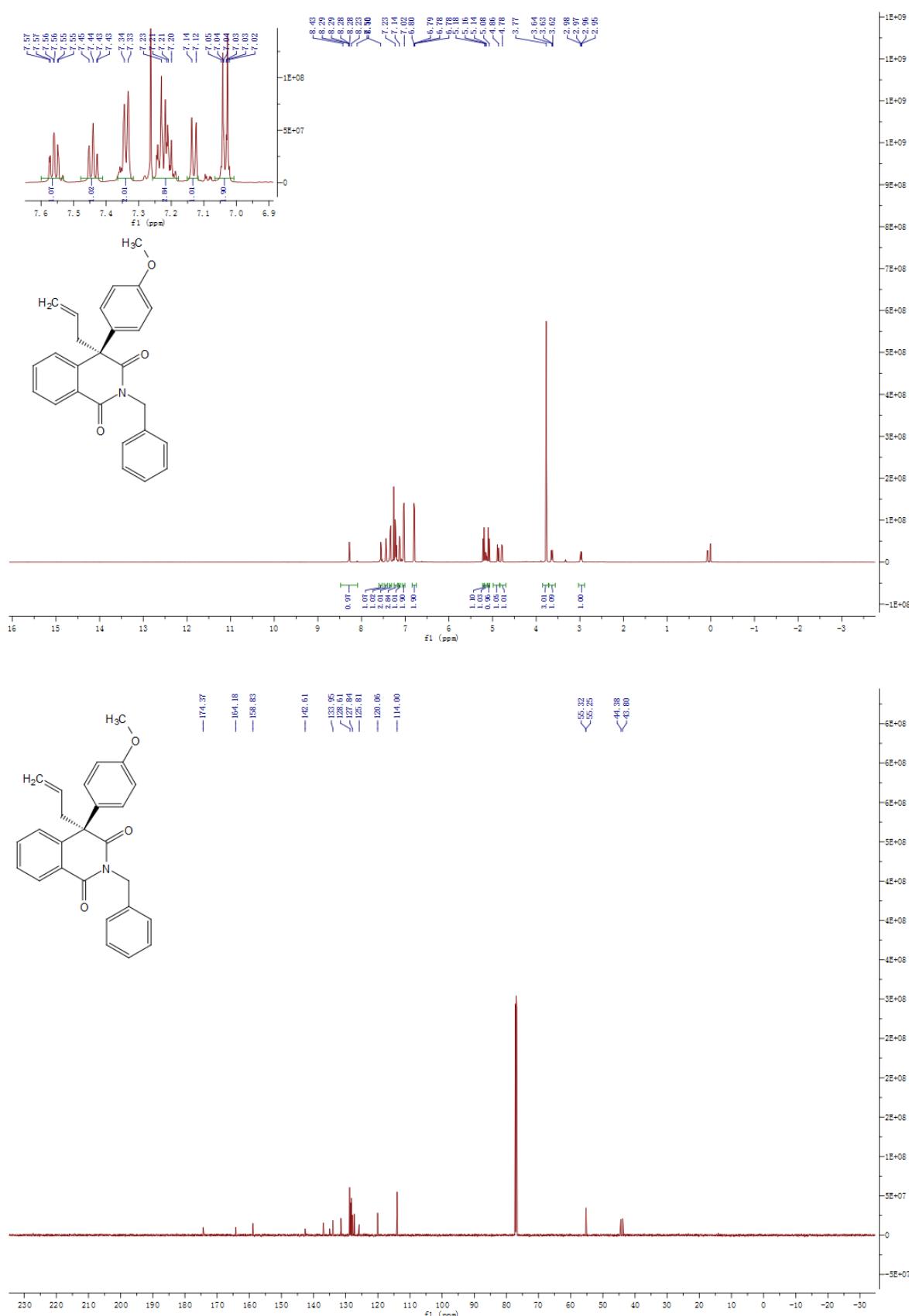
(R)-4-allyl-2-benzyl-4-(4-chlorophenyl)isoquinoline-1,3(2H,4H)-dione(3g):



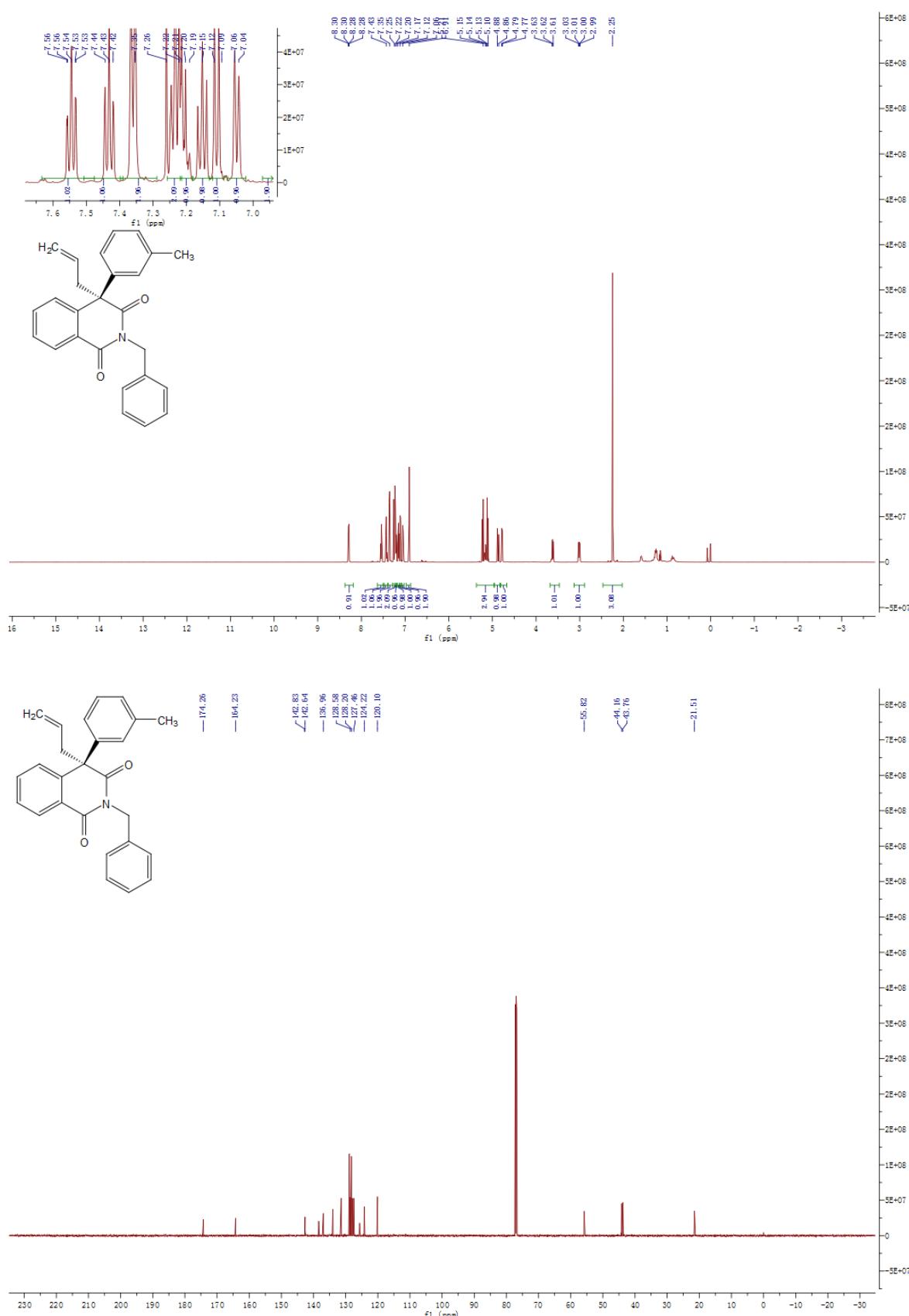
(R)-4-allyl-2-benzyl-4-(p-tolyl)isoquinoline-1,3(2H,4H)-dione(3h):



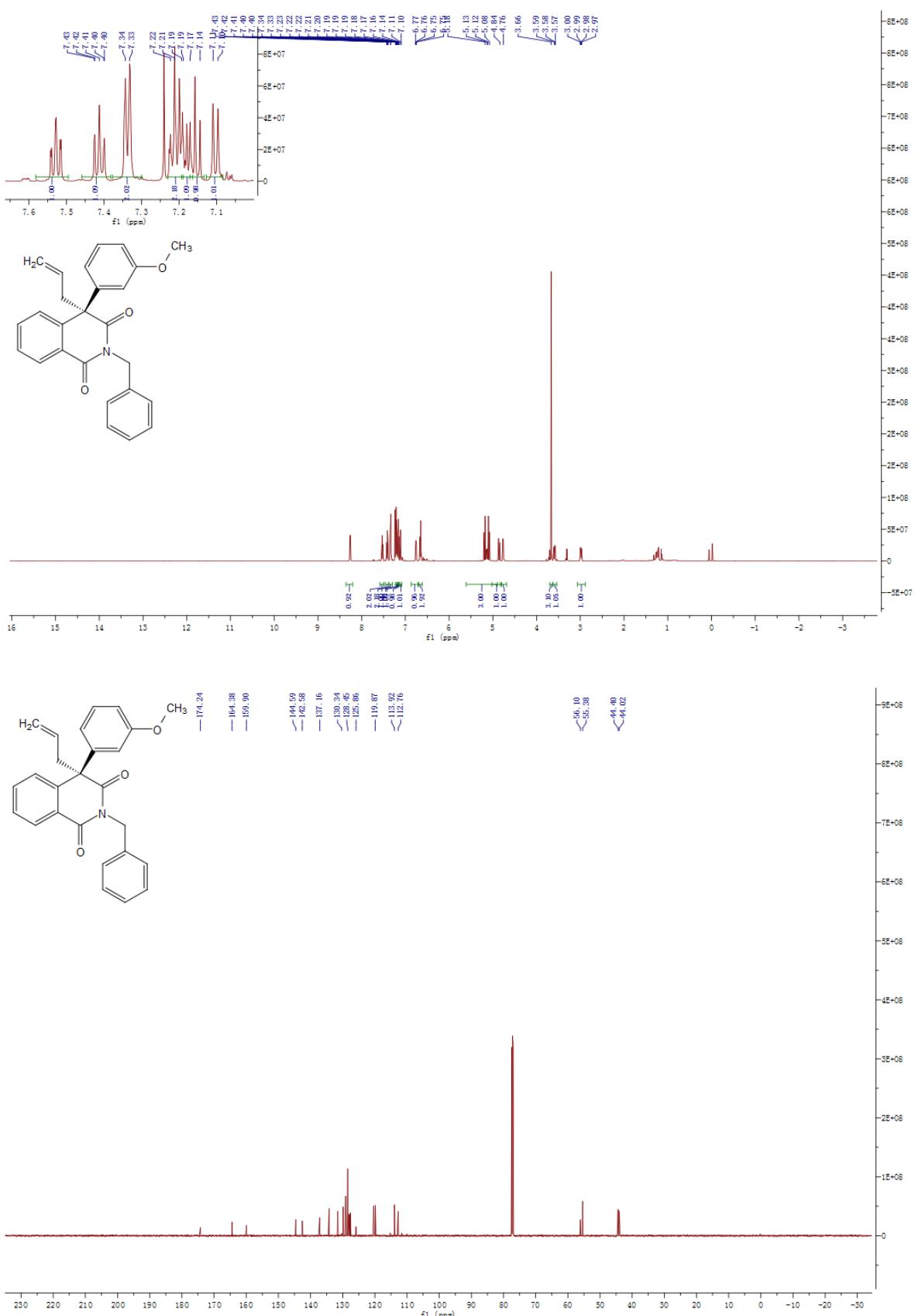
(R)-4-allyl-2-benzyl-4-(4-methoxyphenyl)isoquinoline-1,3(2H,4H)-dione(3i):



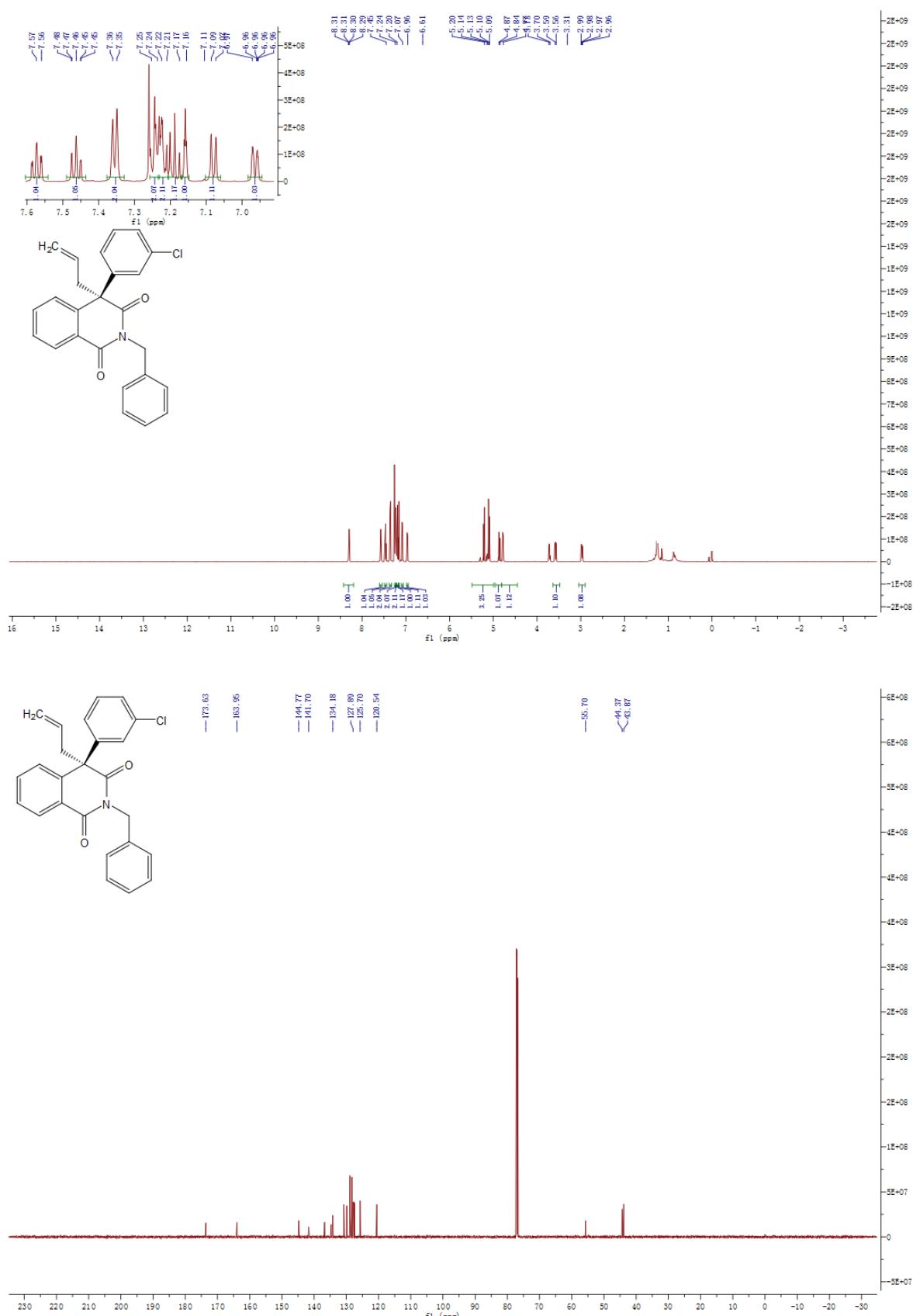
(R)-4-allyl-2-benzyl-4-(m-tolyl)isoquinoline-1,3(2H,4H)-dione(3j):



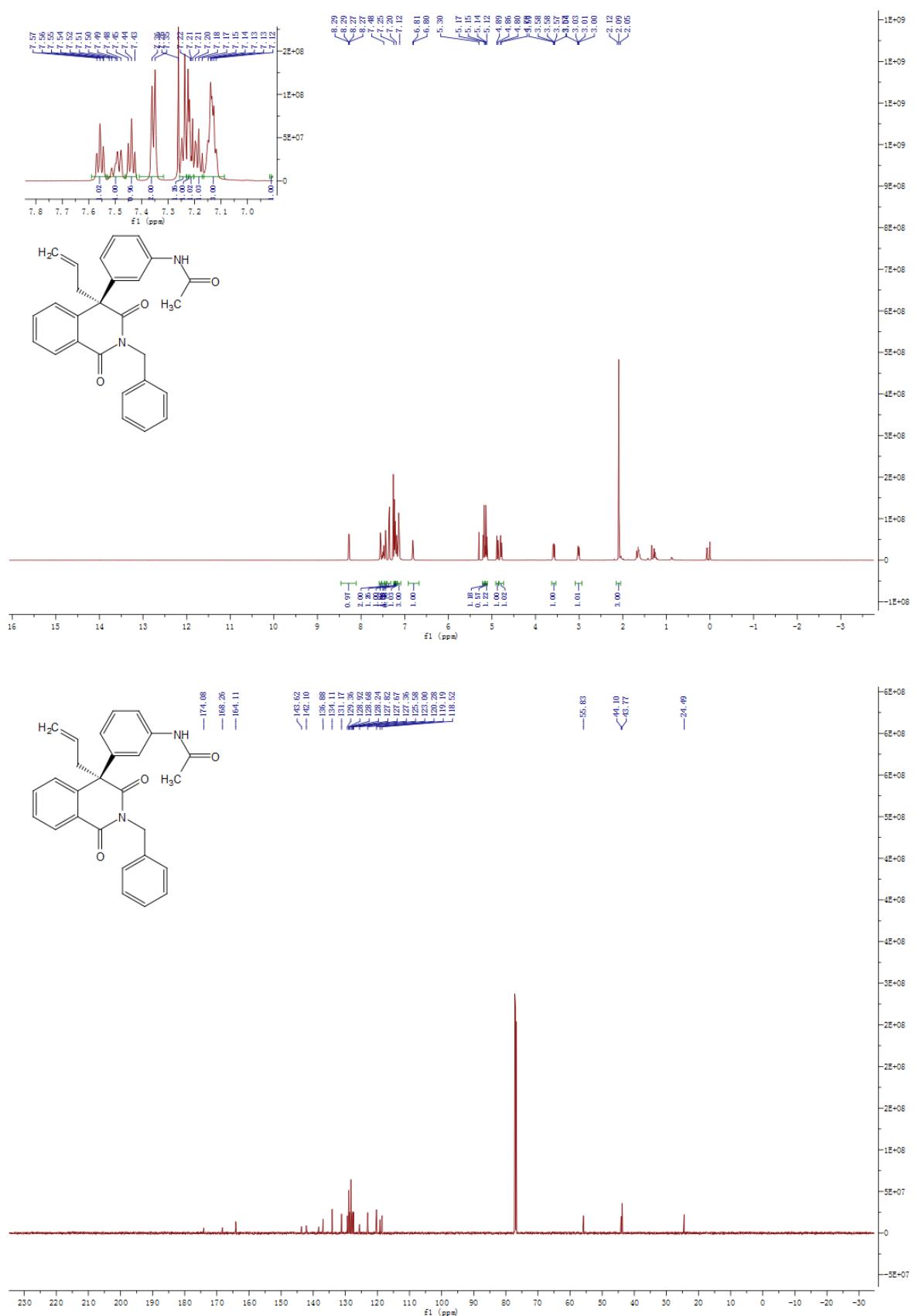
(*R*)-4-allyl-2-benzyl-4-(3-methoxyphenyl)isoquinoline-1,3(2*H*,4*H*)-dione(3k):



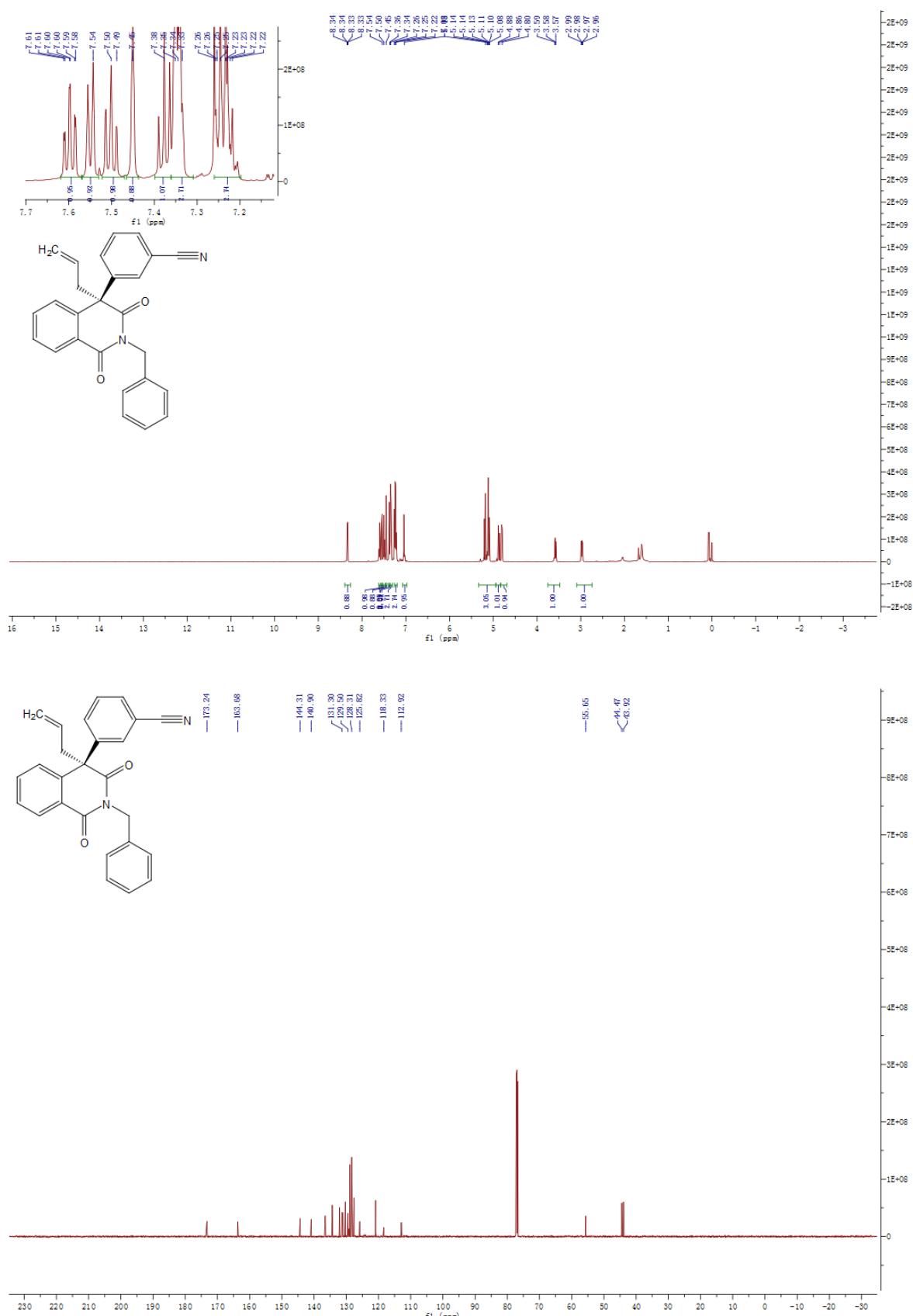
(*R*)-4-allyl-2-benzyl-4-(3-chlorophenyl)isoquinoline-1,3(2*H*,4*H*)-dione(3l):



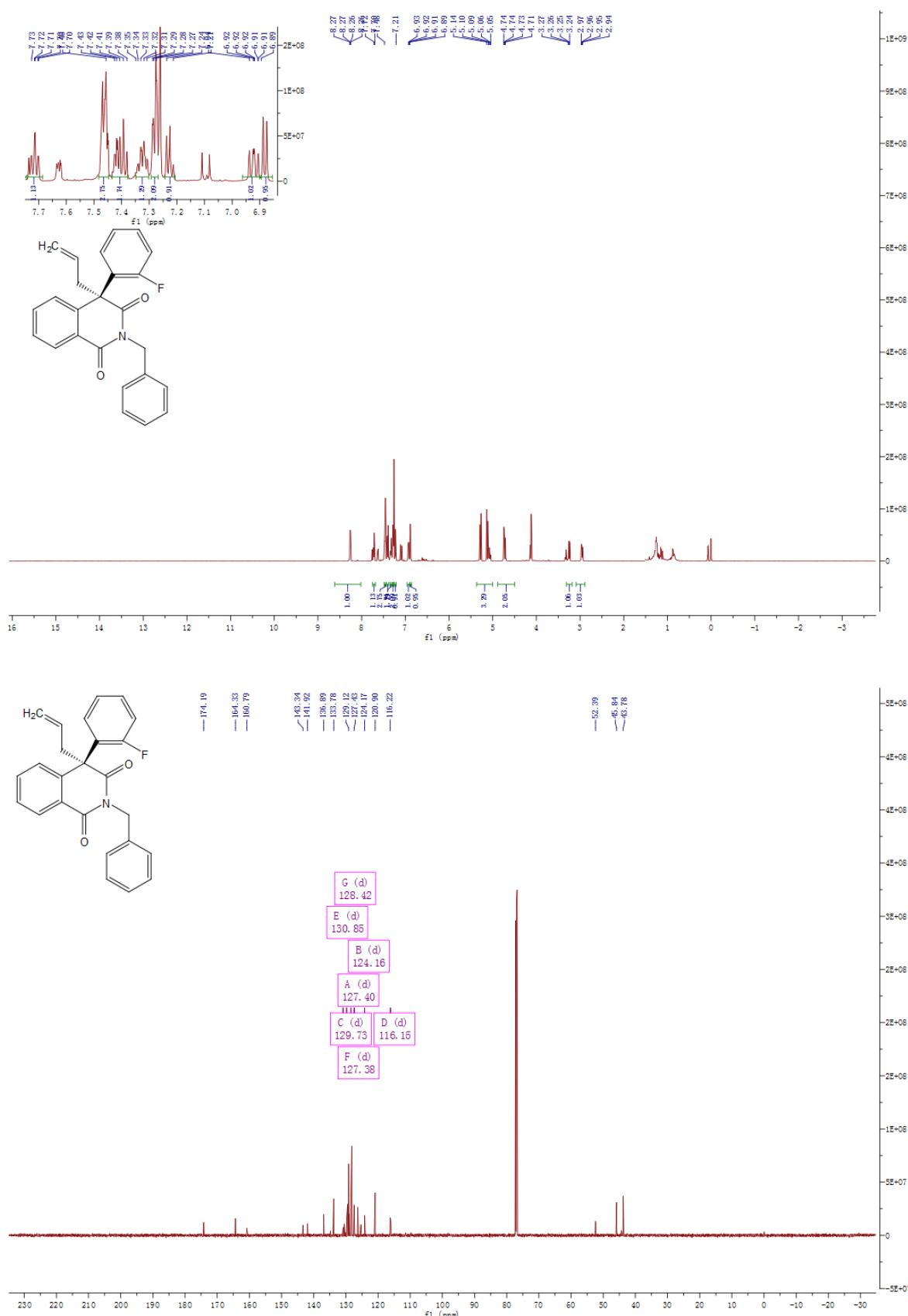
(R)-N-(3-(4-allyl-2-benzyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl)acetamide(3m):



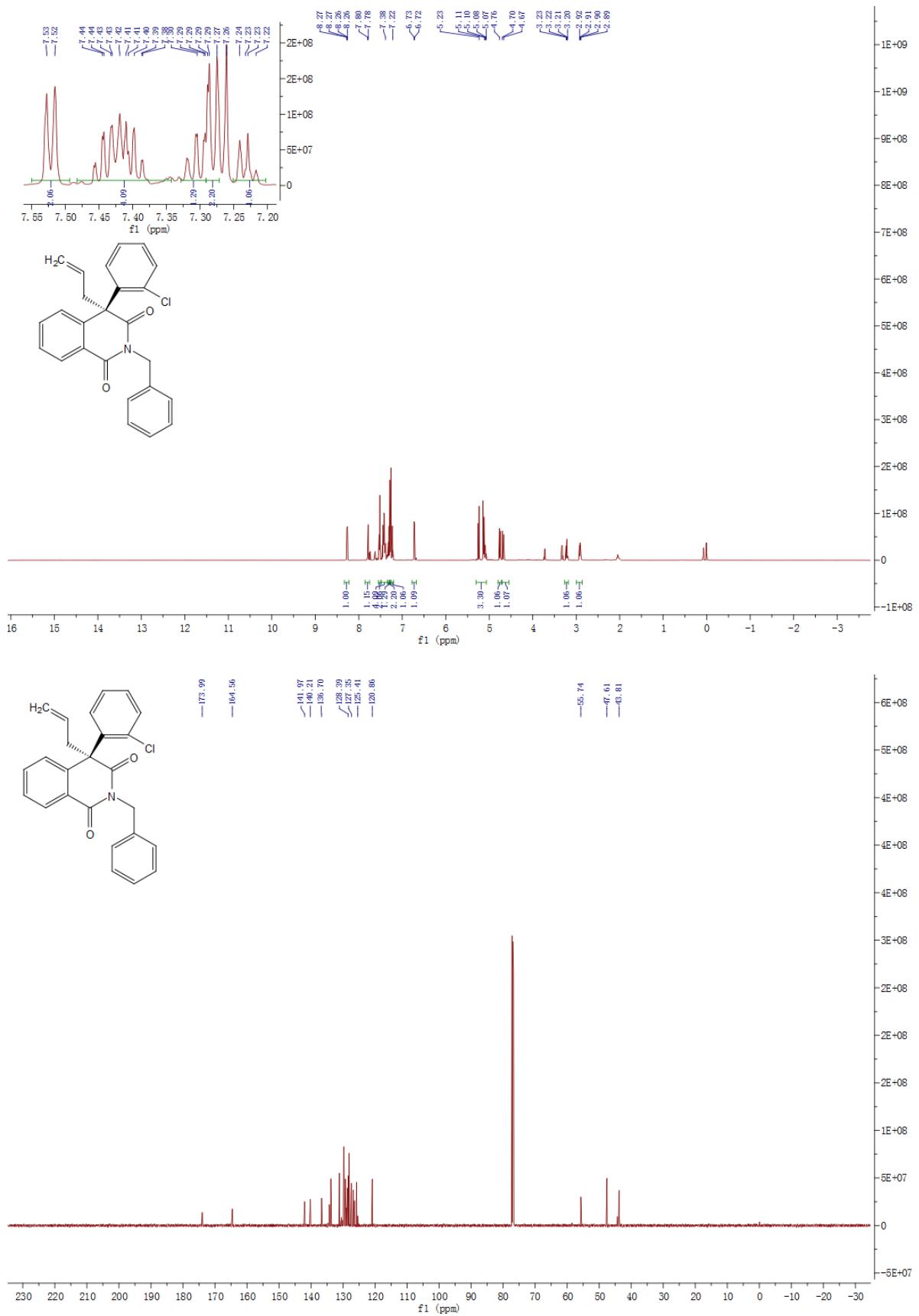
(*R*)-3-(4-allyl-2-benzyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)benzonitrile(3n):



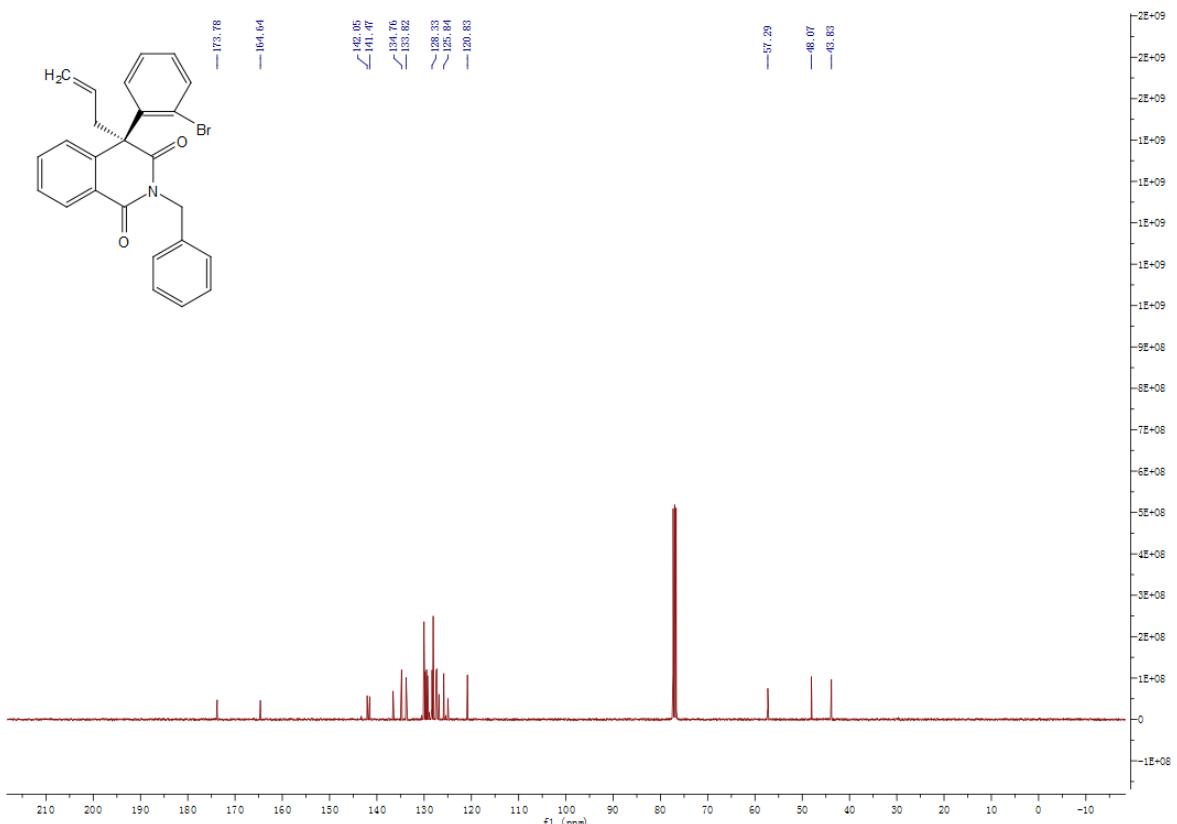
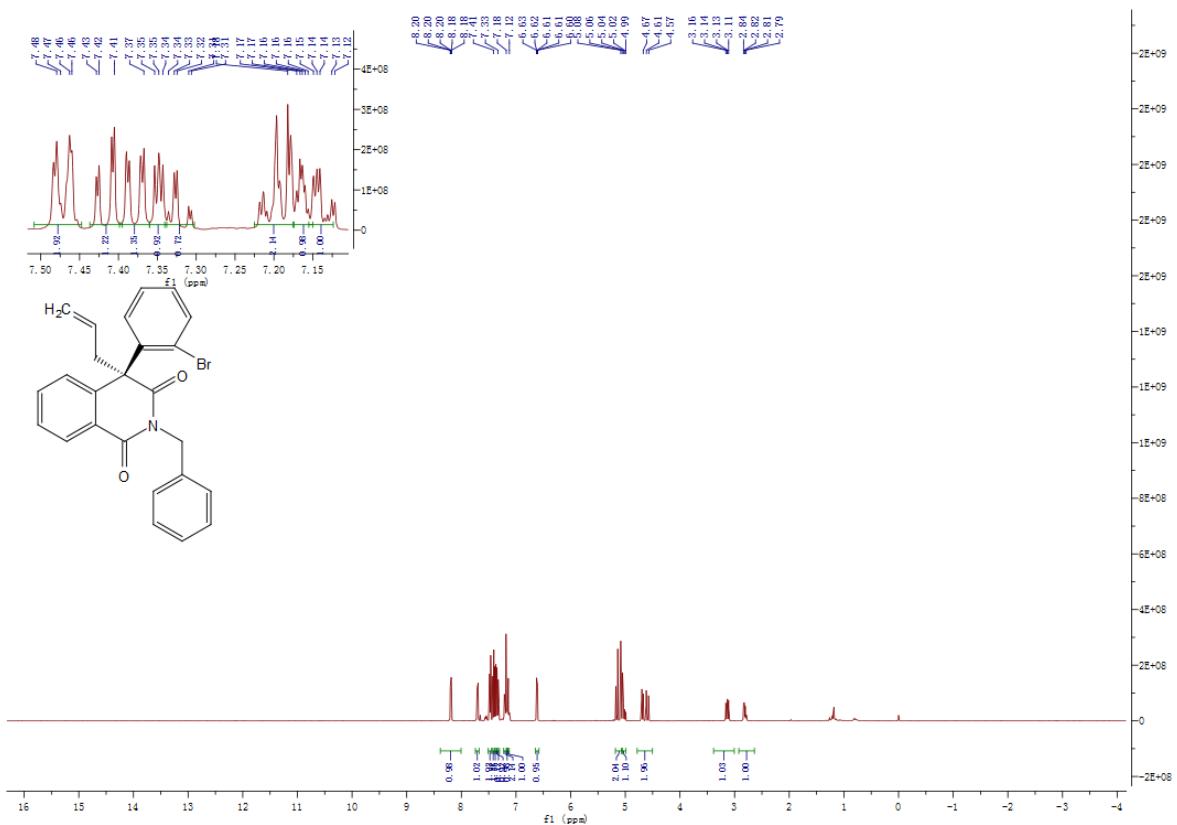
(R)-4-allyl-2-benzyl-4-(2-fluorophenyl)isoquinoline-1,3(2H,4H)-dione(3o):



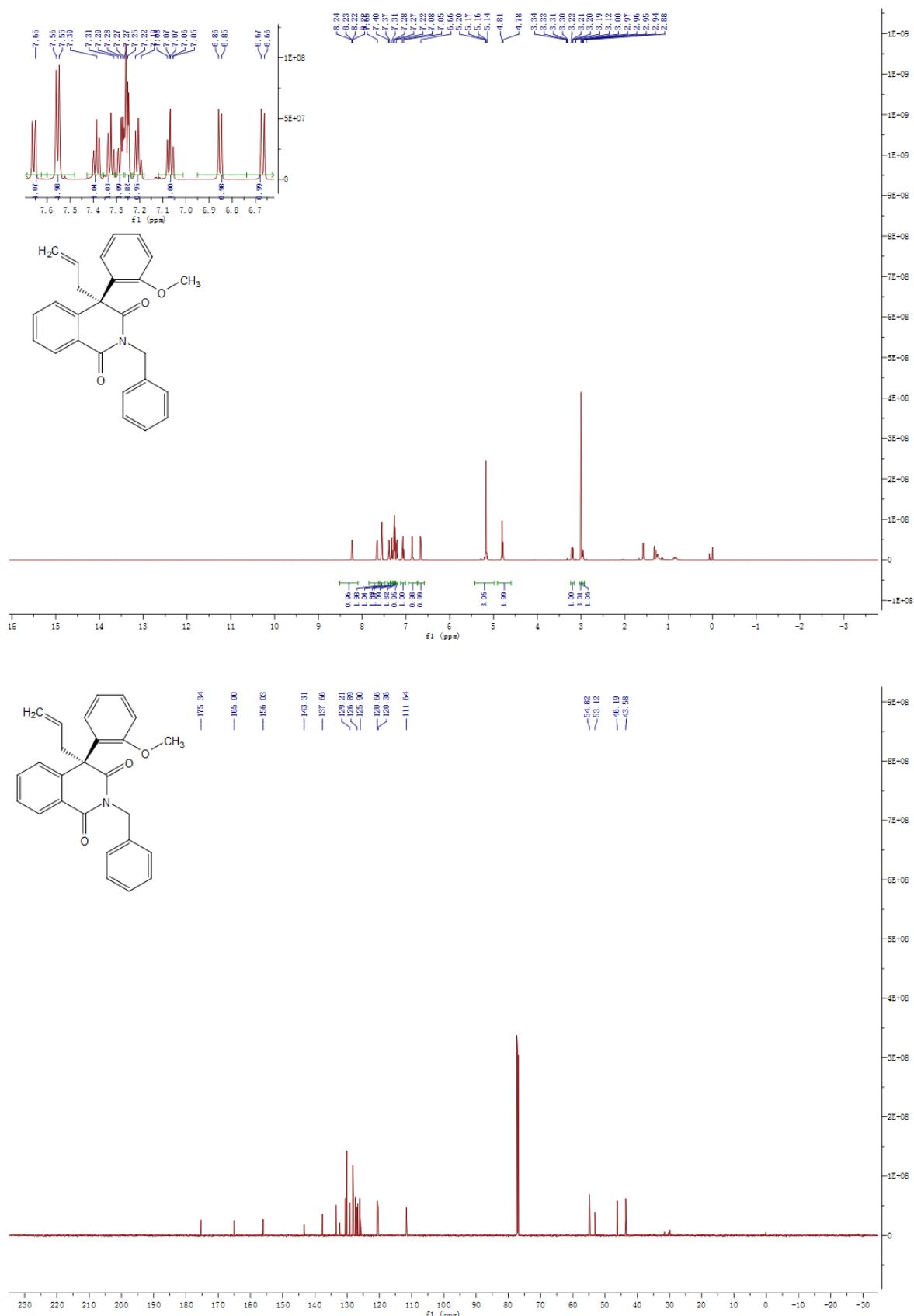
(R)-4-allyl-2-benzyl-4-(2-chlorophenyl)isoquinoline-1,3(2H,4H)-dione(3p):



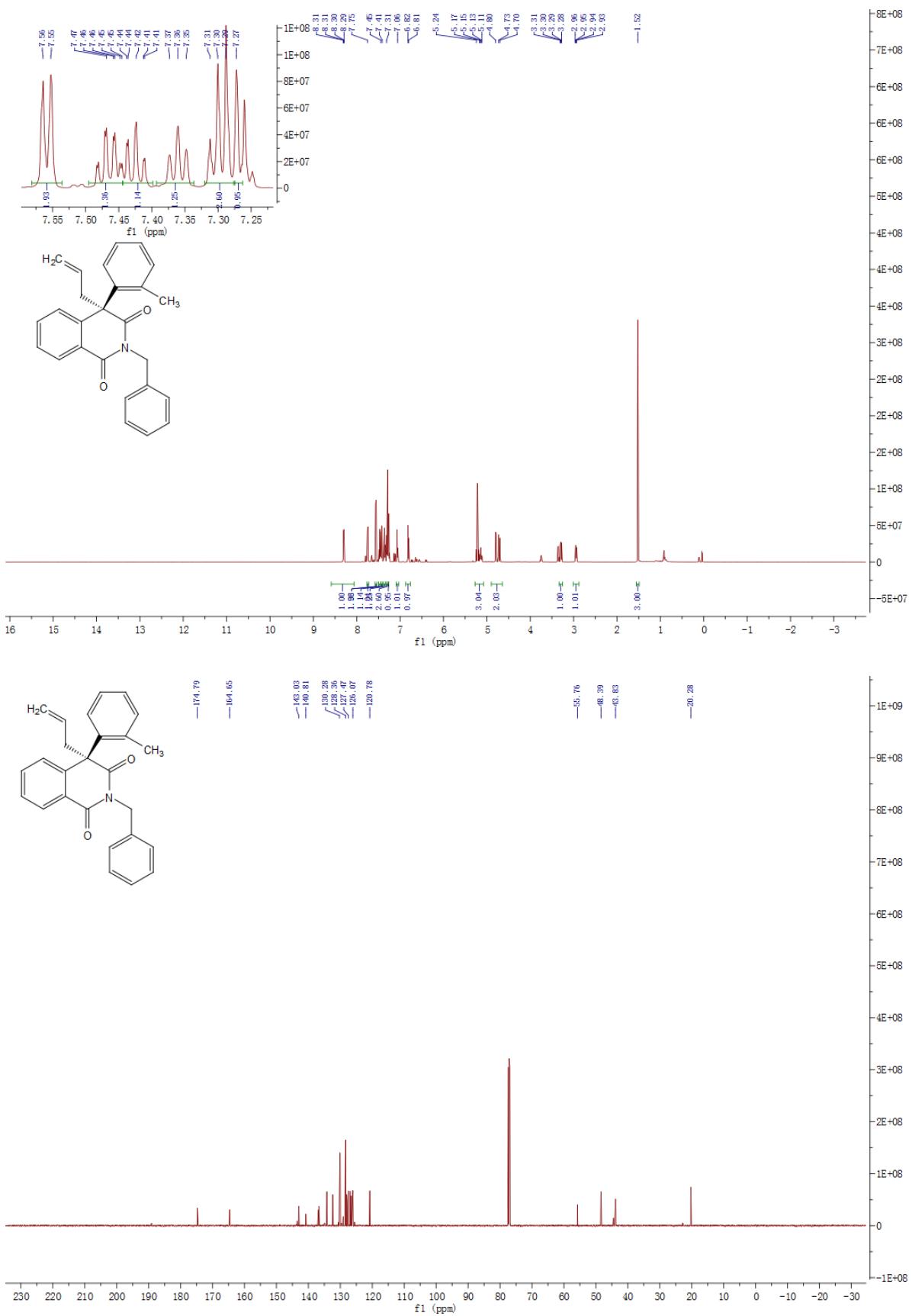
(R)-4-allyl-2-benzyl-4-(2-bromophenyl)isoquinoline-1,3(2H,4H)-dione(3q):



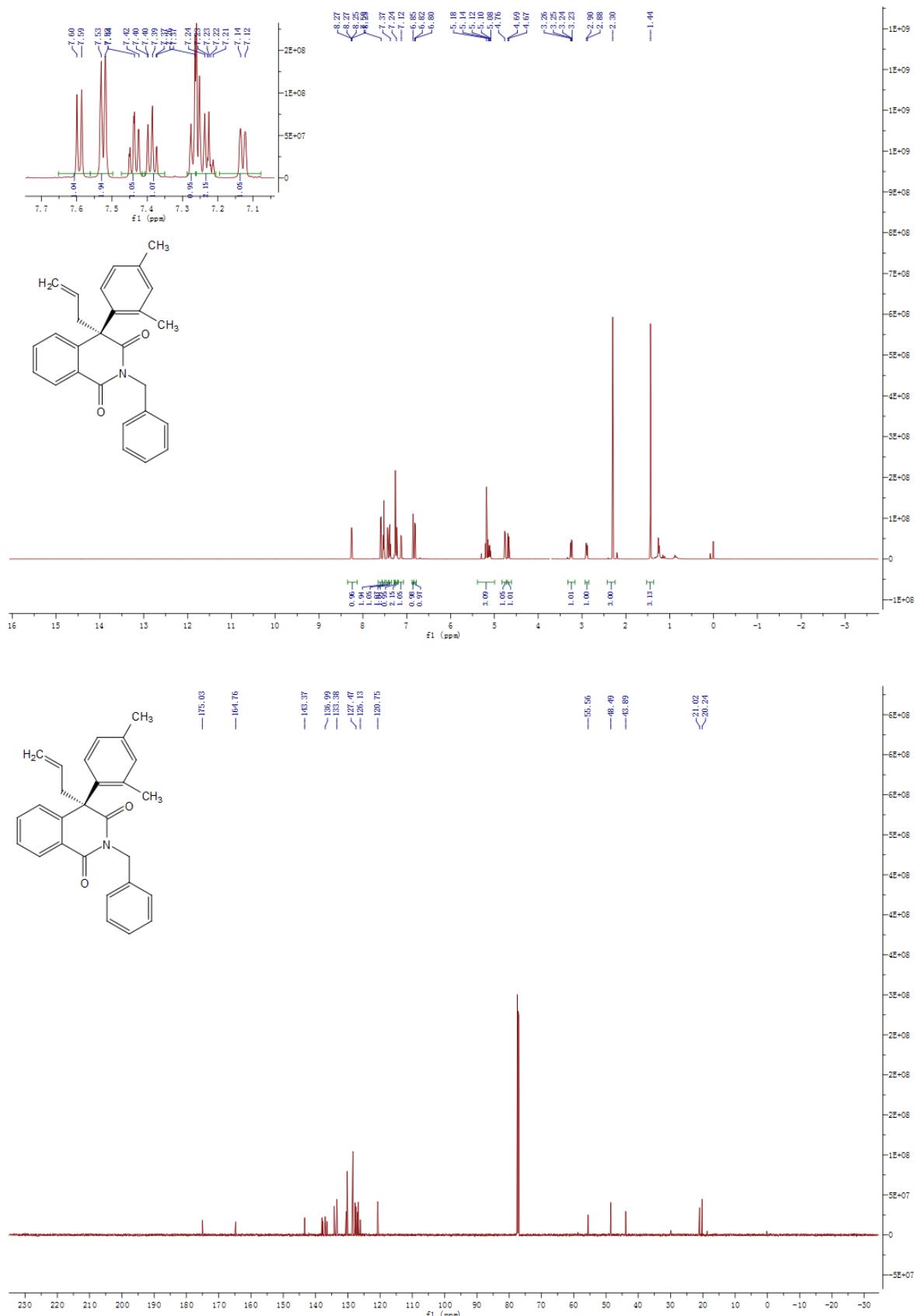
(R)-4-allyl-2-benzyl-4-(2-methoxyphenyl)isoquinoline-1,3(2H,4H)-dione(3r):



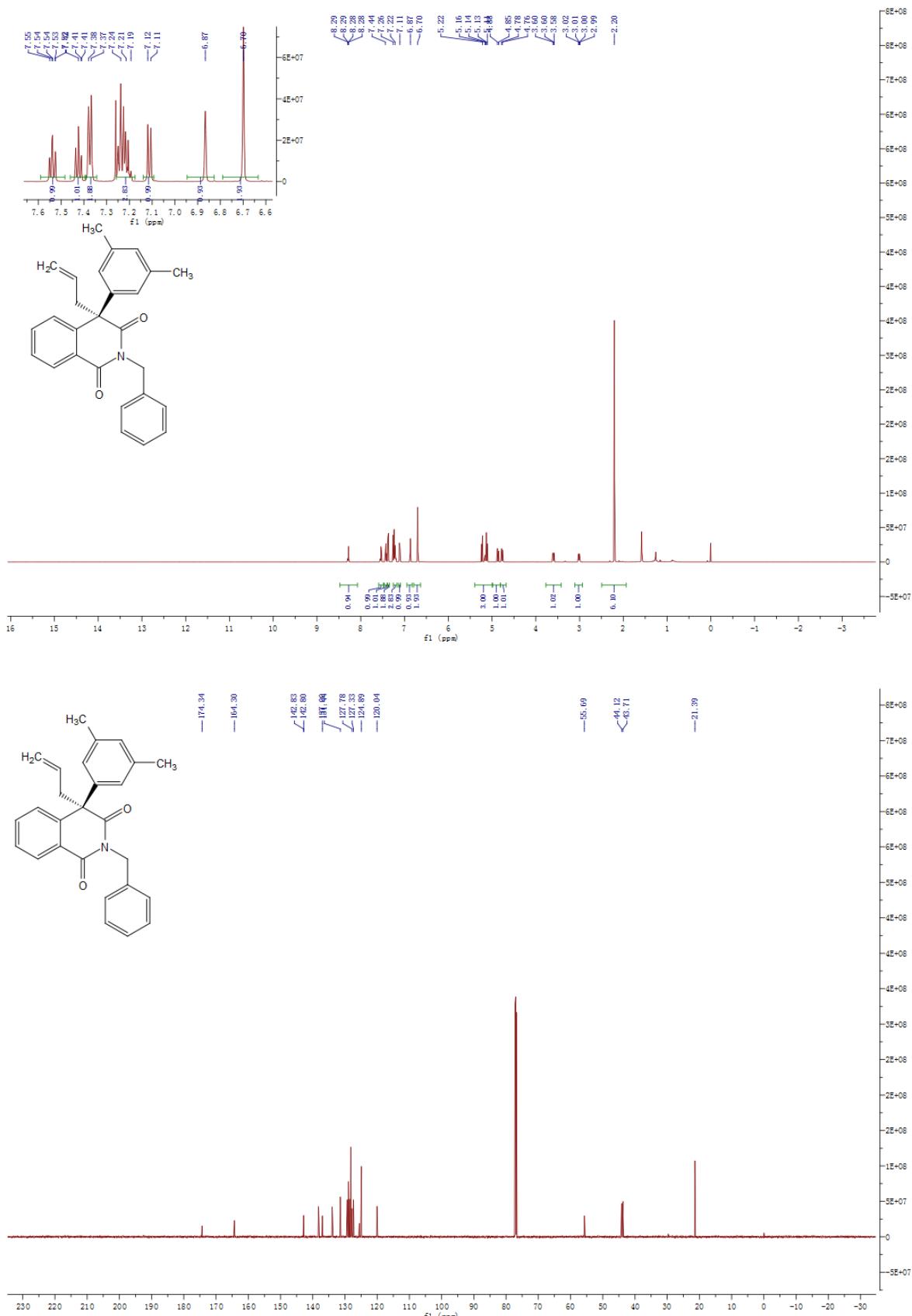
(R)-4-allyl-2-benzyl-4-(o-tolyl)isoquinoline-1,3(2H,4H)-dione(3s):



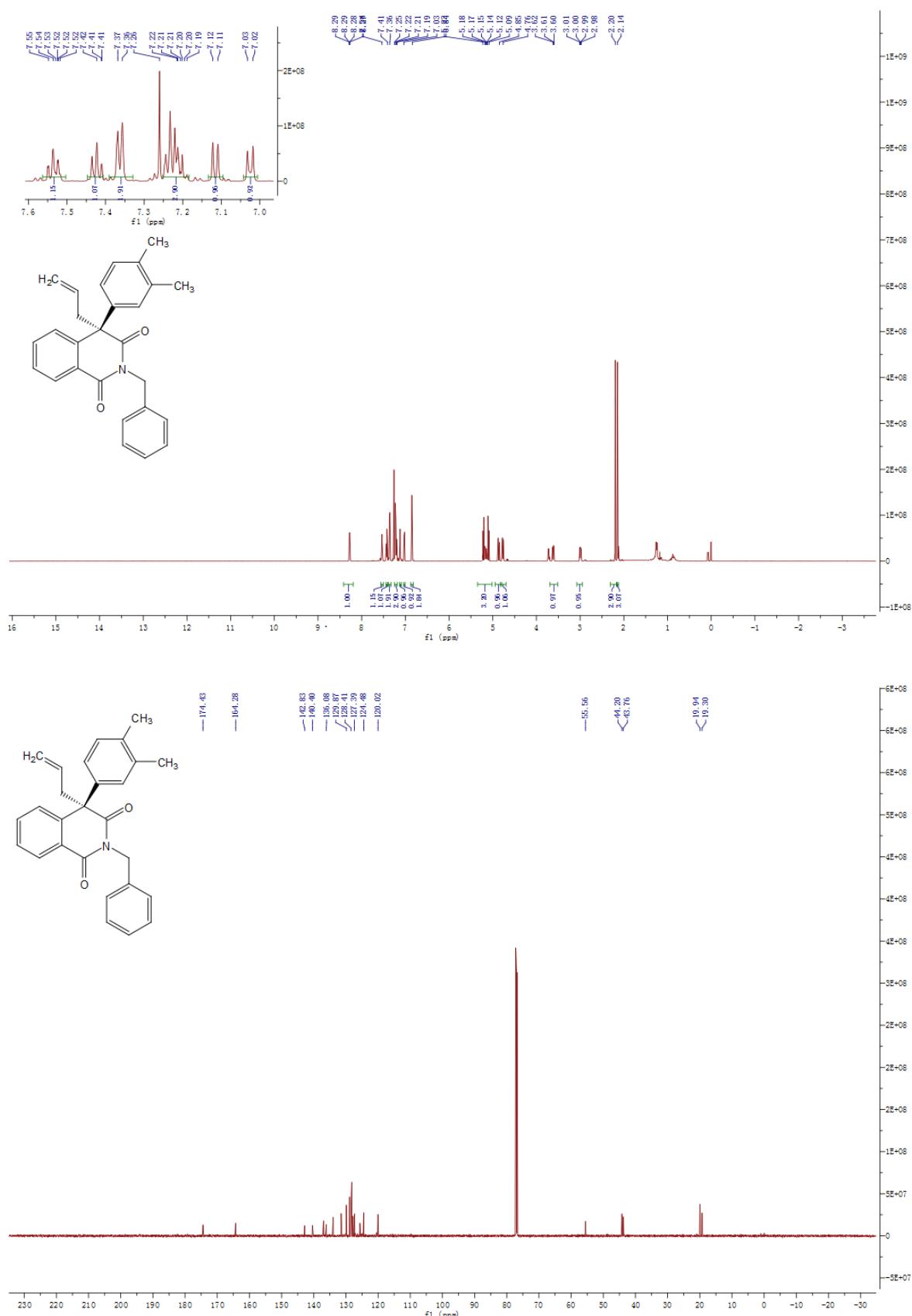
(*R*)-4-allyl-2-benzyl-4-(2,4-dimethylphenyl)isoquinoline-1,3(2*H*,4*H*)-dione(3t):



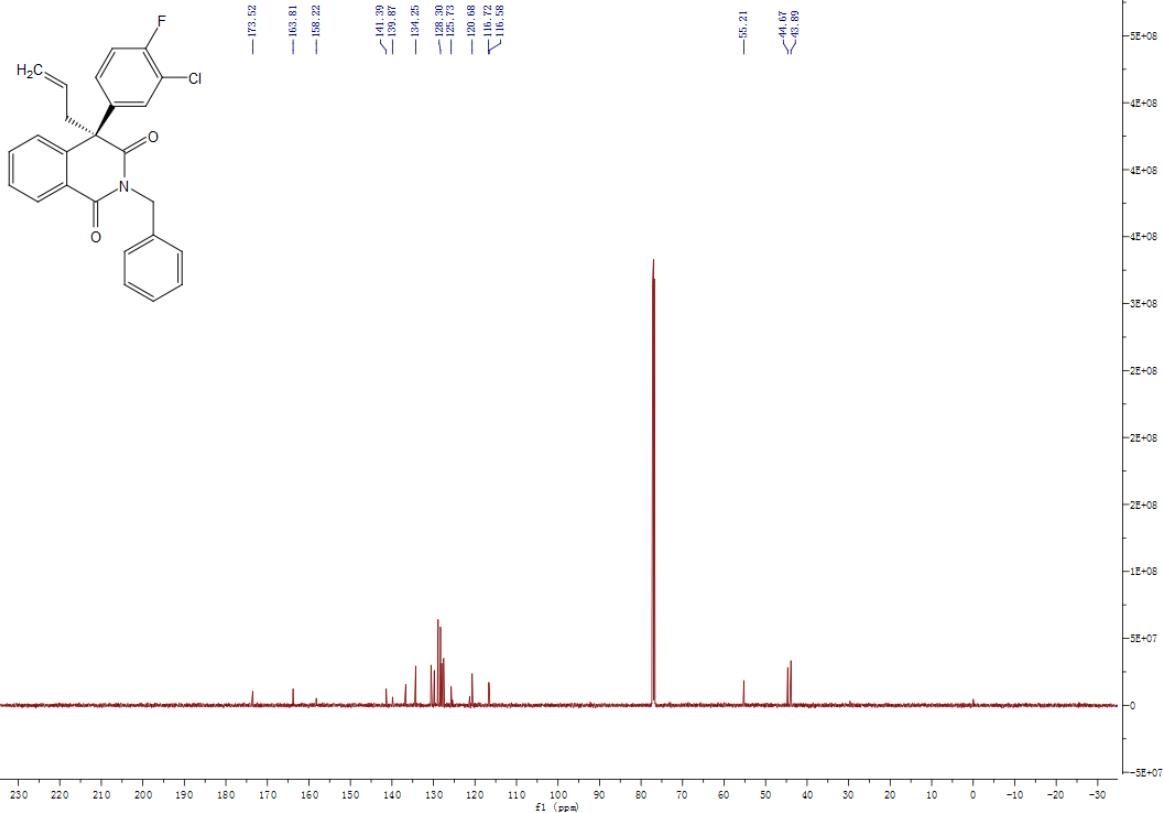
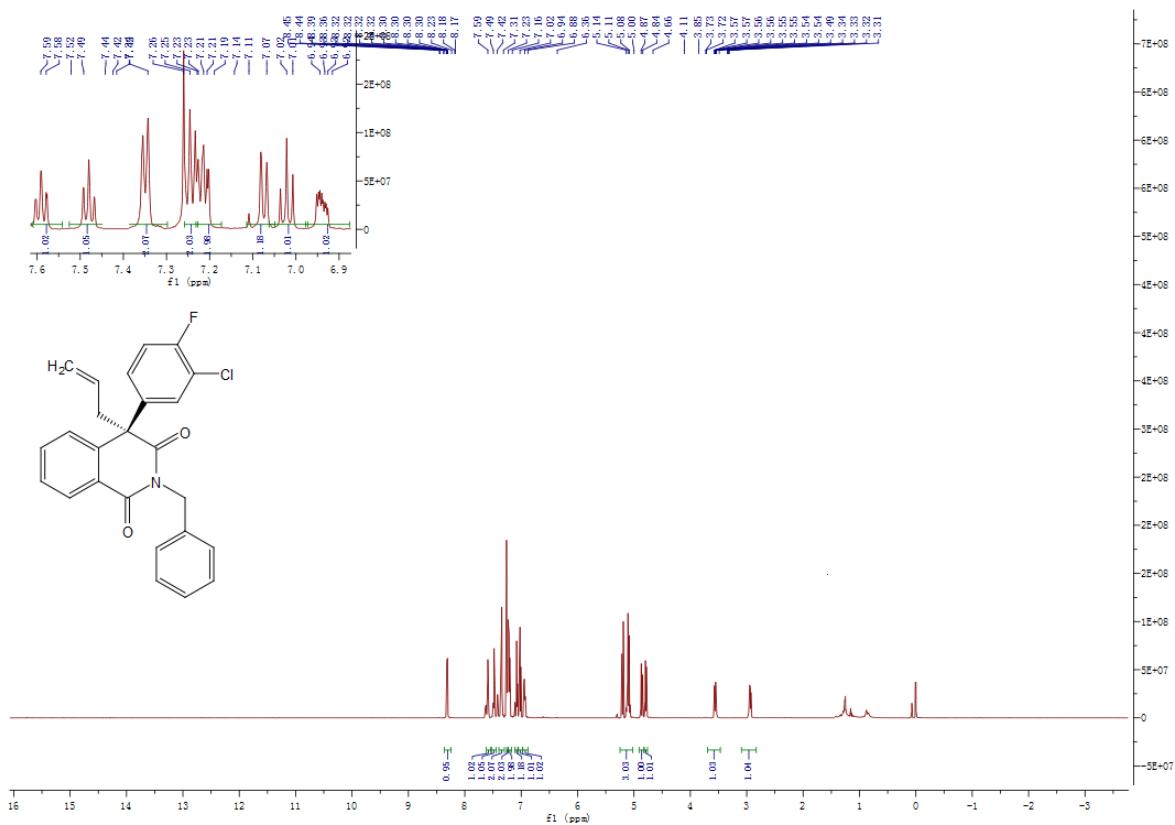
(R)-4-allyl-2-benzyl-4-(3,5-dimethylphenyl)isoquinoline-1,3(2H,4H)-dione(3u):



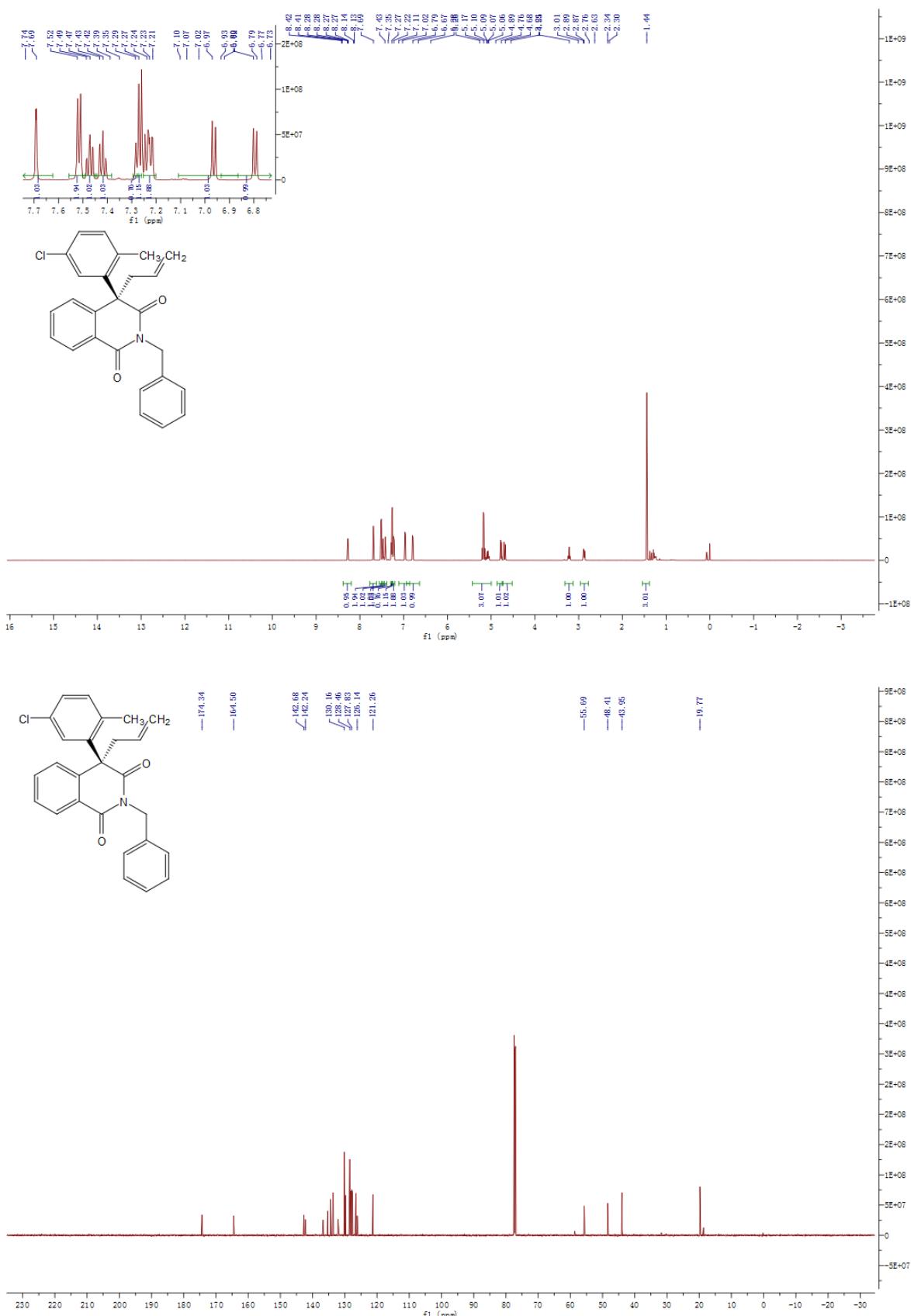
(R)-4-allyl-2-benzyl-4-(3,4-dimethylphenyl)isoquinoline-1,3(2H,4H)-dione(3v):



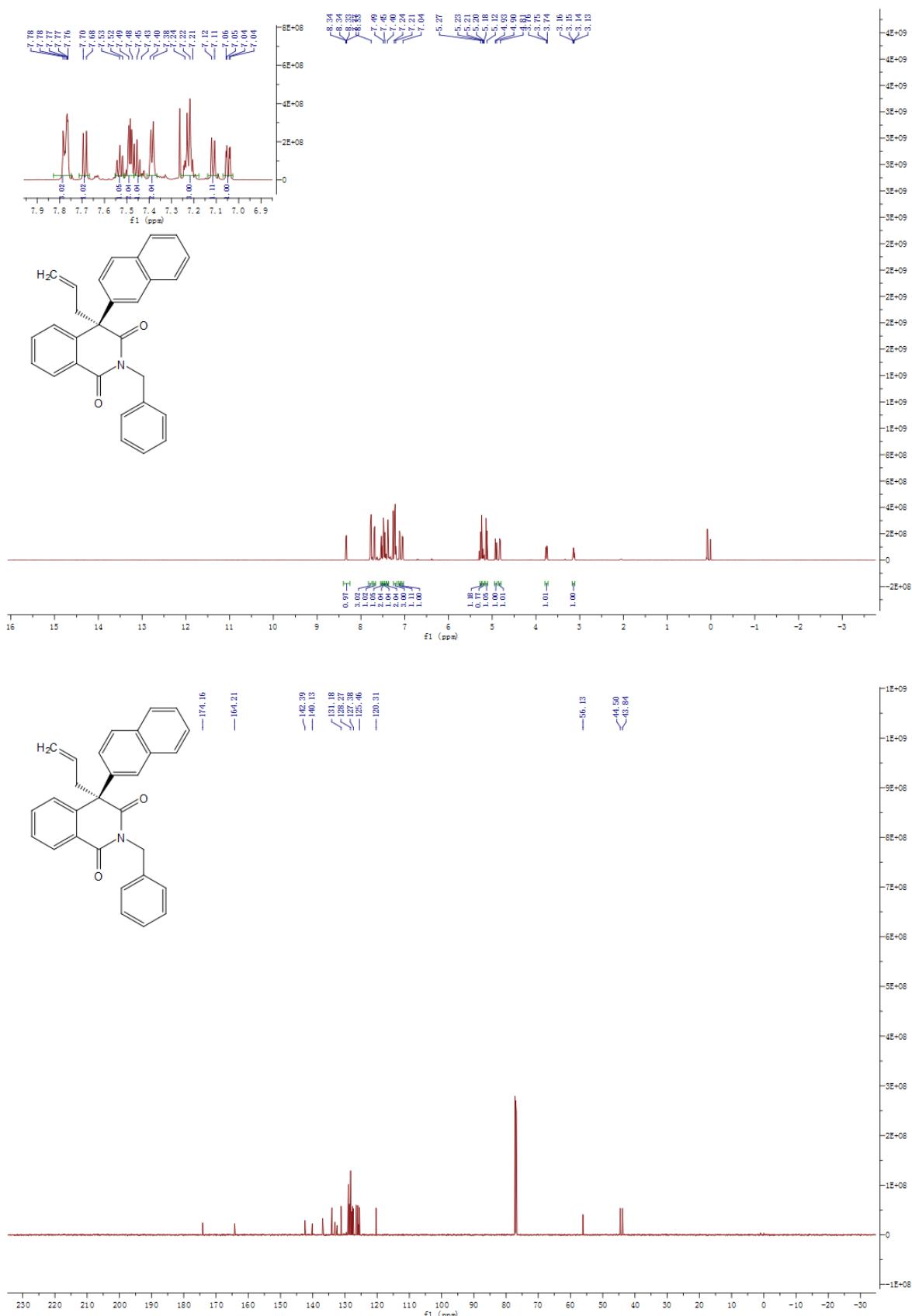
(*R*)-4-allyl-2-benzyl-4-(3-chloro-4-fluorophenyl)isoquinoline-1,3(2*H*,4*H*)-dione(3w):



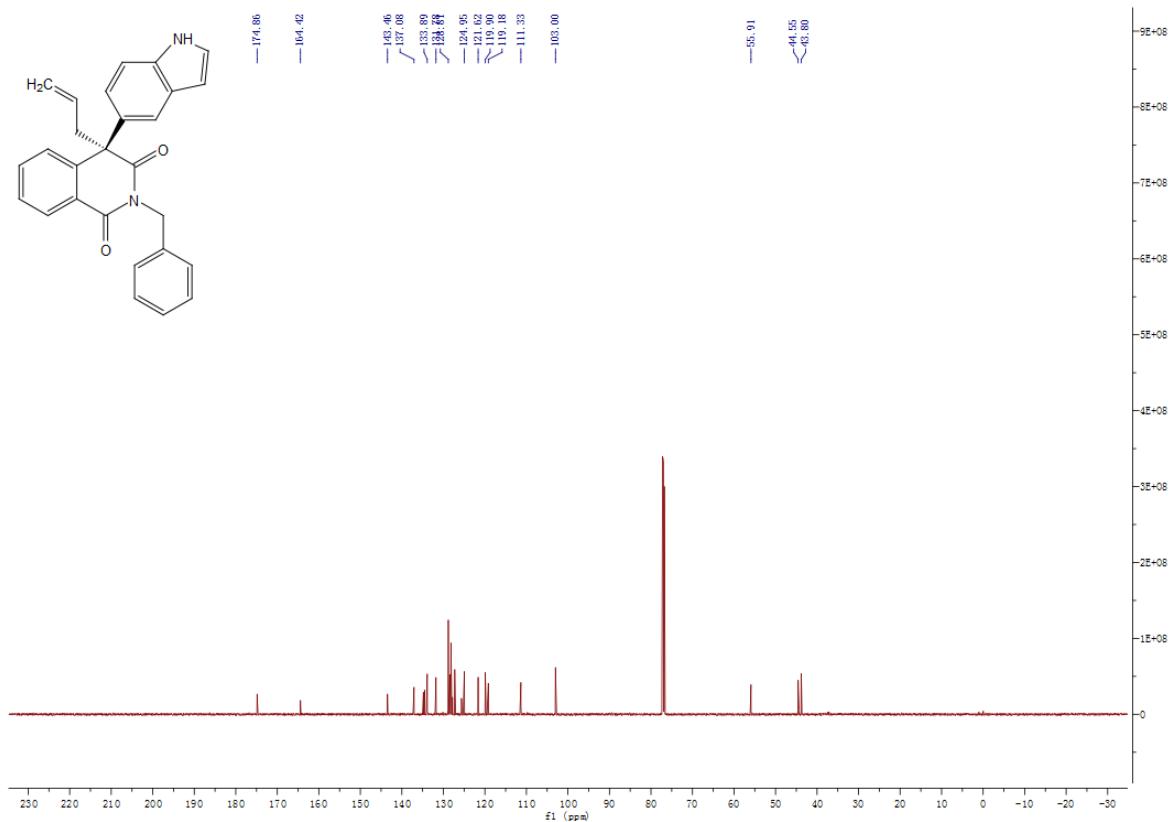
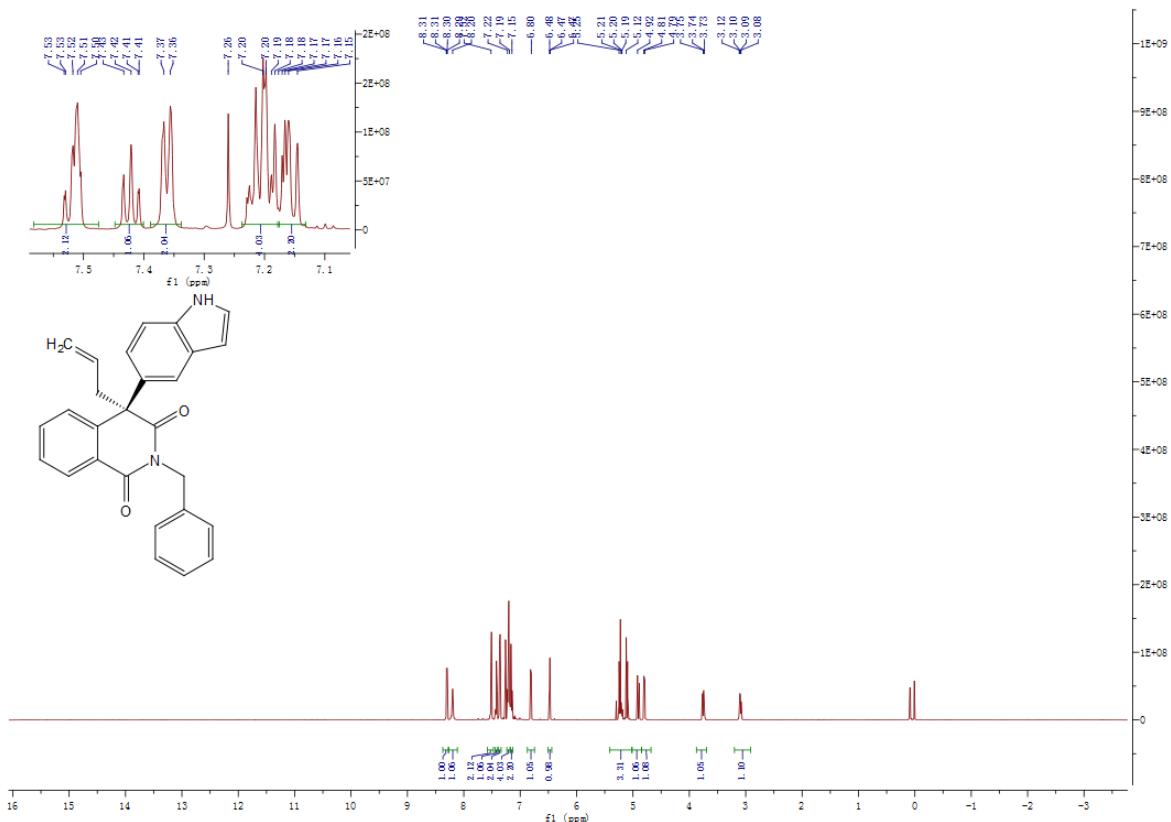
(R)-4-allyl-2-benzyl-4-(5-chloro-2-methylphenyl)isoquinoline-1,3(2H,4H)-dione(3x):



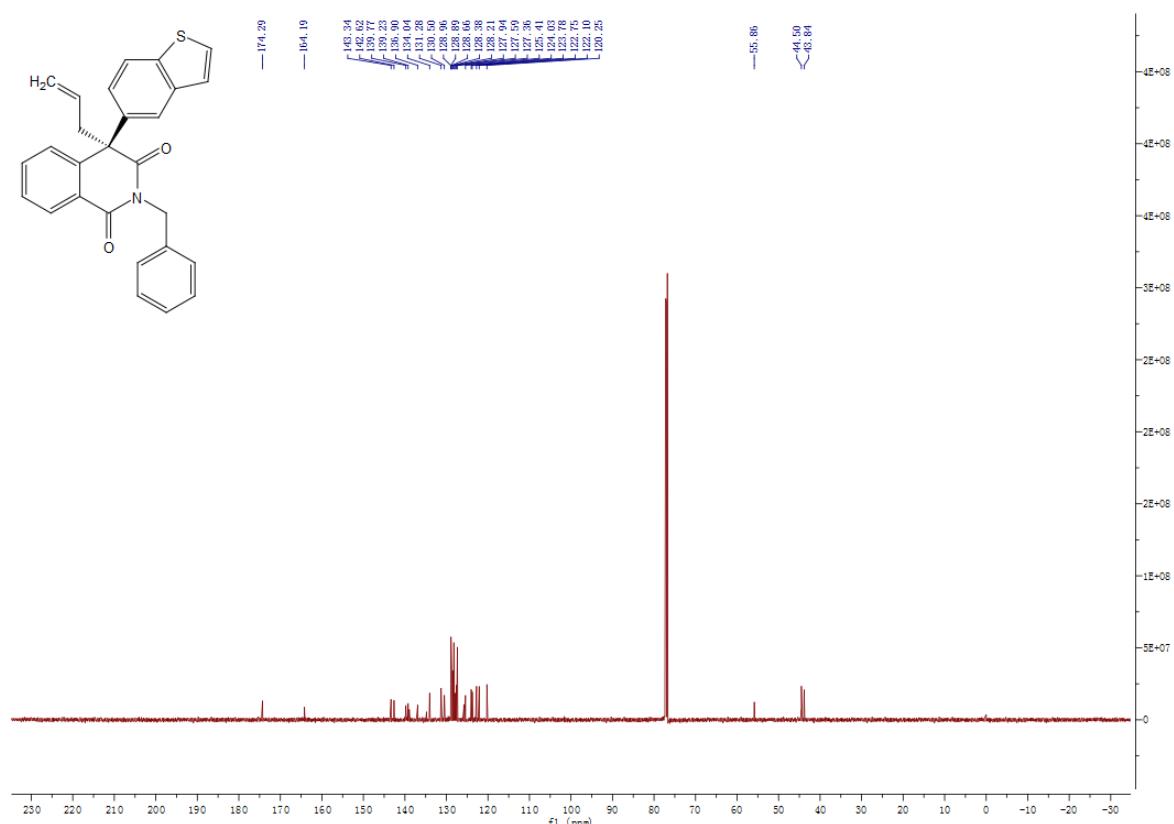
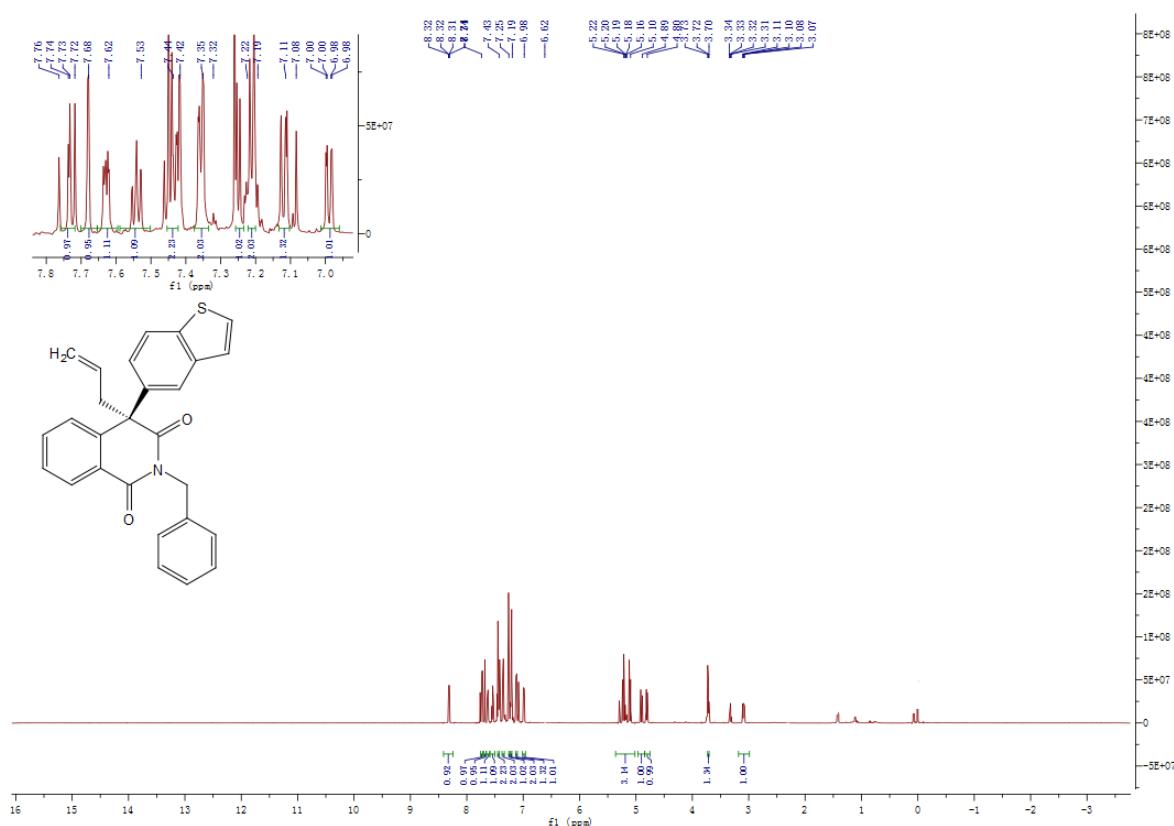
(R)-4-allyl-2-benzyl-4-(naphthalen-2-yl)isoquinoline-1,3(2H,4H)-dione(3y):



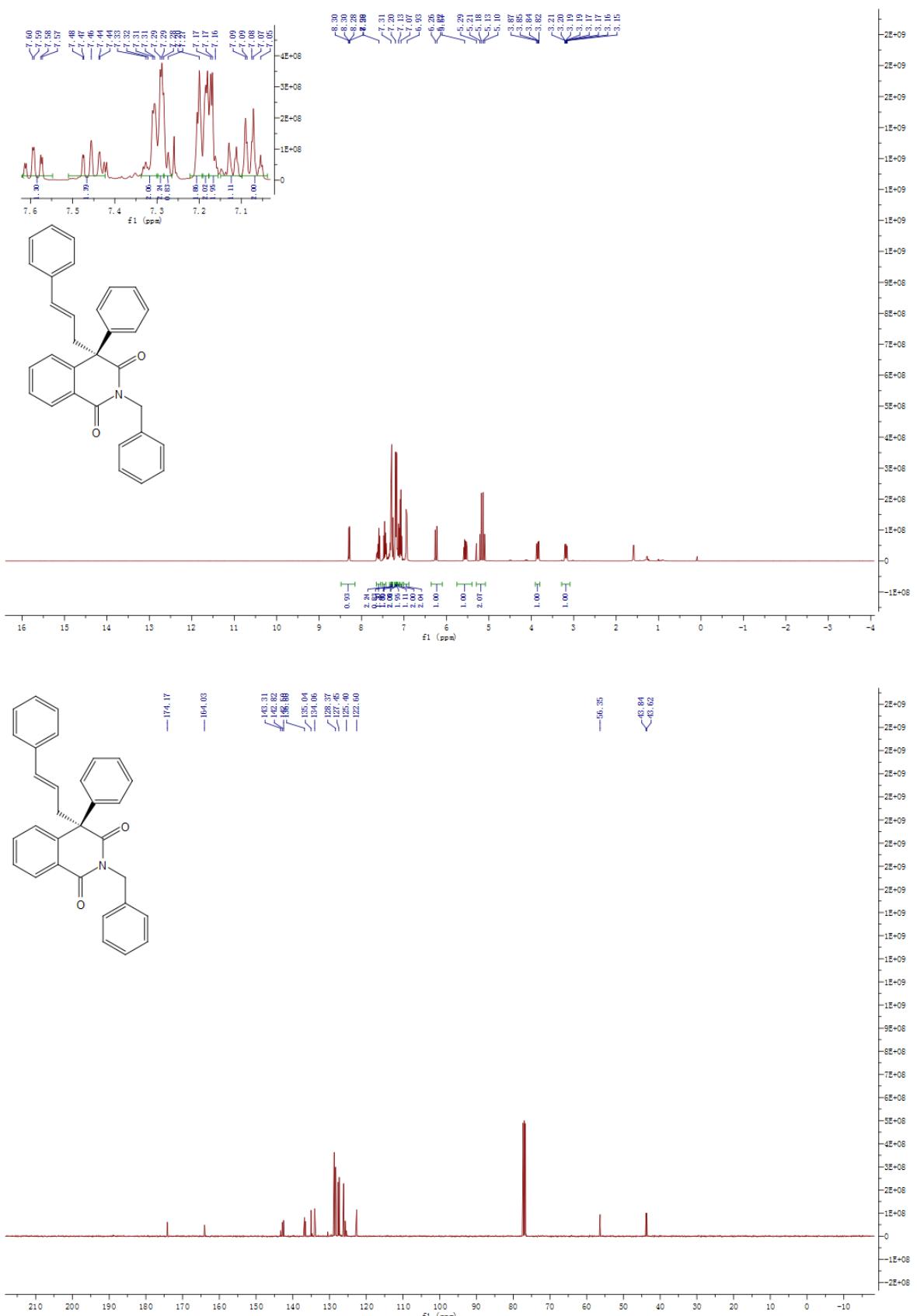
(R)-4-allyl-2-benzyl-4-(1H-indol-5-yl)isoquinoline-1,3(2H,4H)-dione(3z):



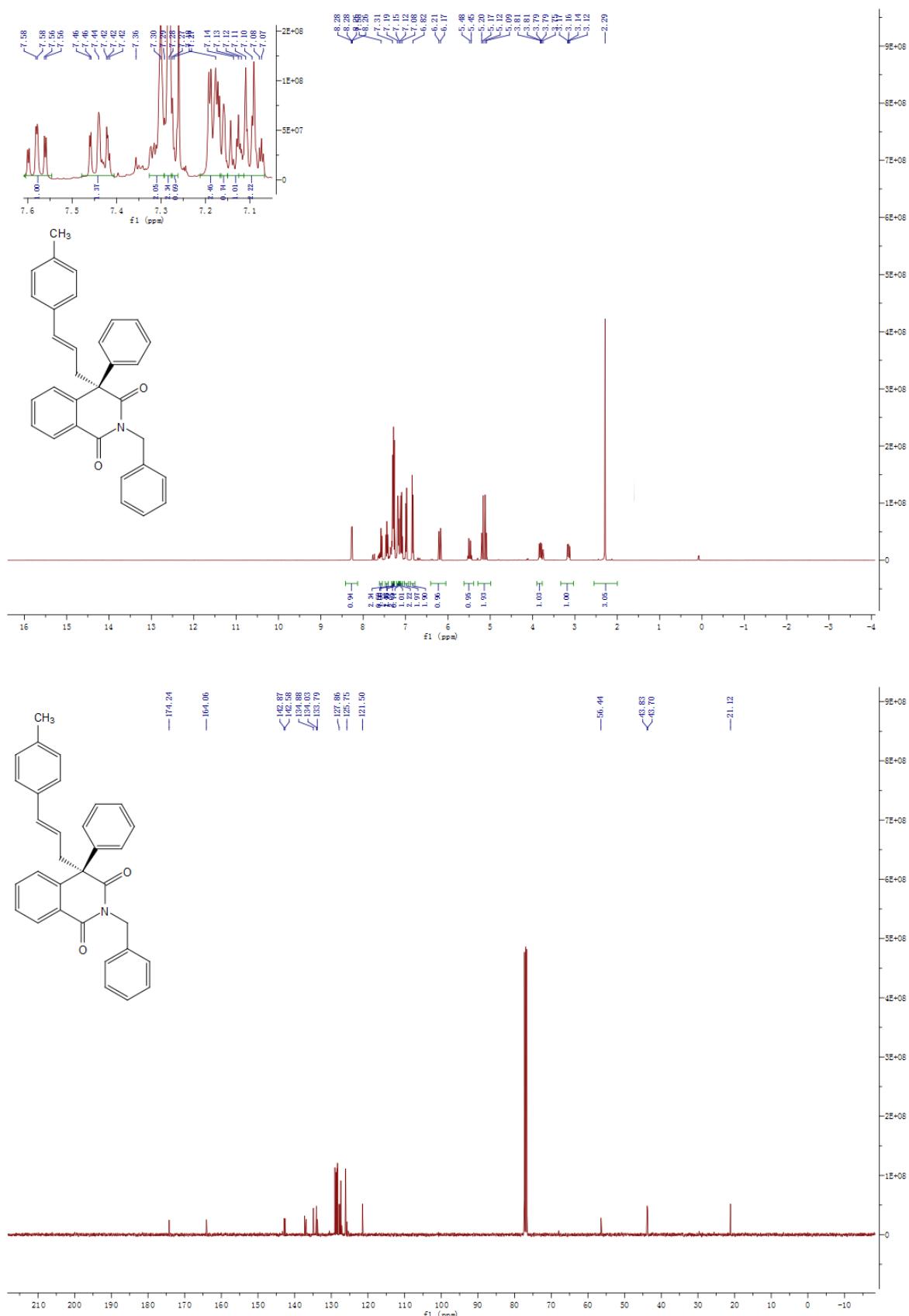
(R)-4-allyl-4-(benzo[b]thiophen-5-yl)-2-benzylisoquinoline-1,3(2H,4H)-dione(3aa):



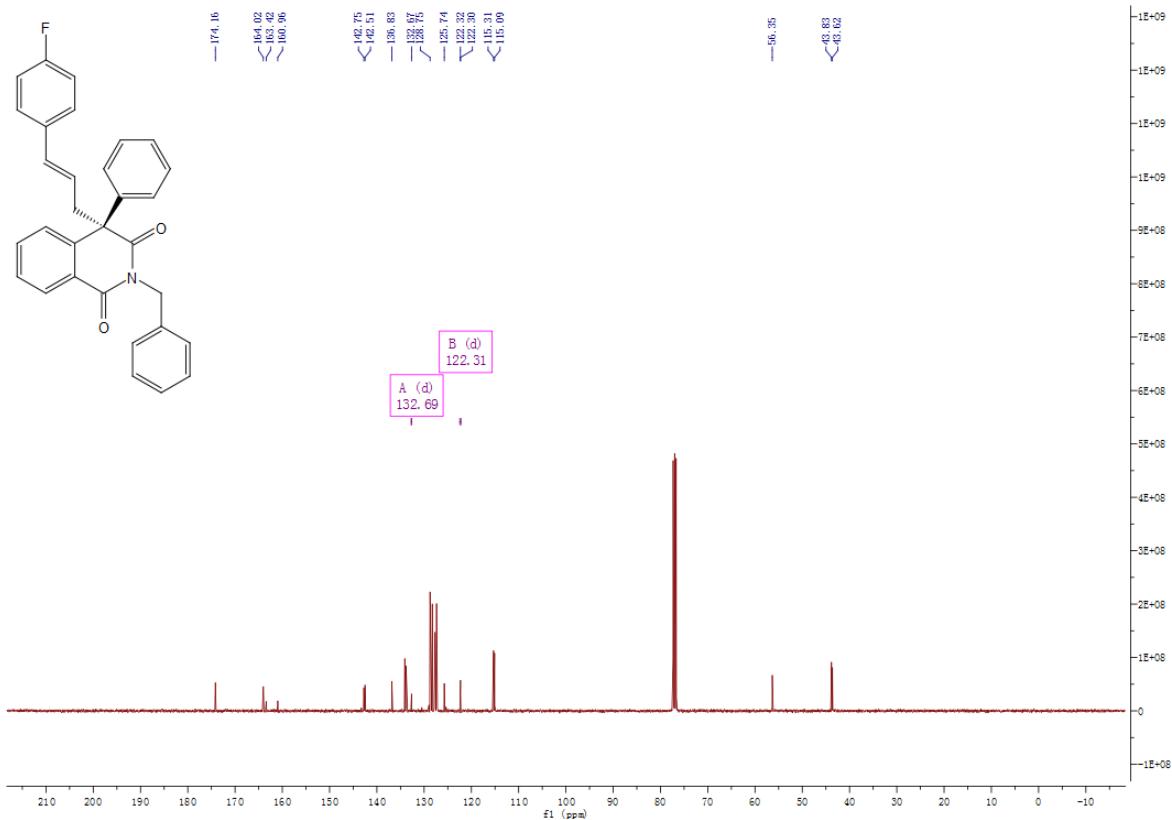
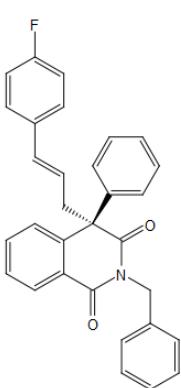
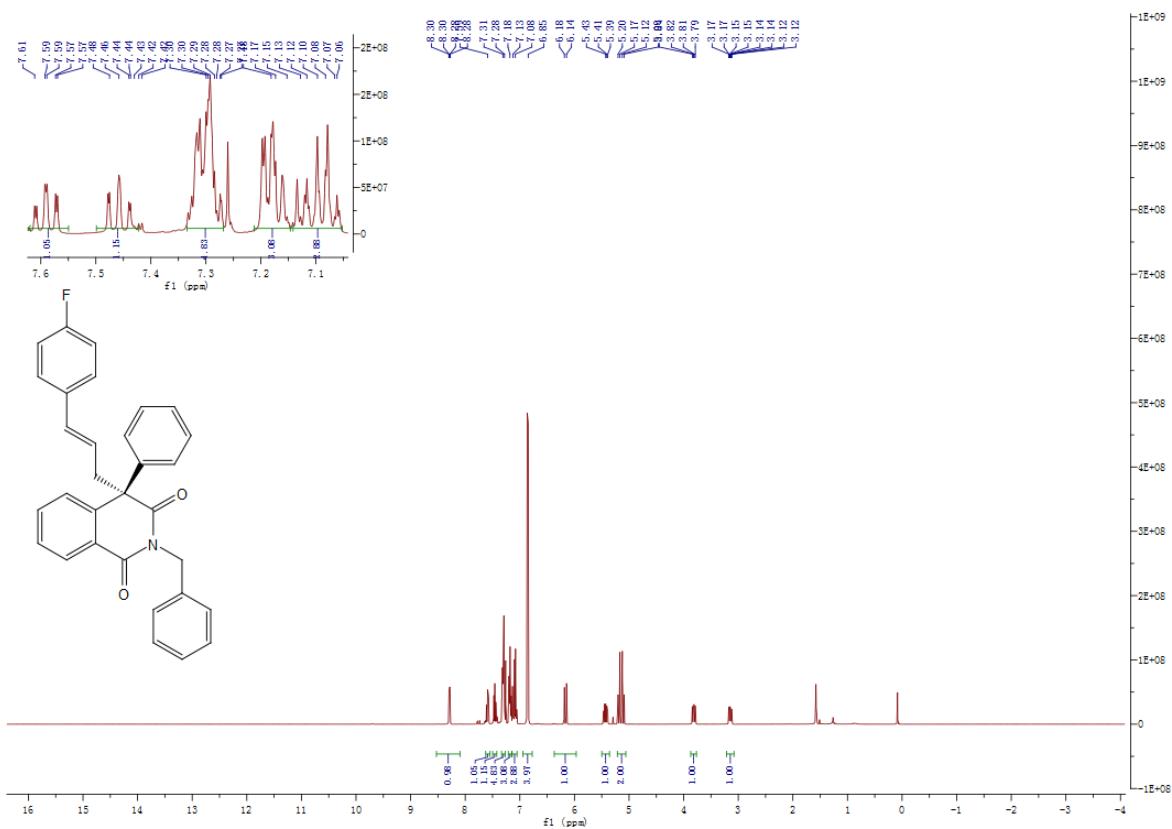
(R)-2-benzyl-4-cinnamyl-4-phenylisoquinoline-1,3(2H,4H)-dione(3ab):



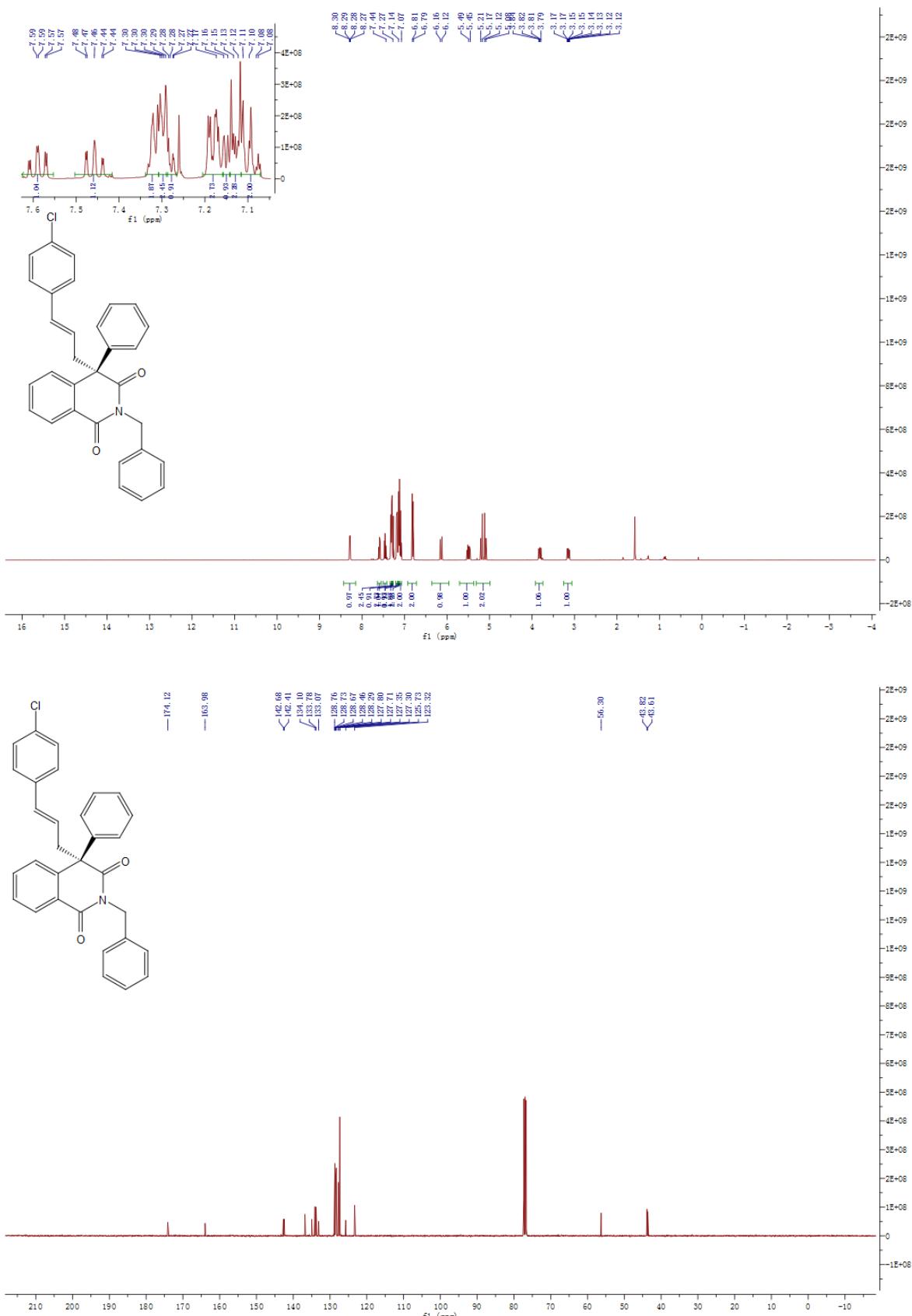
(R,E)-2-benzyl-4-phenyl-4-(3-(p-tolyl)allyl)isoquinoline-1,3(2H,4H)-dione(3ac):



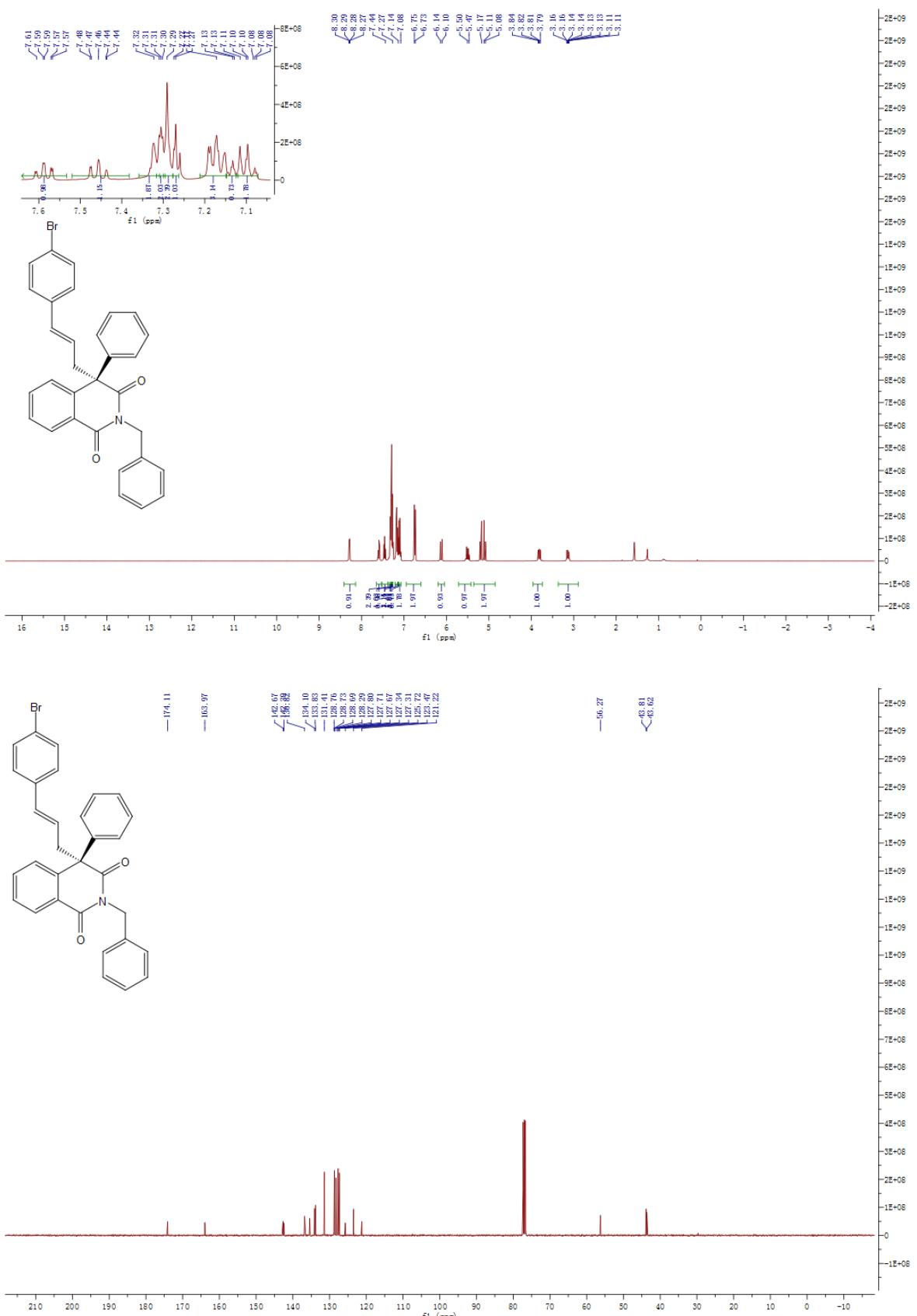
(R,E)-2-benzyl-4-(3-(4-fluorophenyl)allyl)-4-phenylisoquinoline-1,3(2H,4H)-dione(3ad):



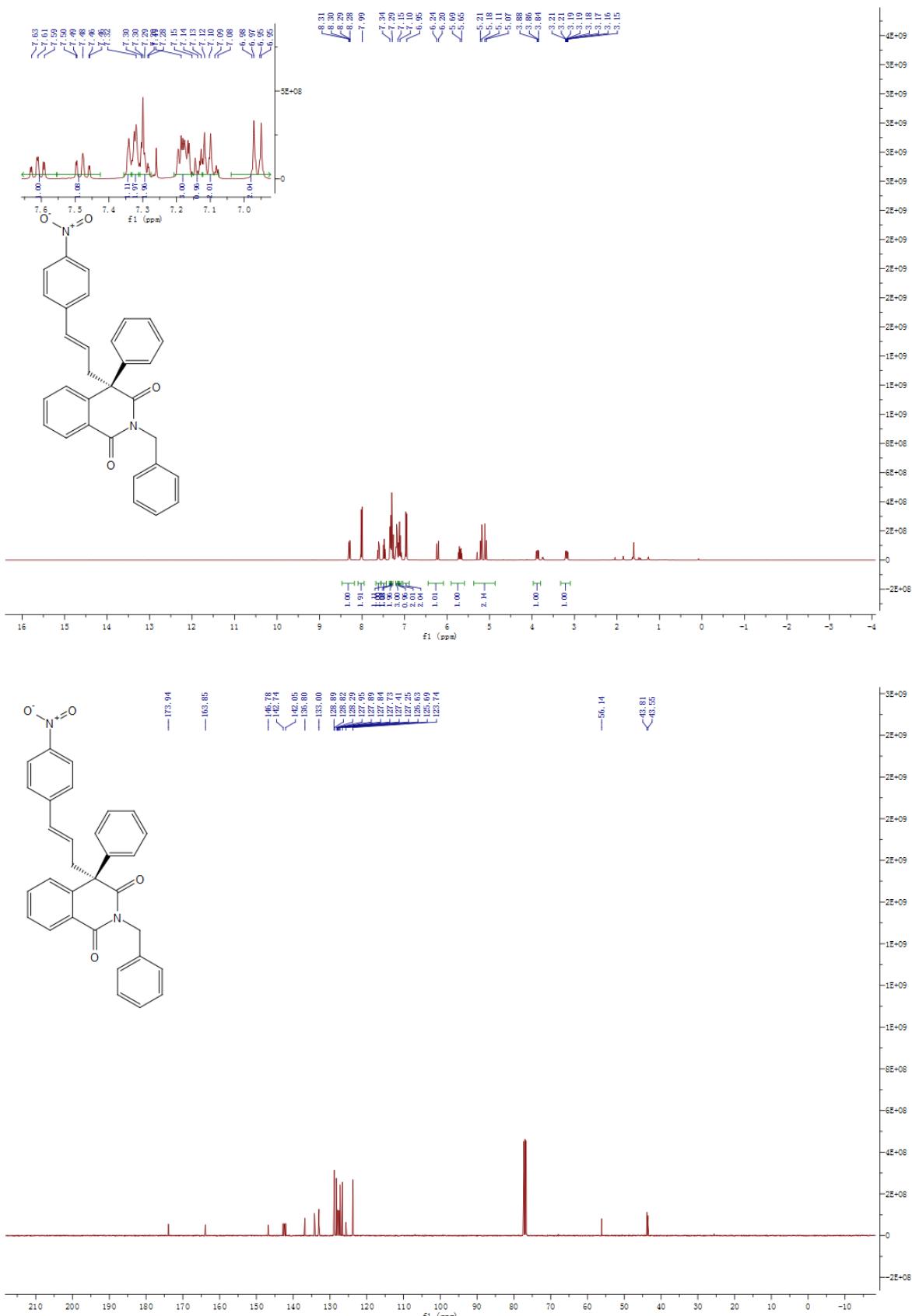
(R,E)-2-benzyl-4-(3-(4-chlorophenyl)allyl)-4-phenylisoquinoline-1,3(2H,4H)-dione(3ae):



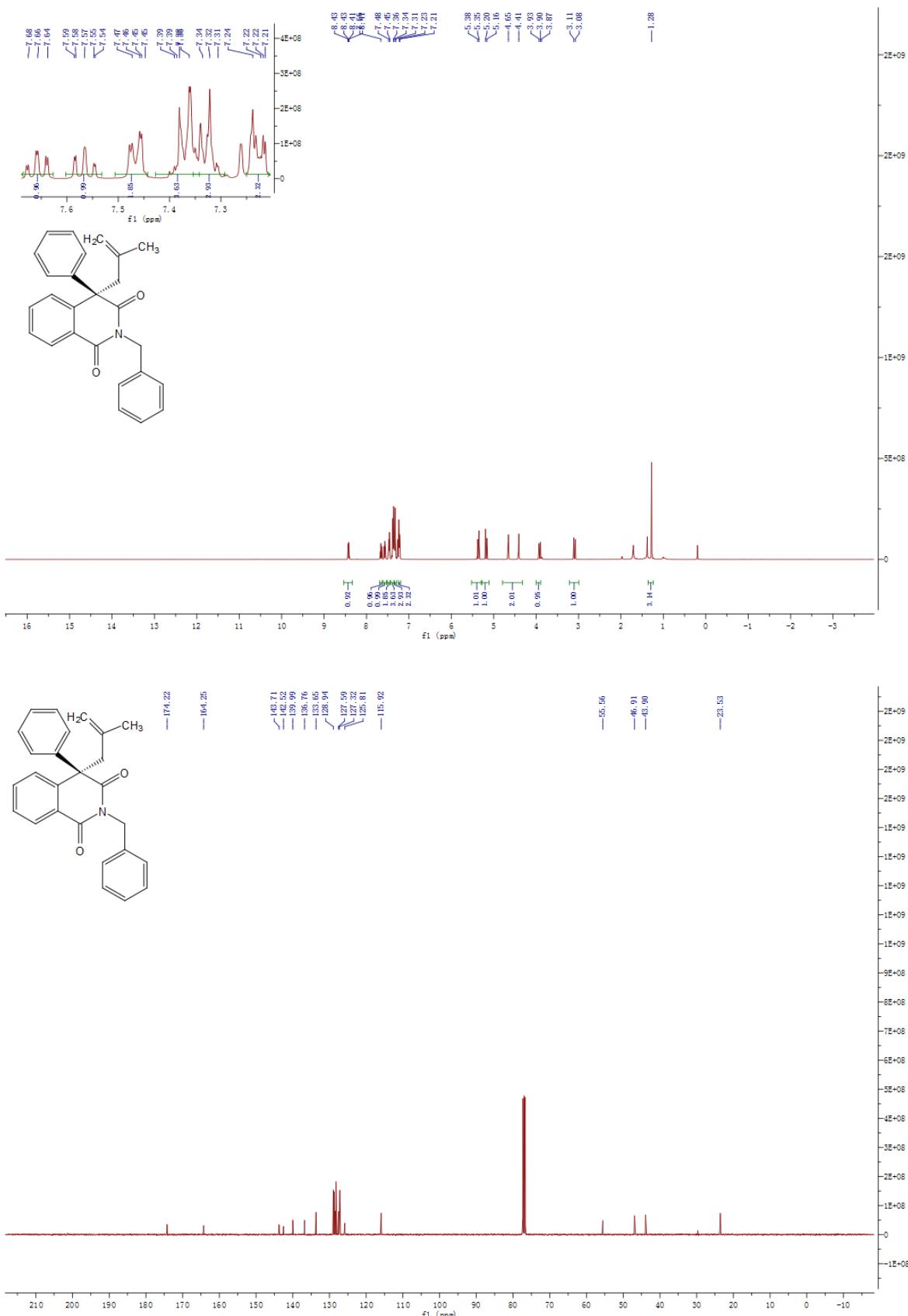
(R,E)-2-benzyl-4-(3-(4-bromophenyl)allyl)-4-phenylisoquinoline-1,3(2H,4H)-dione(3af):



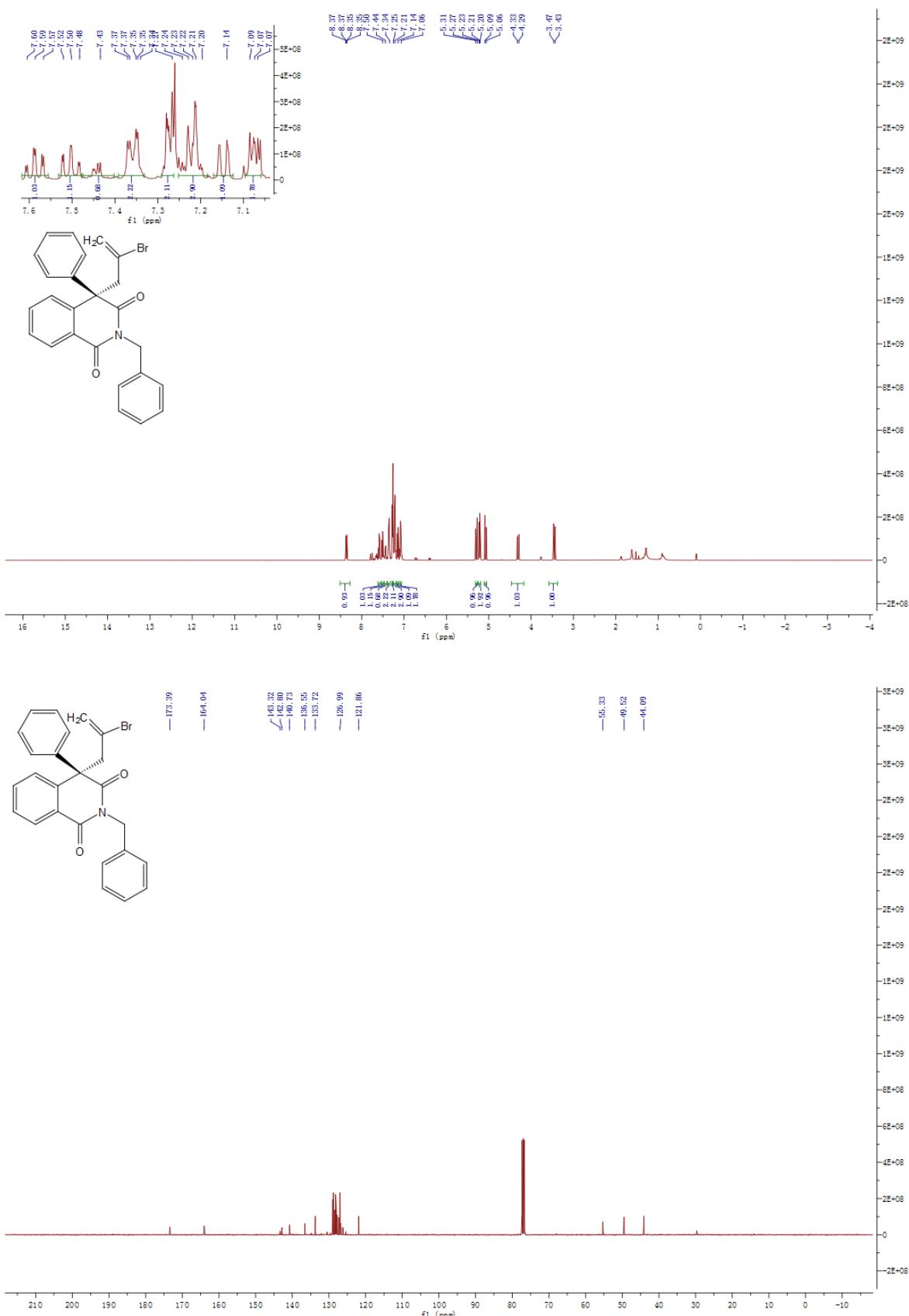
(R,E)-2-benzyl-4-(3-(4-nitrophenyl)allyl)-4-phenylisoquinoline-1,3(2H,4H)-dione(3ag):



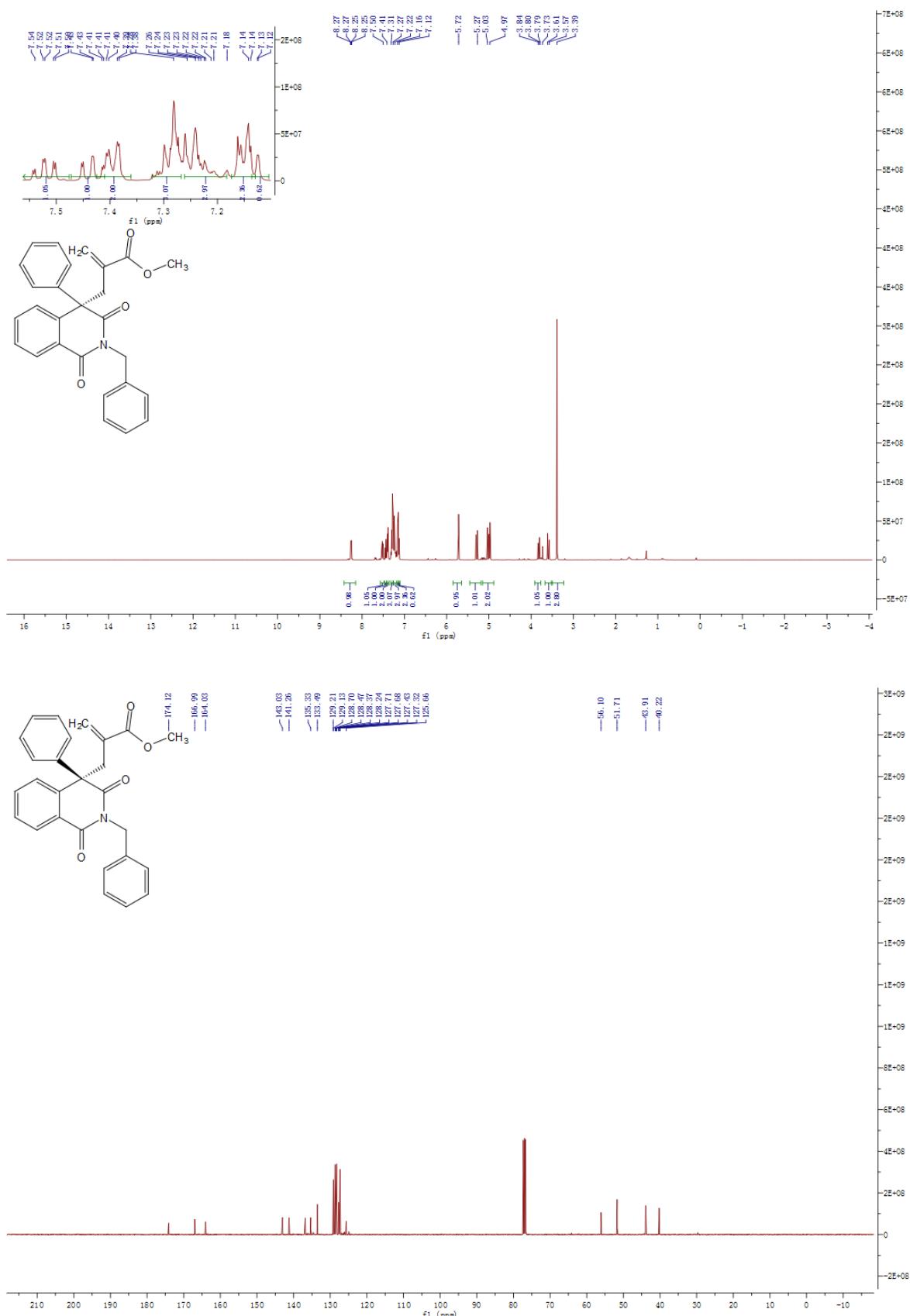
(R)-2-benzyl-4-(2-methylallyl)-4-phenylisoquinoline-1,3(2H,4H)-dione(3ah):



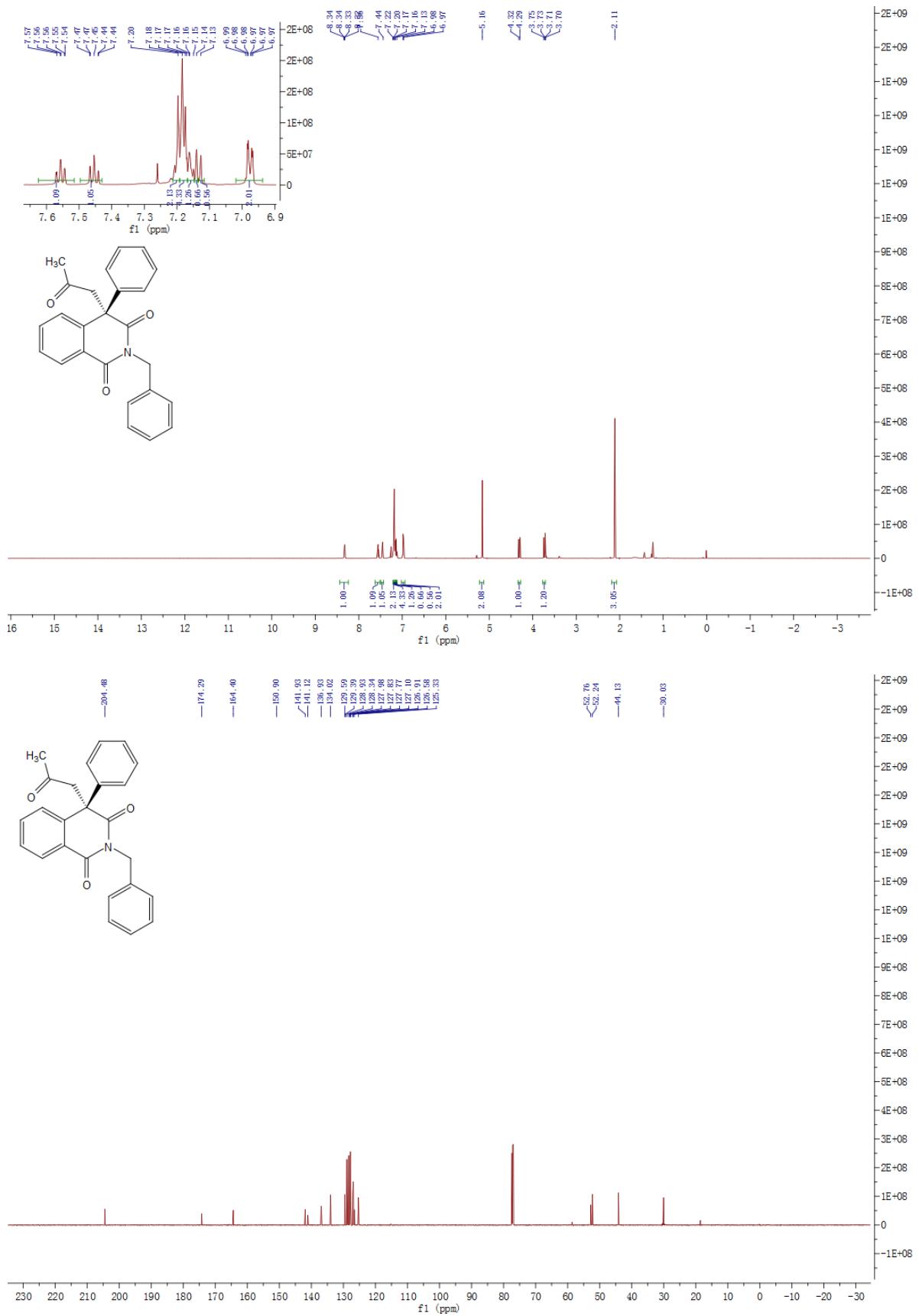
(R)-2-benzyl-4-(2-bromoallyl)-4-phenylisoquinoline-1,3(2H,4H)-dione(3ai):



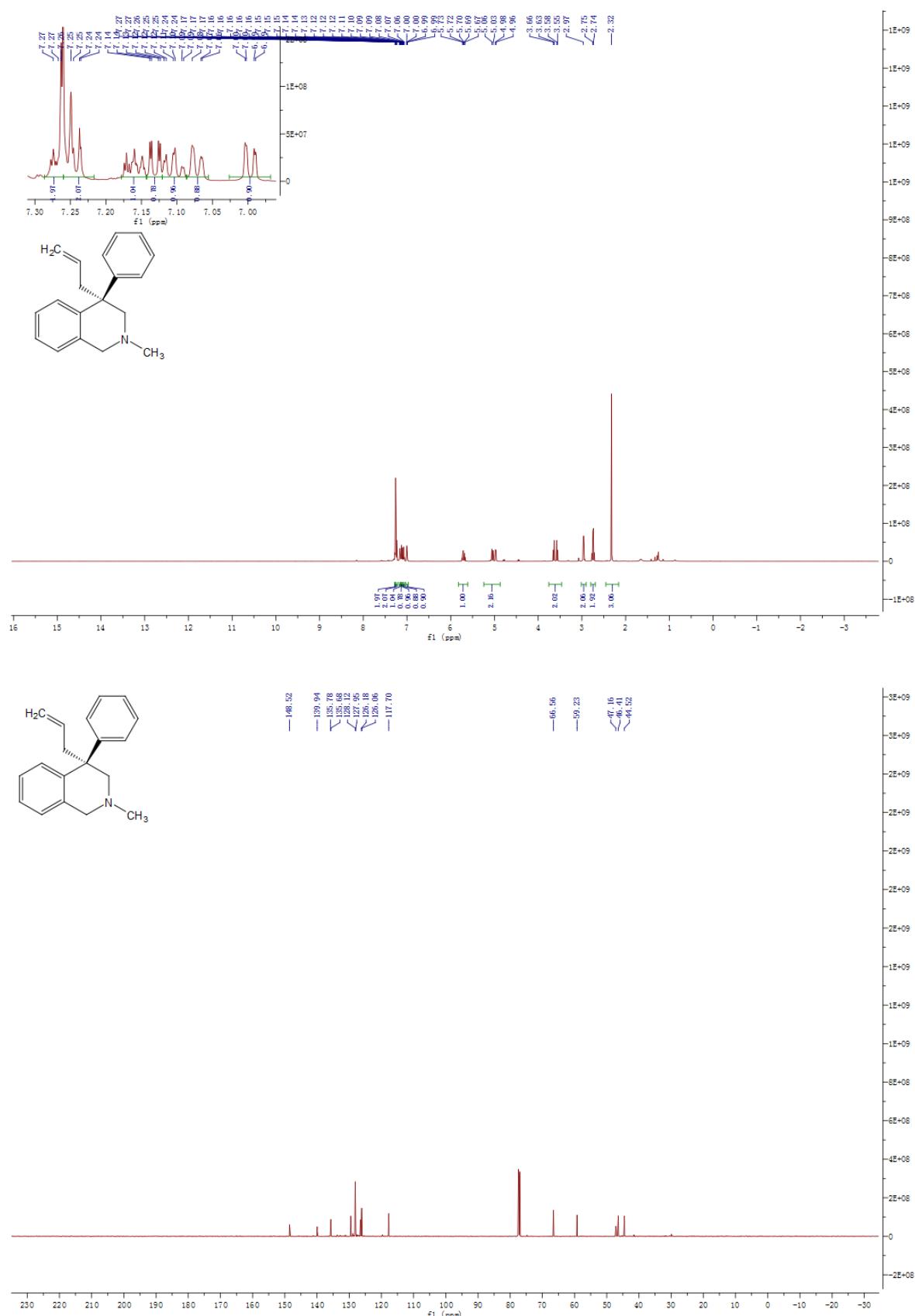
(R)-methyl2-((2-benzyl-1,3-dioxo-4-phenyl-1,2,3,4-tetrahydroisoquinolin-4-yl)methyl)acrylate(3aj):



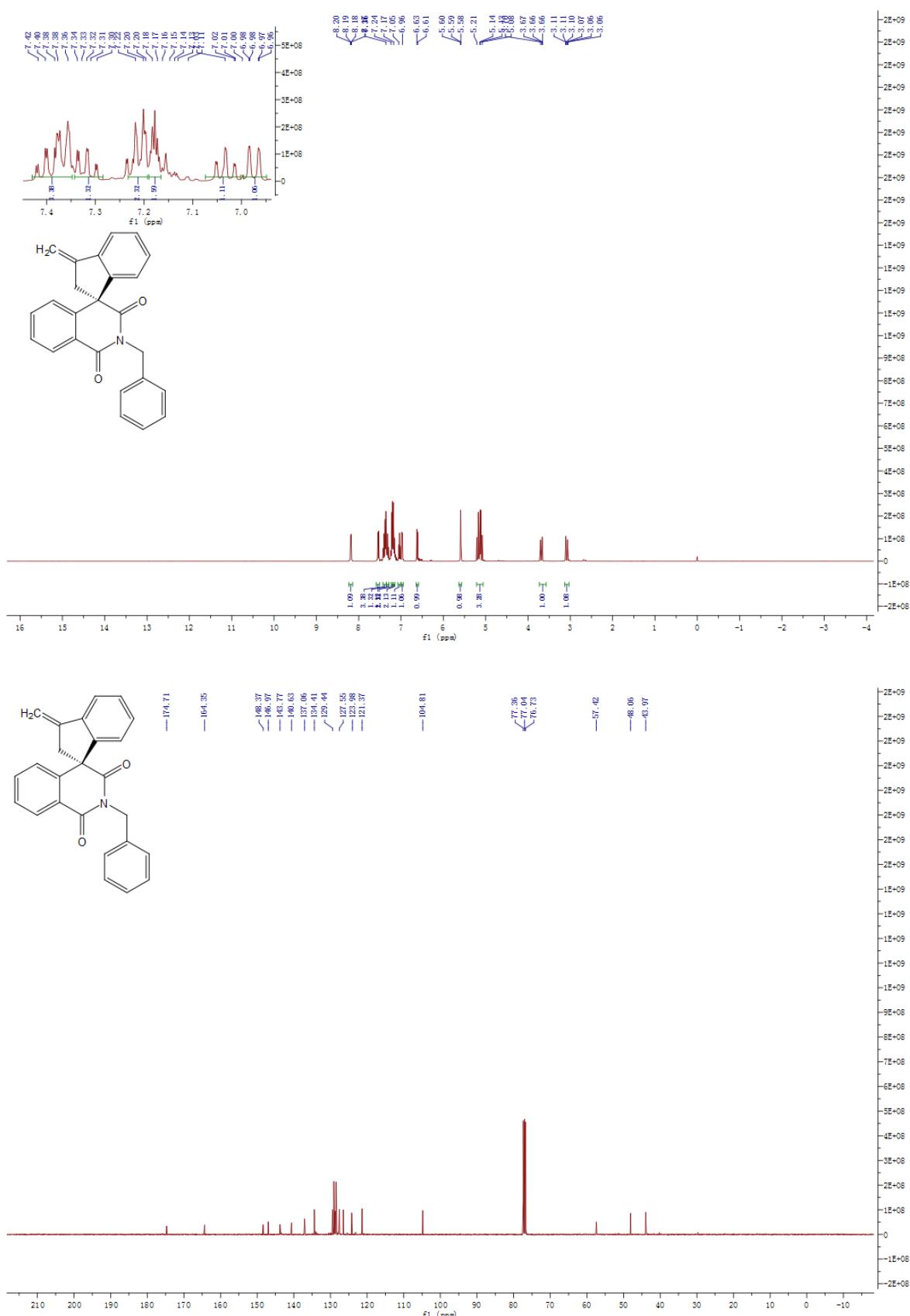
(R)-2-benzyl-4-(2-oxopropyl)-4-phenylisoquinoline-1,3(2H,4H)-dione(4a):



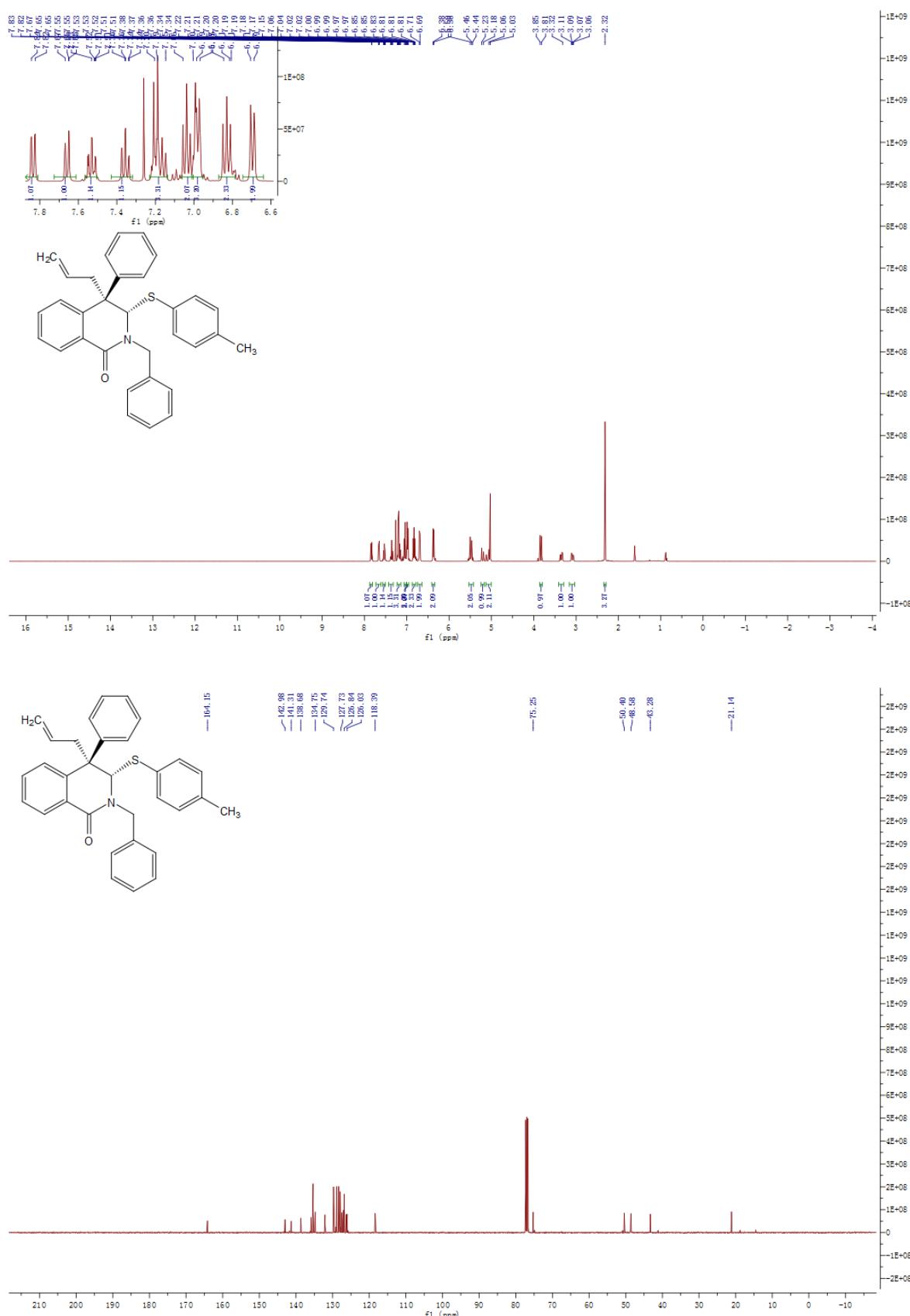
(R)-2'-benzyl-3-methylene-2,3-dihydro-1'H-spiro[indene-1,4'-isoquinoline]-1',3'(2'H)-dione(5b):



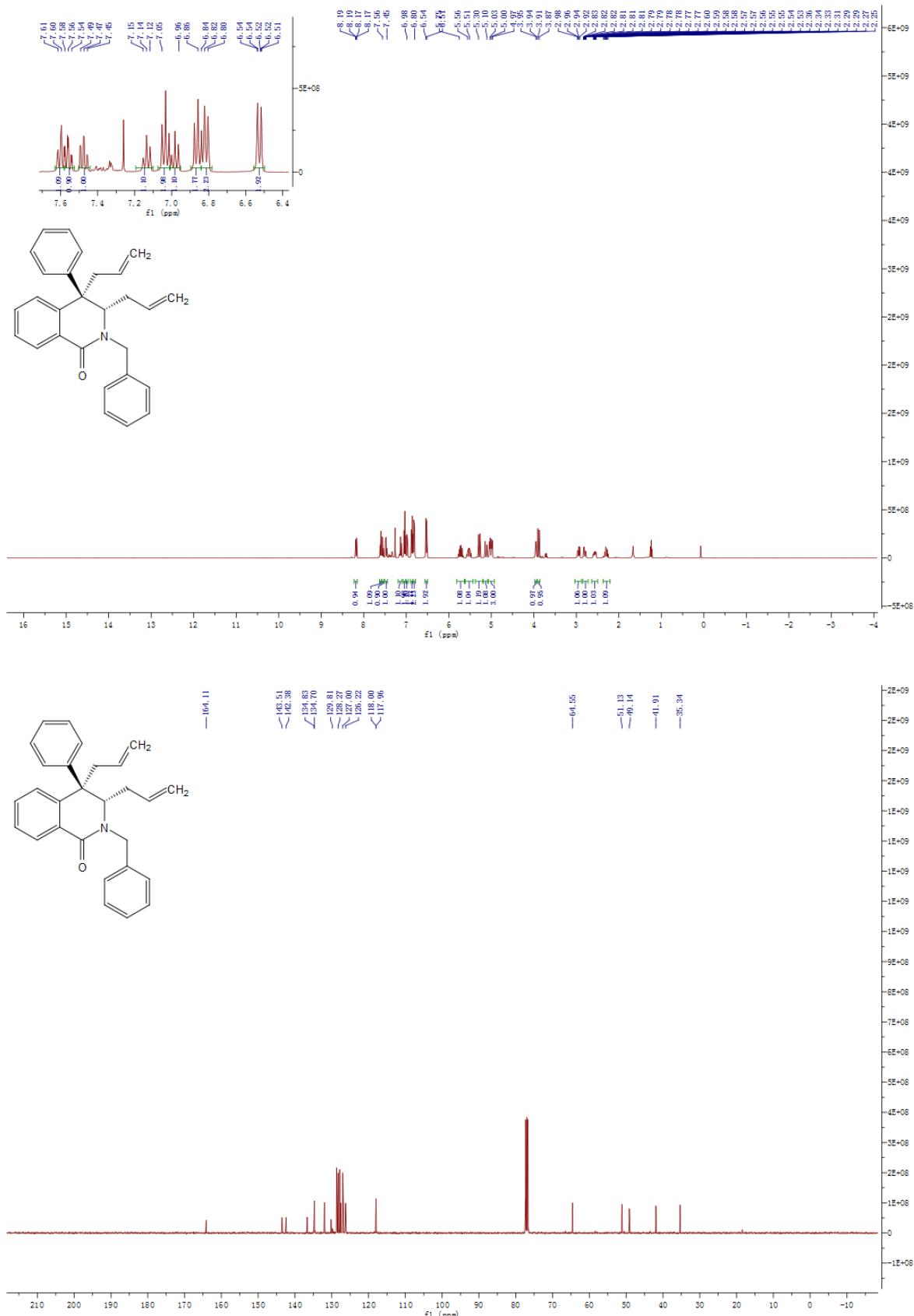
(R)-4-allyl-2-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline(6q):



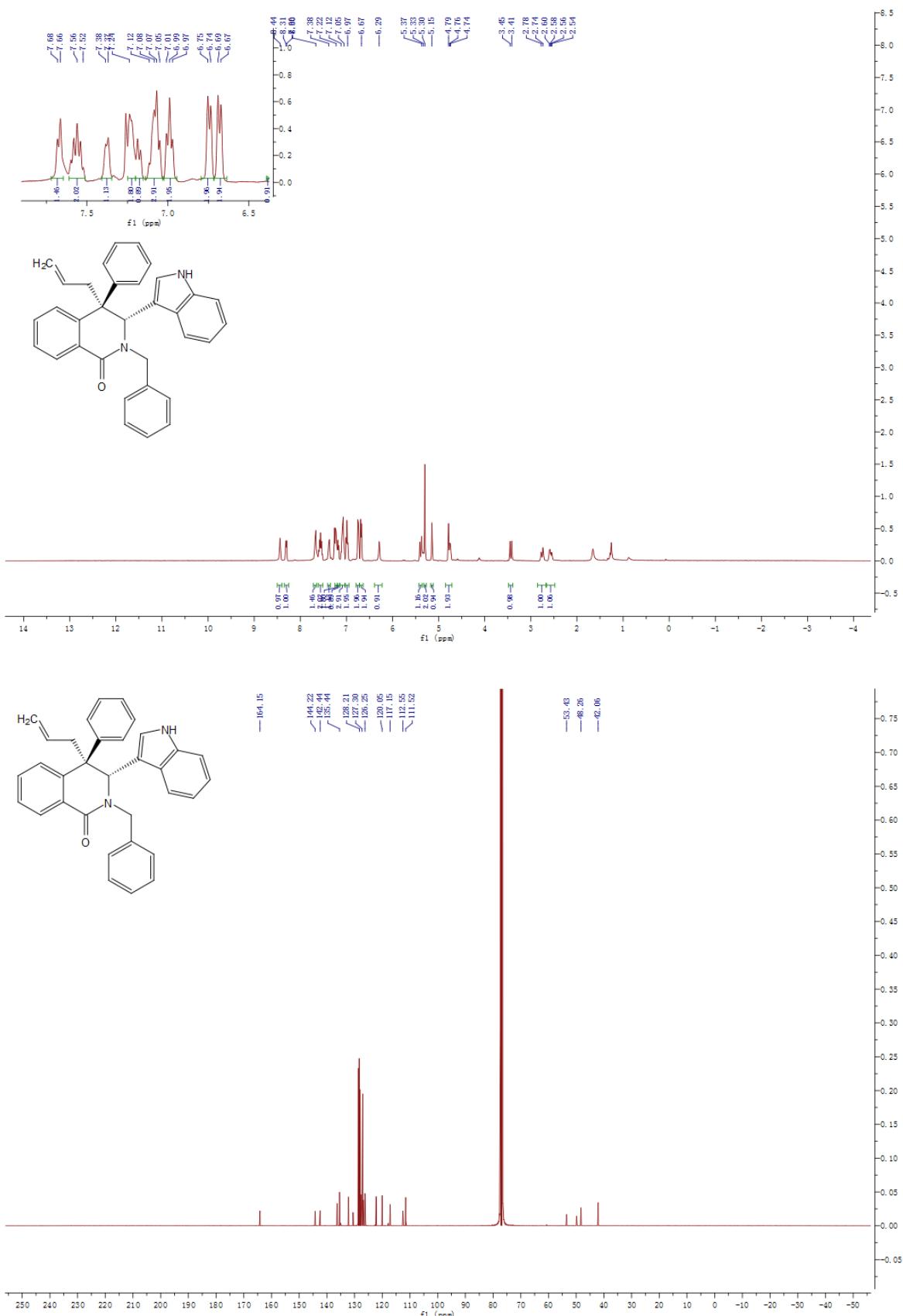
(3*S*,4*R*)-4-allyl-2-benzyl-4-phenyl-3-(*p*-tolylthio)-3,4-dihydroisoquinolin-1(2*H*)-one(8a):



(3*S*,4*R*)-3,4-diallyl-2-benzyl-4-phenyl-3,4-dihydroisoquinolin-1(2*H*)-one(9a):

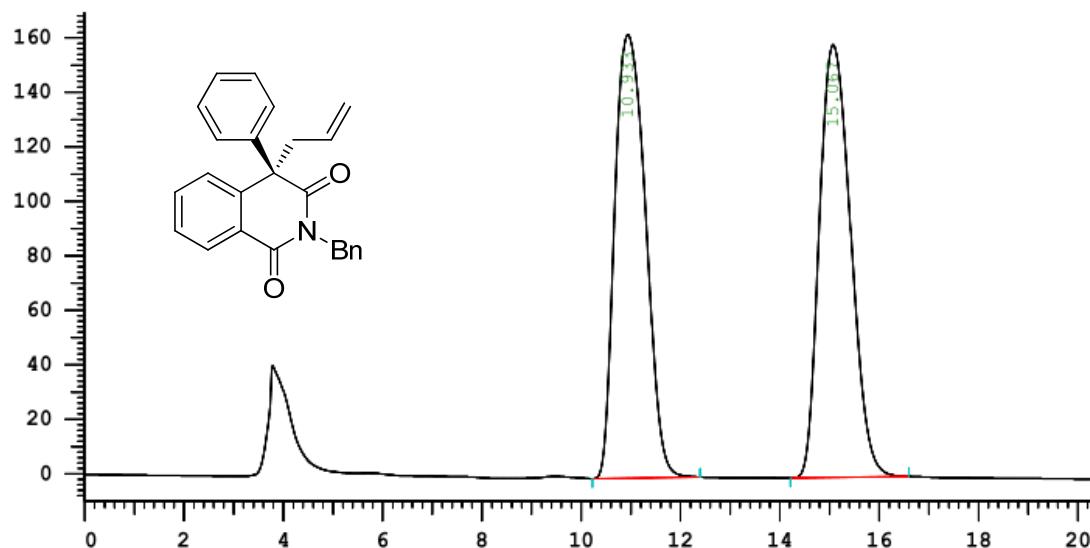


(3*S*,4*R*)-4-allyl-2-benzyl-3-(1*H*-indol-3-yl)-4-phenyl-3,4-dihydroisoquinolin-1(2*H*)-one(10a):

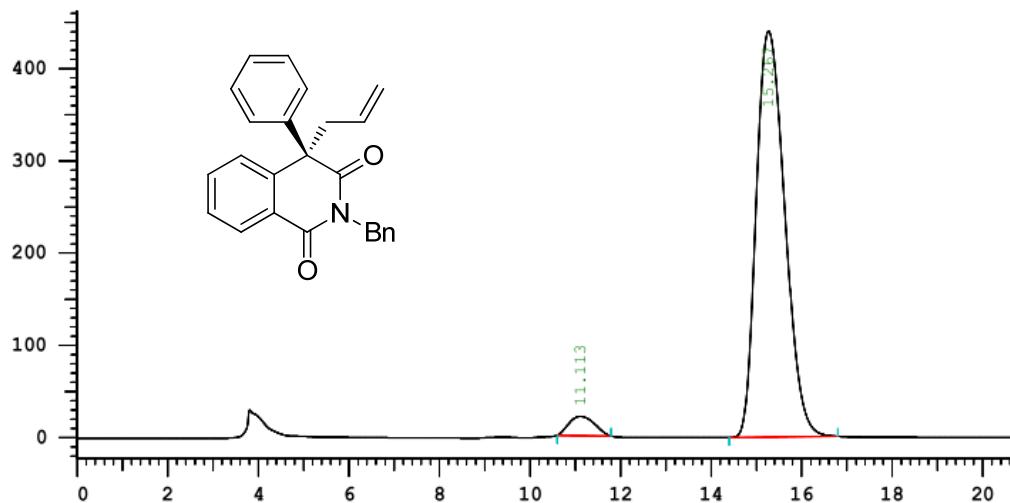


HPPLC spectra:

(R)-4-allyl-2-benzyl-4-phenylisoquinoline-1,3(2H,4H)-dione(3a):

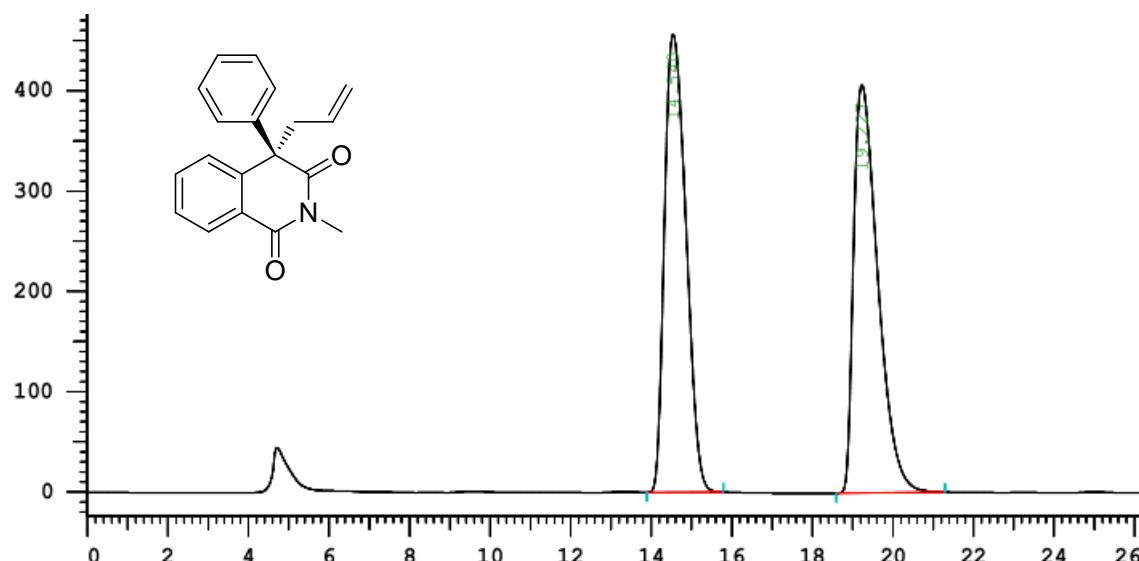


No.	Ret.Time min	Peak Name	Area	Rel.Area
1	10.933	n.a.	7003000	50.195
2	15.067	n.a.	6948573	49.805
Total:			13951573	100.00

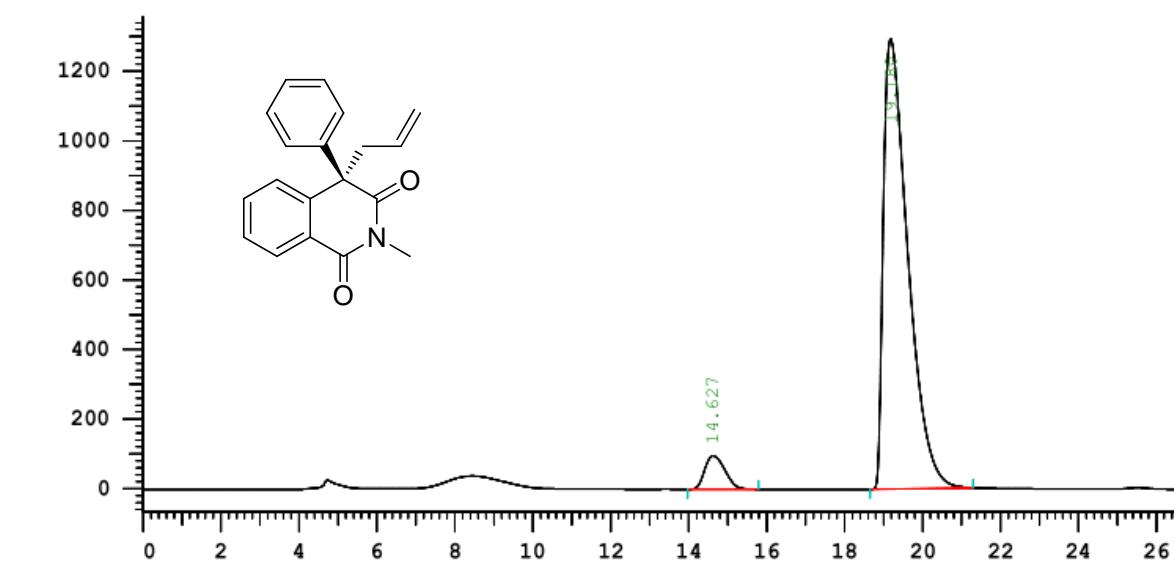


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	11.114	n.a.	821506	4.079
2	15.267	n.a.	19320072	95.921
Total:			20141578	100.00

(R)-4-allyl-2-methyl-4-phenylisoquinoline-1,3(2H,4H)-dione(3b):

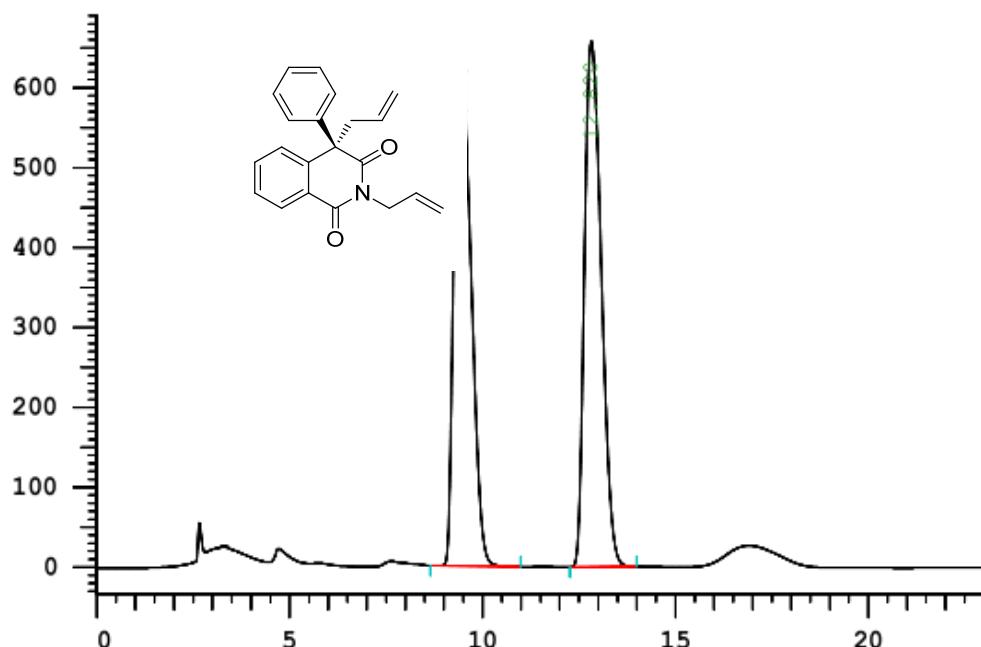
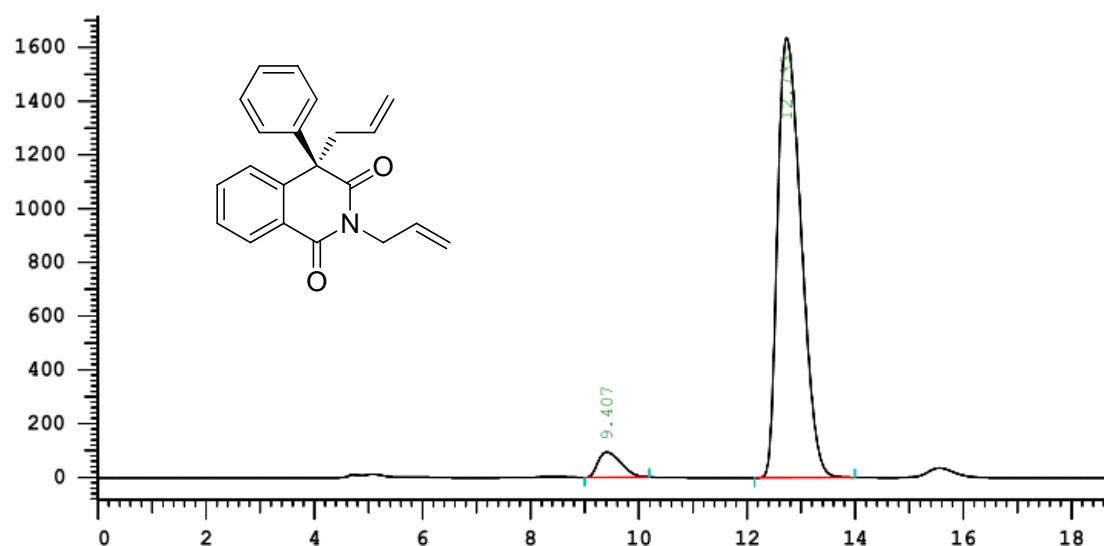


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	14.540	n.a.	16842607	49.824
2	19.227	n.a.	16961552	50.176
Total:			33804159	100.00

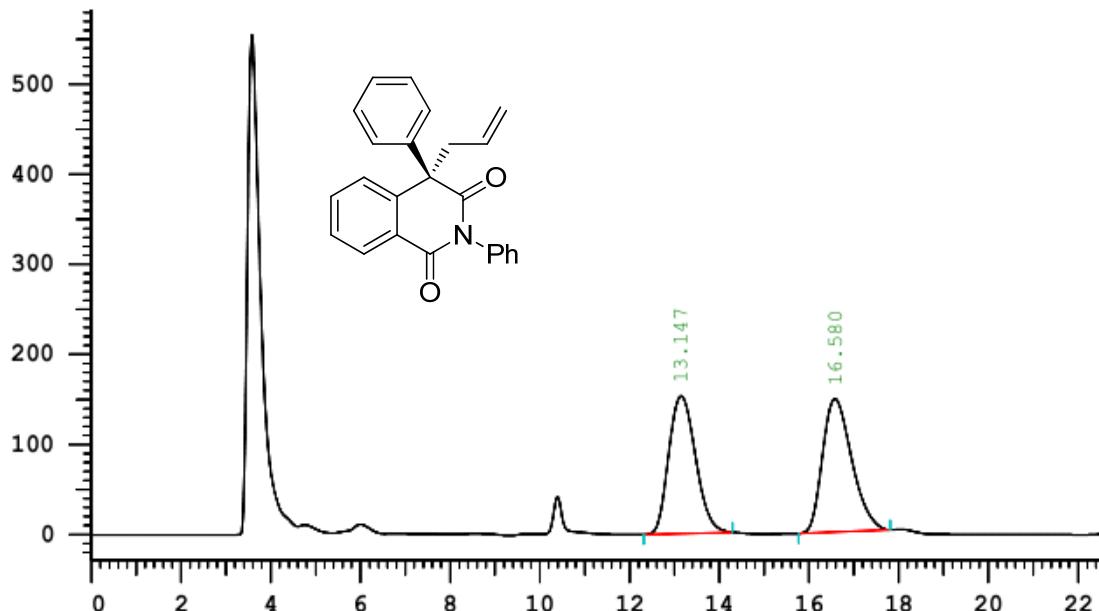


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	14.627	n.a.	3426565	5.744
2	19.180	n.a.	56232852	94.256
Total:			59659417	100.00

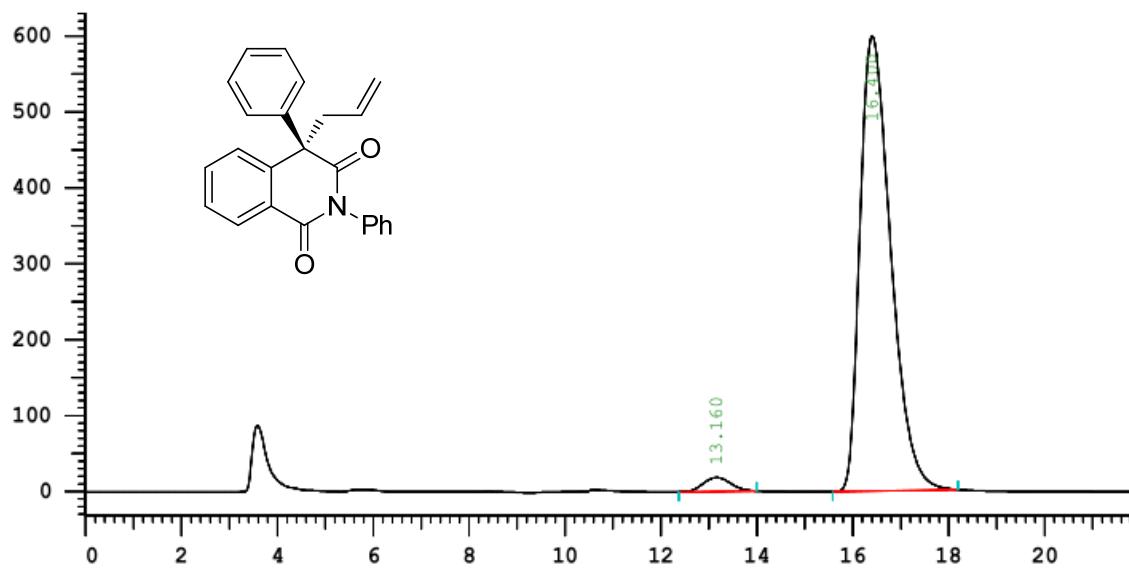
(R)-2,4-diallyl-4-phenylisoquinoline-1,3(2H,4H)-dione(3c):

(R)-4-allyl-2,4-diphenylisoquinoline-1,3(2H,4H)-dione(3d):

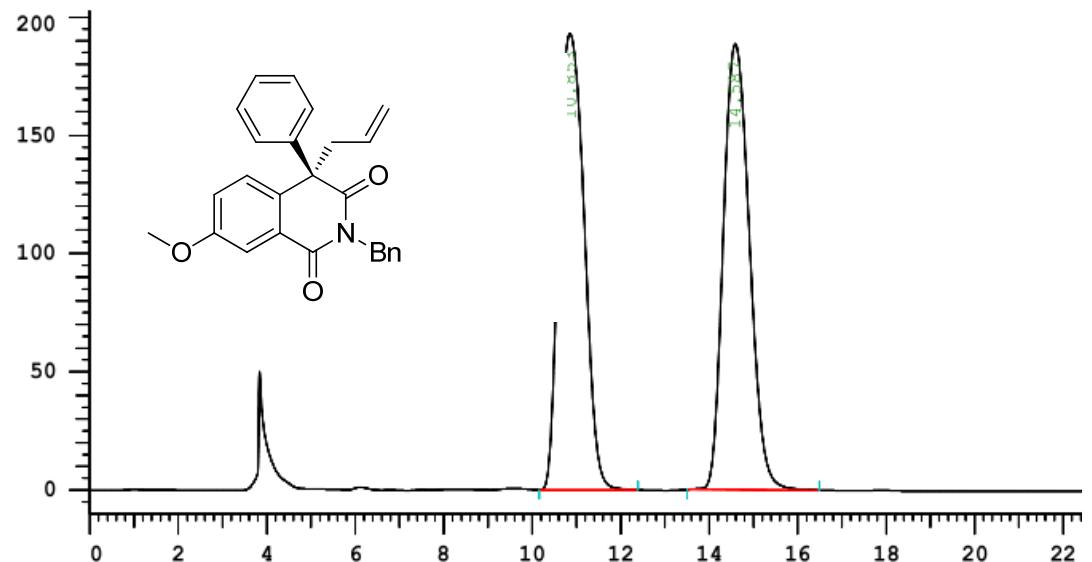


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	13.147	n.a.	6347070	48.609
2	16.580	n.a.	6710332	51.391
Total:			13057402	100.00

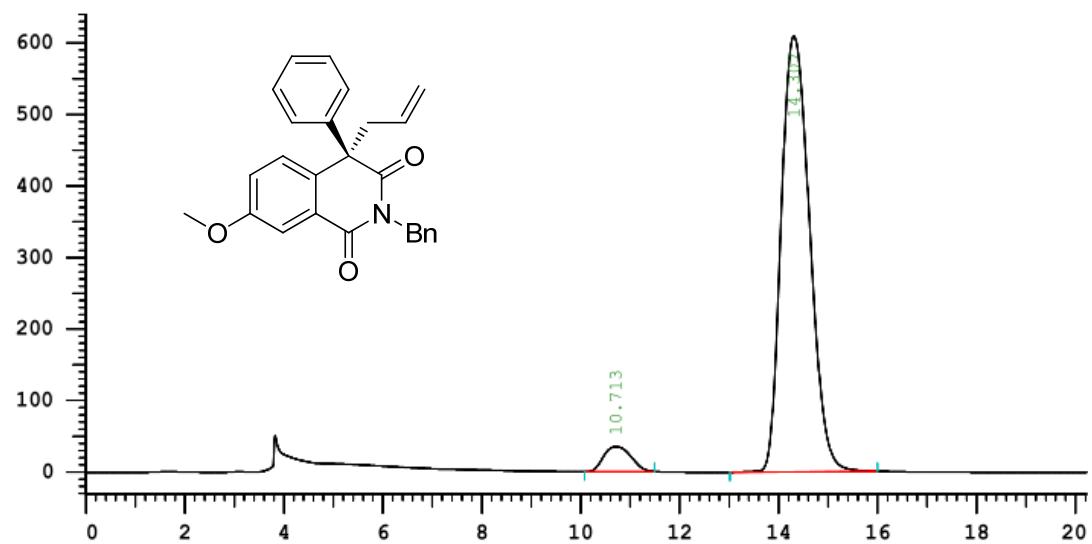


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	13.160	n.a.	732871	2.674
2	16.400	n.a.	26675537	97.326
Total:			27408408	100.00

(R)-4-allyl-2-benzyl-7-methoxy-4-phenylisoquinoline-1,3(2H,4H)-dione(3e):

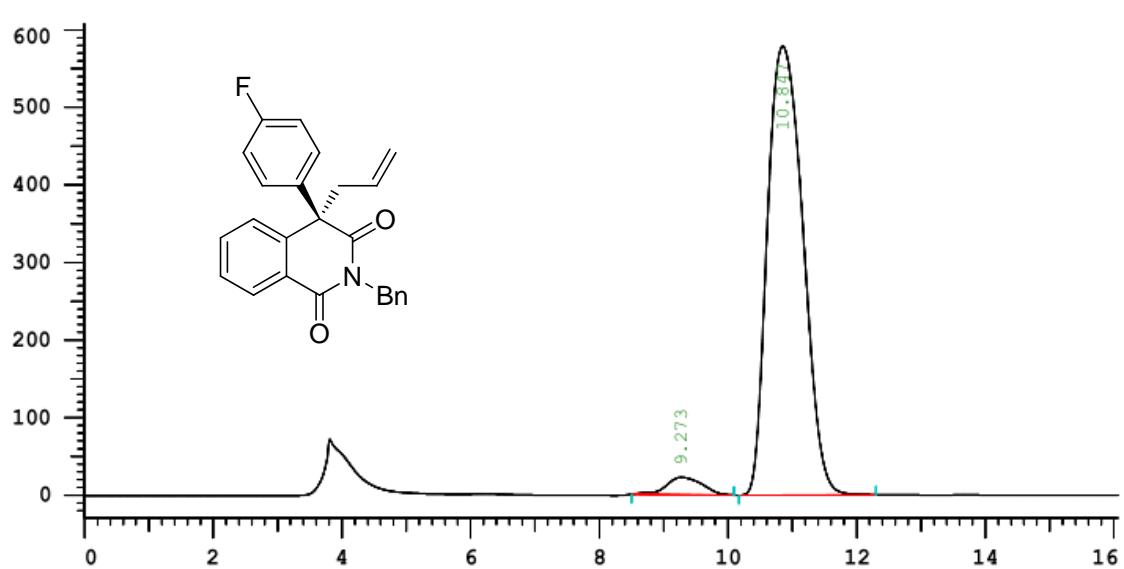
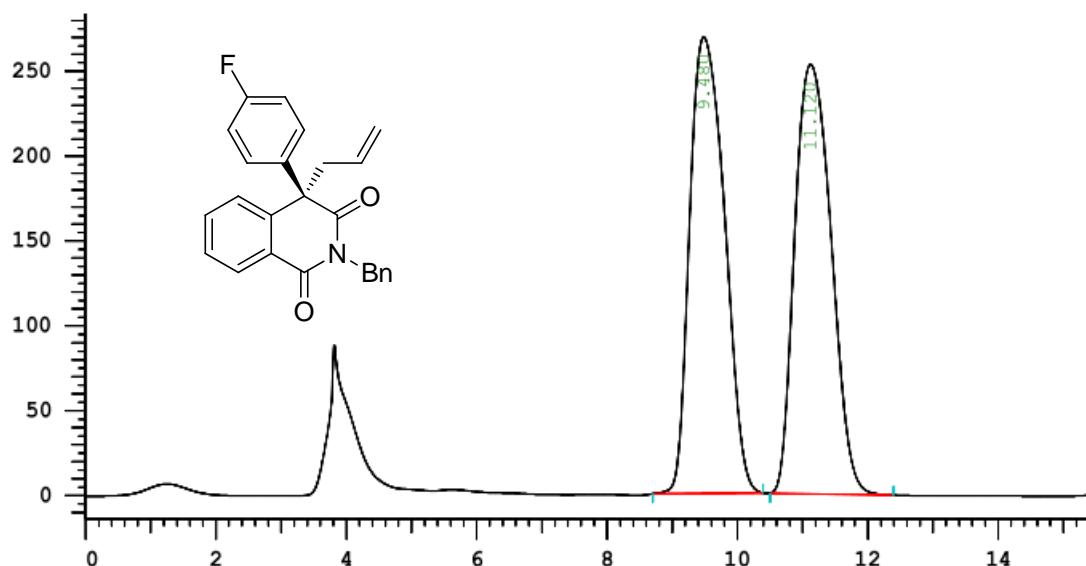


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	10.853	n.a.	7714723	49.970
2	14.587	n.a.	7723911	50.030
Total:			15438634	100.00

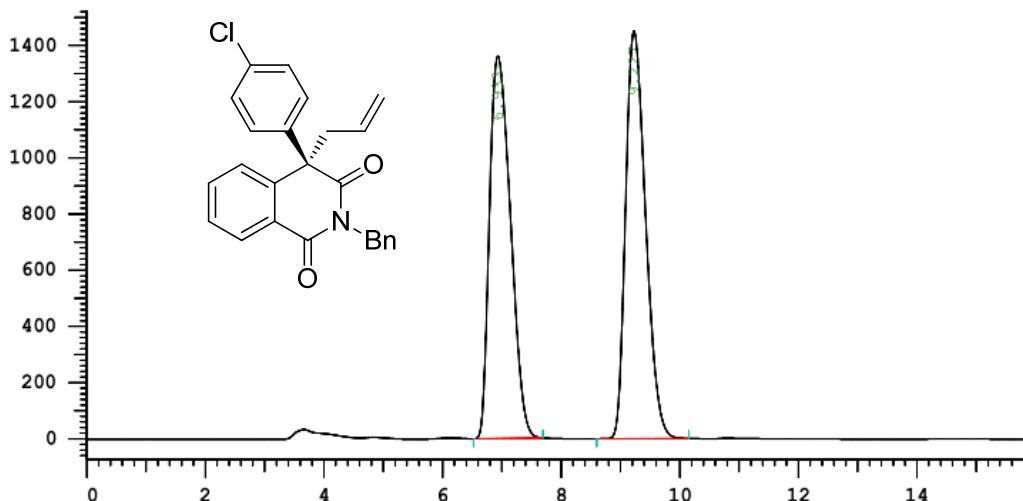


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	10.713	n.a.	1347808	5.254
2	114.307	n.a.	24348920	94.755
Total:			25696728	100.00

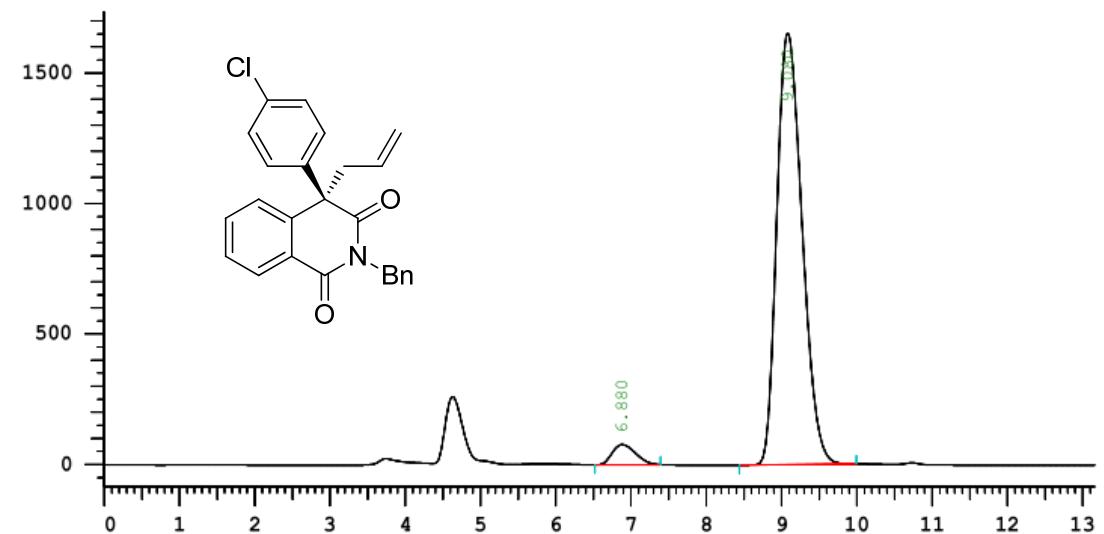
(R)-4-allyl-2-benzyl-4-(4-fluorophenyl)isoquinoline-1,3(2H,4H)-dione(3f):



(R)-4-allyl-2-benzyl-4-(4-chlorophenyl)isoquinoline-1,3(2H,4H)-dione(3g):

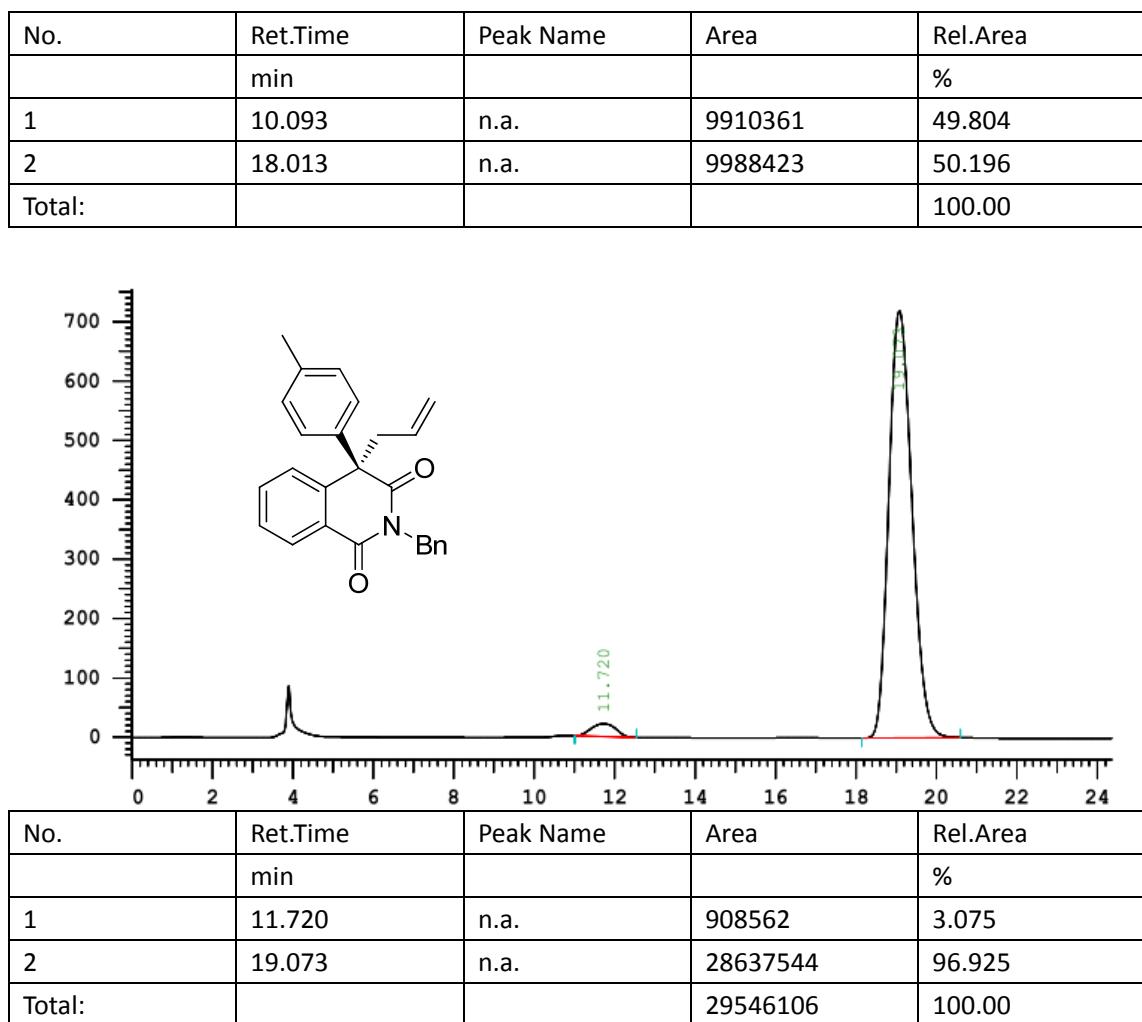
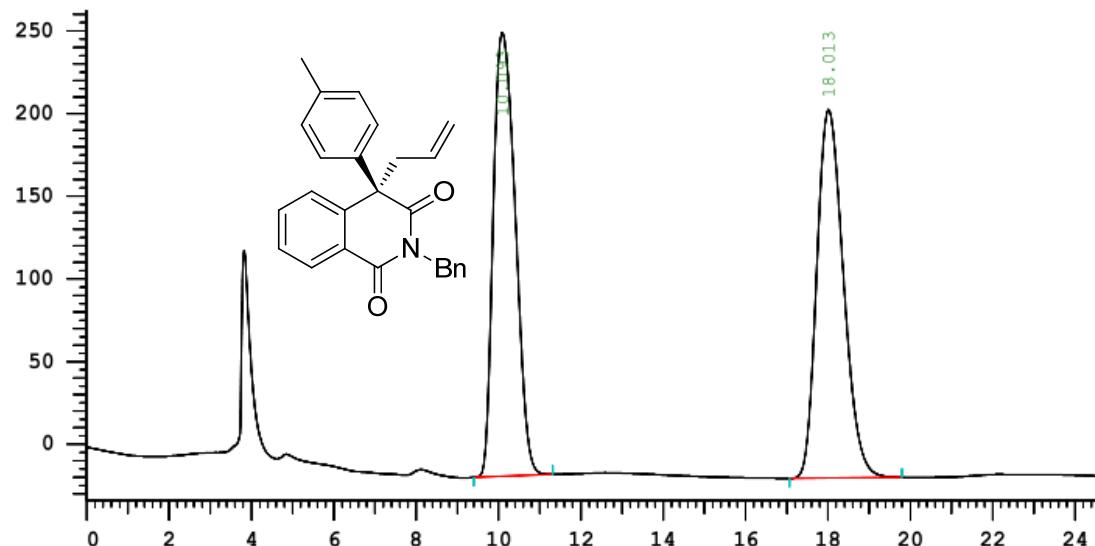


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	6.933	n.a.	33468262	49.655
2	9.227	n.a.	33933196	50.345
Total:			67401458	100.00

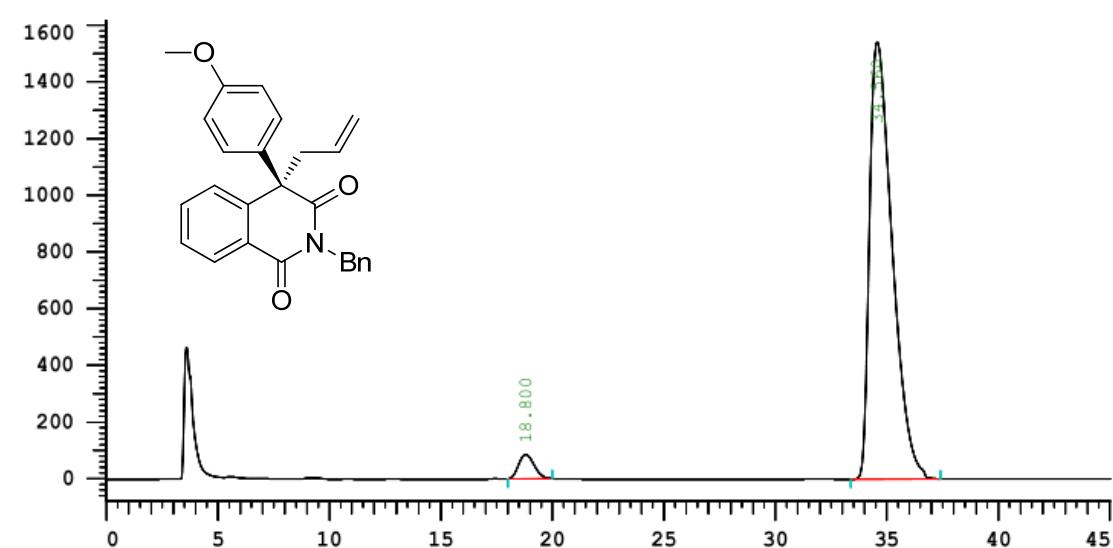
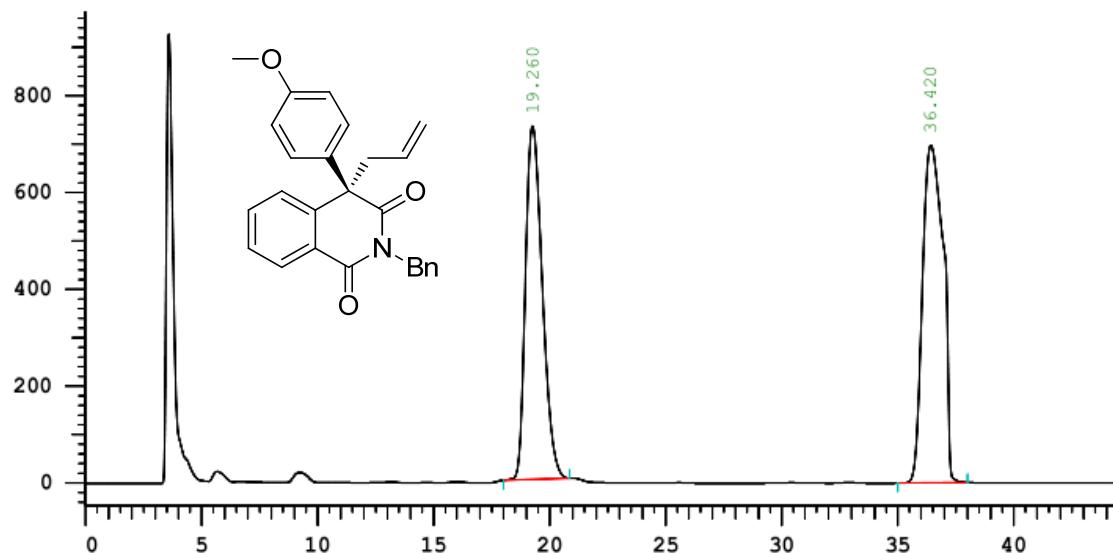


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	6.880	n.a.	1674245	4.162
2	9.080	n.a.	38554949	95.838
Total:			40229194	100.00

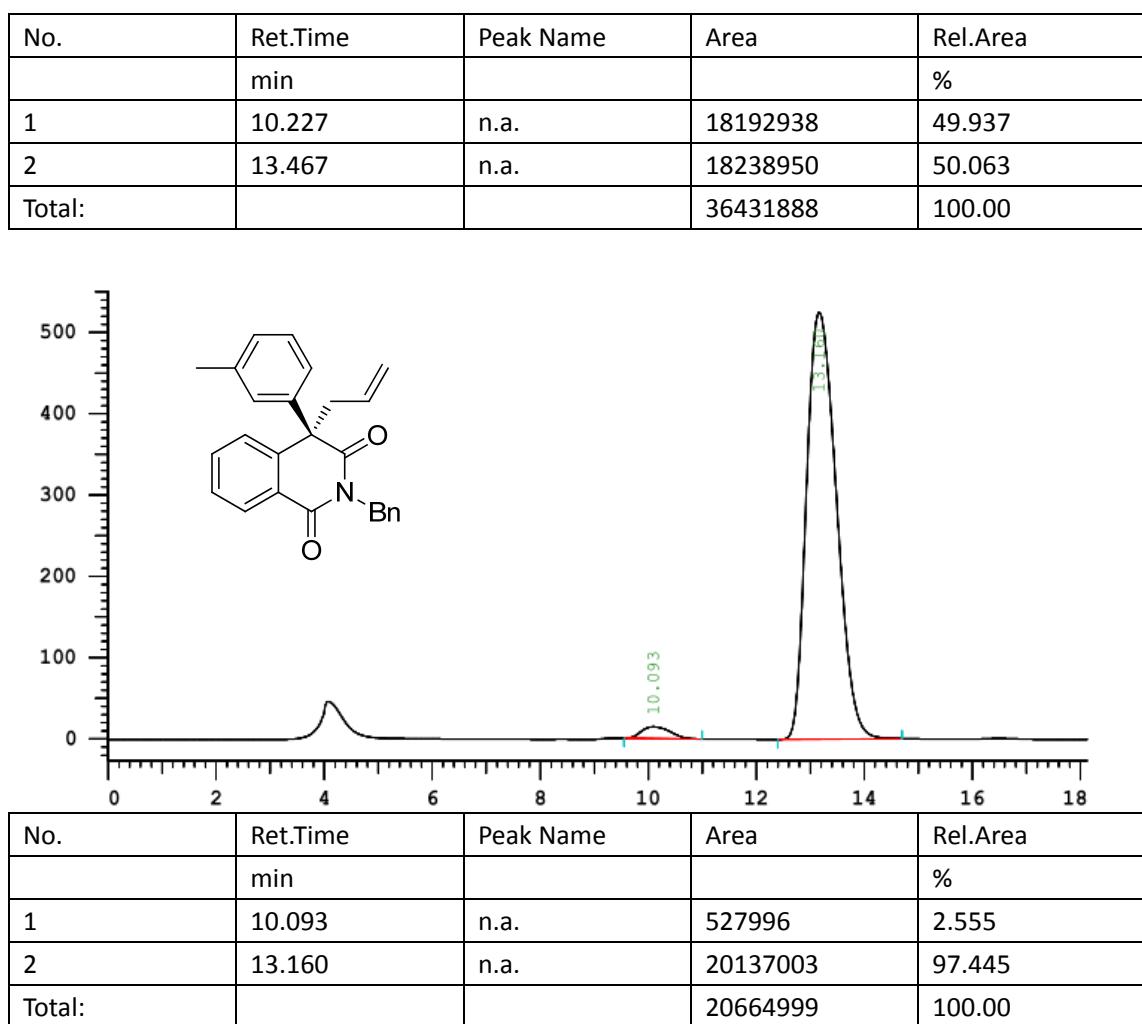
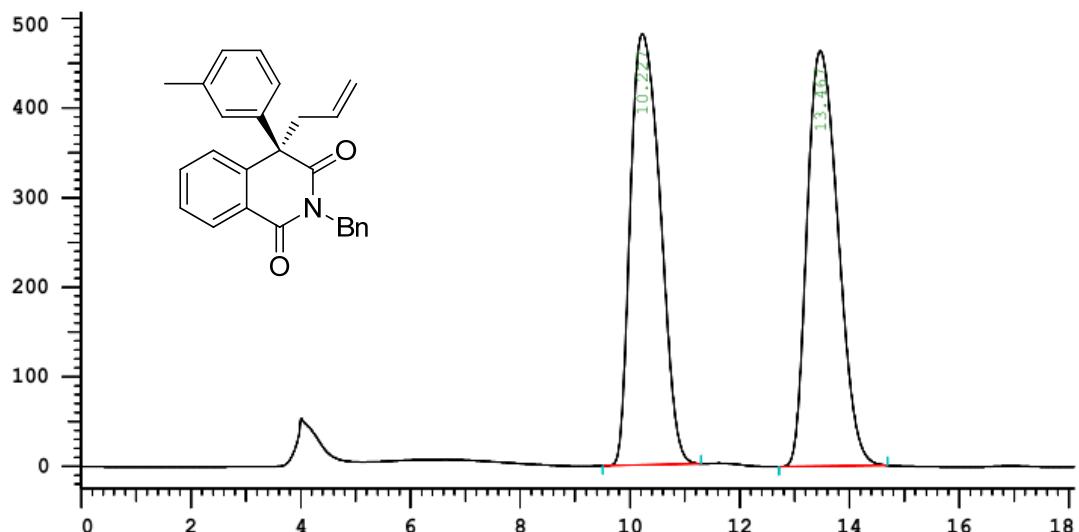
(R)-4-allyl-2-benzyl-4-(p-tolyl)isoquinoline-1,3(2H,4H)-dione(3h):



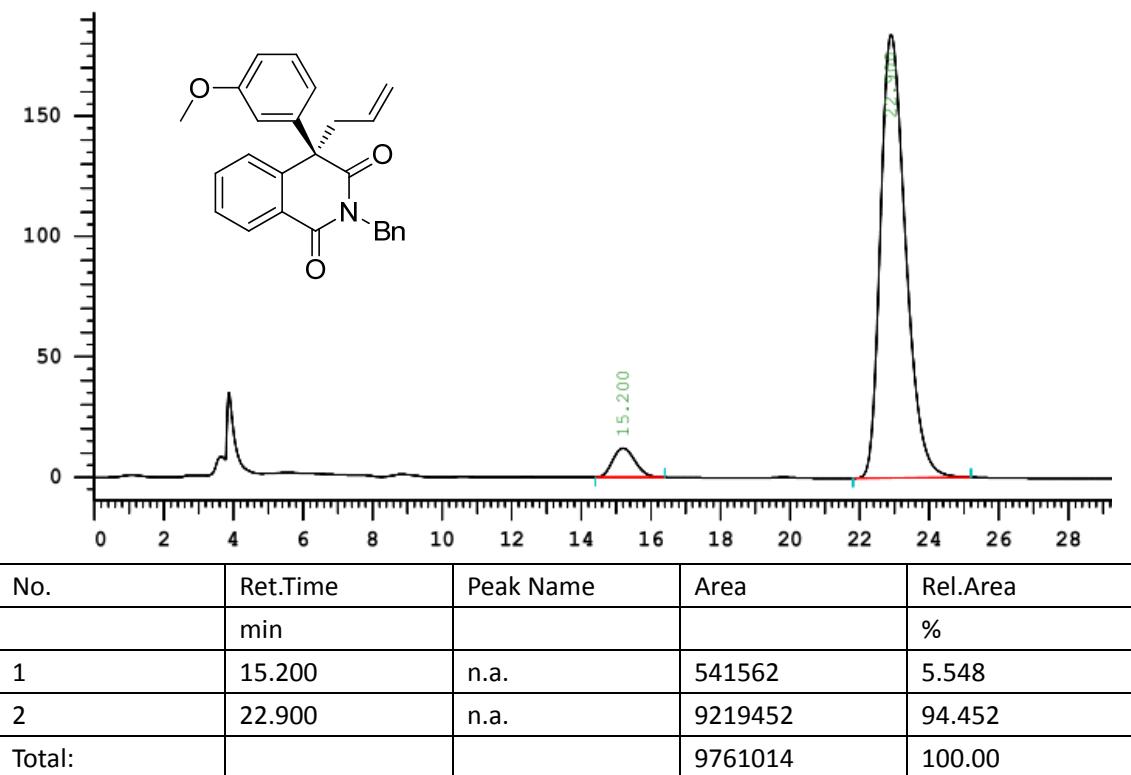
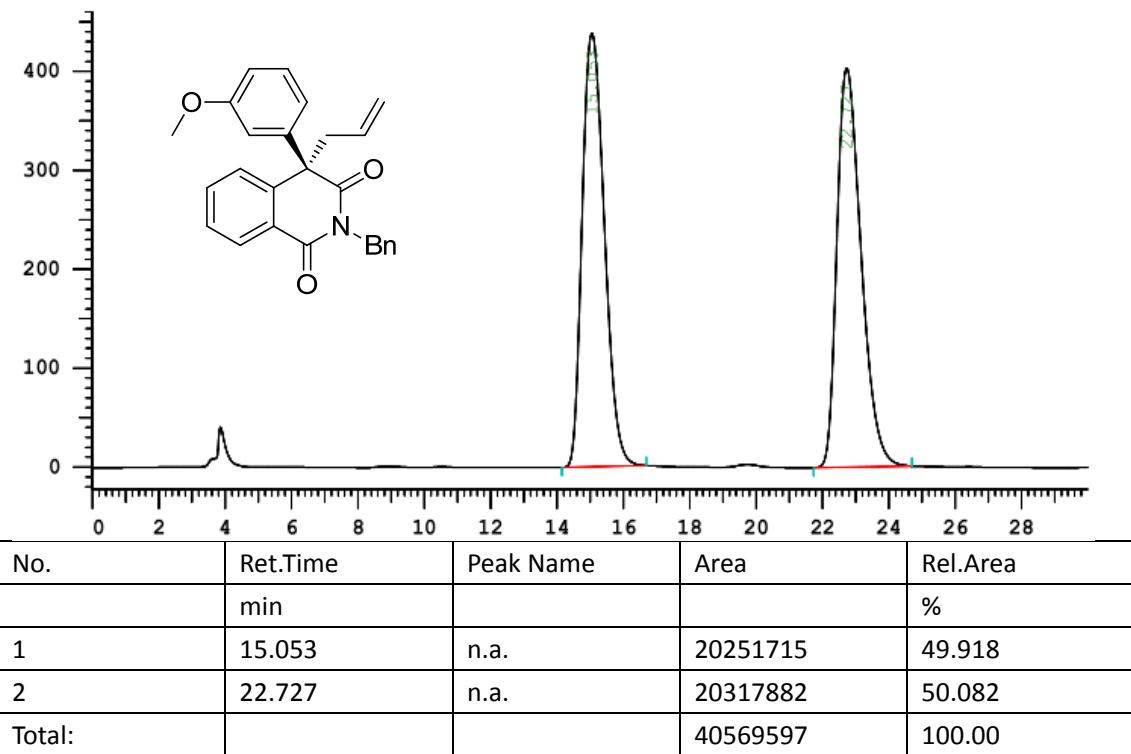
(R)-4-allyl-2-benzyl-4-(4-methoxyphenyl)isoquinoline-1,3(2H,4H)-dione(3i):



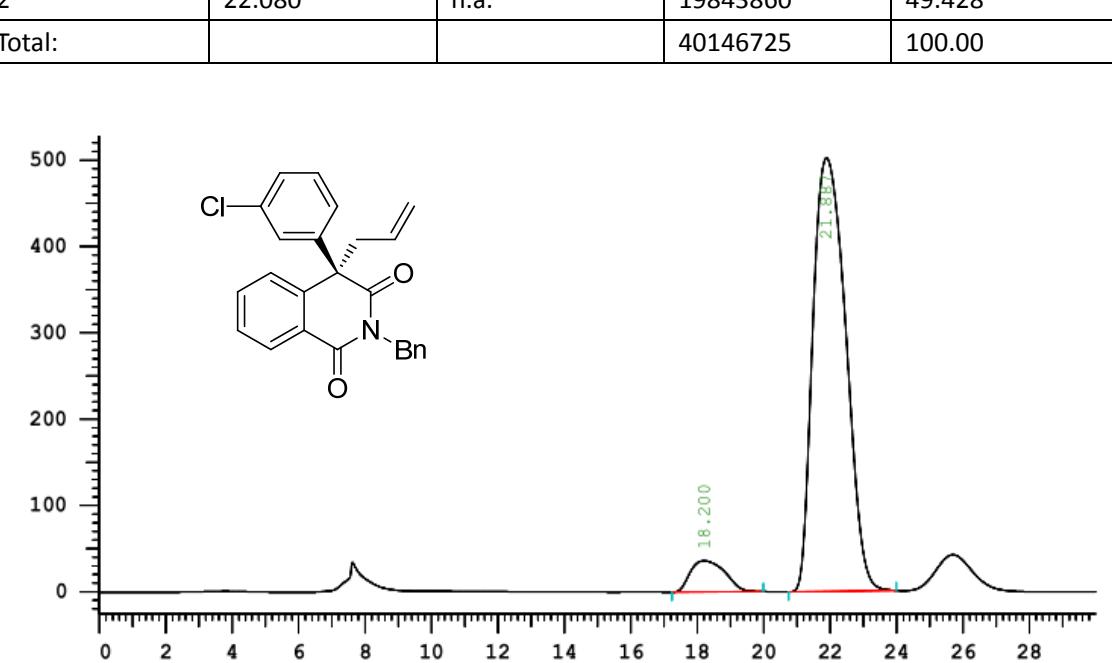
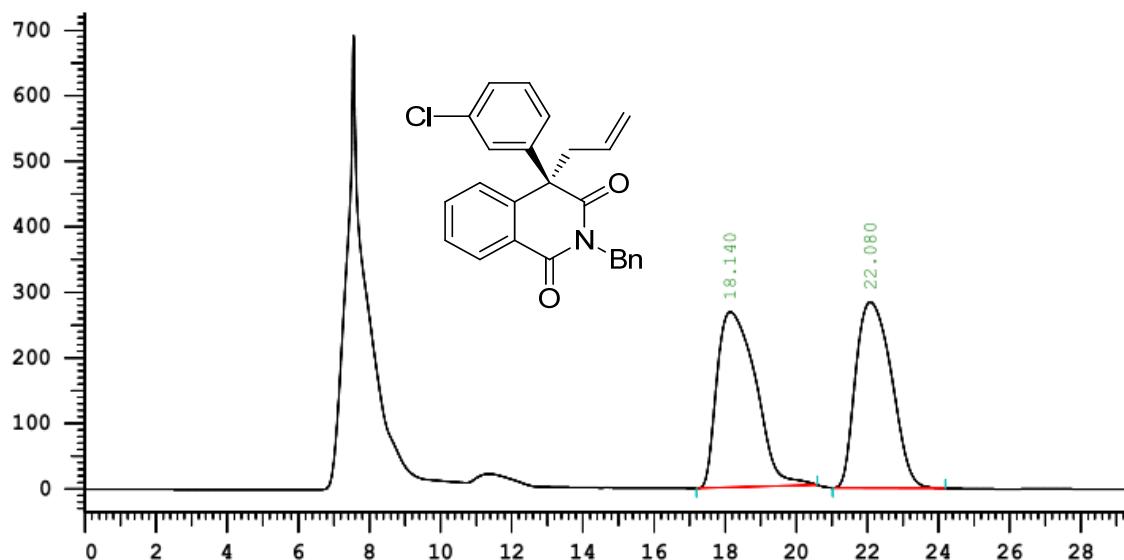
(R)-4-allyl-2-benzyl-4-(m-tolyl)isoquinoline-1,3(2H,4H)-dione(3j):



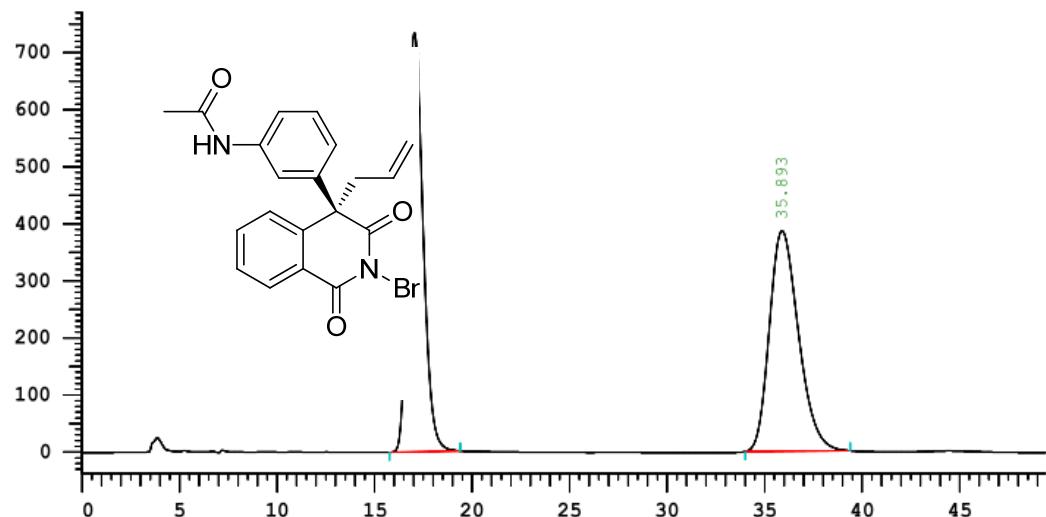
(R)-4-allyl-2-benzyl-4-(3-methoxyphenyl)isoquinoline-1,3(2H,4H)-dione(3k):



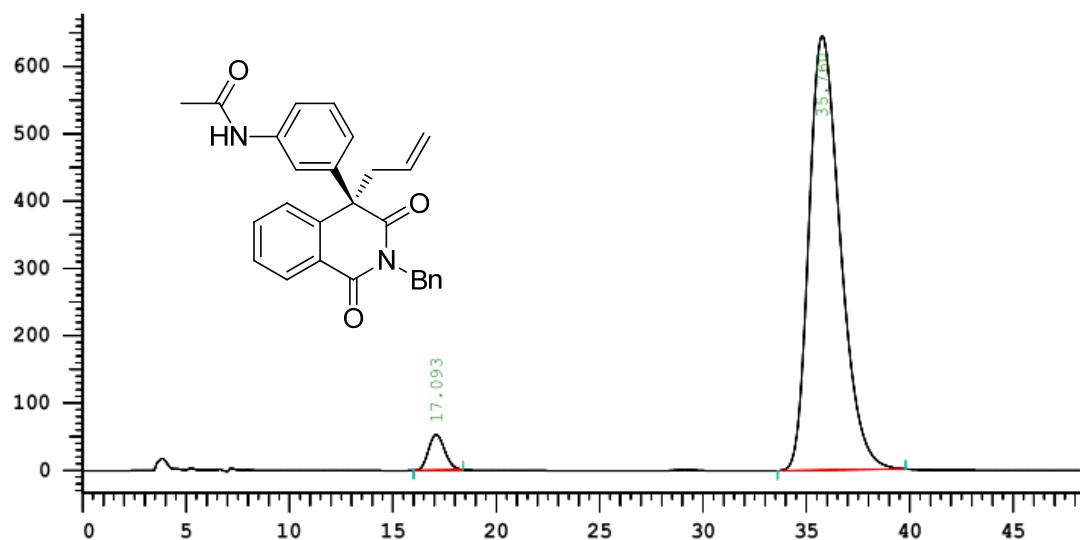
(R)-4-allyl-2-benzyl-4-(3-chlorophenyl)isoquinoline-1,3(2H,4H)-dione(3l):



(R)-N-(3-(4-allyl-2-benzyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)phenyl)acetamide(3m):

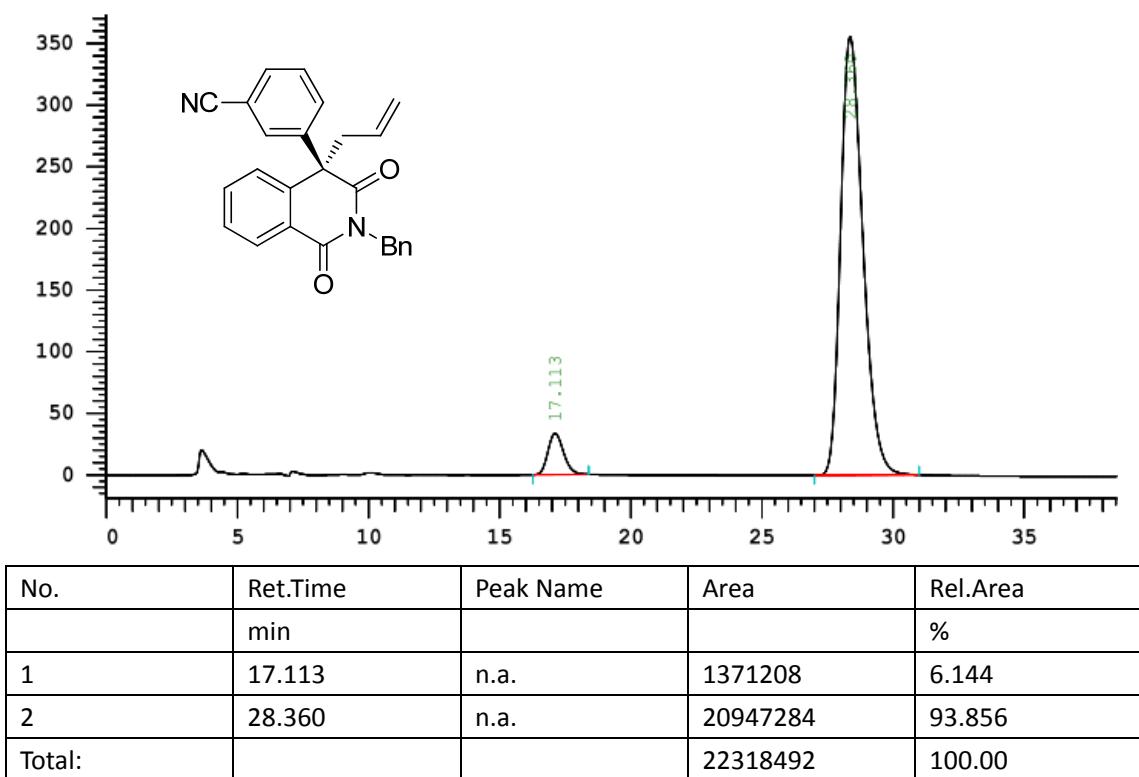
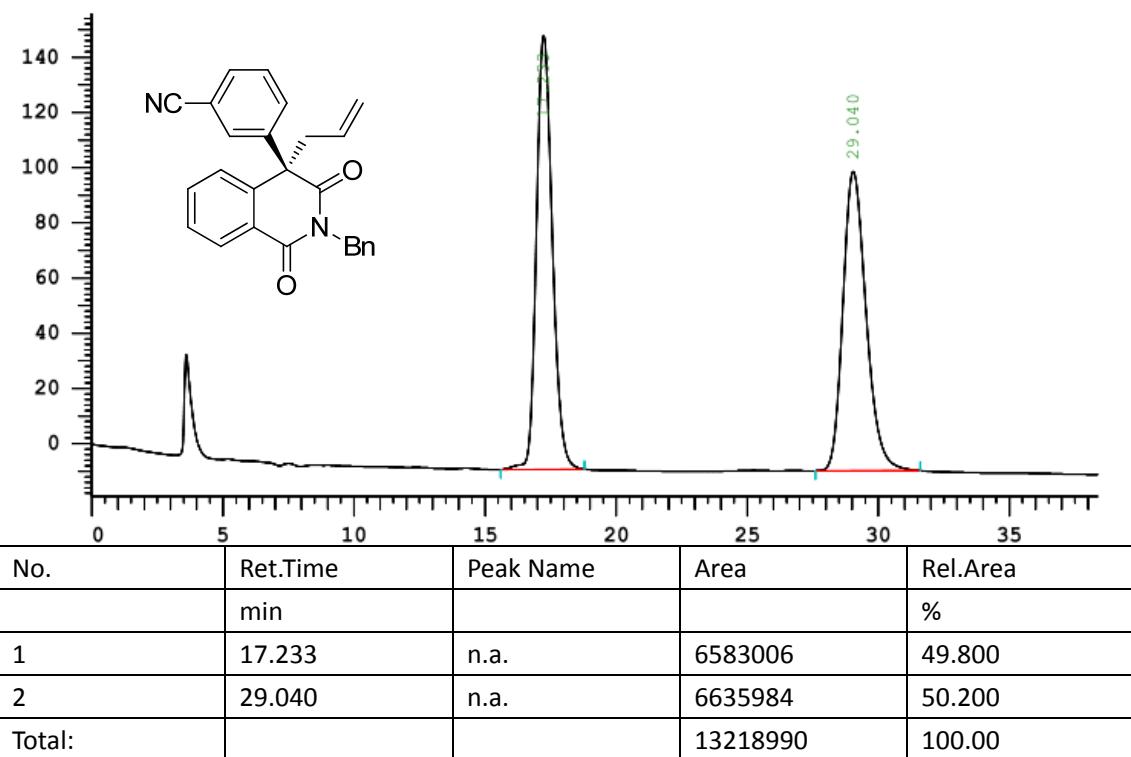


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	17.047	n.a.	40321223	50.213
2	35.893	n.a.	39979934	49.787
Total:			80301157	100.00

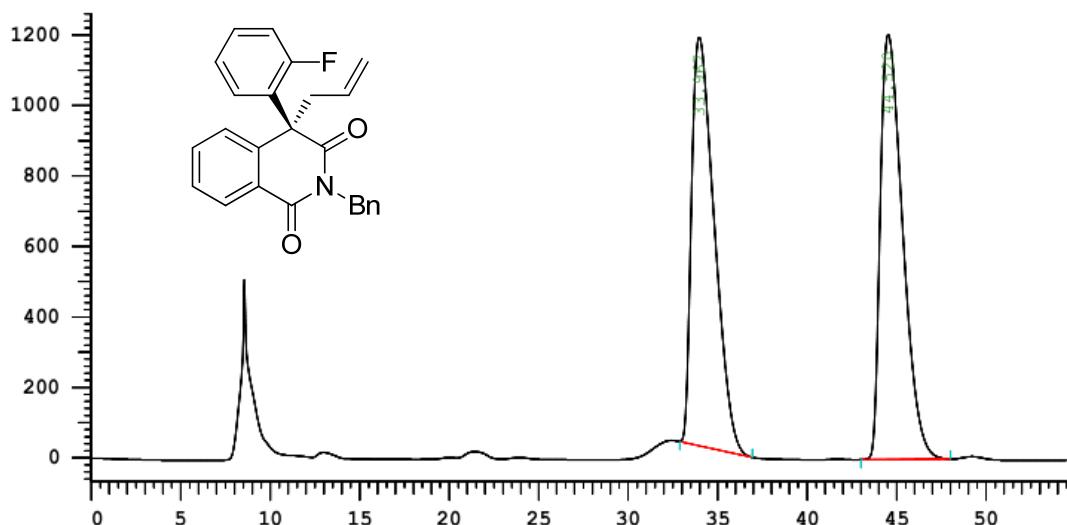


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	17.093	n.a.	2869903	4.067
2	35.760	n.a.	67690234	95.933
Total:			70560137	100.00

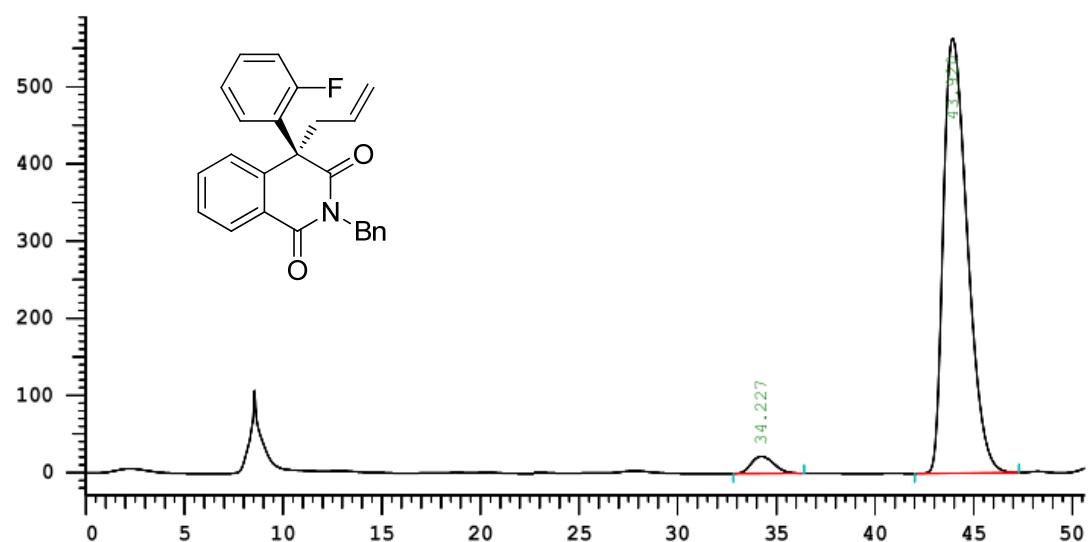
(R)-3-(4-allyl-2-benzyl-1,3-dioxo-1,2,3,4-tetrahydroisoquinolin-4-yl)benzonitrile(3n):



(R)-4-allyl-2-benzyl-4-(2-fluorophenyl)isoquinoline-1,3(2H,4H)-dione(3o):

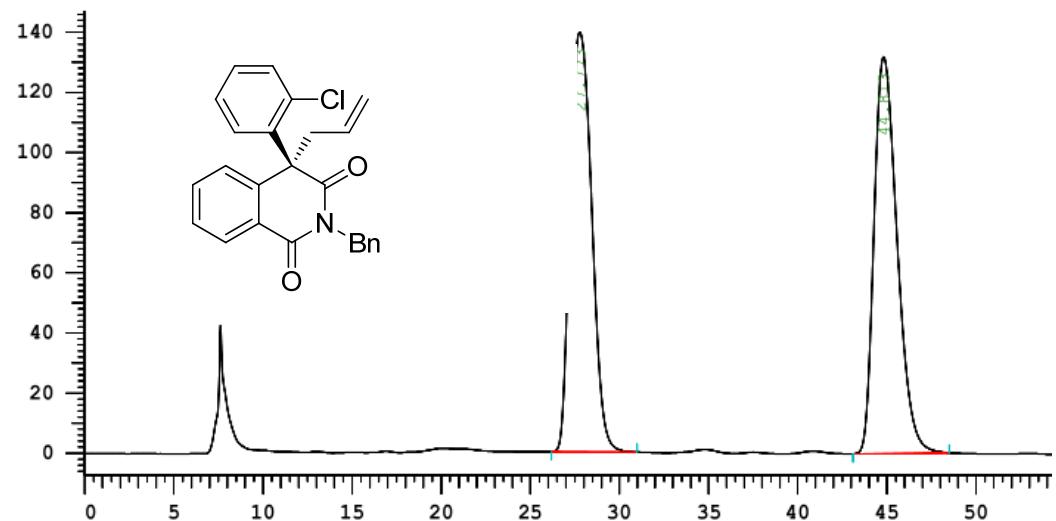


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	33.967	n.a.	1.015E+08	49.373
2	44.520	n.a.	1.041E+08	50.627
Total:			2.057E+08	100.00

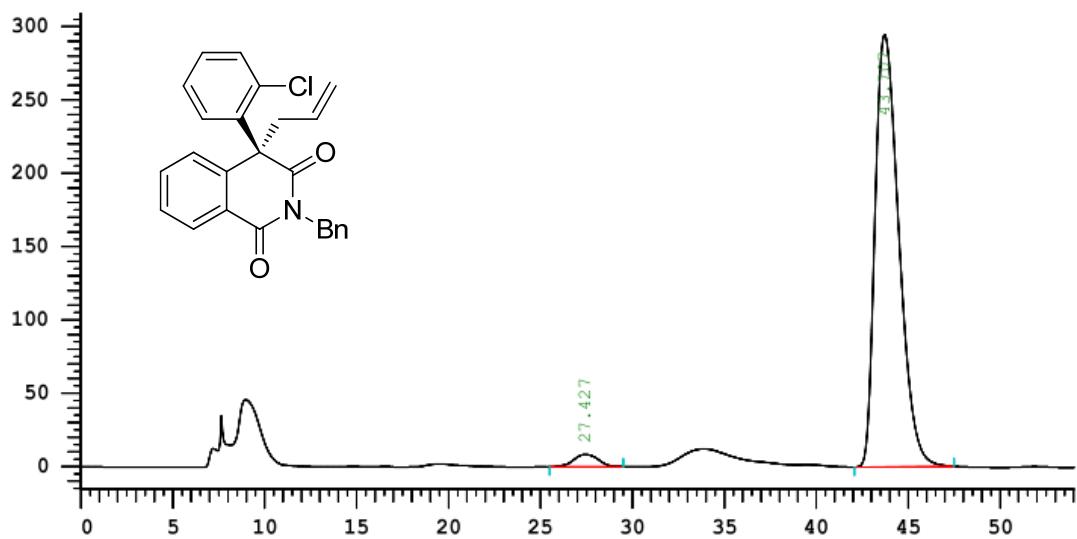


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	34.227	n.a.	1736475	3.533
2	43.920	n.a.	47407759	96.467
Total:			49144234	100.00

(R)-4-allyl-2-benzyl-4-(2-chlorophenyl)isoquinoline-1,3(2H,4H)-dione(3p):

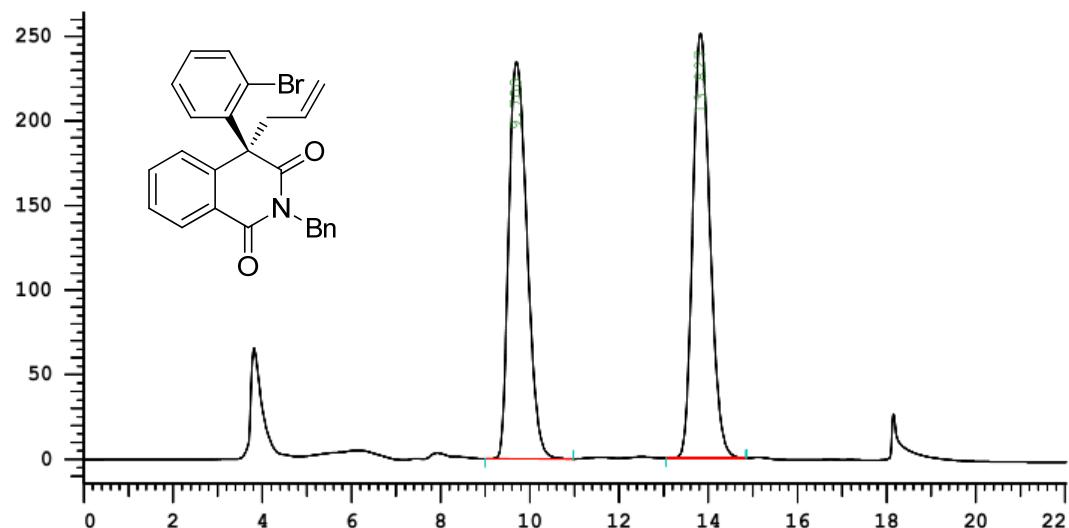
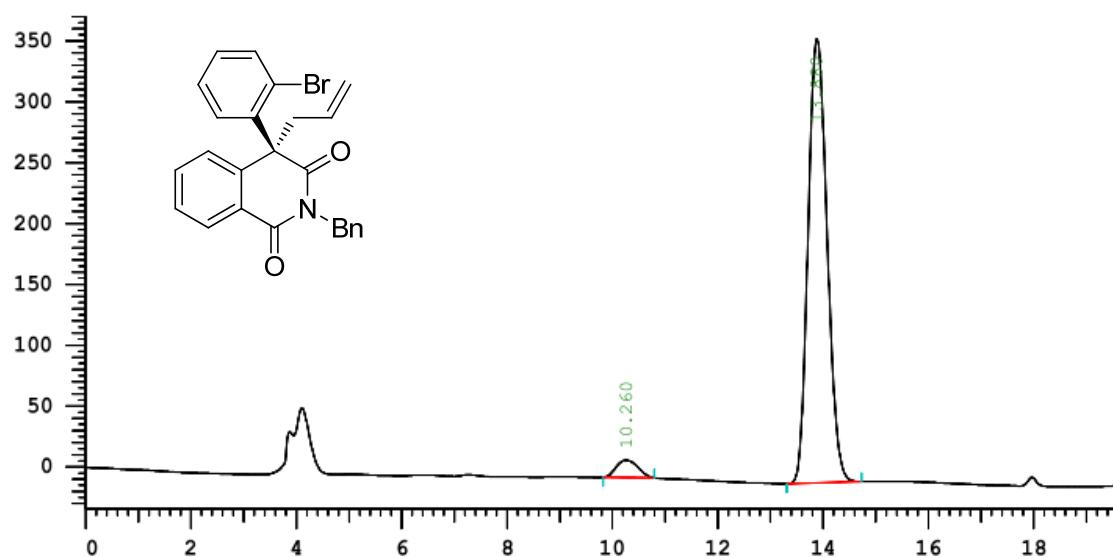


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	27.773	n.a.	11763371	49.961
2	44.813	n.a.	11781928	50.039
Total:			23545299	100.00



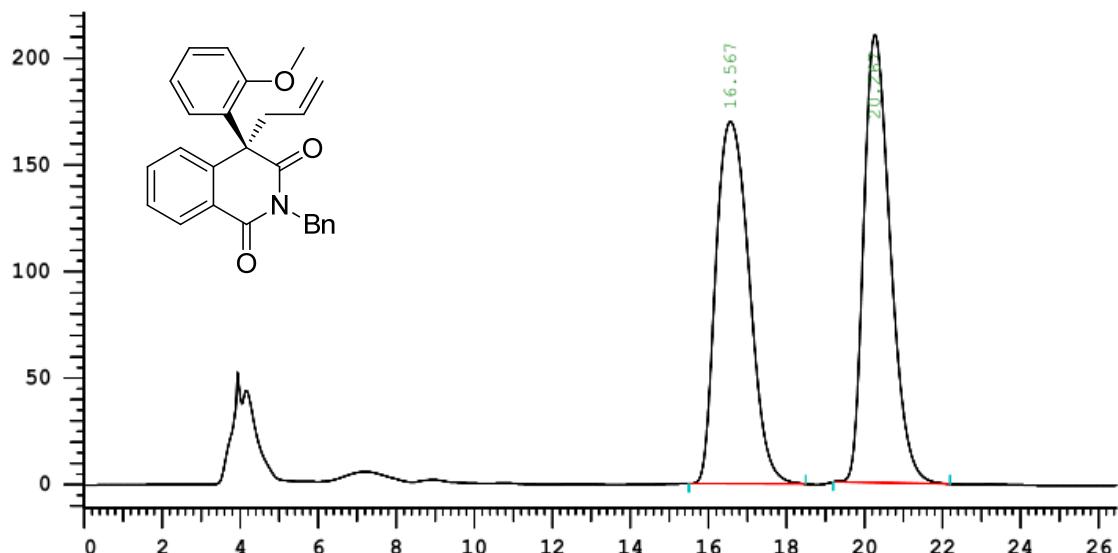
No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	27.427	n.a.	791360	2.918
2	43.707	n.a.	26327905	97.082
Total:			27119265	100.00

(R)-4-allyl-2-benzyl-4-(2-bromophenyl)isoquinoline-1,3(2H,4H)-dione(3q):

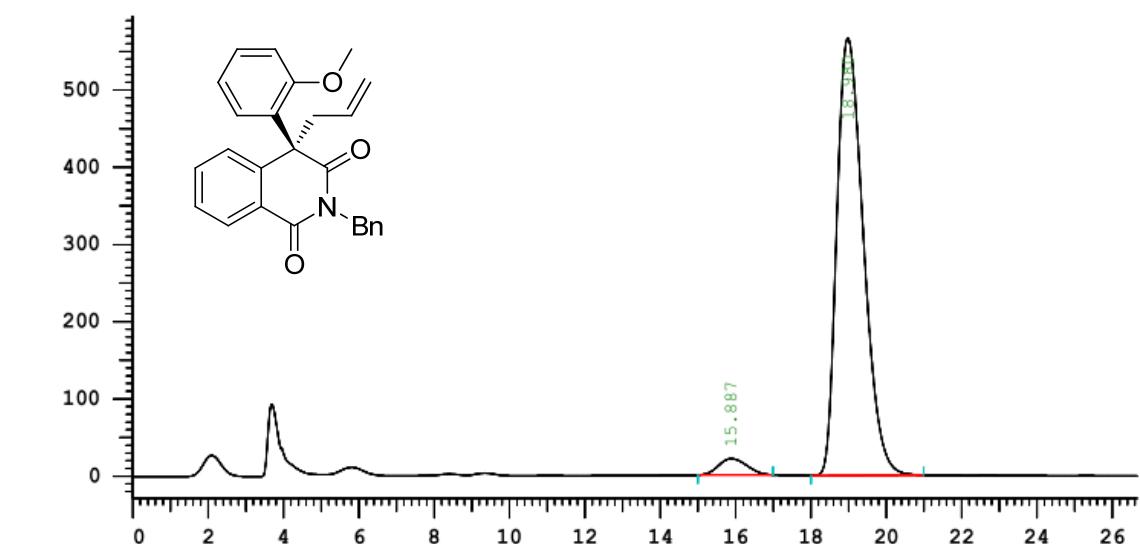



No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	10.260	n.a.	404960	4.248
2	13.880	n.a.	9128309	95.752
Total:			9533269	100.00

(R)-4-allyl-2-benzyl-4-(2-methoxyphenyl)isoquinoline-1,3(2H,4H)-dione(3r):

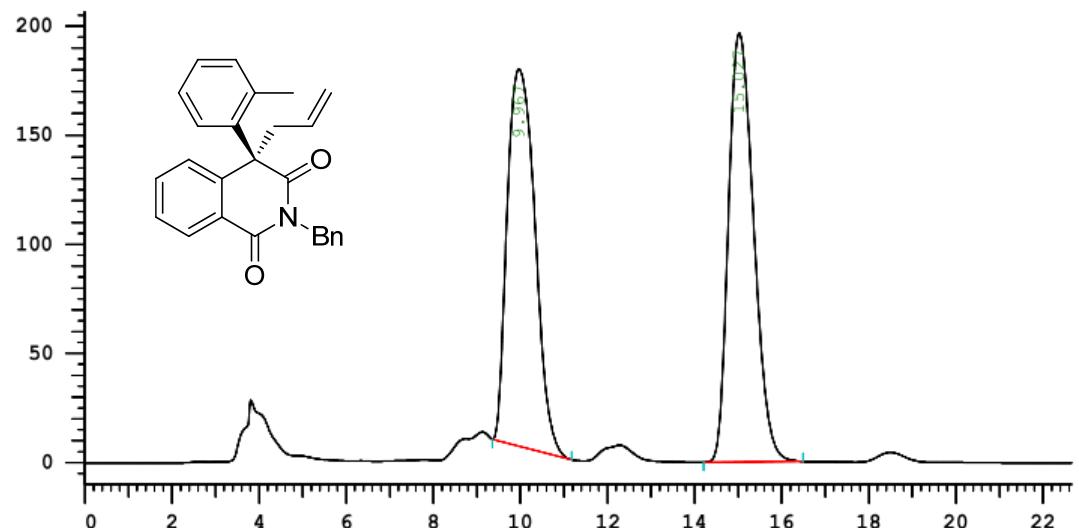


No.	Ret.Time min	Peak Name	Area	Rel.Area
1	16.567	n.a.	10037840	50.258
2	20.267	n.a.	9934624	49.742
Total:				100.00

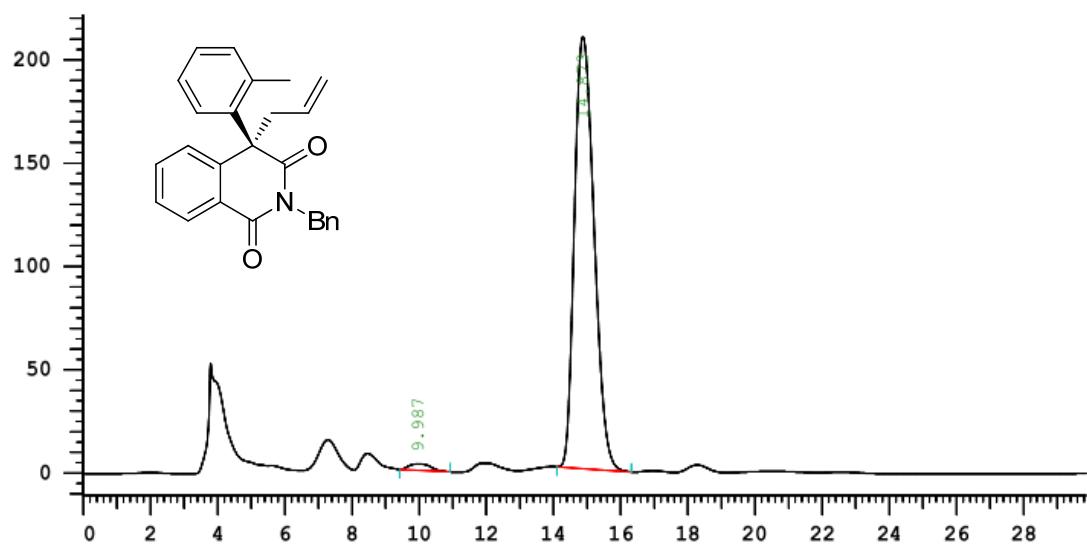


No.	Ret.Time min	Peak Name	Area	Rel.Area
1	15.887	n.a.	1101849	3.828
2	18.980	n.a.	27680706	96.172
Total:			28782555	100.00

(R)-4-allyl-2-benzyl-4-(o-tolyl)isoquinoline-1,3(2H,4H)-dione(3s):

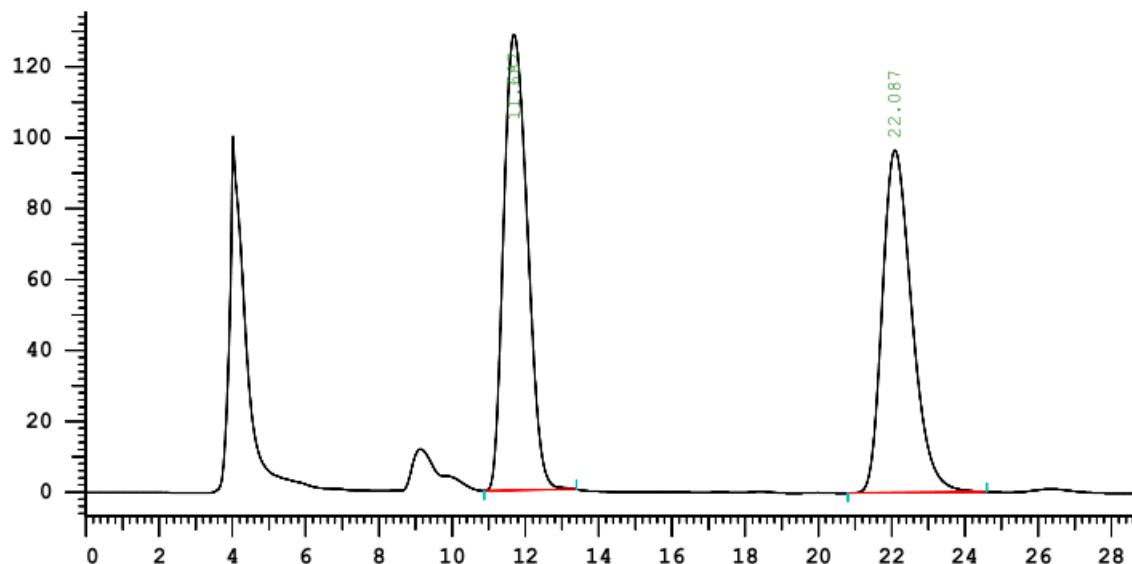


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	9.967	n.a.	7664974	49.288
2	15.027	n.a.	7886312	50.712
Total:			15551286	100.00

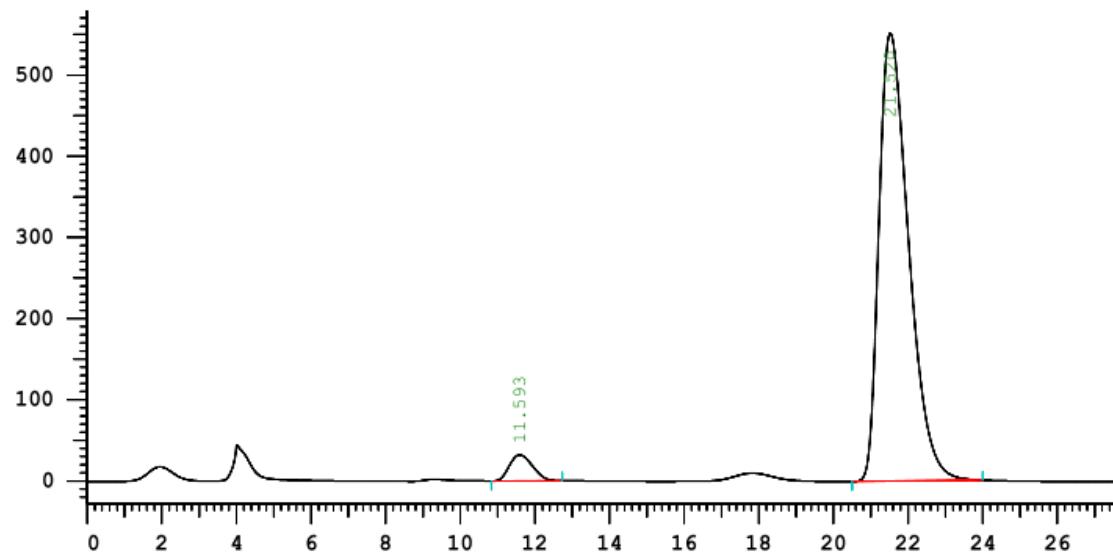


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	9.987	n.a.	139912	1.628
2	14.873	n.a.	8452545	98.372
Total:			8592457	100.00

(R)-4-allyl-2-benzyl-4-(2,4-dimethylphenyl)isoquinoline-1,3(2H,4H)-dione(3t):

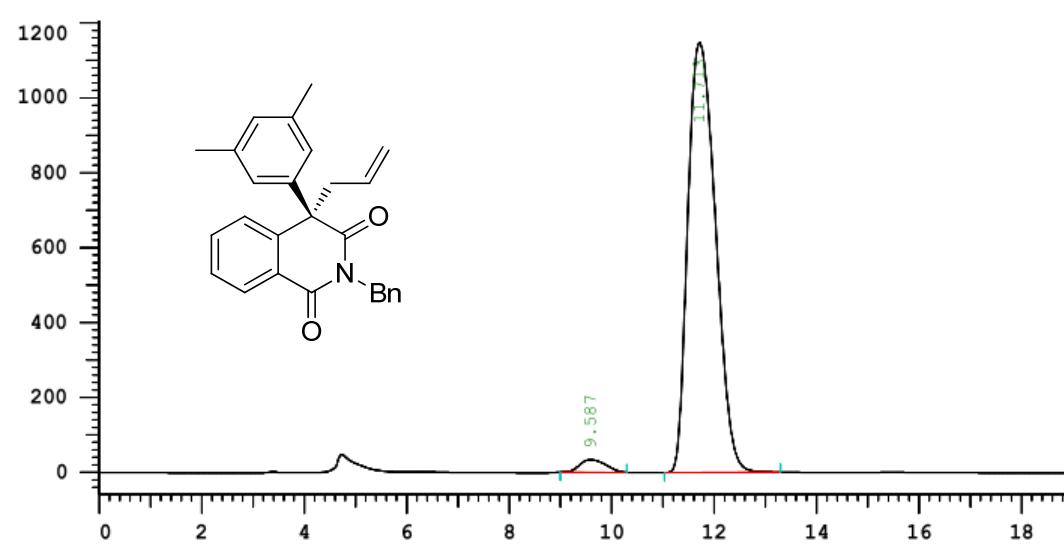
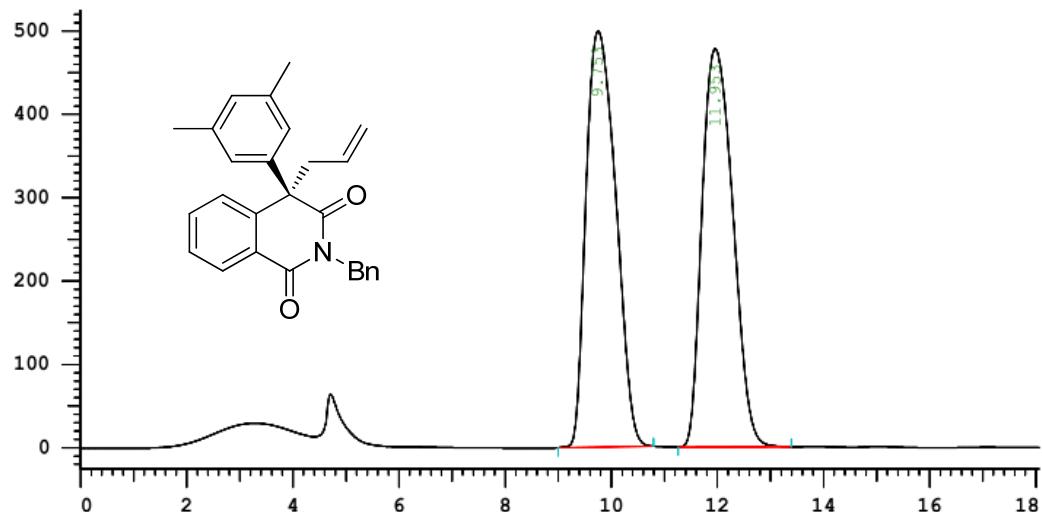


No.	Ret.Time min	Peak Name	Area	Rel.Area
1	11.687	n.a.	5783210	51.721
2	22.087	n.a.	5398335	48.279
Total:			11181545	100.00

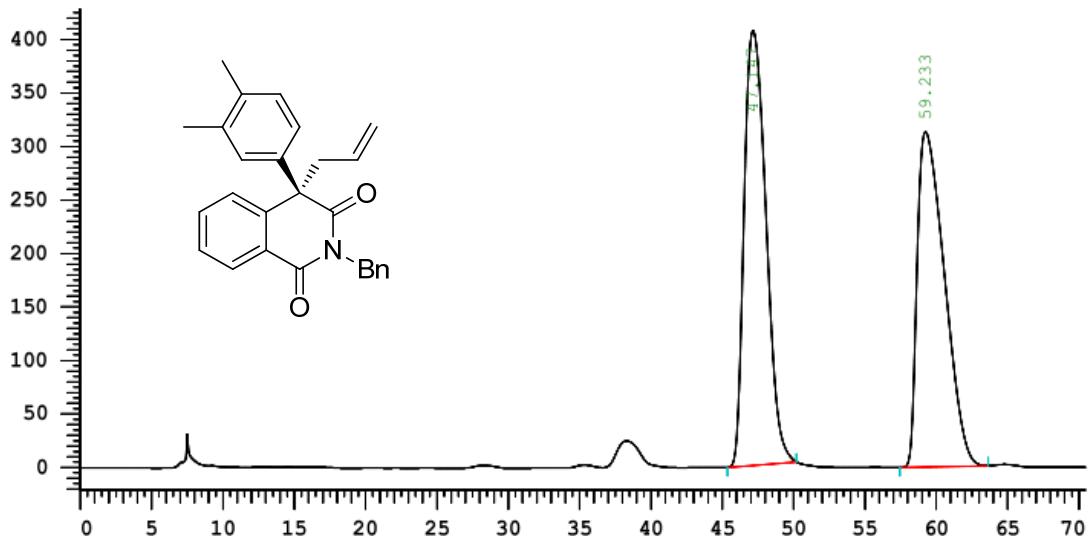


No.	Ret.Time min	Peak Name	Area	Rel.Area
1	11.593	n.a.	1377622	4.333
2	21.520	n.a.	30416691	95.667
Total:			31794313	100.00

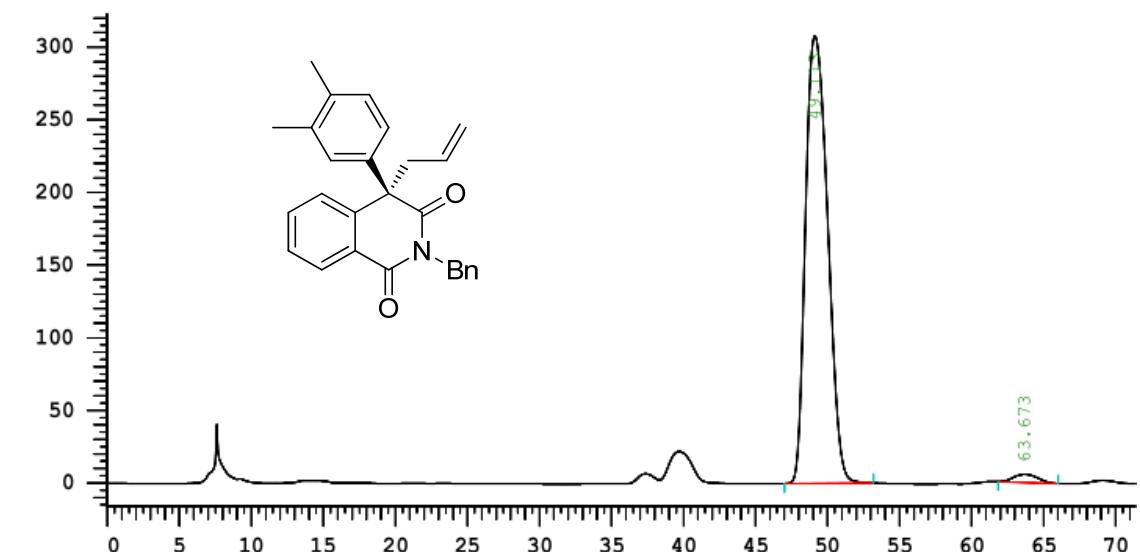
*(R)-4-allyl-2-benzyl-4-(3,5-dimethylphenyl)isoquinoline-1,3(2*H*,4*H*)-dione,(3u):*



*(R)-4-allyl-2-benzyl-4-(3,4-dimethylphenyl)isoquinoline-1,3(2*H*,4*H*)-dione(3v):*

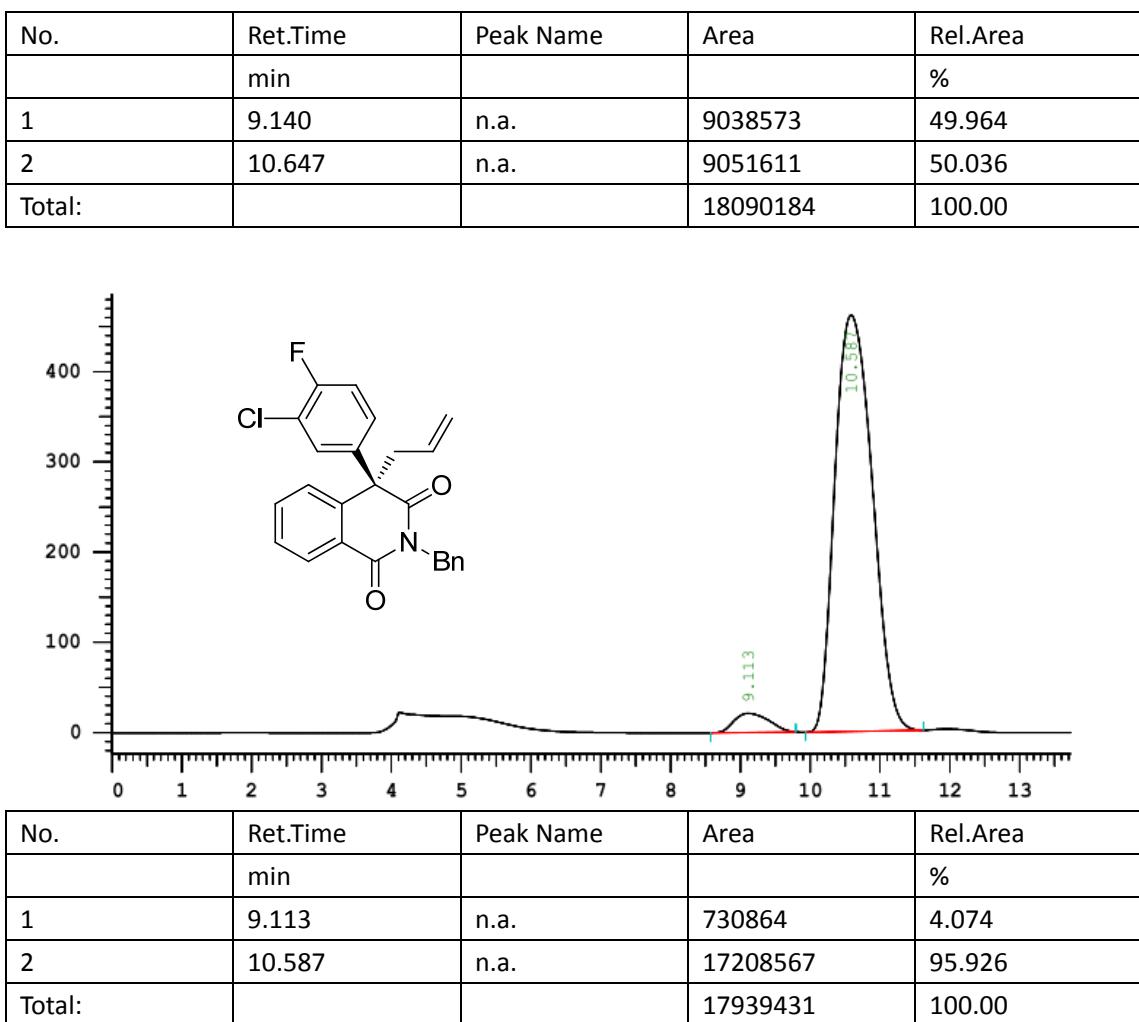
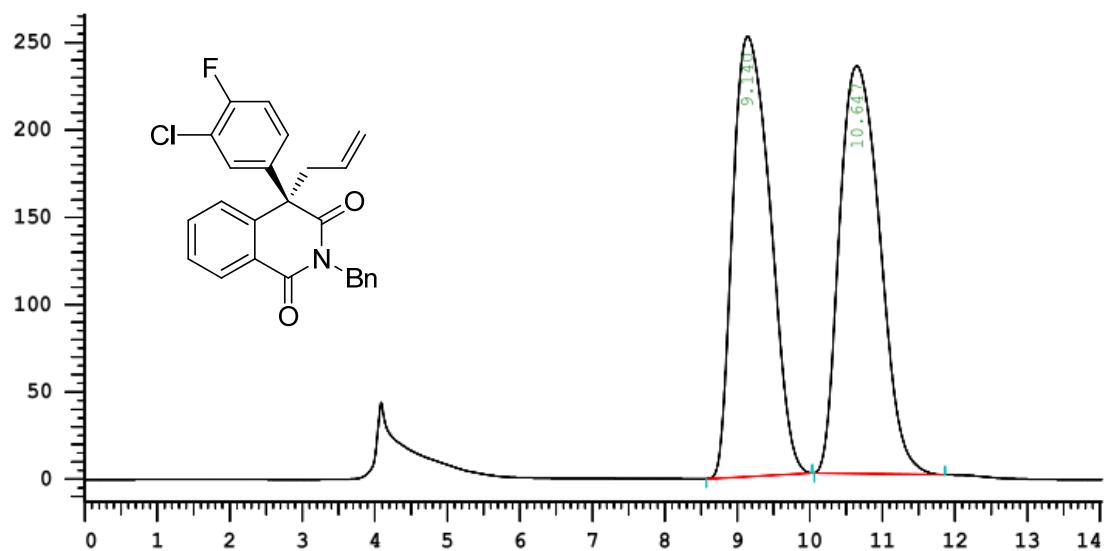


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	47.147	n.a.	42854717	50.982
2	59.233	n.a.	41204090	49.018
Total:			84058807	100.00

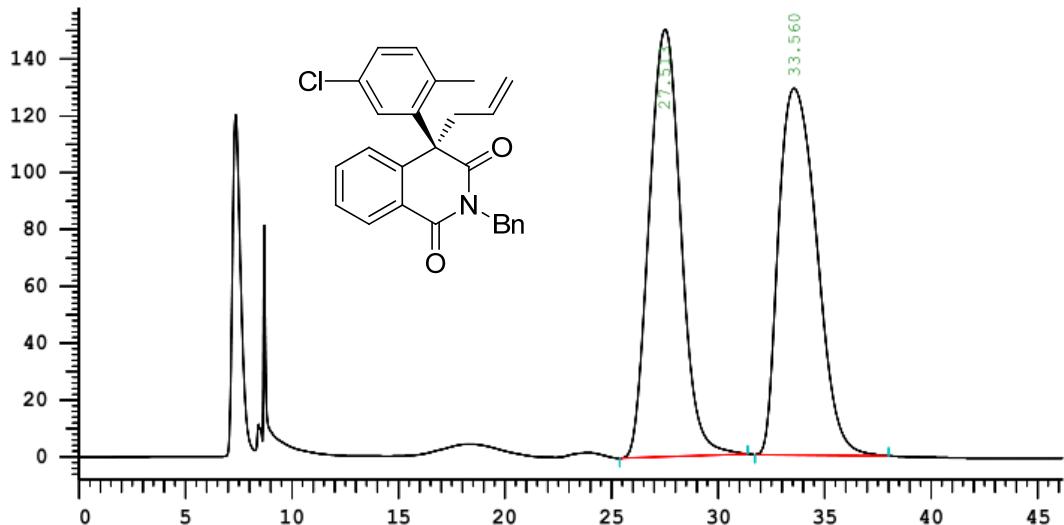


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	49.113	n.a.	32512788	98.012
2	63.673	n.a.	659400	1.988
Total:			33172188	100.00

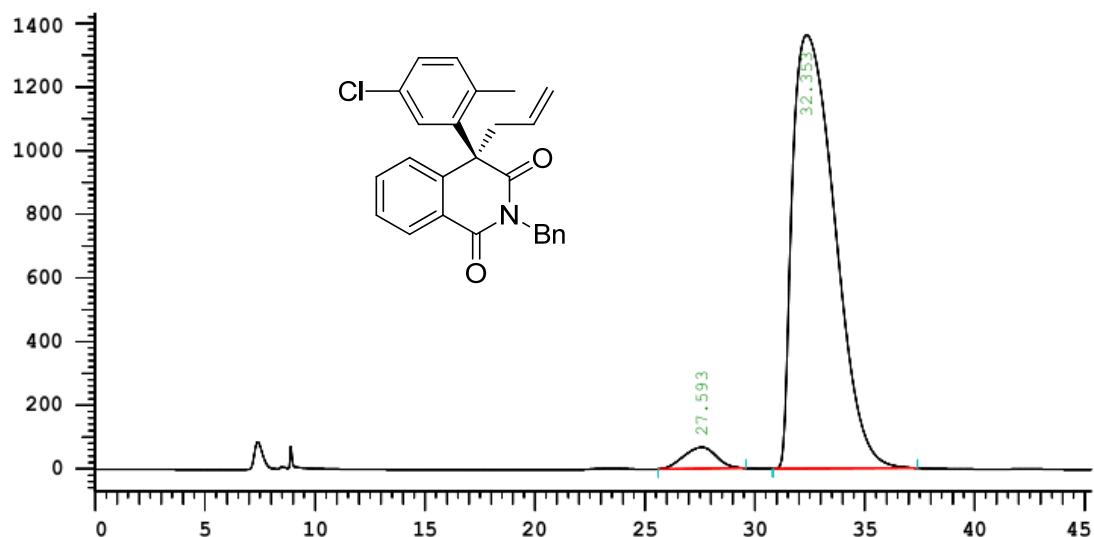
*(R)-4-allyl-2-benzyl-4-(3-chloro-4-fluorophenyl)isoquinoline-1,3(2*H*,4*H*)-dione(3w):*



*(R)-4-allyl-2-benzyl-4-(5-chloro-2-methylphenyl)isoquinoline-1,3(2*H*,4*H*)-dione(3x):*

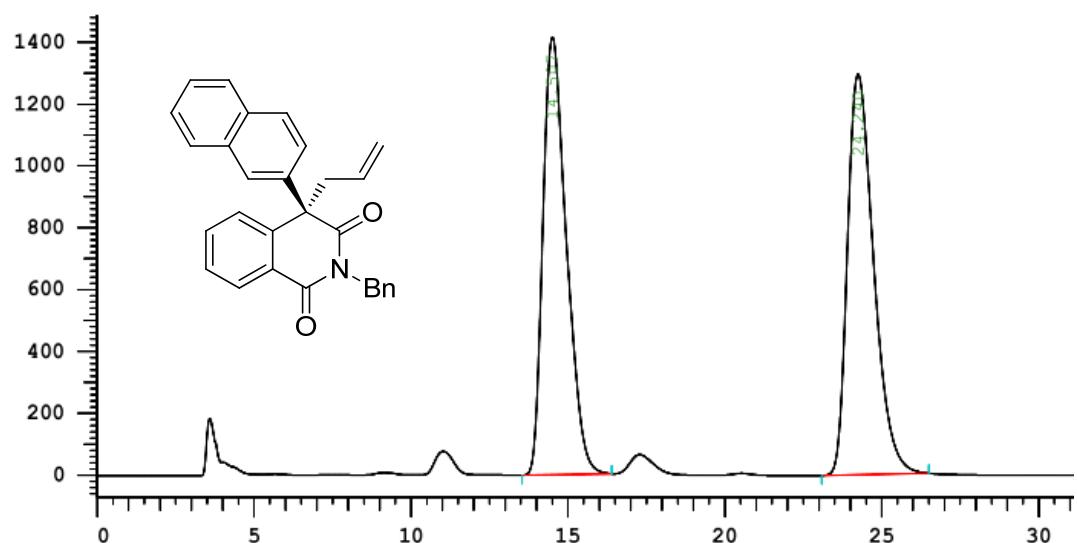


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	27.513	n.a.	15415015	49.146
2	33.560	n.a.	15950810	50.854
Total:			31365825	100.00

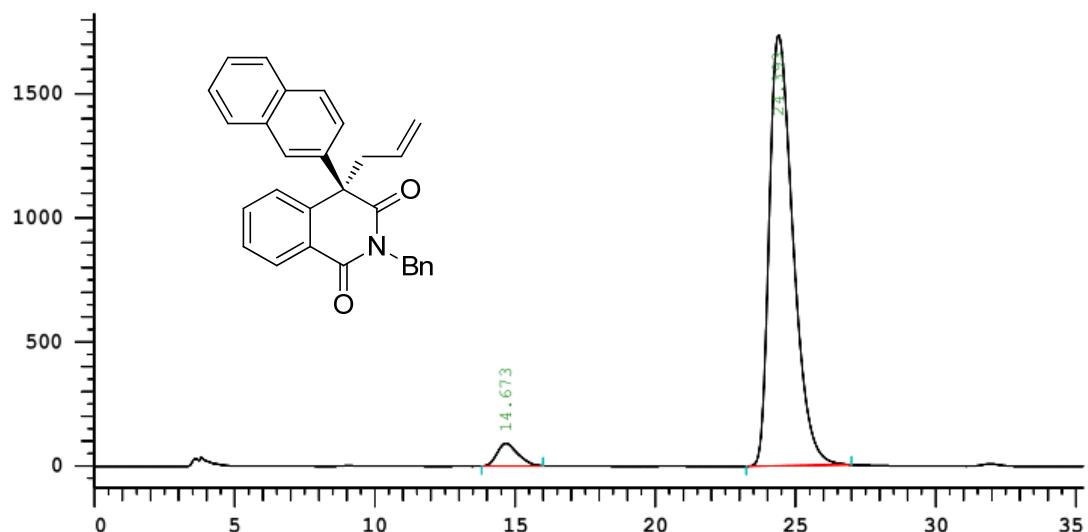


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	27.593	n.a.	6962833	3.697
2	32.353	n.a.	1.813E+08	96.303
Total:			1.883E+08	100.00

*(R)-4-allyl-2-benzyl-4-(naphthalen-2-yl)isoquinoline-1,3(2*H*,4*H*)-dione(3y):*

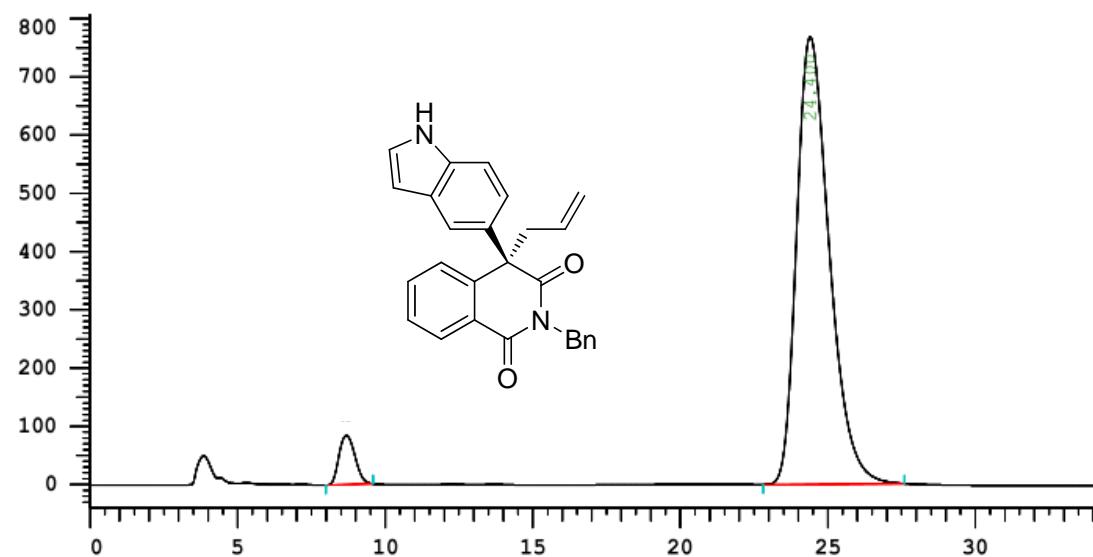
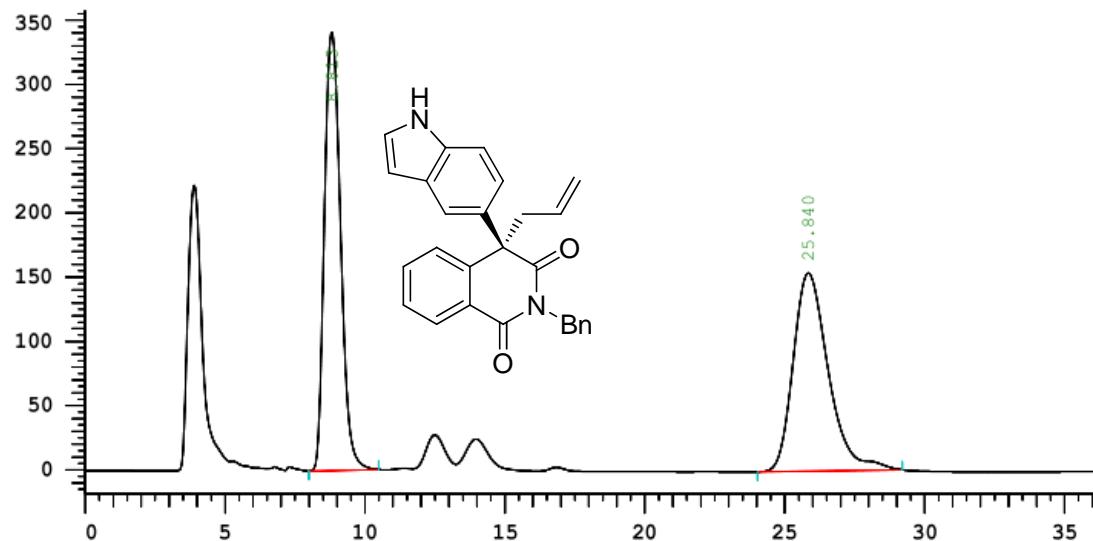


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	14.507	n.a.	73160862	49.428
2	24.240	n.a.	74853790	50.572
Total:			1.480E+08	100.00

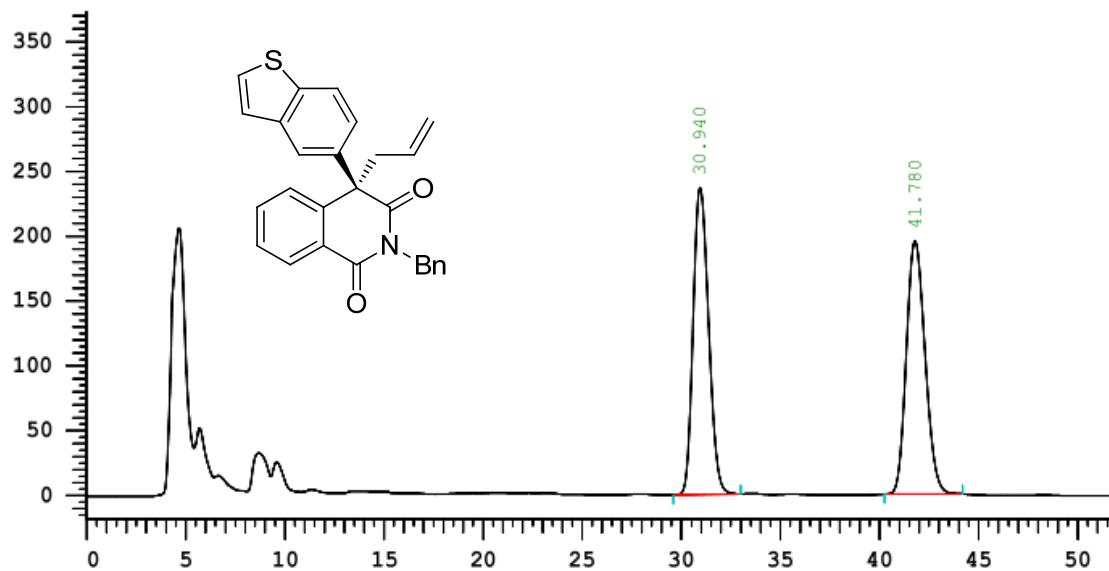


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	14.673	n.a.	4664627	4.379
2	24.393	n.a.	1.018E+08	95.621
Total:			1.065E+08	100.00

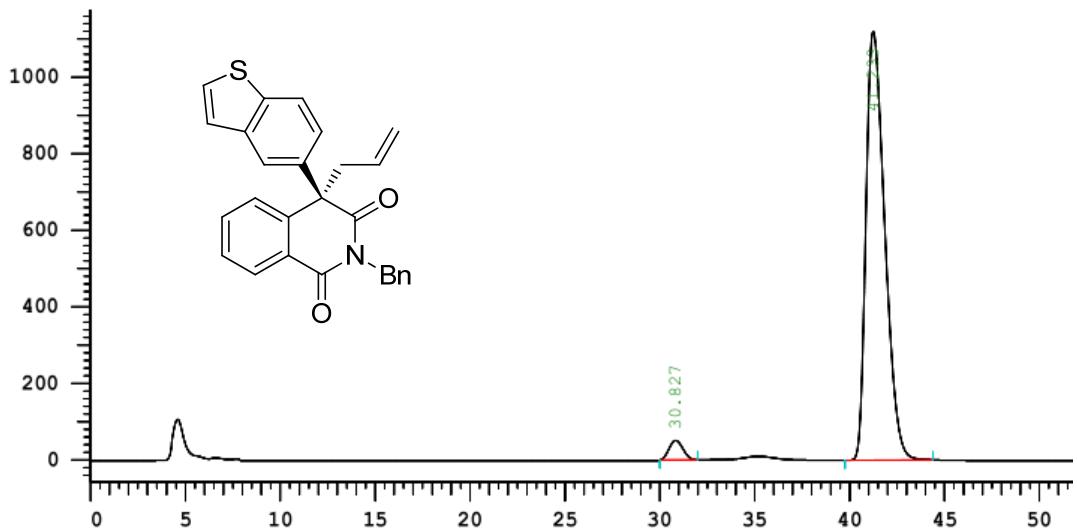
(R)-4-allyl-2-benzyl-4-(1*H*-indol-5-yl)isoquinoline-1,3(2*H*,4*H*)-dione(3z):



(R)-4-allyl-4-(benzo[b]thiophen-5-yl)-2-benzylisoquinoline-1,3(2H,4H)-dione (3aa):

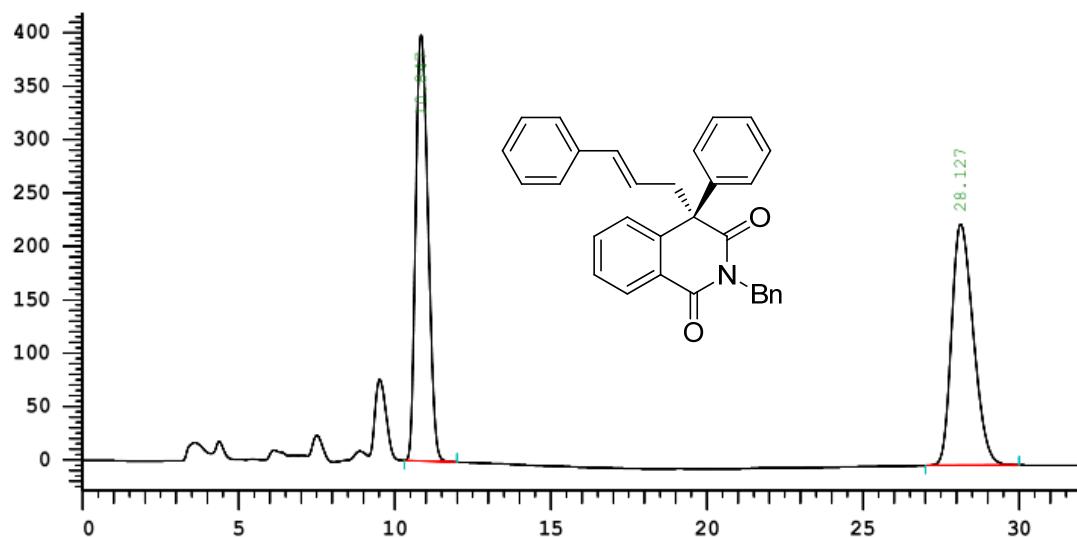


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	30.940	n.a.	12716488	50.084
2	41.780	n.a.	12691868	49.952
Total:				100.00

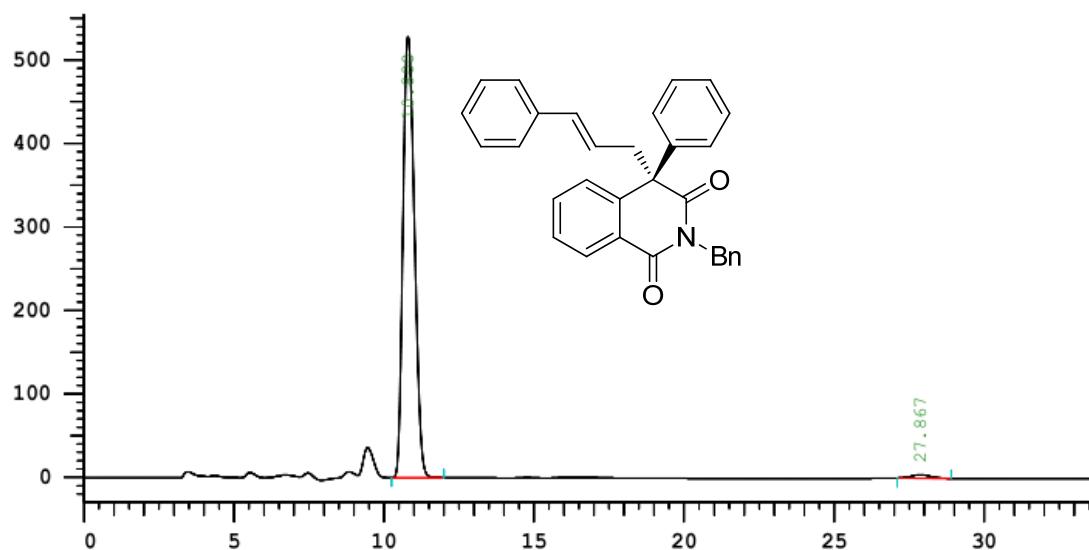


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	30.827	n.a.	2591415	3.288
2	41.233	n.a.	76221532	96.712
Total:				100.00

(R)-2-benzyl-4-cinnamyl-4-phenylisoquinoline-1,3(2H,4H)-dione(3ab):

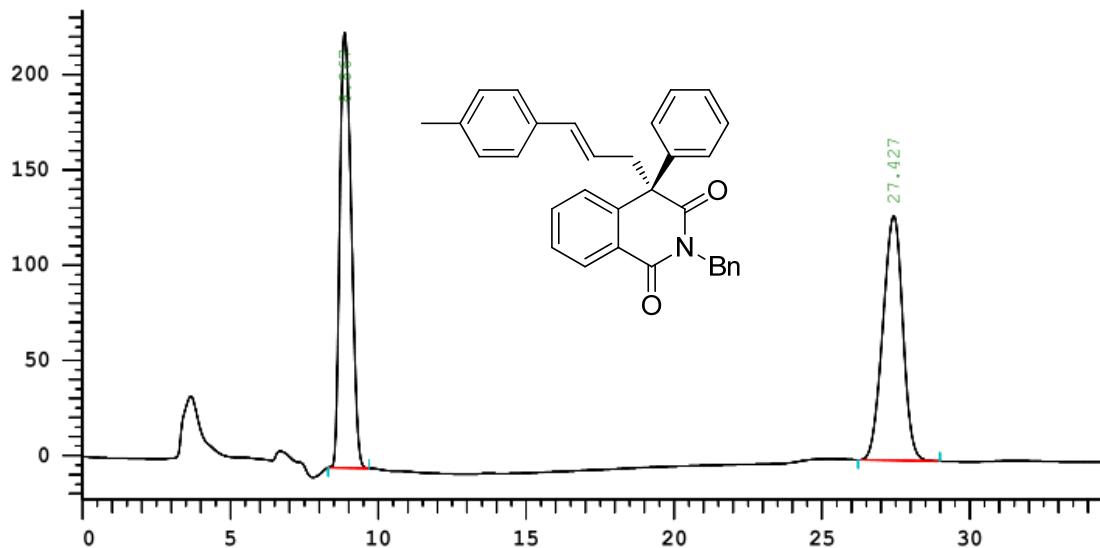


No.	Ret.Time min	Peak Name	Area	Rel.Area
1	10.847	n.a.	10883435	50.057
2	28.127	n.a.	10858592	49.943
Total:			21742027	100.00

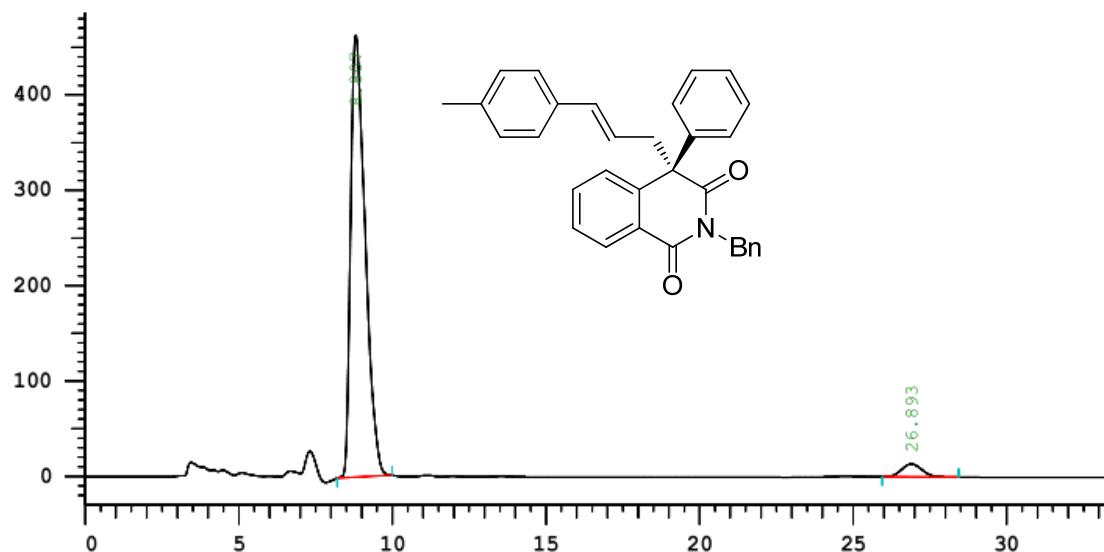


No.	Ret.Time min	Peak Name	Area	Rel.Area
1	10.800	n.a.	13917640	98.713
2	27.867	n.a.	181469	1.287
Total:			14099109	100.00

(R,E)-2-benzyl-4-phenyl-4-(3-(p-tolyl)allyl)isoquinoline-1,3(2H,4H)-dione(3ac):

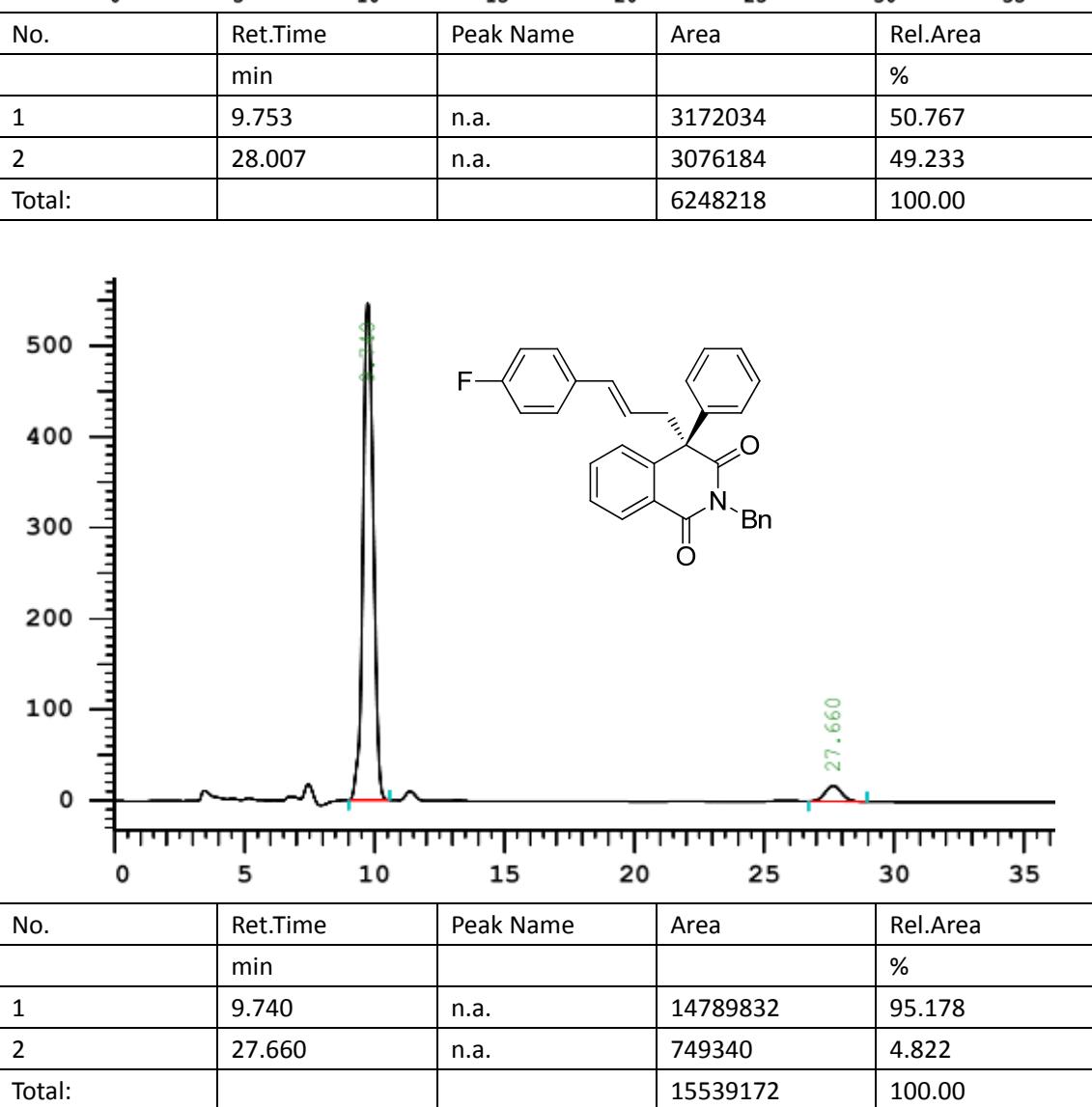
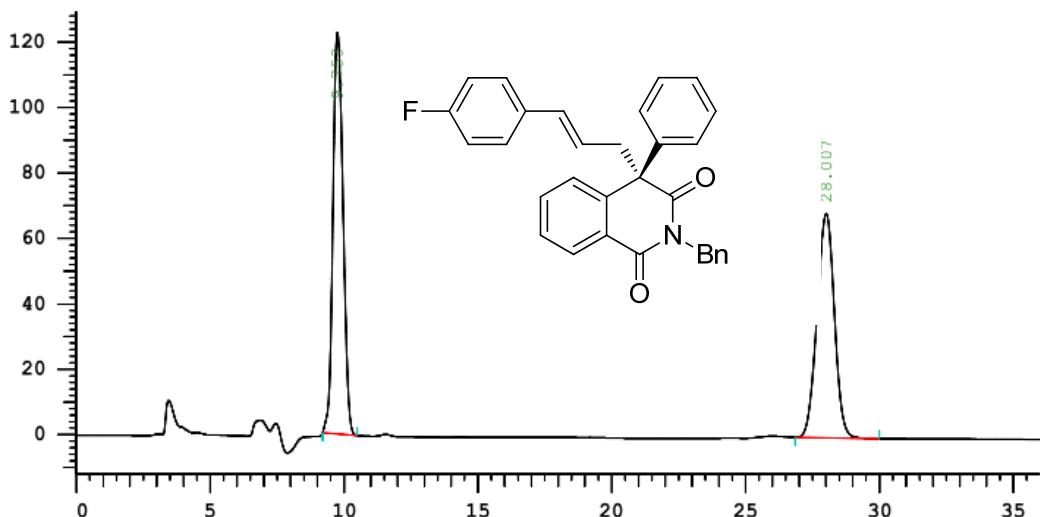


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	8.867	n.a.	6086755	50.402
2	27.427	n.a.	5989625	49.598
Total:			12076380	100.00

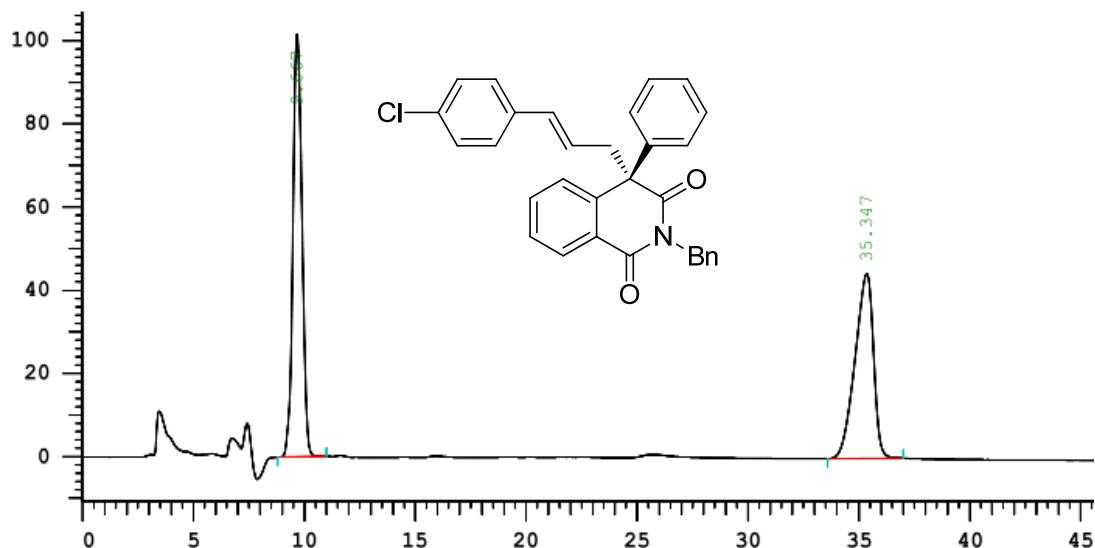


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	8.807	n.a.	15100679	95.977
2	26.893	n.a.	633045	4.023
Total:			15733724	100.00

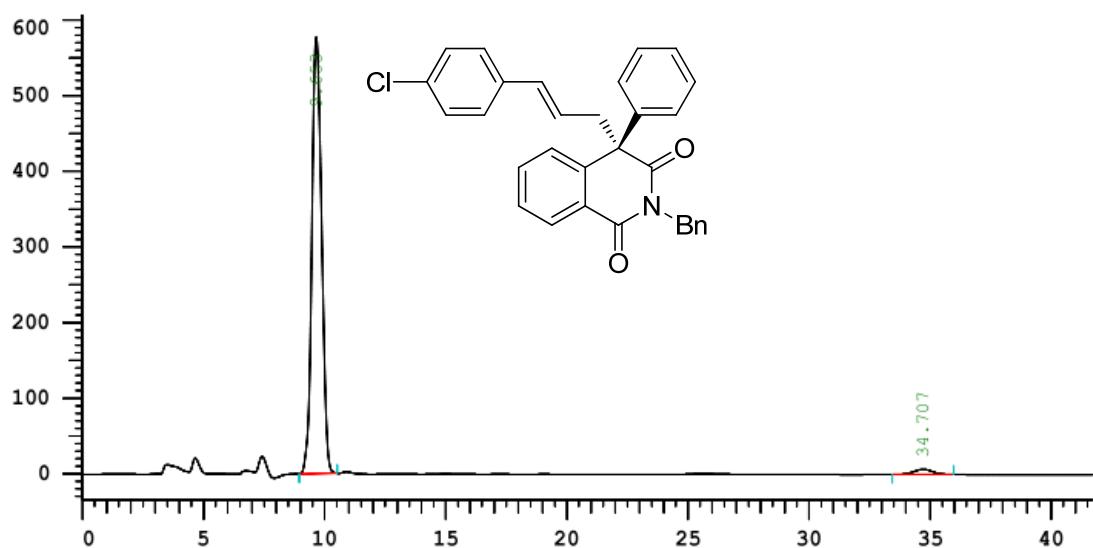
(R,E)-2-benzyl-4-(3-(4-fluorophenyl)allyl)-4-phenylisoquinoline-1,3(2H,4H)-dione(3ad):



(R,E)-2-benzyl-4-(3-(4-chlorophenyl)allyl)-4-phenylisoquinoline-1,3(2H,4H)-dione(3ae):

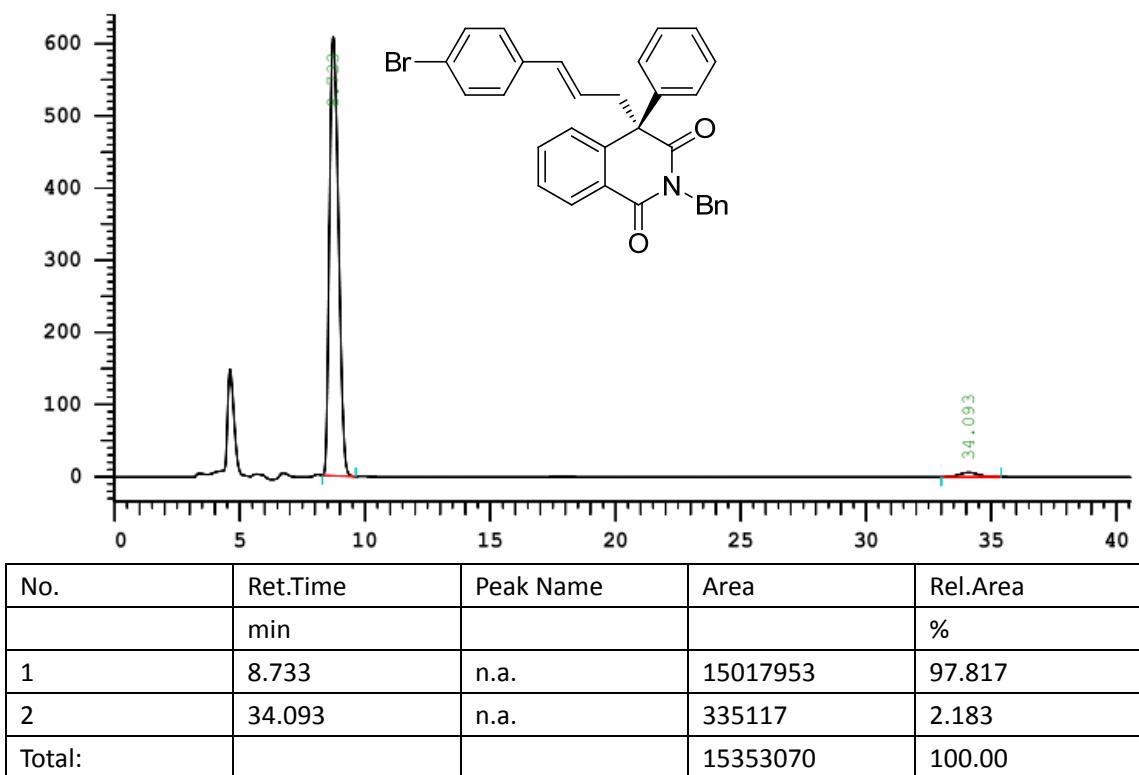
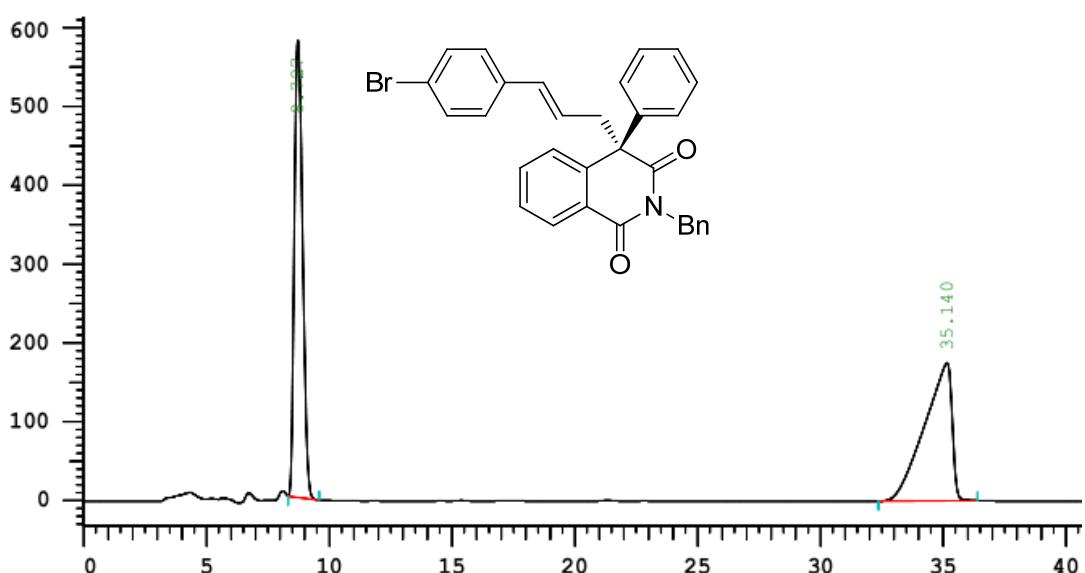


No.	Ret.Time min	Peak Name	Area	Rel.Area
1	9.667	n.a.	2841075	52.692
2	35.347	n.a.	2550778	47.308
Total:			5391853	100.00

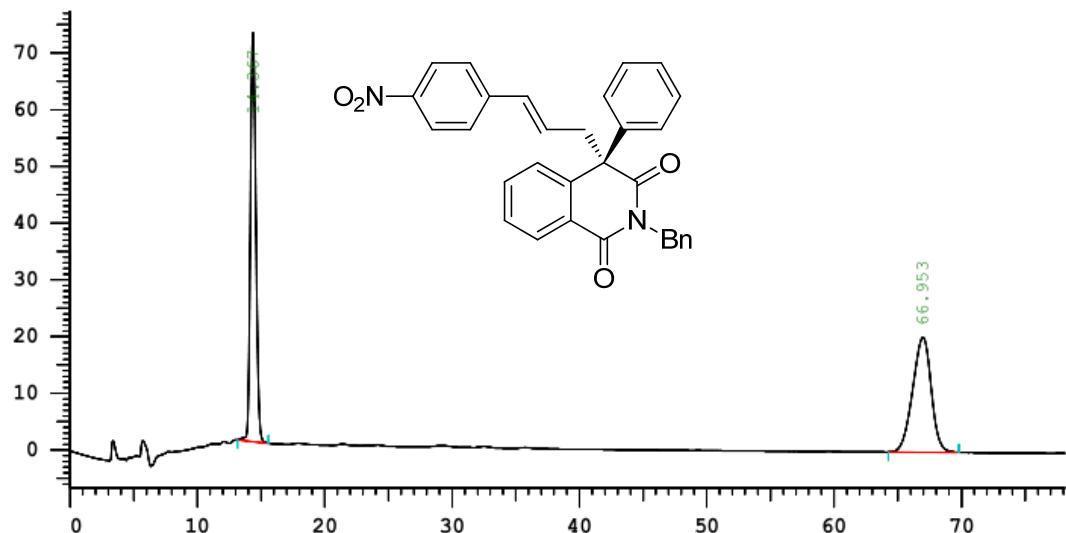


No.	Ret.Time min	Peak Name	Area	Rel.Area
1	9.653	n.a.	15858360	97.729
2	34.707	n.a.	368480	2.271
Total:			16226840	100.00

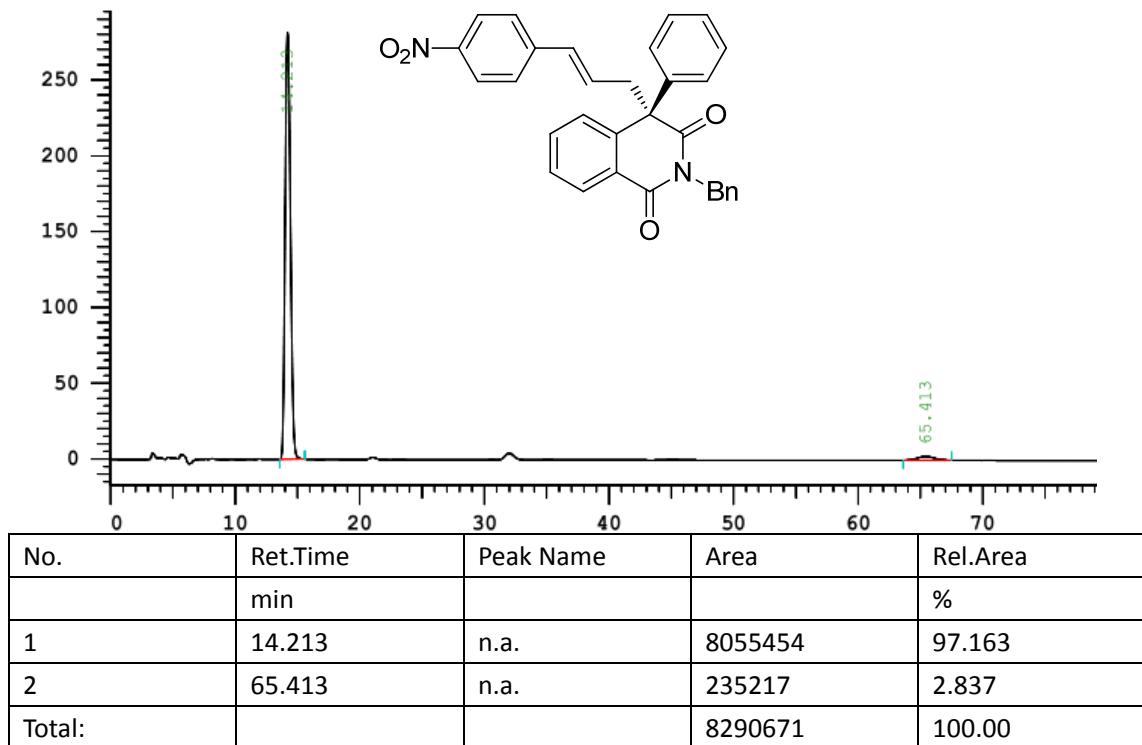
(R,E)-2-benzyl-4-(3-(4-bromophenyl)allyl)-4-phenylisoquinoline-1,3(2H,4H)-dione(3af):



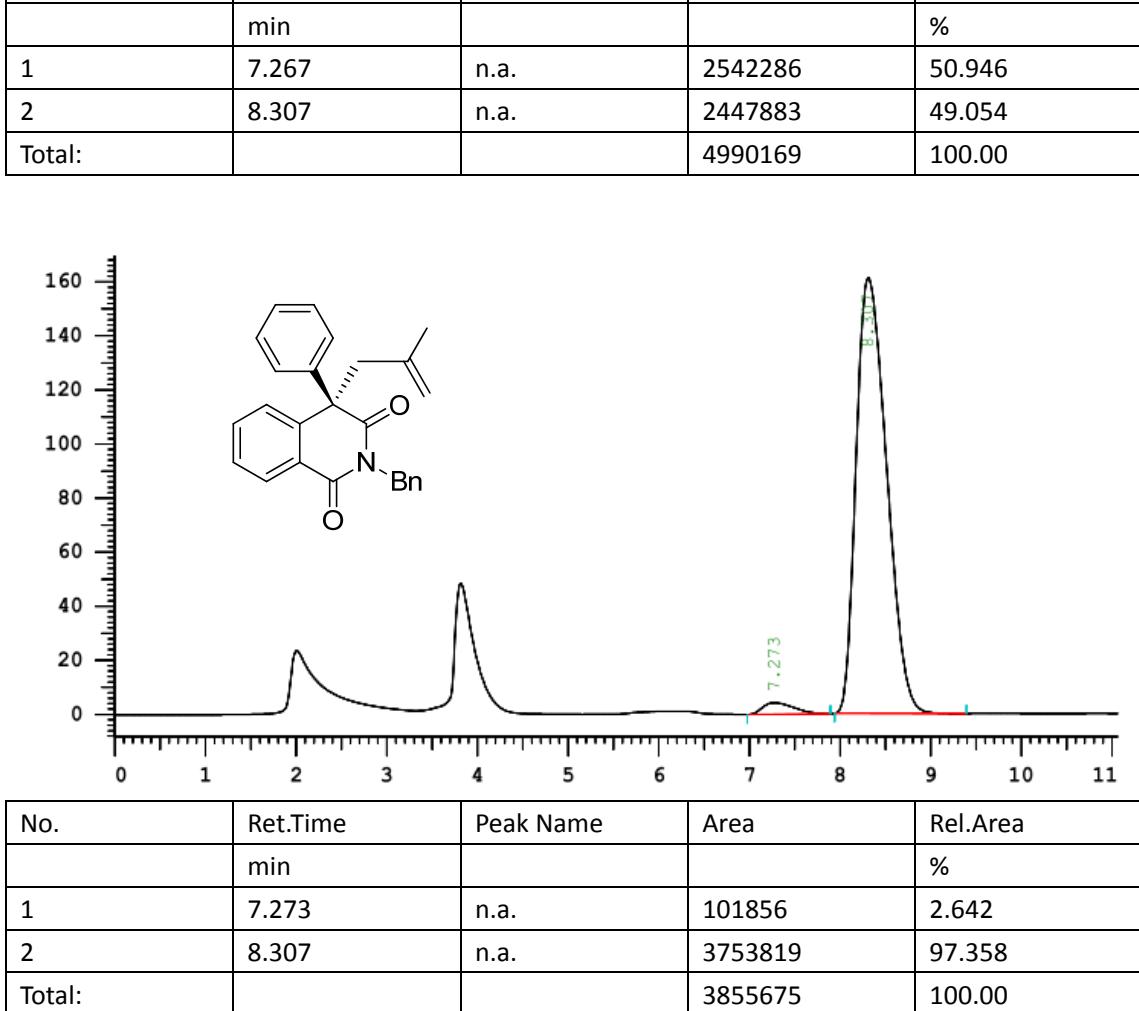
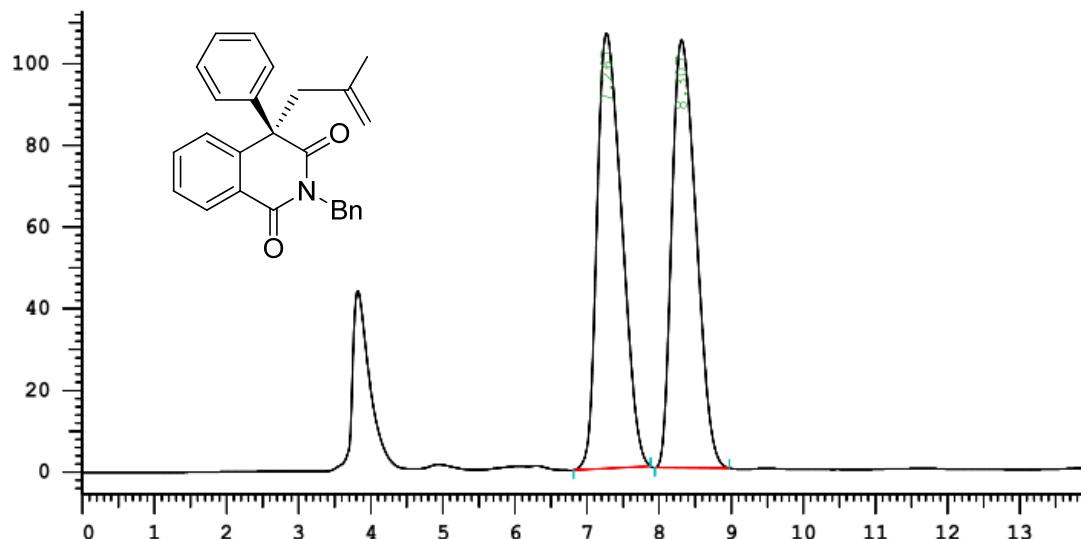
(R,E)-2-benzyl-4-(3-(4-nitrophenyl)allyl)-4-phenylisoquinoline-1,3(2H,4H)-dione(3ag):



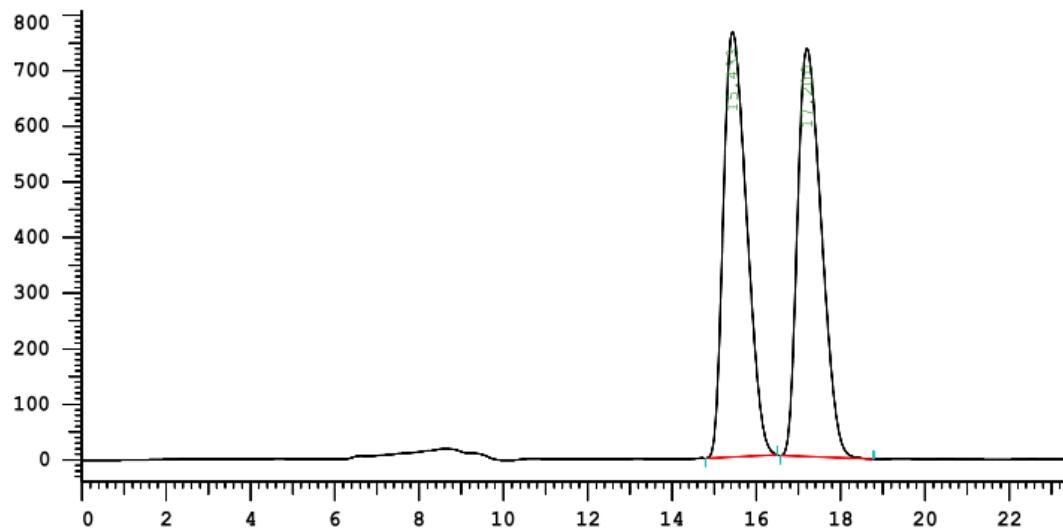
No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	14.367	n.a.	2101513	50.829
2	66.953	n.a.	2032981	49.171
Total:			4134494	100.00



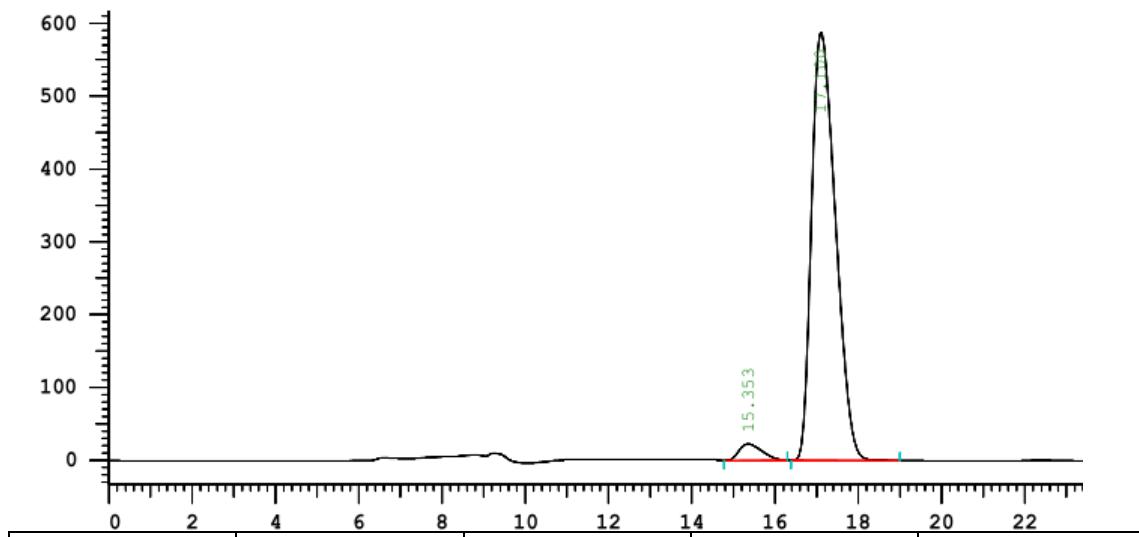
(R)-2-benzyl-4-(2-methylallyl)-4-phenylisoquinoline-1,3(2H,4H)-dione(3ah):



*(R)-2-benzyl-4-(2-bromoallyl)-4-phenylisoquinoline-1,3(2*H*,4*H*)-dione(3ai):*

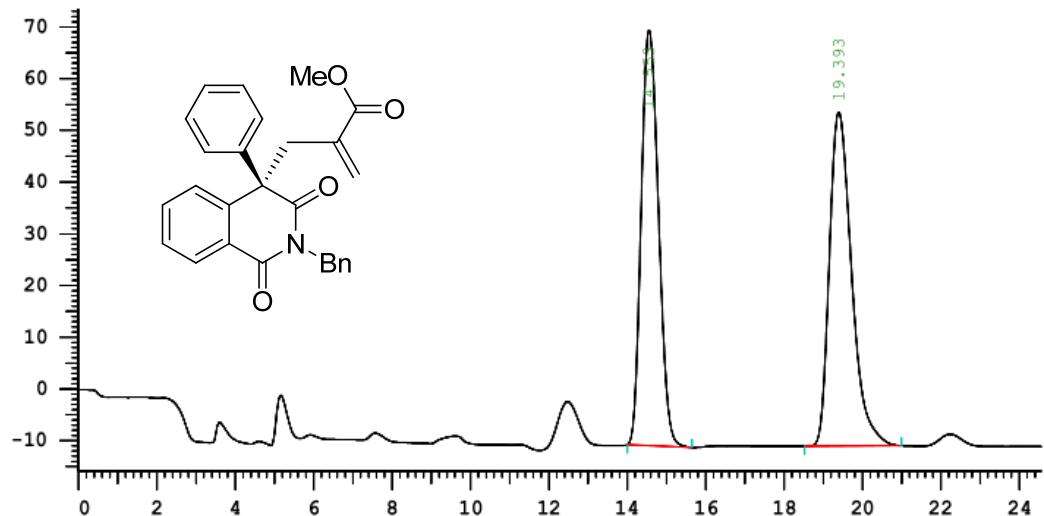


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	15.433	n.a.	29295900	50.283
2	17.200	n.a.	28966279	49.717
Total:			58262179	100.00

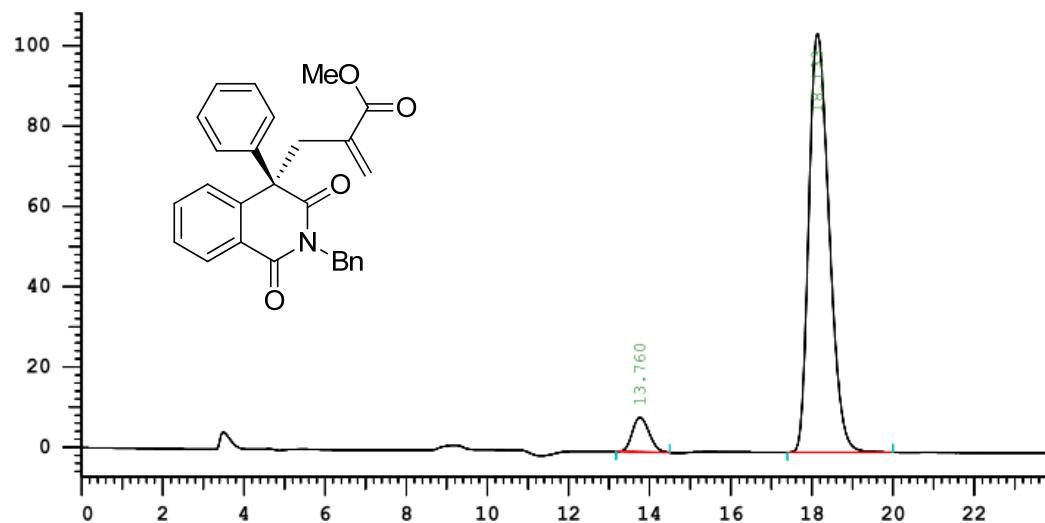


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	15.353	n.a.	866079	3.565
2	17.100	n.a.	23425226	96.435
Total:			24291305	100.00

(R)-methyl2-((2-benzyl-1,3-dioxo-4-phenyl-1,2,3,4-tetrahydroisoquinolin-4-yl)methyl)acrylate
(3aj):

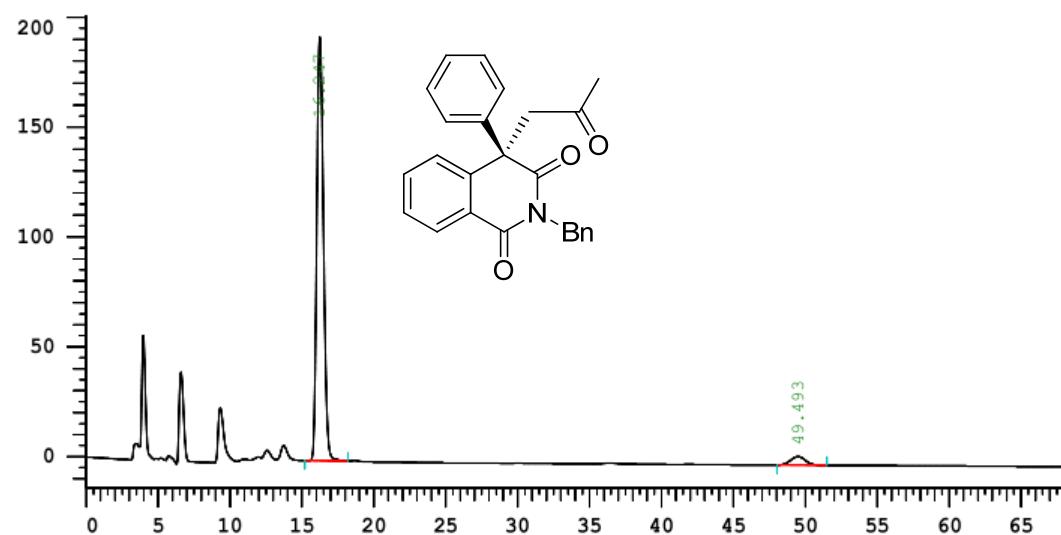
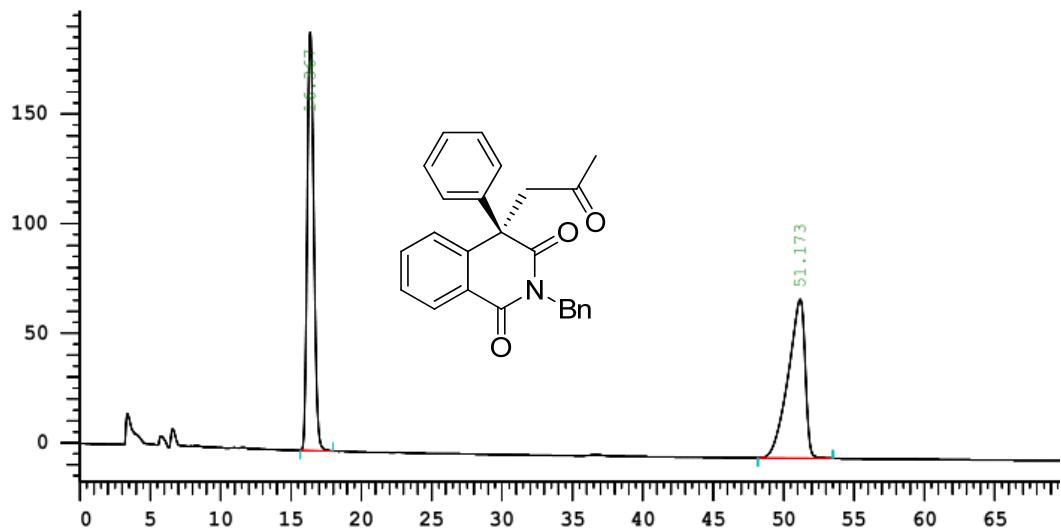


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	14.553	n.a.	2449223	49.114
2	19.393	n.a.	2537636	50.886
Total:			4986859	100.00

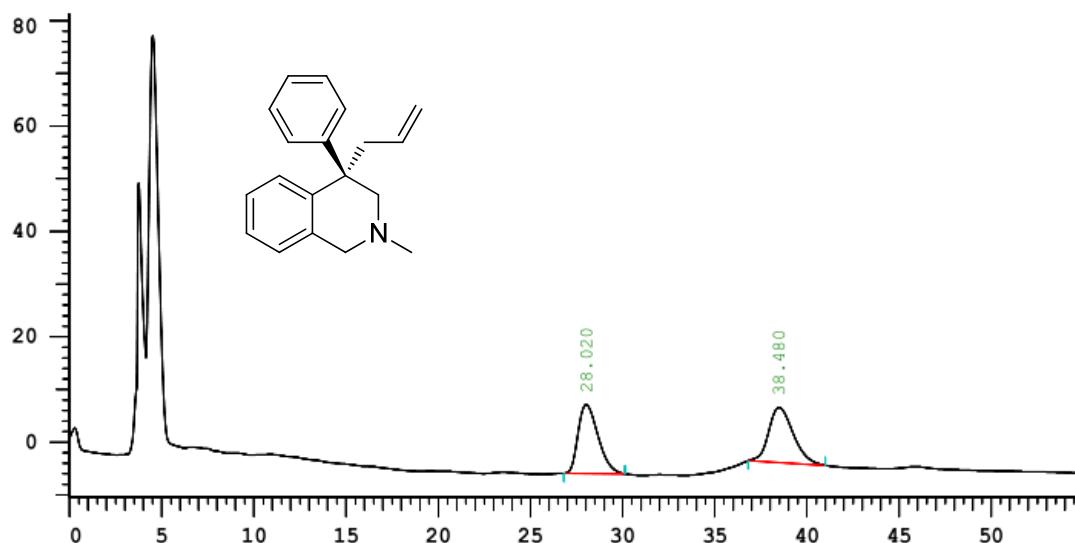


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	13.760	n.a.	247748	6.416
2	18.133	n.a.	3613562	93.584
Total:			3861310	100.00

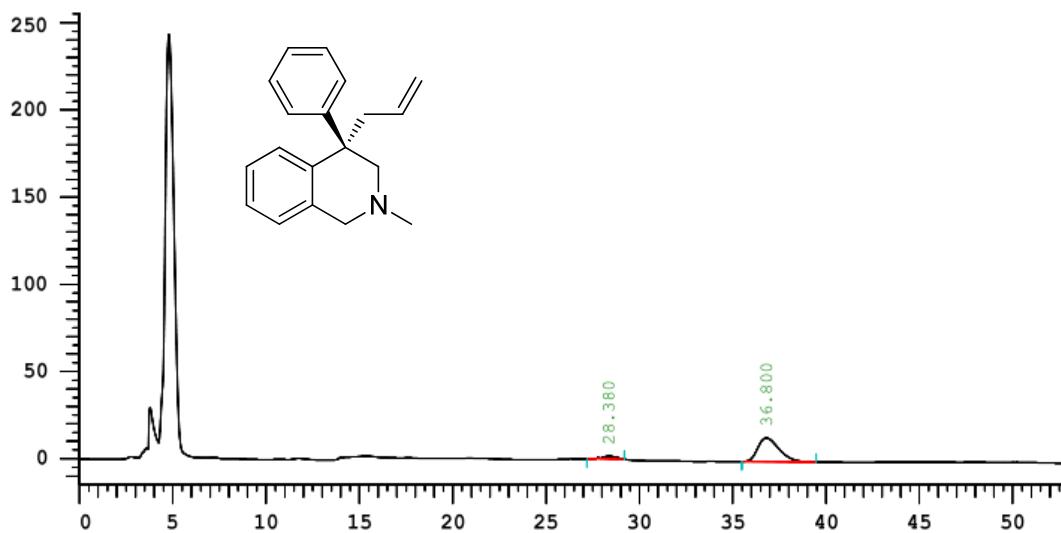
(R)-2-benzyl-4-(2-oxopropyl)-4-phenylisoquinoline-1,3(2H,4H)-dione(4a):



(*R*)-2'-benzyl-3-methylene-2,3-dihydro-1'H-spiro[indene-1,4'-isoquinoline]-1',3'(*2'H*)-dione(5b):

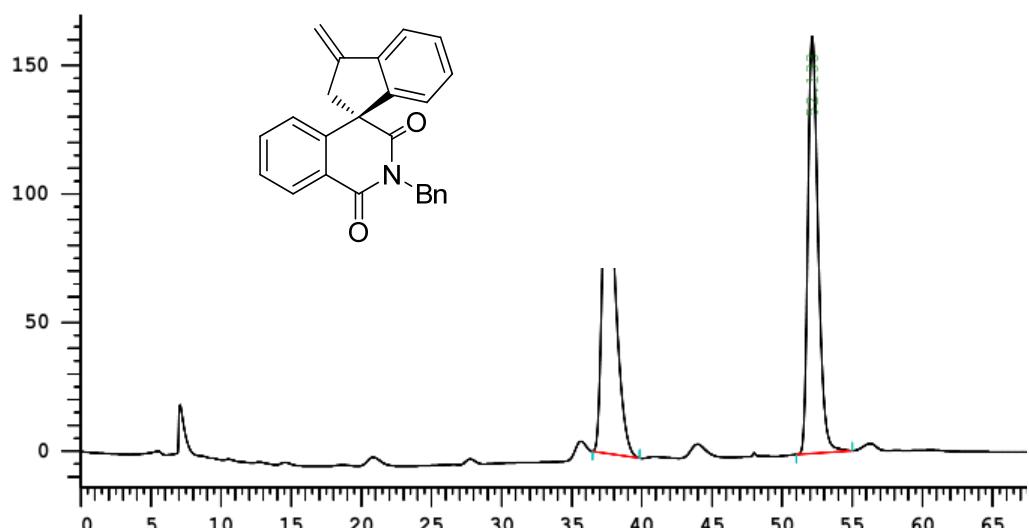


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	28.020	n.a.	978305	50.300
2	38.480	n.a.	966626	49.700
Total:				100.00

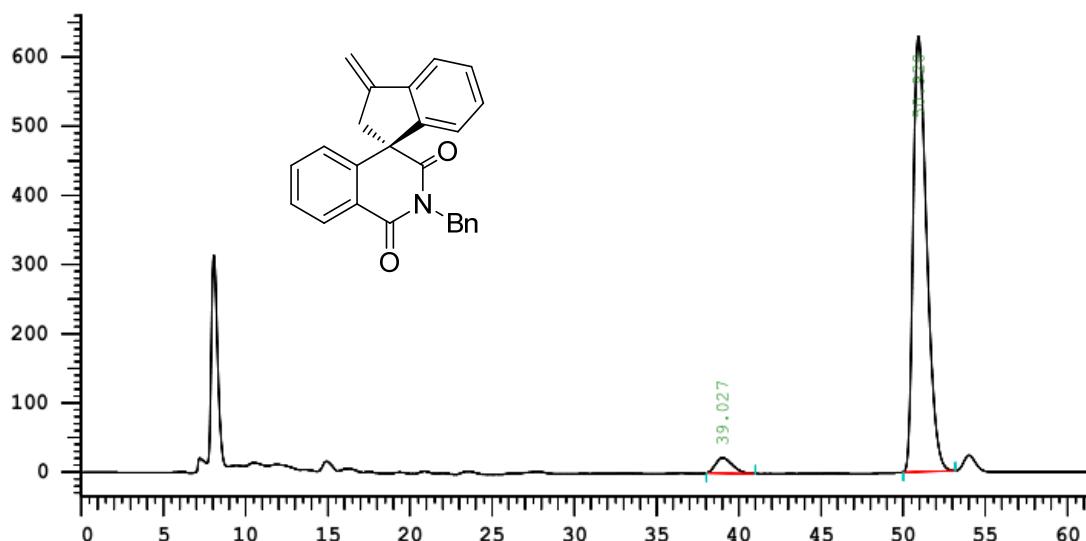


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	28.380	n.a.	79365	6.832
2	36.800	n.a.	1082275	93.168
Total:			1161640	100.00

(R)-4-allyl-2-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline(6q):

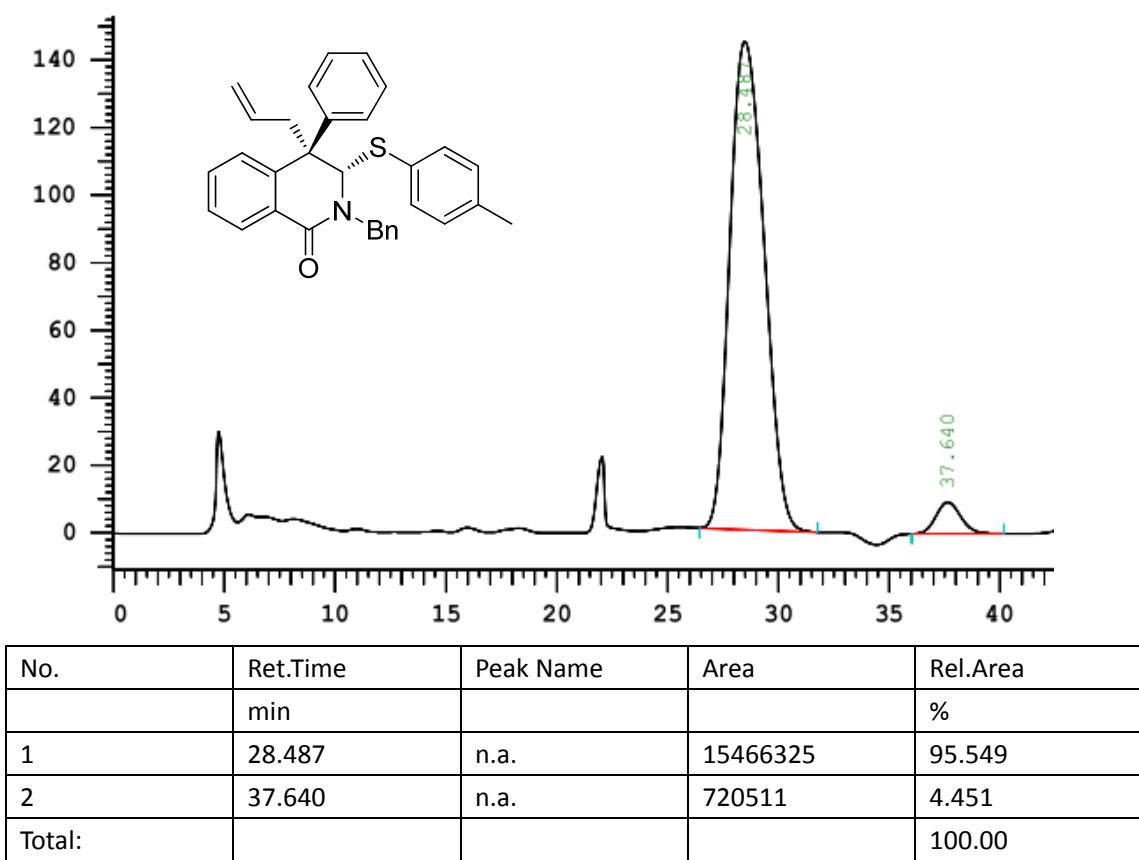
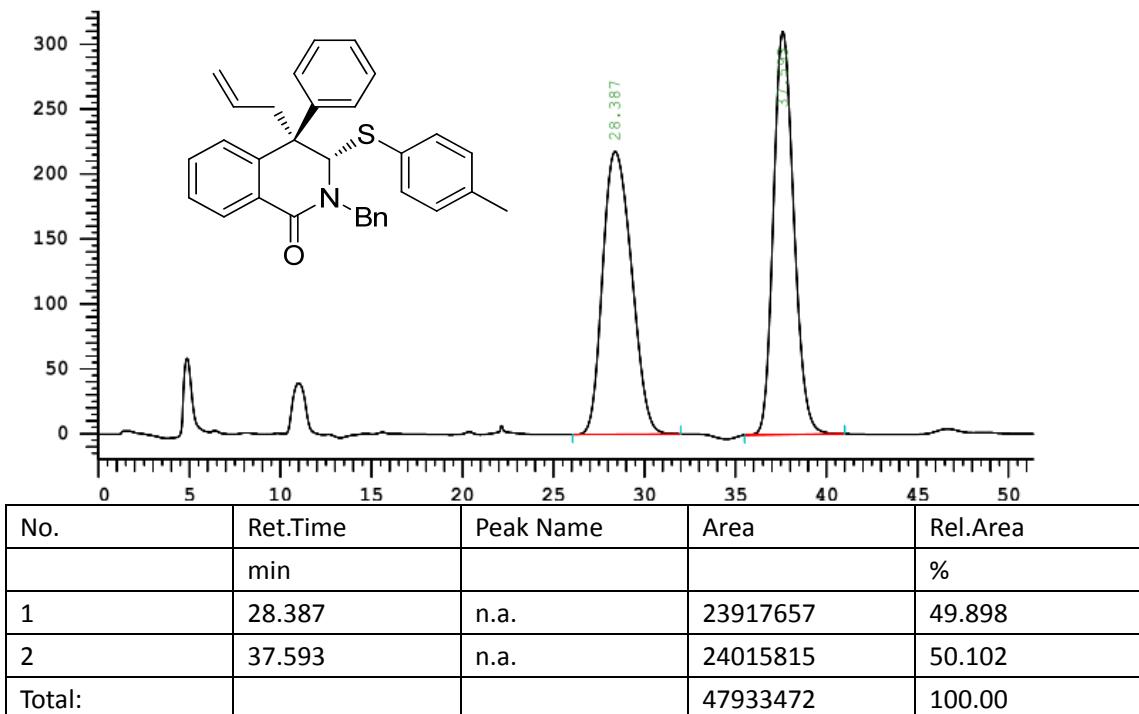


No.	Ret.Time min	Peak Name	Area	Rel.Area
1	37.527	n.a.	7779780	49.046
2	52.133	n.a.	8082520	50.954
Total:			15862300	100.00

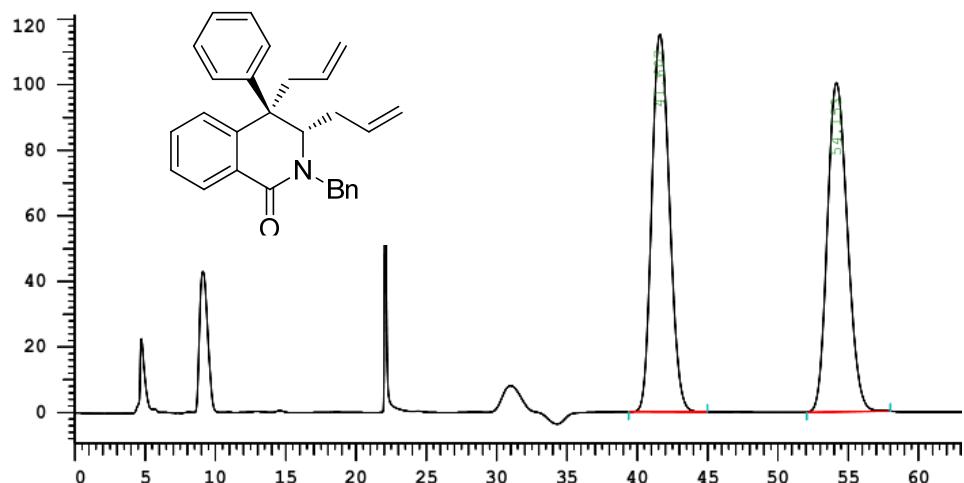


No.	Ret.Time min	Peak Name	Area	Rel.Area
1	39.027	n.a.	1617600	4.352
2	50.920	n.a.	35554785	95.648
Total:			37172385	100.00

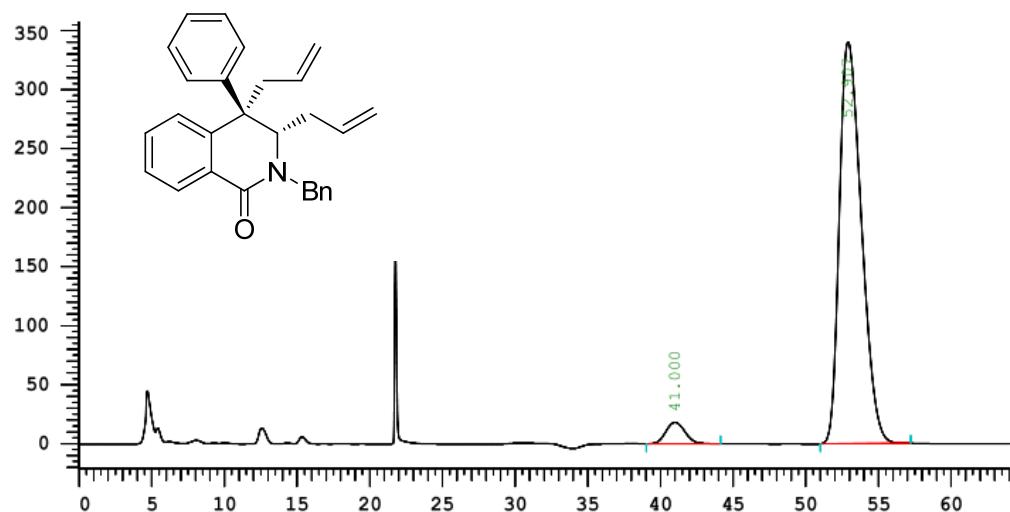
(3S,4R)-4-allyl-2-benzyl-4-phenyl-3-(p-tolylthio)-3,4-dihydroisoquinolin-1(2H)-one(8a):



(3*S*,4*R*)-3,4-diallyl-2-benzyl-4-phenyl-3,4-dihydroisoquinolin-1(2*H*)-one(9a):

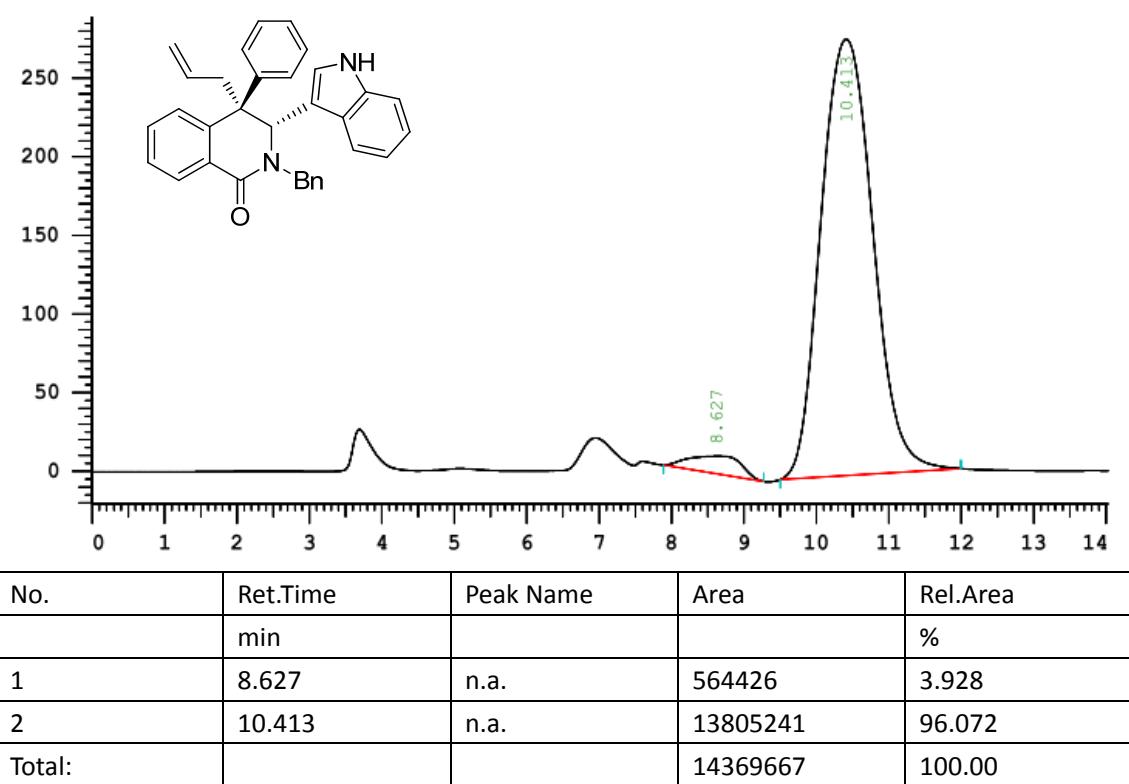
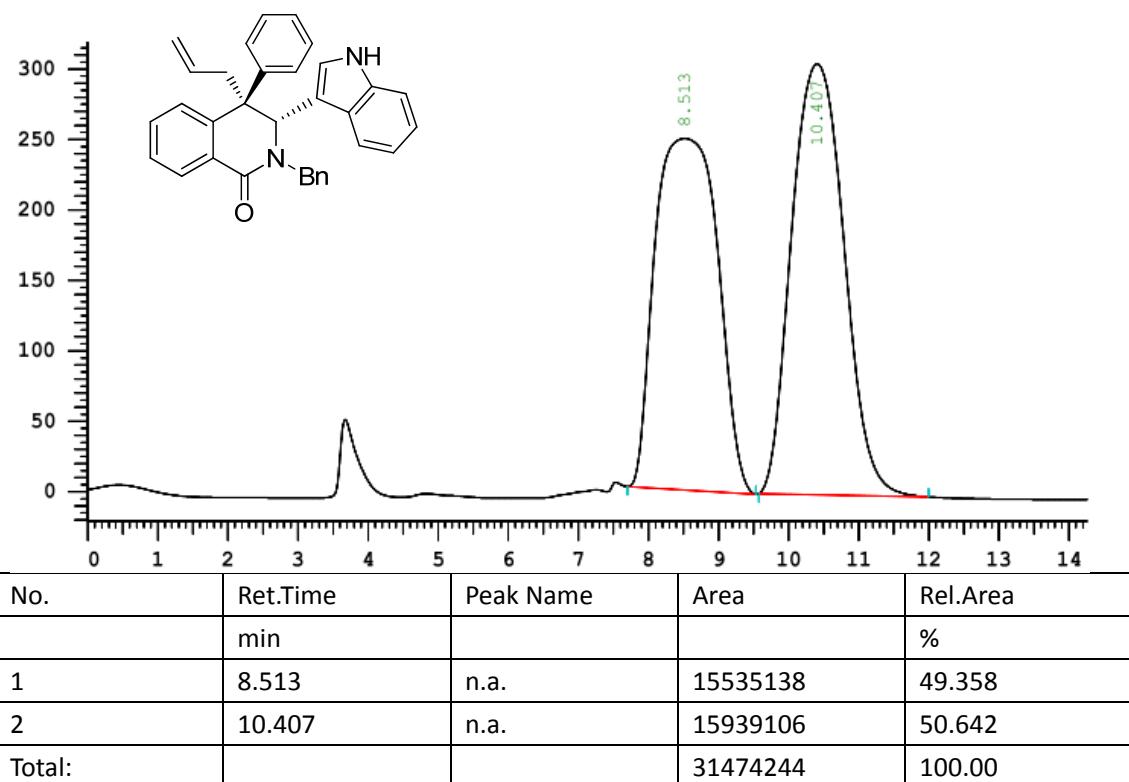


No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	41.607	n.a.	9961452	50.188
2	54.153	n.a.	9886666	49.812
Total:			19848118	100.00



No.	Ret.Time	Peak Name	Area	Rel.Area
	min			%
1	41.000	n.a.	1654045	4.442
2	52.907	n.a.	35584878	95.558
Total:			37238923	100.00

(3S,4R)-4-allyl-2-benzyl-3-(1H-indol-3-yl)-4-phenyl-3,4-dihydroisoquinolin-1(2H)-one(10a):



References:

1. Yuanyong Yang, Yingxian Li, Cheng Cheng, Guo Yang, Jiquan Zhang, Yi Zhang, Yonglong Zhao, Lin Zhang, Chun Li, Lei Tang, Synthesis of 4-Aryl Isoquinolinedione Derivatives by Palladium-catalyzed Coupling Reaction of Aryl Halides with Isoquinoline-1,3(2H, 4H)-diones. *The Journal of Organic Chemistry*, 2018, 83, 3348–3353.
2. Cheng Cheng, Ying-Xian Li, Ji-Quan Zhang, Yong-Long Zhao, Lin Zhang, Chun Li, Yu-she Yang, Lei Tang, and Yuan-Yong Yang Organo-Catalyzed Asymmetric Amination of 4-Arylisoquinoline-1,3(2H,4H)-dione Derivatives in the Construction of Quaternary Stereocenters, *Adv. Synth. Catal.* 2019, 361, 5317–5321.