Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Enantioselective Construction of Spiro-1,3-indandiones with Three Stereocenters via Organocatalytic Michael-Aldol Reaction of 2-Arylideneindane-1,3-diones and Nitro Aldehydes

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Supporting Information

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Experimental section

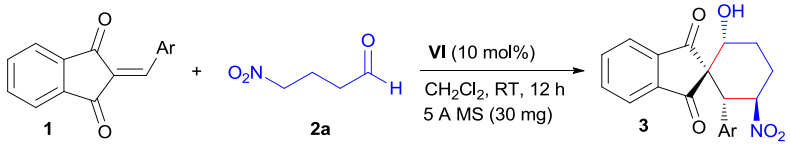
General

All reactions were carried out with dry, freshly distilled solvents in anhydrous conditions. Toluene and THF were distilled from sodium, while dichloromethane was distilled from CaH_2 immediately prior to use. All chemicals were used without further purification as commercially available unless otherwise noted. All reactions were performed under an atmosphere of dry nitrogen. Thin-layer chromatography (TLC) was performed on silica gel plates (60F-254) using UV-light (254 and 365 nm). Flash chromatography was conducted on silica gel (300–400 mesh). NMR (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR) spectra were recorded in $CDCl_3$ or Acetone with TMS as the internal standard. Chemical shifts are reported in ppm and coupling constants are given in Hz. Data for ^{1}H NMR are recorded as follows: chemical shift (ppm), multiplicity (s, singlet; d, doublet; t, triplet; q, quarter; m, multiplet), coupling constant (Hz), integration. Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm). High resolution mass spectral (HRMS) analyses were measured using ESI techniques. Melting points were determined in a hanon auto melting point system (MP 450).

A variety of 2-arylidene-1,3-indandiones **1** were synthesized via Knoevenagel reactions as reported in the literature.[1] 4-nitrobutanal and 3-nitropropanal were prepared using general procedures reported in the literature.[2] All the organocatalysts were purchased from Daicel Chiral Technologies (China) Co., LTD.

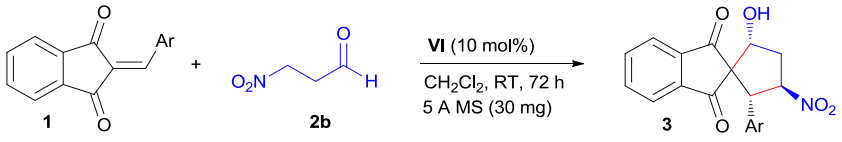
General procedure for the enantioselective construction of spiro-1,3-indandiones

Procedure A:



To a stirred solution of 2-arylidene-1,3-indandiones **1** (0.2 mmol), 5Å MS (30 mg) and catalyst **VI** (0.02 mmol) in dichloromethane (2.0 mL) was added 4-nitrobutanal **2a** (0.24 mmol) and then stirred for 12 h at room temperature. After removal of the solvent, the crude residue was purified by column chromatography (petroleum ether/acetone 4/1 v/v) on silica gel to give the corresponding product.

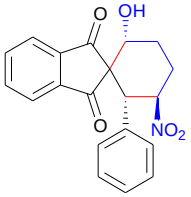
Procedure B:



To a stirred solution of 2-arylidene-1,3-indandiones **1** (0.2 mmol), 5Å MS (30 mg) and catalyst **VI** (0.02 mmol) in dichloromethane (2.0 mL) was added 3-nitropropanal **2b** (0.24 mmol) and then stirred for 72 h at room temperature. After removal of the solvent, the crude residue was purified by column chromatography (petroleum ether/acetone 4/1 v/v) on silica gel to give the corresponding product.

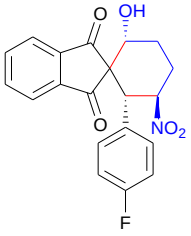
Compounds characterization

(2R,3R,6R)-6-Hydroxy-3-nitro-2-phenylspiro[cyclohexane-1,2'-indene]-1',3'-dione (3aa)



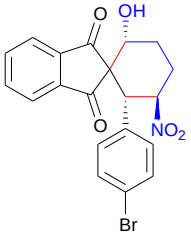
Prepared according to general procedure A to afford **3aa** (58 mg, 83 % yield) as a white solid; m.p. 203-205 ^{o}C; $[\alpha]_D^{22}$ = - 91.4 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, Acetone-D_6) δ 7.85-7.72(m, 4H), 7.07-6.97 (m, 5H), 5.89-5.83 (m, 1H), 4.69 (d, *J* = 4.4 Hz, 1H), 4.42-4.37 (m, 1H), 3.79 (d, *J* = 12.0 Hz, 1H), 2.67-2.61 (m, 1H), 2.53-2.43 (m, 1H), 2.34-2.23 (m, 1H), 2.17-2.11 (m, 1H); ^{13}C NMR (100 MHz, Acetone-D_6) δ 202.2, 200.8, 143.3, 142.8, 135.8, 135.7, 134.3, 128.6, 128.4, 128.0, 122.4, 122.2, 84.8, 73.2, 63.2, 49.4, 28.7; HRMS (ESI): m/z calcd for $C_{20}H_{17}NNaO_5$ [M+Na] 374.1004, Found 374.1006; HPLC conditions: Daicel Chiralpak OD-H column, *n*-hexane/2-propanol = 85/15, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_R (minor) = 17.1 min, t_R (major) = 20.1 min, 90% ee.

(2R,3R,6R)-2-(4-Fluorophenyl)-6-hydroxy-3-nitrospiro[cyclohexane-1,2'-indene]-1',3'-dione (3ba)



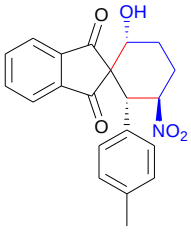
Prepared according to general procedure A to afford **3ba** (59 mg, 80 % yield) as a white solid; m.p. 195-197 ^{o}C; $[\alpha]_D^{22}$ = - 95.8 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, Acetone-D_6) δ 7.87-7.76(m, 4H), 7.09-7.06 (m, 2H), 6.87-6.83 (m, 2H), 5.86-5.79 (m, 1H), 4.72 (d, *J* = 4.0 Hz, 1H), 4.42-4.37 (m, 1H), 3.80 (d, *J* = 12.0 Hz, 1H), 2.67-2.62 (m, 1H), 2.52-2.41 (m, 1H), 2.34-2.27 (m, 1H), 2.17-2.13 (m, 1H); ^{13}C NMR (100 MHz, Acetone-D_6) δ 207.3, 205.9, 168.5($J_{C\text{-}F}$ = 244.1 Hz), 148.5, 147.9, 141.2, 141.1, 135.8, 135.7($J_{C\text{-}F}$ = 3.0 Hz), 127.6($J_{C\text{-}F}$ = 6.7 Hz), 127.5, 120.5 ($J_{C\text{-}F}$ = 20.7 Hz), 90.1, 78.3, 68.4, 53.8, 34.7; HRMS (ESI): m/z calcd for $C_{20}H_{16}FNNaO_5$ [M+Na] 392.0910, Found 392.0912; HPLC conditions: Daicel Chiralpak IB-3 column, *n*-hexane/2-propanol = 85/15, flow rate = 1.5 mL/min, λ = 254 nm, retention time: t_R (major) = 9.3 min, t_R (minor) = 13.4 min, 89% ee.

(2R,3R,6R)-2-(4-Bromophenyl)-6-hydroxy-3-nitrospiro[cyclohexane-1,2'-indene]-1',3'-dione (3ca)



Prepared according to general procedure A to afford **3ca** (64 mg, 75 % yield) as a white solid; m.p. 232-235 ^{o}C; $[\alpha]_D^{22}$ = -78.5 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82-7.81(m, 1H), 7.72-7.66 (m, 3H), 7.13 (d, *J* = 8.4 Hz, 2H), 6.89 (d, *J* = 8.4 Hz, 2H), 5.82-5.77 (m, 1H), 4.40-4.36 (m, 1H), 3.79 (d, *J* = 12.0 Hz, 1H), 2.65-2.61 (m, 1H), 2.53-2.49 (m, 1H), 2.23-2.19 (m, 1H), 2.15-2.09 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.9, 200.9, 143.1, 142.5, 136.1, 135.9, 132.4, 131.8, 130.2, 122.9, 122.7, 122.5, 84.1, 73.3, 62.9, 48.8, 29.6, 28.6; HRMS (ESI): m/z calcd for $C_{20}H_{16}BrNNaO_5$ [M+Na] 452.0110, Found 452.0109; HPLC conditions: Daicel Chiralpak IB-3 column, *n*-hexane/2-propanol = 85/15, flow rate = 1.5 mL/min, λ = 254 nm, retention time: t_R (major) = 9.9 min, t_R (minor) = 14.3 min, 86% ee.

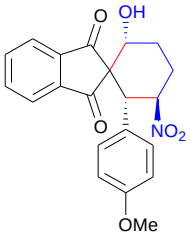
(2R,3R,6R)-6-Hydroxy-3-nitro-2-(p-tolyl)spiro[cyclohexane-1,2'-indene]-1',3'-dione (3da)



Prepared according to general procedure A to afford **3da** (55 mg, 76 % yield) as a white solid; m.p. 228-230 ^{o}C; $[\alpha]_D^{22}$ = -82.8 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, Acetone-D_6) δ 7.87-7.73 (m, 4H), 6.92-6.84 (m, 4H), 5.86-5.79 (m, 1H), 4.65 (d, *J* = 4.4 Hz, 1H), 4.39-4.34 (m, 1H), 3.75 (d, *J* = 11.6 Hz, 1H), 2.65-2.59 (m, 1H), 2.48-2.40 (m, 1H), 2.32-2.25 (m, 1H), 2.15-2.09 (m, 1H), 2.04 (s, 3H); ^{13}C NMR (100 MHz, Acetone-D_6) δ 202.3, 200.8, 143.4, 142.9,

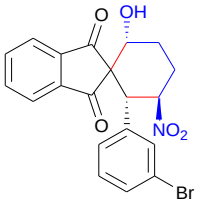
137.6, 135.8, 135.7, 131.3, 128.9, 128.5, 122.4, 122.2, 85.0, 73.2, 73.1，63.2, 48.9, 28.7, 19.9; HRMS (ESI): m/z calcd for $C_{21}H_{19}NNaO_5$ [M+Na] 388.1161, Found 388.1156; HPLC conditions: Daicel Chiralpak IB-3 column, *n*-hexane/2-propanol = 85/15, flow rate = 1.5 mL/min, λ = 254 nm, retention time: t_R (major) = 8.4 min, t_R (minor) = 11.8 min, 86% ee.

(2R,3R,6R)-6-Hydroxy-2-(4-methoxyphenyl)-3-nitrospiro[cyclohexane-1,2'-indene]-1',3'-dione (3ea)



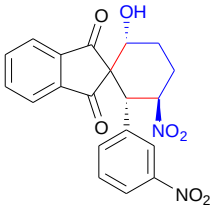
Prepared according to general procedure A to afford **3ea** (61 mg, 80 % yield) as a white solid; m.p. 230-232 ^oC; $[\alpha]_D^{22}$ = -40.9 (c = 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.79-7.78 (m, 1H), 7.68-7.58 (m, 3H), 6.90 (d, J = 8.5 Hz, 2H), 6.50 (d, J = 8.5 Hz, 2H), 5.79-5.74 (m, 1H), 4.38-4.36 (m, 1H), 3.74 (d, J = 12.0 Hz, 1H), 3.56 (s, 3H), 2.61-2.56 (m, 1H), 2.53-2.47 (m, 1H), 2.24-2.14 (m, 2H), 2.11-2.07 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.2, 201.4, 159.1, 143.2, 142.6, 135.7, 135.6, 129.6, 125.2, 122.8, 122.6, 113.9, 84.5, 73.2, 63.3, 54.9, 48.8, 29.6, 28.6; HRMS (ESI): m/z calcd for $C_{21}H_{19}NNaO_6$ [M+Na] 404.1110, Found 404.1112; HPLC conditions: Daicel Chiralpak IB-3 column, *n*-hexane/2-propanol = 85/15, flow rate = 1.5 mL/min, λ = 254 nm, retention time: t_R (major) = 11.6 min, t_R (minor) = 16.5 min, 88% ee.

(2R,3R,6R)-2-(3-Bromophenyl)-6-hydroxy-3-nitrospiro[cyclohexane-1,2'-indene]-1',3'-dione (3fa)



Prepared according to general procedure A to afford **3fa** (69 mg, 80 % yield) as a white solid; m.p. 226-228 ^oC; $[\alpha]_D^{22}$ = -74.7 (c = 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.85-7.83 (m, 1H), 7.75-7.65 (m, 3H), 7.15-7.09 (m, 2H), 6.97-6.95 (m, 1H), 6.89-6.86 (m, 1H), 5.81-5.74 (m, 1H), 4.43-4.37 (m, 1H), 3.78 (d, *J* = 12.0 Hz, 1H), 2.67-2.61 (m, 1H), 2.56-2.49 (m, 1H), 2.28-2.19 (m,1H), 2.17-2.11 (m,1H), 1.89 (d, *J* = 5.2 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 201.6, 200.7, 143.1, 142.4, 135.9, 135.8, 135.6, 131.5, 130.1, 122.9, 122.7, 122.6, 83.9, 73.2, 62.8, 48.9, 29.6, 28.7; HRMS (ESI): m/z calcd for $C_{20}H_{16}BrNNaO_5$ [M+Na] 452.0110, Found 452.0108; HPLC conditions: HPLC conditions: Daicel Chiralpak IB-3 column, *n*-hexane/2-propanol = 85/15, flow rate = 1.5 mL/min, λ = 254 nm, retention time: t_R (major) = 10.0 min, t_R (minor) = 13.3 min, 77% ee.

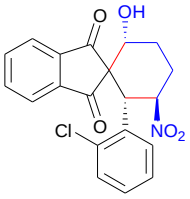
(2R,3R,6R)-6-Hydroxy-3-nitro-2-(3-nitrophenyl)spiro[cyclohexane-1,2'-indene]-1',3'-dione (3ga)



Prepared according to general procedure A to afford **3ga** (54 mg, 68 % yield) as a white solid; m.p. 241-242 ^oC; $[\alpha]_D^{22}$ = -75.4 (c = 1.0, $CHCl_3$); ^1H NMR (400 MHz, Acetone-D_6) δ 7.93-7.78 (m, 6H), 7.50-7.44 (m, 2H), 5.94-5.93 (m, 1H), 4.82 (m, 1H), 4.44 (m, 1H), 4.00-3.97 (m, 1H), 2.72-2.69 (m, 1H), 2.49-2.34 (m, 2H), 2.20-2.17 (m, 1H); ^{13}C NMR (100 MHz, Acetone-D_6) δ 201.8, 200.4, 147.9, 143.2, 142.6, 136.6, 136.3, 136.2, 134.9, 130.1, 123.1, 122.6, 122.4, 84.5, 73.2, 63.1, 48.7; HRMS (ESI): m/z calcd for $C_{20}H_{16}N_2NaO_7$ [M+Na] 419.0855, Found 419.0852; HPLC conditions: Daicel Chiralpak IB-3 column, *n*-hexane/2-propanol = 80/20, flow rate = 1.5 mL/min, λ = 254 nm, retention time: t_R (major) = 10.6 min, t_R (minor) = 13.8 min, 66% ee.

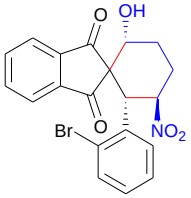
(2S,3R,6R)-2-(2-Chlorophenyl)-6-hydroxy-3-nitrospiro[cyclohexane-1,2'-indene]-1',3'-dione (3ha)

Prepared according to general procedure A to afford **3ha** (56 mg, 73 % yield) as a white solid; m.p. 206-208 ^oC; $[\alpha]_D^{22}$ = -68.7 (c = 1.0, $CHCl_3$); 1H NMR (400 MHz, Acetone-D_6) δ 7.94-7.92 (m, 1H), 7.87-7.73 (m, 4H), 7.26-7.21 (m, 2H), 7.03-7.01 (m, 2H), 5.78-5.71 (m, 1H), 4.81 (d, J =



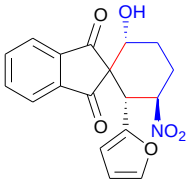
4.0 Hz, 1H), 4.57 (d, *J* = 12.0 Hz, 1H), 4.47-4.42 (m, 1H), 2.67-2.63 (m, 1H), 2.57-2.44 (m, 1H), 2.38-2.28 (m, 1H), 2.19-2.15 (m, 1H); ^{13}C NMR (100 MHz, Acetone-D_6) δ 202.8, 198.9, 143.4, 142.7, 135.9, 135.8, 134.6, 132.3, 130.4, 129.5, 128.4, 127.1, 122.5, 122.4, 85.6, 73.3, 73.1，62.3, 44.2, 28.5; HRMS (ESI): m/z calcd for $C_{20}H_{16}ClNNaO_5$ [M+Na] 408.0615, Found 408.0612; HPLC conditions: Daicel Chiralpak IB-3 column, *n*-hexane/2-propanol = 85/15, flow rate = 1.5 mL/min, λ = 254 nm, retention time: t_R (major) = 11.7 min, t_R (minor) = 13.6 min, 86% ee.

(2S,3R,6R)-2-(2-Bromophenyl)-6-hydroxy-3-nitrospiro[cyclohexane-1,2'-indene]-1',3'-dione (3ia)



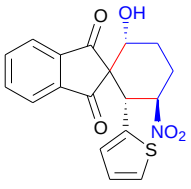
Prepared according to general procedure A to afford **3ia** (64 mg, 75 % yield) as a white solid; m.p. 225-227 °C; $[\alpha]_D^{22}$ = -35.4 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, Acetone-D_6) δ 7.94 (d, *J* = 7.6 Hz, 1H), 7.88-7.73 (m, 3H), 7.41 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.25 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.07-7.03 (m, 1H), 6.96-6.91 (m, 1H), 5.77-5.70 (m, 1H), 4.76 (d, *J* = 4.4 Hz, 1H), 4.55 (d, *J* = 12.0 Hz, 1H), 4.48-4.42 (m, 1H), 2.67-2.62 (m, 1H), 2.58-2.48 (m, 1H), 2.39-2.28 (m, 1H), 2.20-2.14 (m, 1H); ^{13}C NMR (100 MHz, Acetone-D_6) δ 202.8, 198.8, 143.5, 142.8, 135.9, 135.8, 133.9, 129.7, 128.5, 127.6, 125.6, 122.5, 122.4, 85.6, 73.3, 62.3, 46.9, 29.5, 28.5; HRMS (ESI): m/z calcd for $C_{20}H_{16}BrNNaO_5$ [M+Na] 452.0110, Found 452.0108; HPLC conditions: Daicel Chiralpak IB-3 column, *n*-hexane/2-propanol = 85/15, flow rate = 1.5 mL/min, λ = 254 nm, retention time: t_R (major) = 9.8 min, t_R (minor) = 15.3 min, 86% ee.

(2R,3R,6R)-2-(Furan-2-yl)-6-hydroxy-3-nitrospiro[cyclohexane-1,2'-indene]-1',3'-dione (3ja)



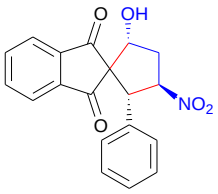
Prepared according to general procedure A to afford **3ja** (57 mg, 84 % yield)as a white solid; m.p. 135-137 °C; $[\alpha]_D^{22}$ = -60.1 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, Acetone-D_6) δ 7.91-7.84 (m, 4H), 7.07 (d, *J* = 1.2 Hz, 1H), 6.03-5.97 (m, 2H), 5.70-5.63 (m, 1H), 4.65 (d, *J* = 4.4 Hz, 1H), 4.38-4.33 (m, 1H), 3.93 (d, *J* = 8.0 Hz, 1H), 2.63-2.57 (m, 1H), 2.47-2.39 (m, 1H), 2.31-2.23 (m, 1H), 2.14-2.09 (m, 1H); ^{13}C NMR (100 MHz, Acetone-D_6) δ 200.9, 200.3, 148.5, 143.1, 142.7, 142.5, 135.8, 135.6，122.5, 122.4, 110.1, 108.8, 84.1, 72.6, 61.4, 43.2, 29.2, 28.4; HRMS (ESI): m/z calcd for $C_{18}H_{15}NNaO_6$ [M+Na] 364.0797, Found 364.0795; HPLC conditions: Daicel Chiralpak IB-3 column, *n*-hexane/2-propanol = 85/15, flow rate = 1.5 mL/min, λ = 254 nm, for major diastereomer: retention time: t_R (major) = 7.9 min, t_R (minor) = 10.1 min, 88% ee, 97.8:2.1 dr.

(2R,3R,6R)-6-Hydroxy-3-nitro-2-(thiophen-2-yl)spiro[cyclohexane-1,2'-indene]-1',3'-dione (3ka)



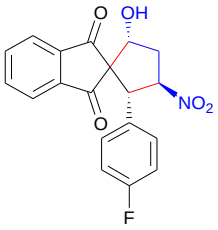
Prepared according to general procedure A to afford **3ka** (43 mg, 61 % yield) as a white solid; m.p. 151-153 °C; $[\alpha]_D^{22}$ = -81.7 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, Acetone-D_6) δ 7.91-7.82 (m, 4H), 7.09 (d, *J* = 5.2 Hz, 1H), 6.73-6.67 (m, 2H), 5.75-5.68 (m, 1H), 4.75 (d, *J* = 5.2 Hz, 1H), 4.39-4.34 (m, 1H), 4.10 (d, *J* = 11.6 Hz, 1H), 2.65-2.59 (m, 1H), 2.45-2.38 (m, 1H), 2.32-2.25 (m, 1H), 2.16-2.09 (m, 1H); ^{13}C NMR (100 MHz, Acetone-D_6) δ 202.1, 200.7, 143.5, 142.9, 136.0, 135.9, 135.8, 127.4, 126.5, 125.5, 122.5, 122.3, 86.4, 73.0, 63.3, 44.5, 29.5, 28.5; HRMS (ESI): m/z calcd for $C_{18}H_{15}NNaO_5S$ [M+Na] 380.0569, Found 380.0566; HPLC conditions: Daicel Chiralpak IA-3 column, *n*-hexane/2-propanol = 85/15, flow rate = 1.5 mL/min, λ = 254 nm, retention time: t_R (minor) = 11.4 min, t_R (major) = 12.2 min, 74% ee.

(2R,3R,5R)-5-Hydroxy-3-nitro-2-phenylspiro[cyclopentane-1,2'-indene]-1',3'-dione (3ab)



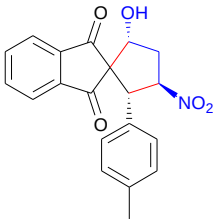
Prepared according to general procedure B to afford **3ab** (63mg, 94 % yield) as a pale off-white sticky oil; $[\alpha]_D^{22}$ = - 58.7 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, Acetone-D_6) δ 7.94-7.91 (m, 1H), 7.89-7.86 (m, 3H), 7.23-7.09 (m, 5H), 6.11-6.05 (m, 1H), 5.08 (s, 1H), 5.05-5.00 (m, 1H), 4.31 (d, *J* = 9.6 Hz, 1H), 2.97-2.92 (m, 2H); ^{13}C NMR (100 MHz, Acetone-D_6) δ 199.8, 199.5, 143.2, 142.9, 136.4, 136.1, 134.3, 128.7, 128.2, 128.1, 122.8, 122.7, 86.1, 76.9, 70.3, 53.5, 37.2; HRMS (ESI): m/z calcd for $C_{19}H_{15}NNaO_5$ [M+Na] 360.0848, Found 360.0842; HPLC conditions: Daicel Chiralpak OD-H column, *n*-hexane/2-propanol = 80/20, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_R (major) = 11.4 min, t_R (minor) = 14.4 min, 90% ee.

(2R,3R,5R)-2-(4-Fluorophenyl)-5-hydroxy-3-nitrospiro[cyclopentane-1,2'-indene]-1',3'-dione (3bb)



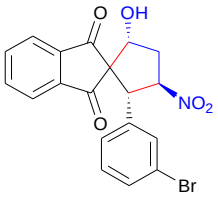
Prepared according to general procedure B to afford **3bb** (64 mg, 90 % yield) as a pale off-white sticky oil; $[\alpha]_D^{22}$ = -84.2 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, Acetone-D_6) δ 7.96-7.89 (m, 4H), 7.29-7.25 (m, 2H), 6.99-6.94(m, 2H), 6.08-6.02(m, 1H), 5.10 (s, 1H), 5.03-4.99 (m, 1H), 4.31 (d, *J* = 9.6 Hz, 1H), 2.97-2.92 (m, 2H); ^{13}C NMR (100 MHz, Acetone-D_6) δ 199.7, 199.5, 163.5($J_{C\text{-}F}$ = 243.7 Hz), 143.1 ($J_{C\text{-}F}$ = 15.4 Hz), 136.5, 136.2, 130.5($J_{C\text{-}F}$ = 2.8 Hz), 130.3($J_{C\text{-}F}$ = 8.5 Hz), 122.9, 122.7, 115.5, 115.3, 86.2, 76.9, 70.3, 52.6, 37.1; HRMS (ESI): m/z calcd for $C_{19}H_{14}FNNaO_5$ [M+Na] 378.0754, Found 378.0751; HPLC conditions: Daicel Chiralpak IB-3 column, *n*-hexane/2-propanol = 85/15, flow rate = 1.5 mL/min, λ = 254 nm, retention time: t_R (major) = 9.0 min, t_R (minor) = 11.1 min, 87% ee.

(2R,3R,5R)-5-Hydroxy-3-nitro-2-(p-tolyl)spiro[cyclopentane-1,2'-indene]-1',3'-dione (3db)



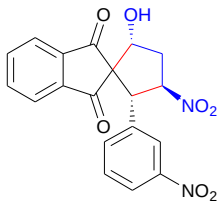
Prepared according to general procedure B to afford **3db** (43 mg, 62 % yield) as a pale off-white sticky oil; $[\alpha]_D^{22}$ = -59.7 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, Acetone-D_6) δ 7.94-7.90 (m, 1H), 7.89-7.83 (m, 3H), 7.11-7.08 (m, 2H), 6.97-6.95 (m, 2H), 6.06-6.00 (m, 1H), 5.06-4.99 (m, 2H), 4.28 (d, *J* = 10.0 Hz, 1H), 2.95-2.90 (m, 2H), 2.12-2.10 (m, 3H); ^{13}C NMR (101 MHz, Acetone-D_6) δ 199.9, 199.6, 143.2, 143.0, 137.8, 136.4, 136.1, 131.2, 129.3, 128.1, 122.8, 122.7, 86.4, 76.9, 70.3, 53.3, 37.2, 20.00; HRMS (ESI): m/z calcd for $C_{20}H_{17}NNaO_5$ [M+Na] 374.1004, Found 374.1007; HPLC conditions: Daicel Chiralpak IB-3 column, *n*-hexane/2-propanol = 85/15, flow rate = 1.5 mL/min, λ = 254 nm, retention time: t_R (major) = 7.9 min, t_R (minor) = 9.5 min, 87% ee.

(2R,3R,5R)-2-(3-Bromophenyl)-5-hydroxy-3-nitrospiro[cyclopentane-1,2'-indene]-1',3'-dione(3fb)



Prepared according to general procedure B to afford **3fb** (63 mg, 76 % yield) as a pale off-white sticky oil; $[\alpha]_D^{22}$ = -64.2 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, Acetone-D_6) δ 7.96-7.95 (m, 1H), 7.92-7.90 (m, 3H), 7.48-7.44 (m, 1H), 7.33-7.31 (m, 1H), 7.25-7.23 (m, 1H), 7.16-7.13(m, 1H), 6.11-6.07 (m, 1H), 5.12 (s, 1H), 5.04-4.99 (m, 1H), 4.32 (d, *J* = 10.0 Hz, 1H), 2.99-2.94 (m, 2H); ^{13}C NMR (100 MHz, Acetone-D_6) δ 199.5, 199.3, 143.1, 142.9, 137.2, 136.6, 136.3, 131.2, 131.1, 130.6, 127.3, 122.9, 122.7, 122.2, 85.7, 77.0, 70.4, 52.5, 36.9; HRMS (ESI): m/z calcd for $C_{19}H_{14}BrNNaO_5$ [M+Na] 437.9953, Found 437.9947; HPLC conditions: Daicel Chiralpak IB-3 column, *n*-hexane/2-propanol = 85/15, flow rate = 1.5 mL/min, λ = 254 nm, retention time: t_R (major) = 8.9 min, t_R (minor) = 10.3 min, 68% ee.

(2R,3R,5R)-5-Hydroxy-3-nitro-2-(3-nitrophenyl)spiro[cyclopentane-1,2'-indene]-1',3'-dione (3gb)



Prepared according to general procedure B to afford **3gb** (55 mg, 72 % yield) as a pale off-white sticky oil; $[\alpha]_D^{22}$ = -59.5 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, Acetone-D_6) δ 8.14 (s, 1H), 8.05-8.03 (m, 1H), 7.97-7.88 (m, 4H), 7.71-7.69 (m, 1H), 7.56-7.52(m, 1H), 6.24-6.18 (m, 1H), 5.18 (s, 1H), 5.06-5.02 (m, 1H), 4.50 (d, *J* = 9.6 Hz, 1H), 3.04-2.96 (m, 2H); ^{13}C NMR (100MHz, Acetone-D_6) δ 199.3, 199.2, 148.3, 143.0, 142.9, 137.0, 136.7, 136.3, 134.8, 130.1, 123.0, 123.0, 122.8, 85.5, 77.1, 70.5, 52.1, 36.8; HRMS (ESI): m/z calcd for $C_{19}H_{14}N_2NaO_7$ [M+Na] 405.0699, Found 405.0697; HPLC conditions: Daicel Chiralpak IB-3 column, *n*-hexane/2-propanol = 85/15, flow rate = 1.5 mL/min, λ = 254 nm, retention time: t_R (major) = 18.9 min, t_R (minor) = 23.7 min, 65% ee.

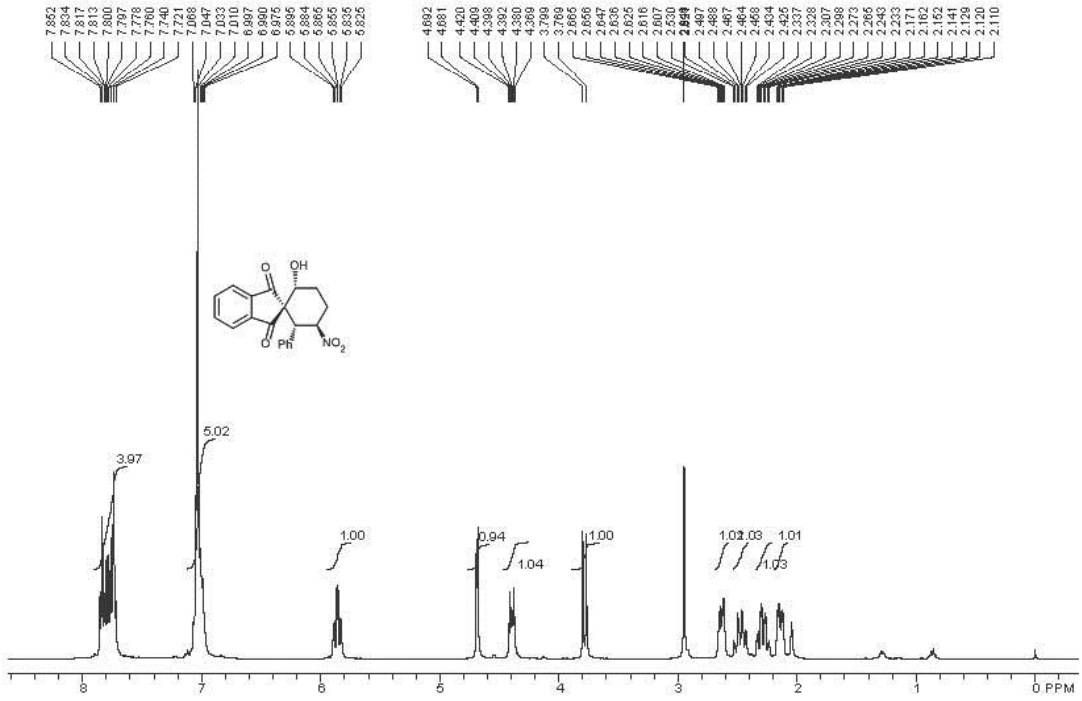
References

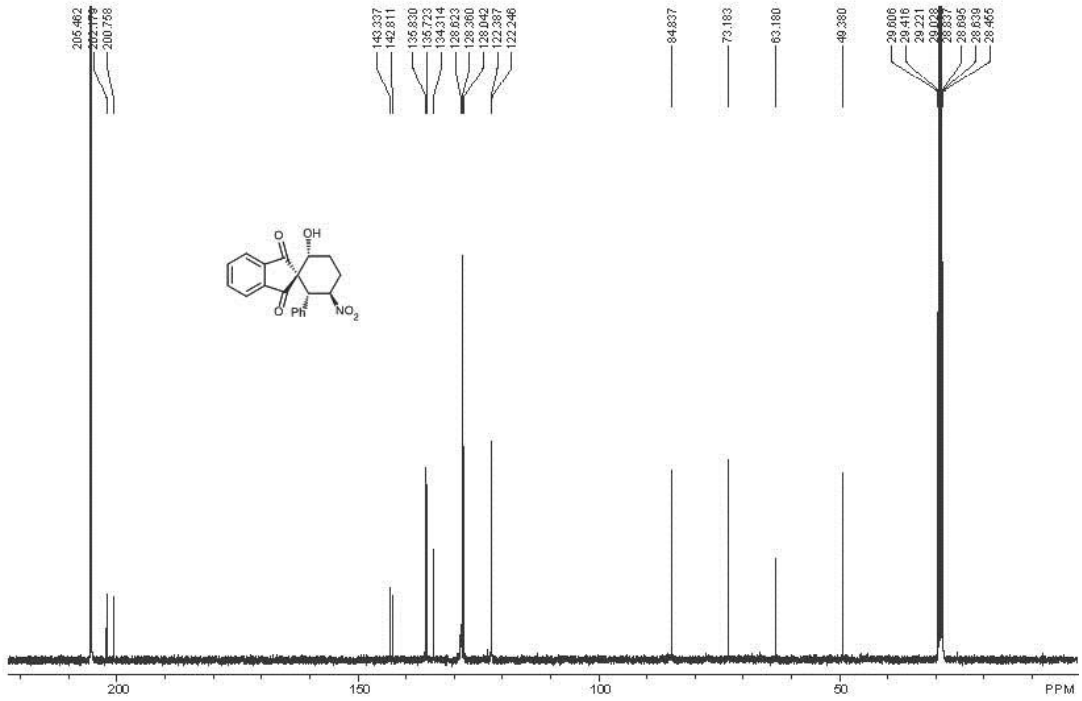
1 E. Li, Y. Huang, L. Liang and P. Xie, *Org. Lett.*, 2013, **15**, 3138.

2 (a) L. E. Blidi, D. Crestia, E. Gallienne, C. Demuynck, J. Bolte and M. Lemaire, *Tetrahedron: Asymmetry*, 2004, **15**, 2951; (b) L. Hu, F. Xiong, X. Chen, W. Chen, Q. He and F. Chen, *Tetrahedron: Asymmetry*, 2013, **24**, 207.

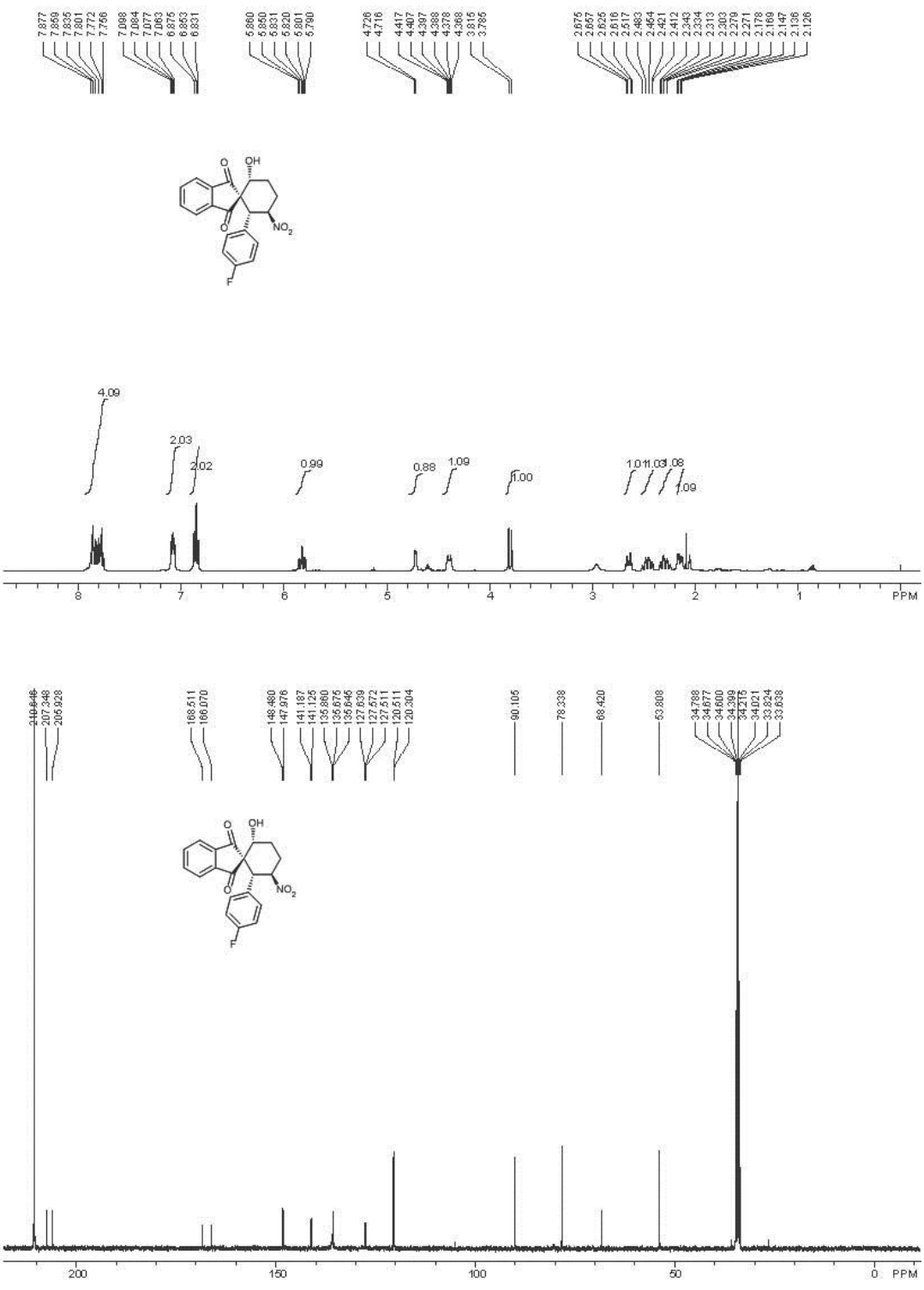
NMR Spectra of compounds

(2R,3R,6R)-6-Hydroxy-3-nitro-2-phenylspiro[cyclohexane-1,2'-indene]-1',3'-dione(3aa)

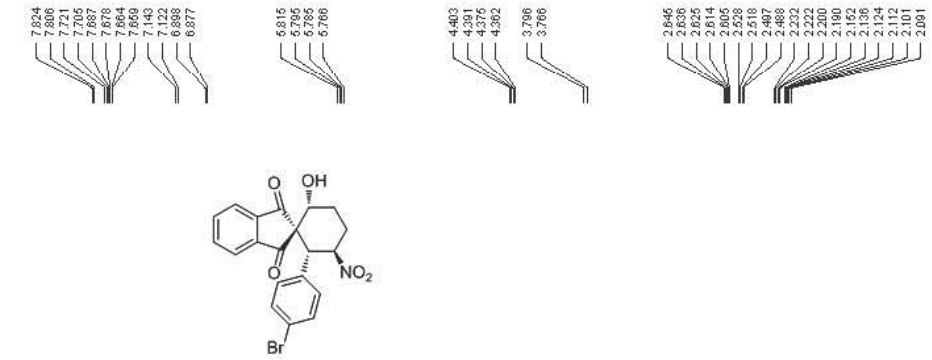


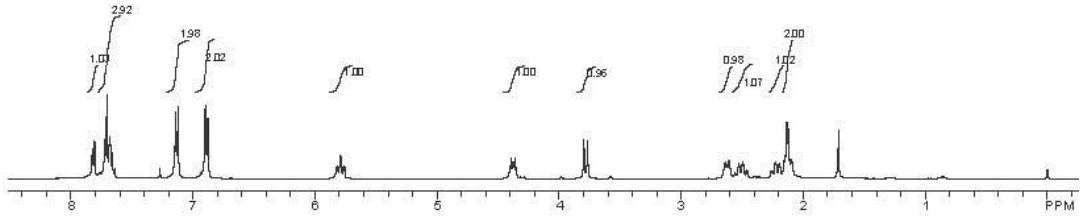


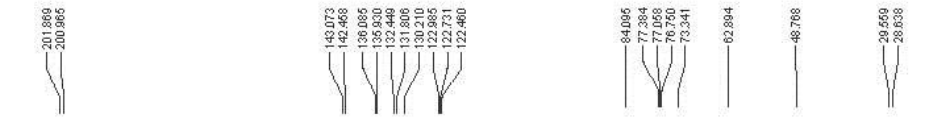
(2R,3R,6R)-2-(4-Fluorophenyl)-6-hydroxy-3-nitrospiro[cyclohexane-1,2'-indene]-1',3'-dione(3ba)

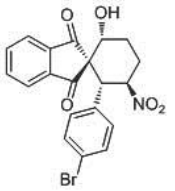


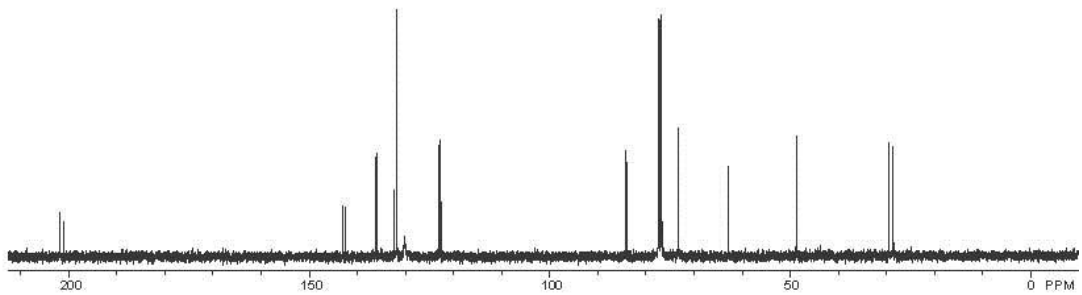
(2R,3R,6R)-2-(4-Bromophenyl)-6-hydroxy-3-nitrospiro[cyclohexane-1,2'-indene]-1',3'-dione(3ca)



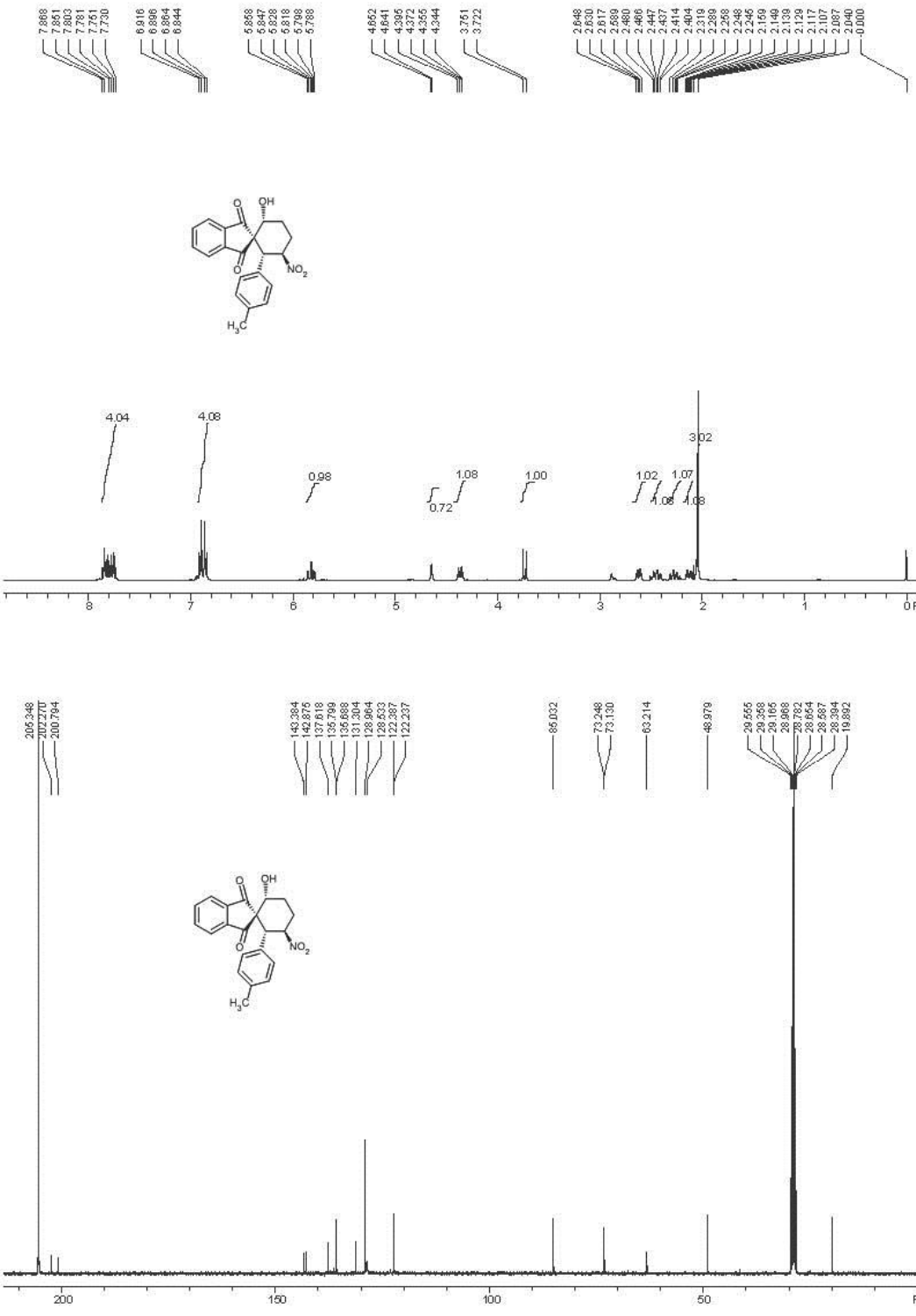




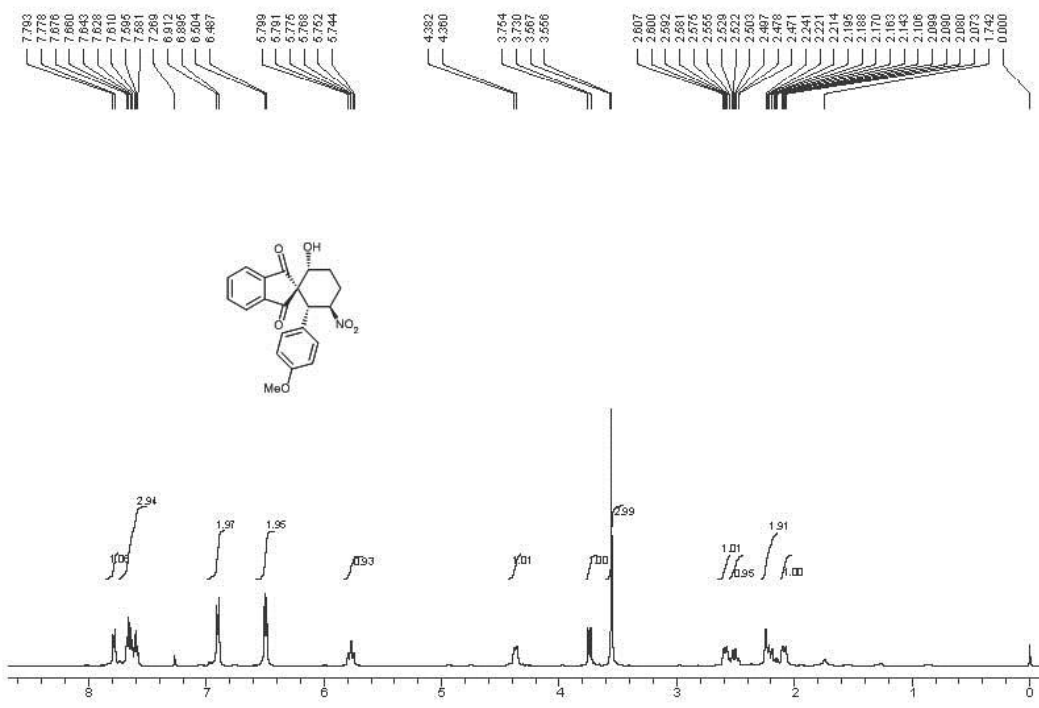


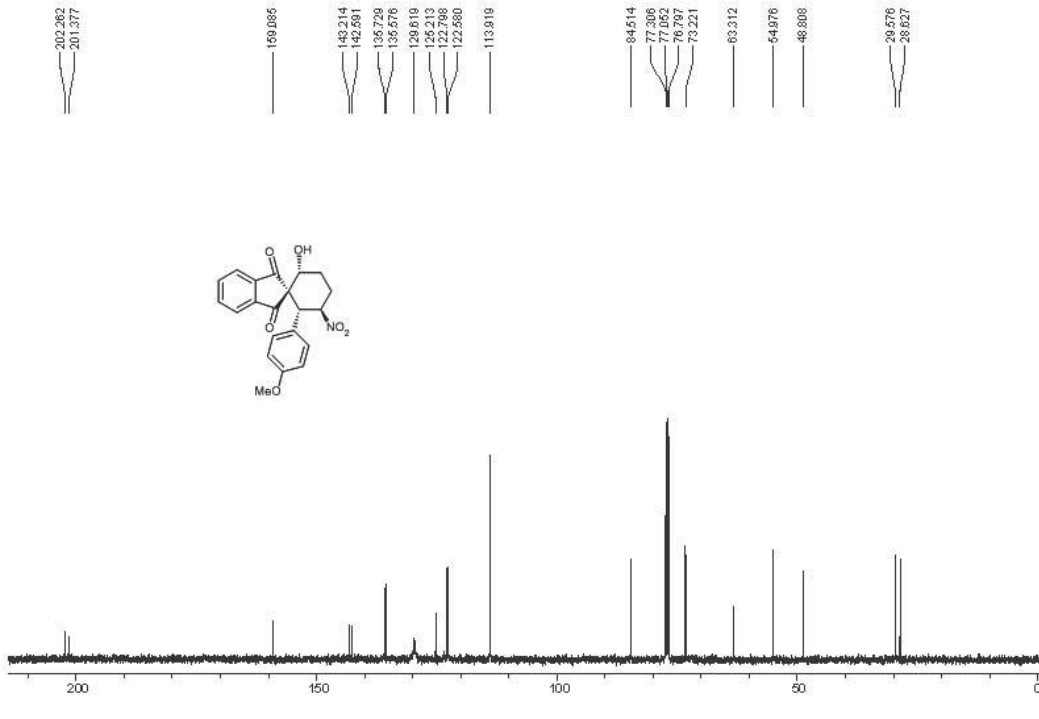


(2R,3R,6R)-6-Hydroxy-3-nitro-2-(p-tolyl)spiro[cyclohexane-1,2'-indene]-1',3'-dione(3da)

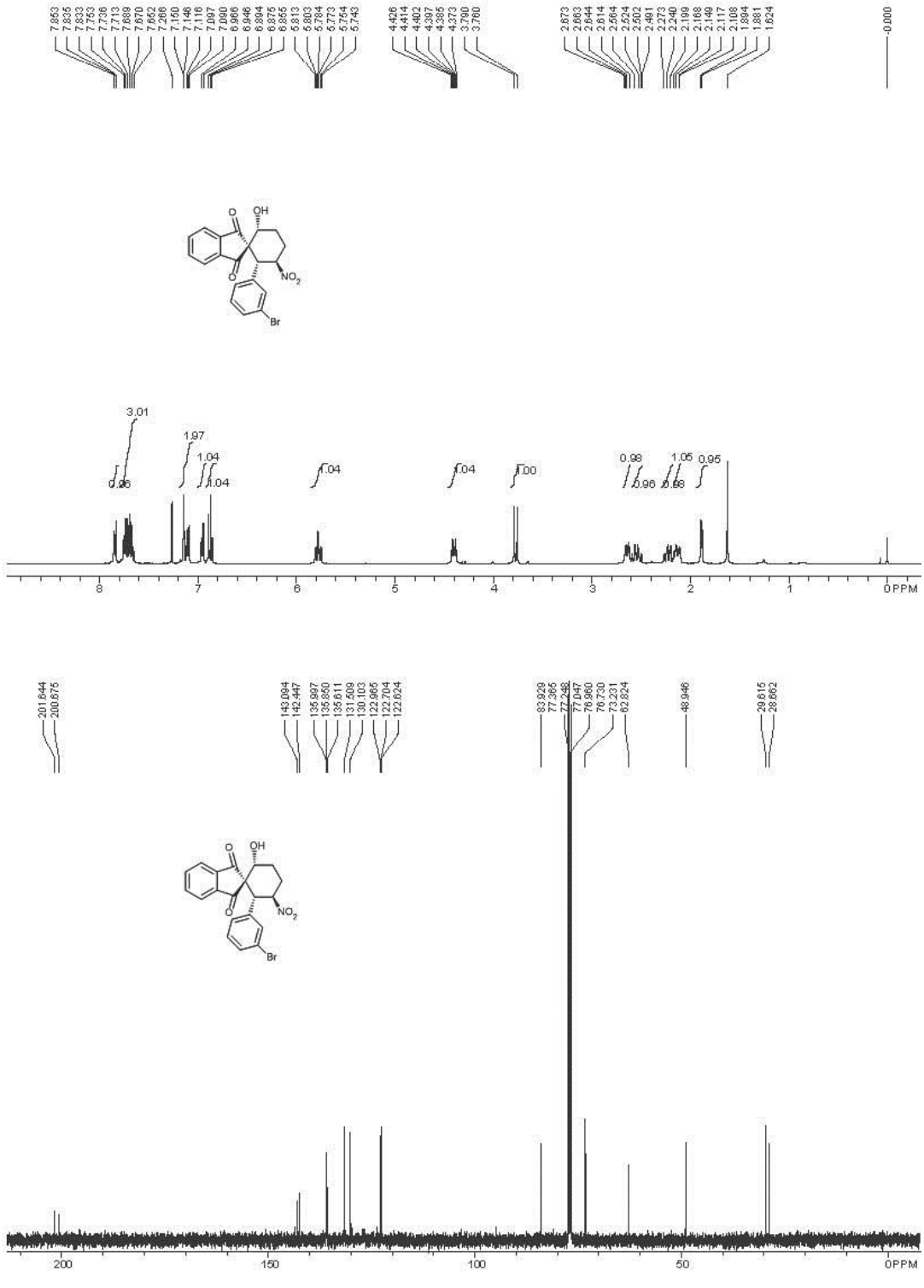


(2R,3R,6R)-6-Hydroxy-2-(4-methoxyphenyl)-3-nitrospiro[cyclohexane-1,2'-indene]-1',3'-dione(3ea)

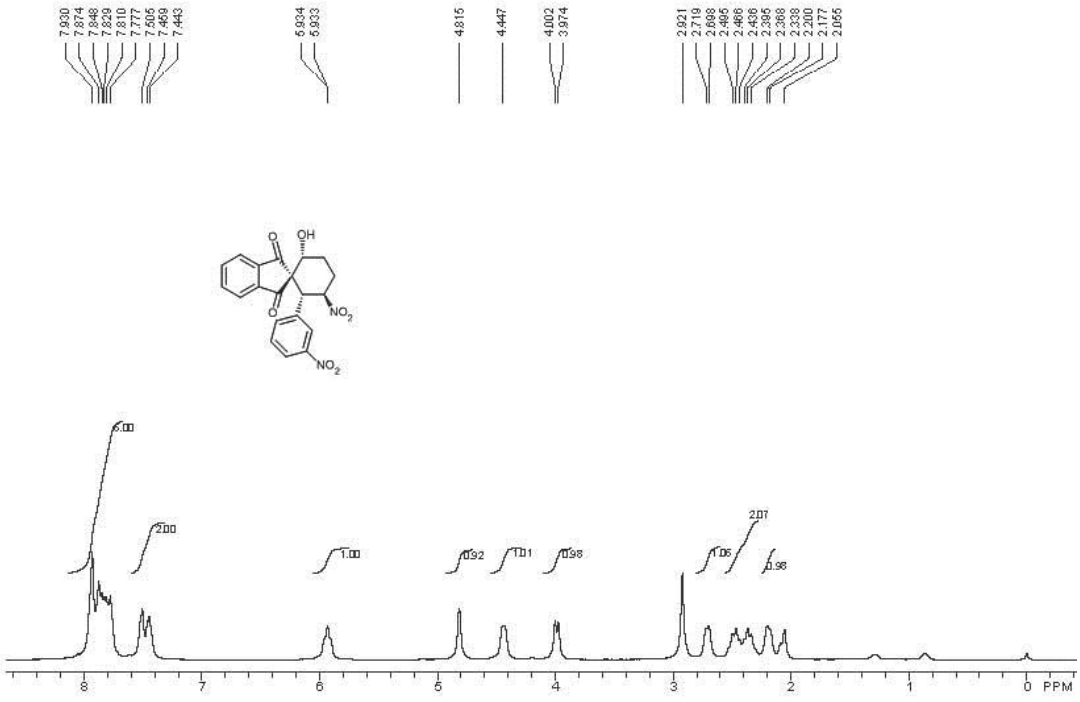


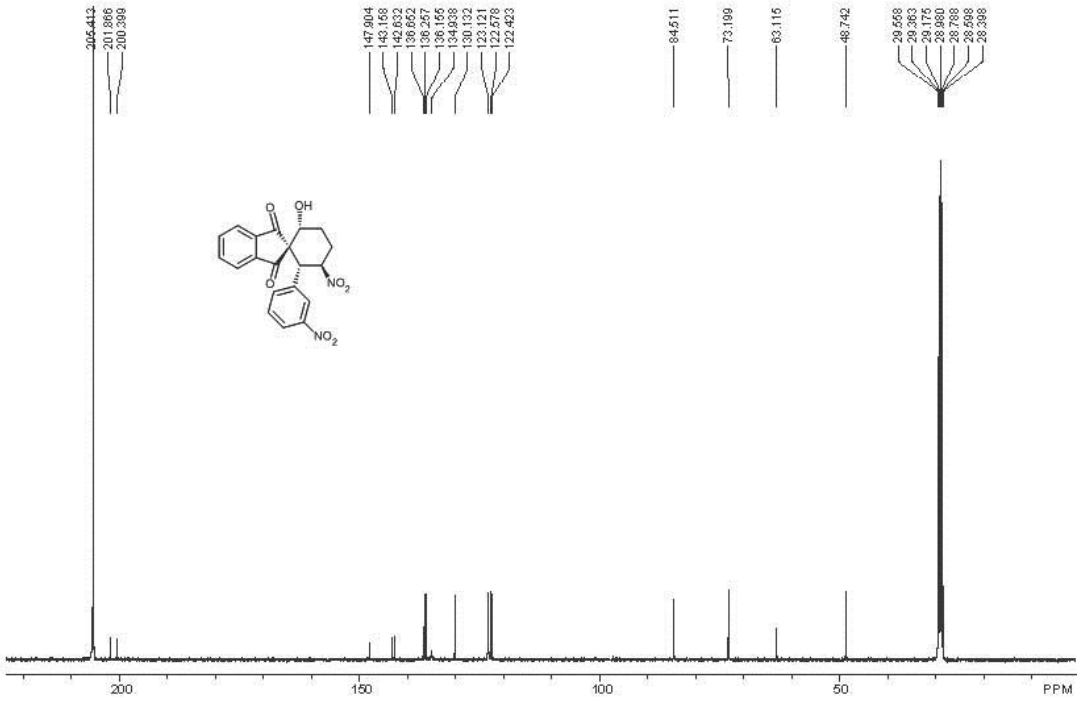


(2R,3R,6R)-2-(3-Bromophenyl)-6-hydroxy-3-nitrospiro[cyclohexane-1,2'-indene]-1',3'-dione(3fa)

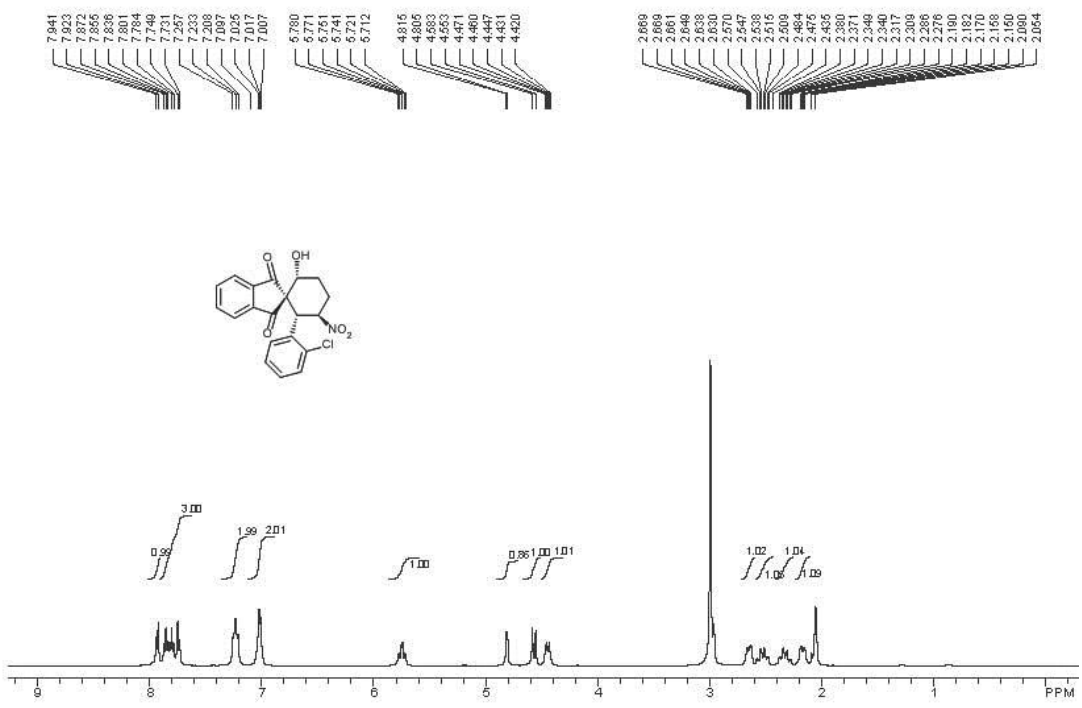


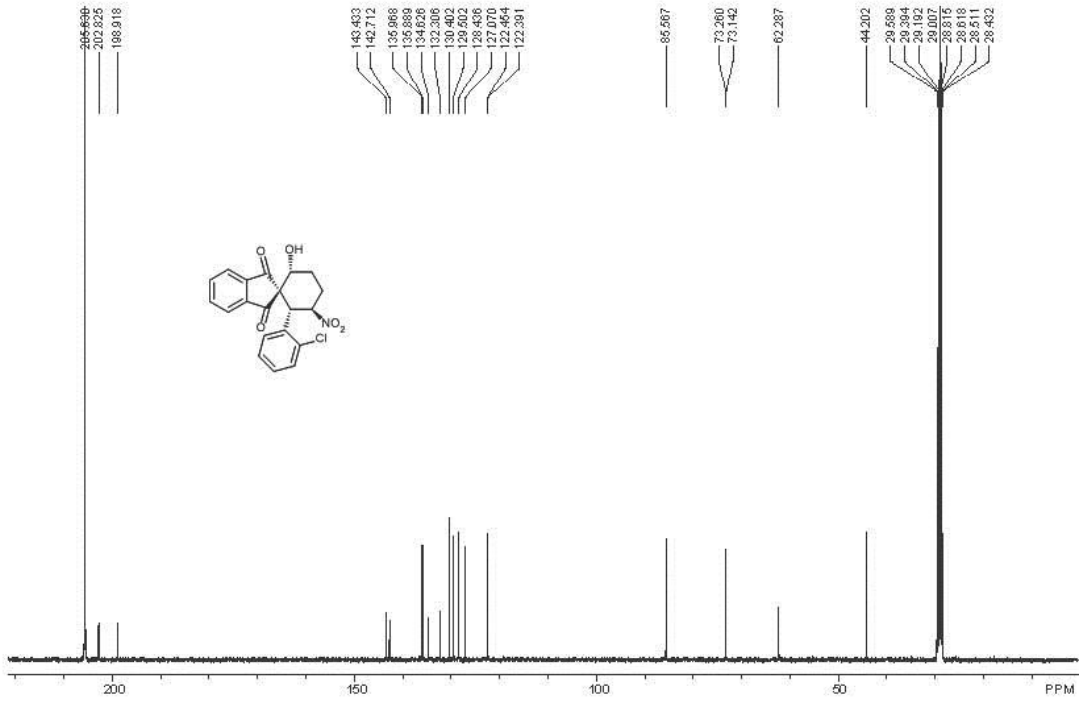
(2R,3R,6R)-6-Hydroxy-3-nitro-2-(3-nitrophenyl)spiro[cyclohexane-1,2'-indene]-1',3'-dione(3ga)



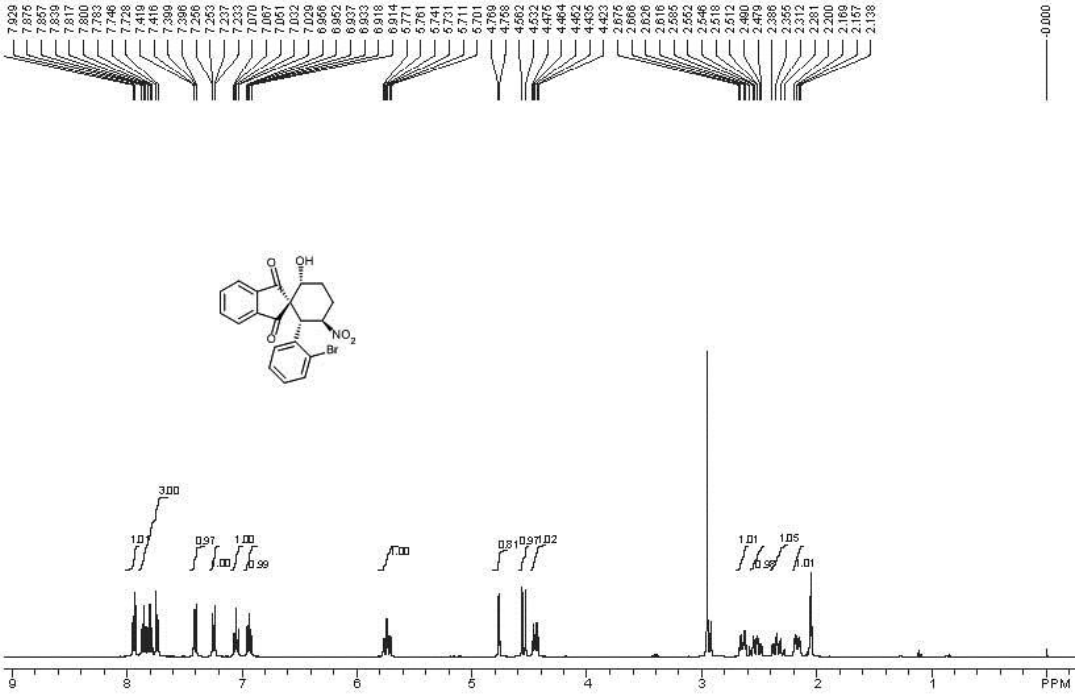


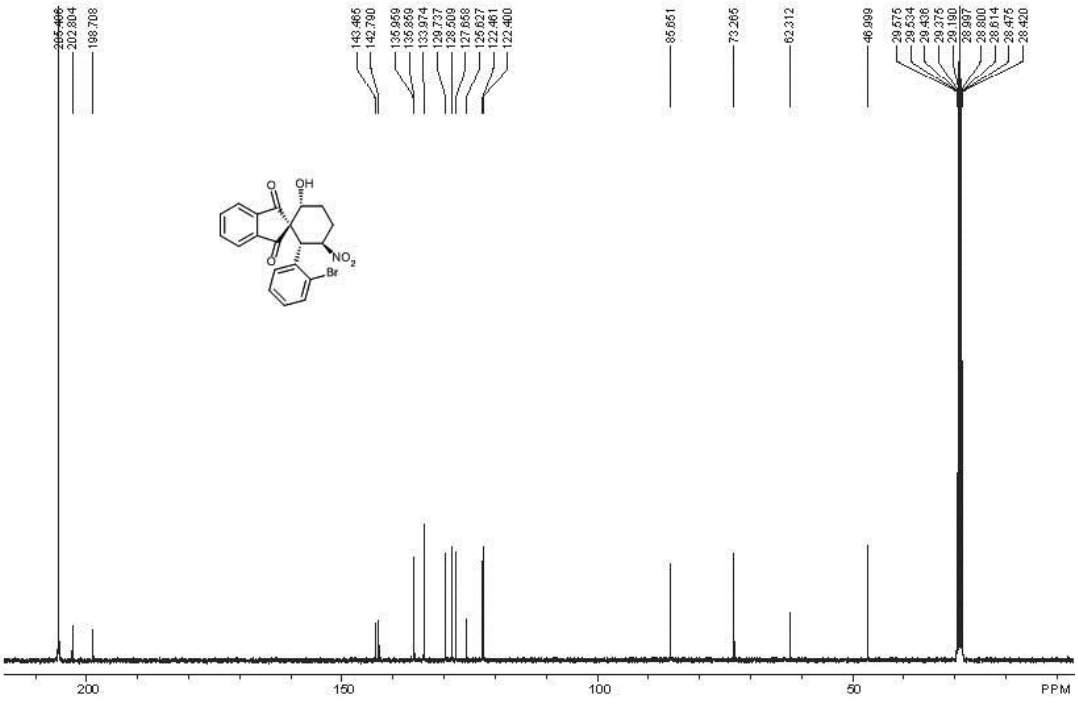
(2S,3R,6R)-2-(2-Chlorophenyl)-6-hydroxy-3-nitrospiro[cyclohexane-1,2'-indene]-1',3'-dione(3ha)



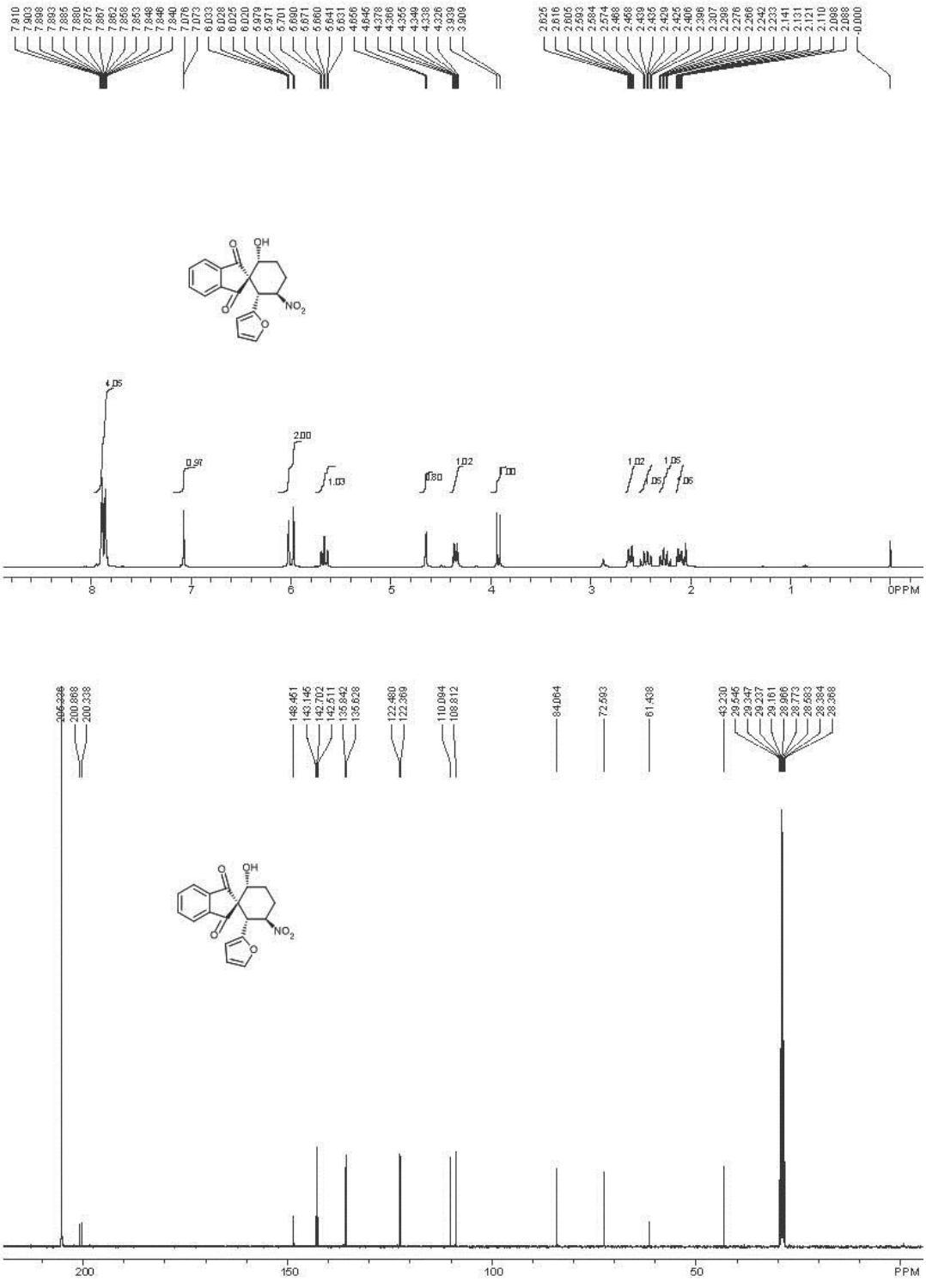


(2S,3R,6R)-2-(2-Bromophenyl)-6-hydroxy-3-nitrospiro[cyclohexane-1,2'-indene]-1',3'-dione(3ia)

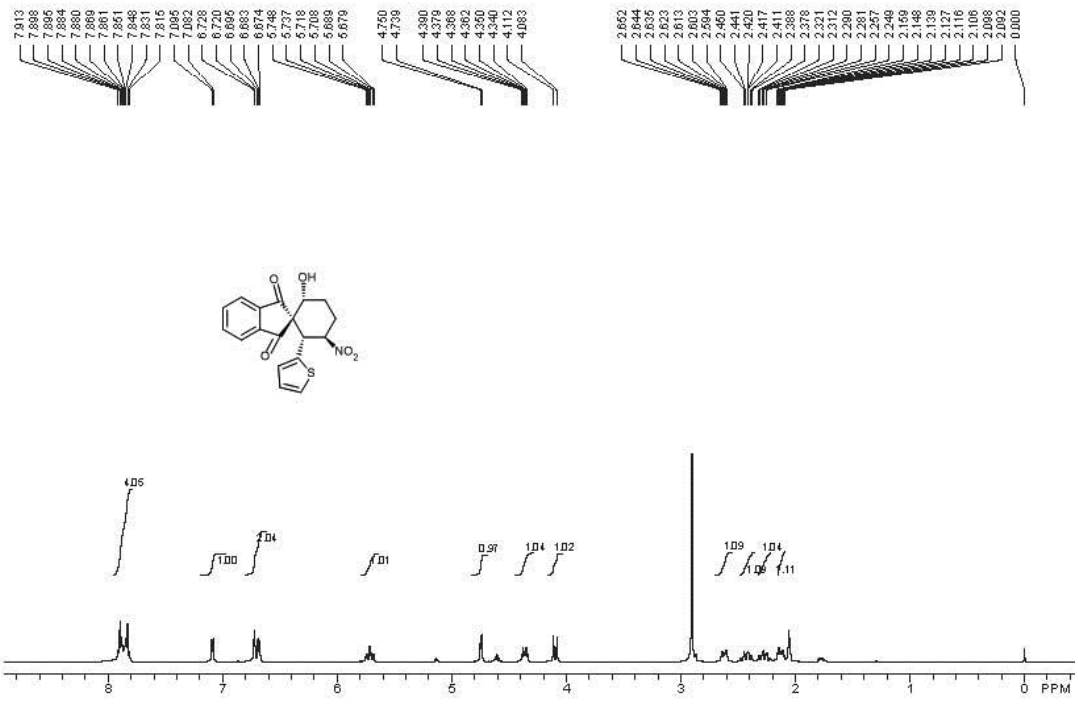


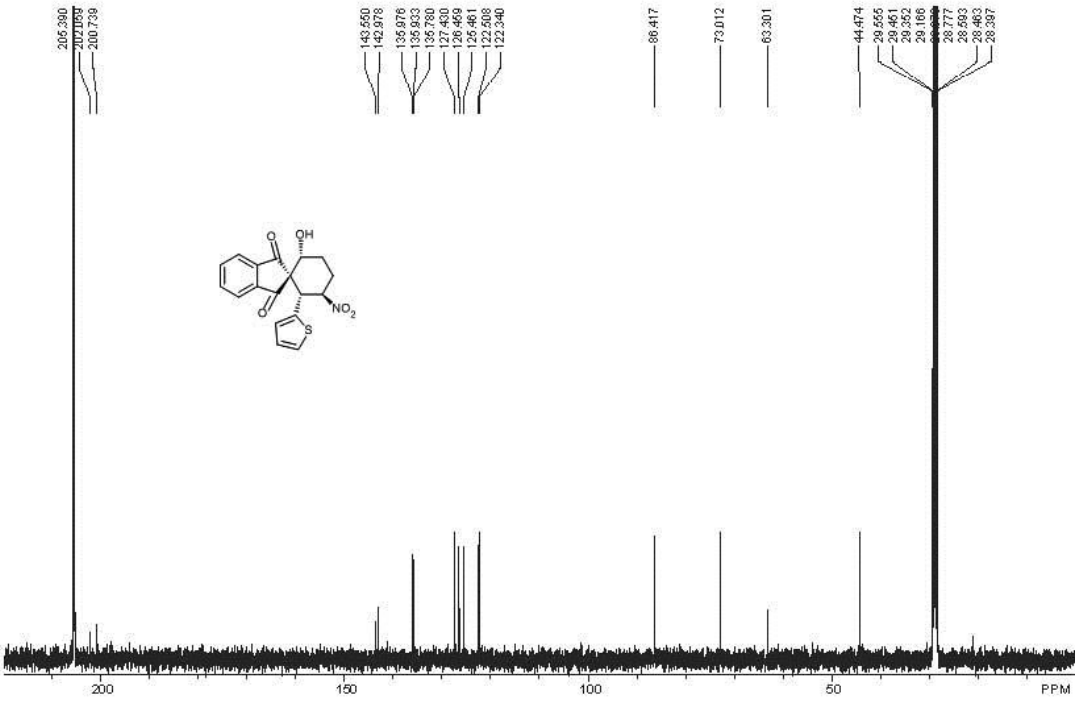


(2R,3R,6R)-2-(Furan-2-yl)-6-hydroxy-3-nitrospiro[cyclohexane-1,2'-indene]-1',3'-dione(3ja)

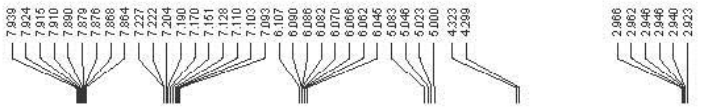


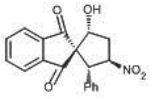
(2R,3R,6R)-6-Hydroxy-3-nitro-2-(thiophen-2-yl)spiro[cyclohexane-1,2'-indene]-1',3'-dione(3ka)

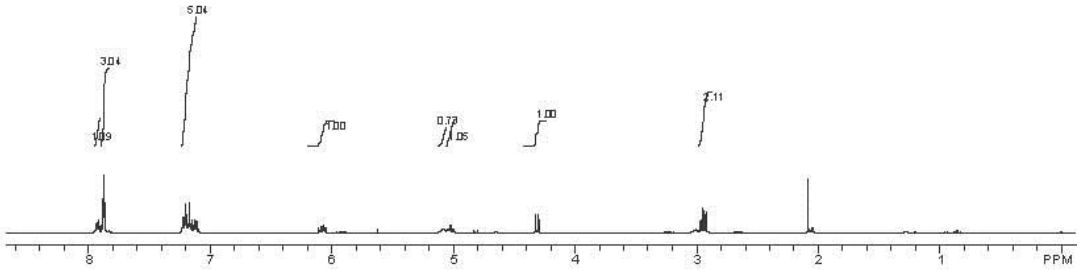


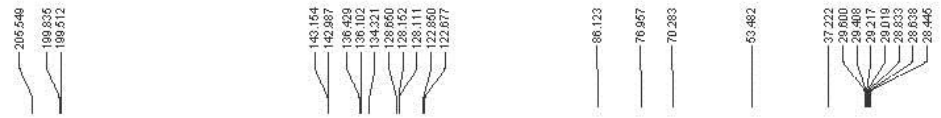


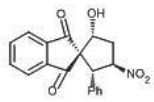
(2R,3R,5R)-5-Hydroxy-3-nitro-2-phenylspiro[cyclopentane-1,2'-indene]-1',3'-dione(3ab)

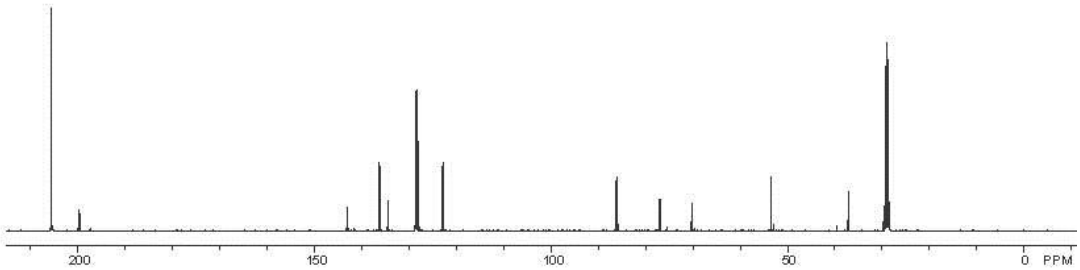




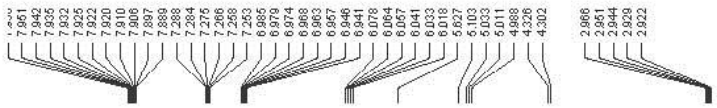


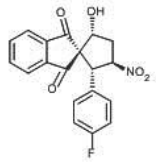


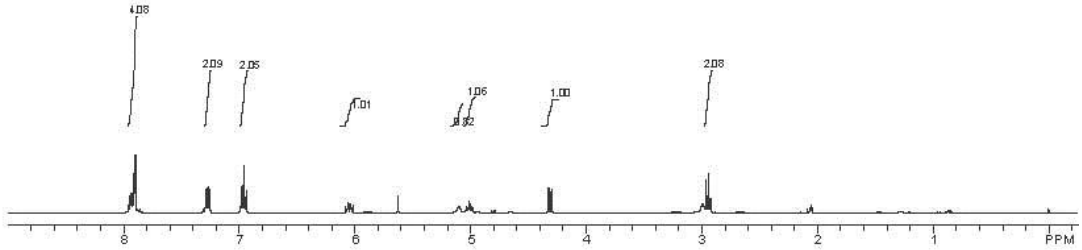


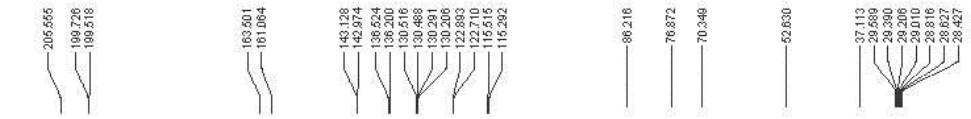


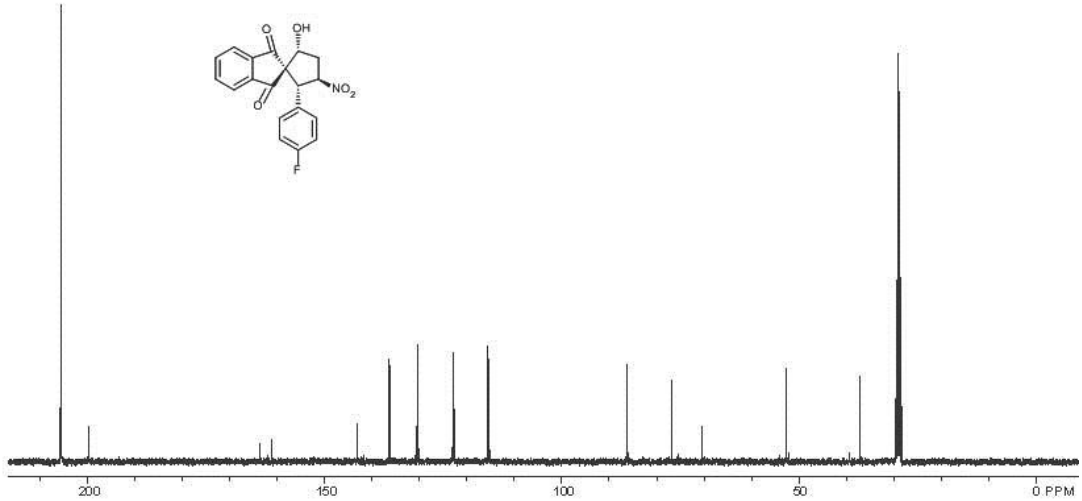
(2R,3R,5R)-2-(4-Fluorophenyl)-5-hydroxy-3-nitrospiro[cyclopentane-1,2'-indene]-1',3'-dione(3bb)



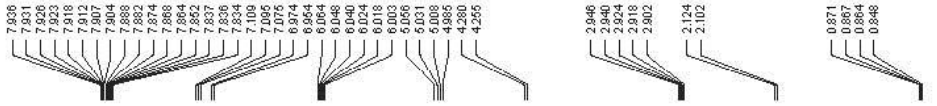


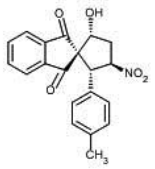


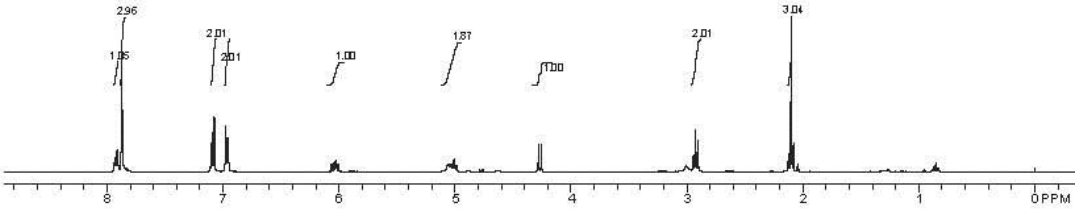


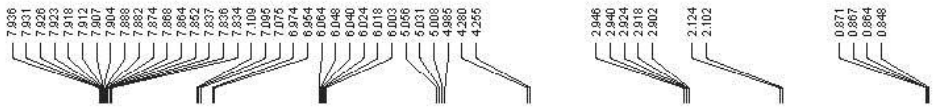


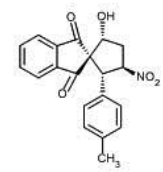
(2R,3R,5R)-5-Hydroxy-3-nitro-2-(p-tolyl)spiro[cyclopentane-1,2'-indene]-1',3'-dione(3db)

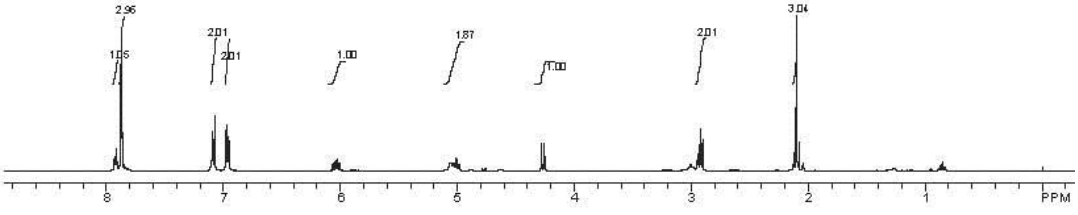




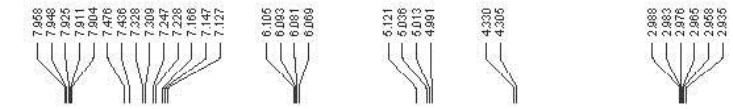


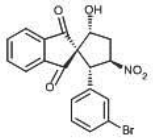


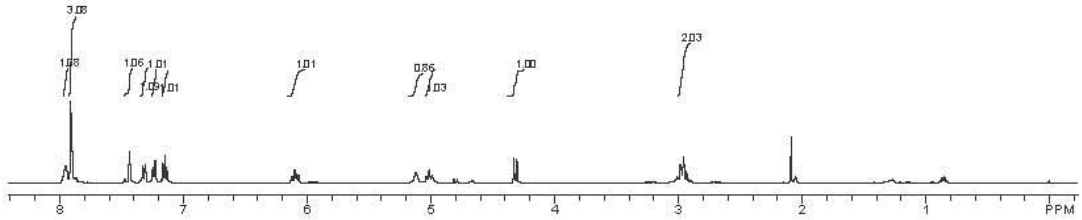


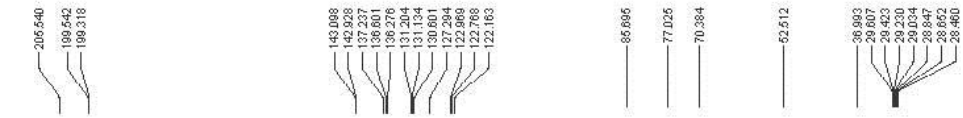


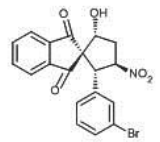
(2R,3R,5R)-2-(3-Bromophenyl)-5-hydroxy-3-nitrospiro[cyclopentane-1,2'-indene]-1',3'-dione(3fb)

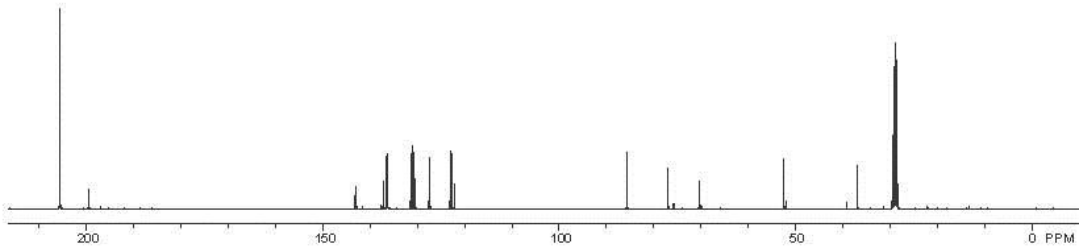




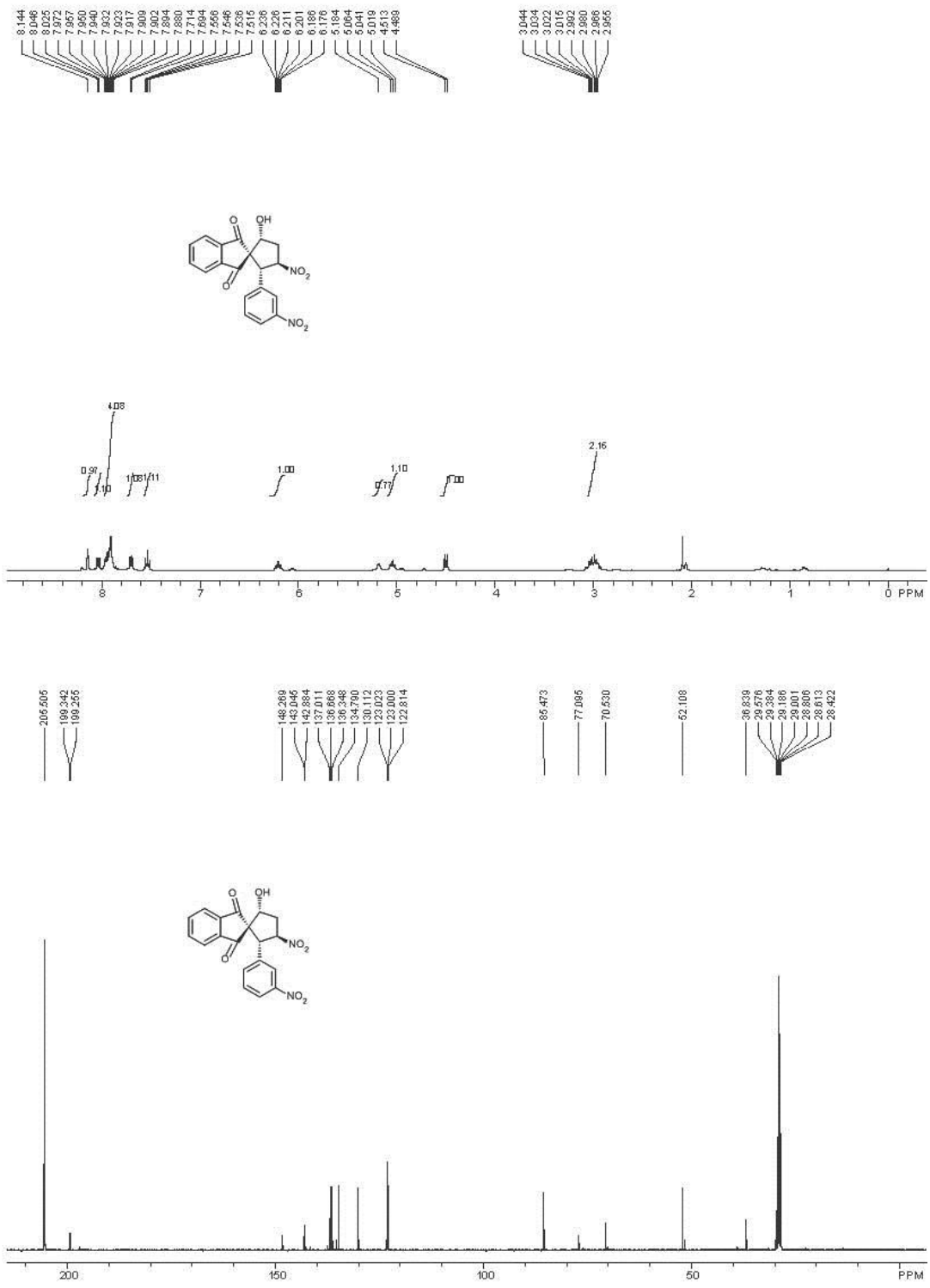






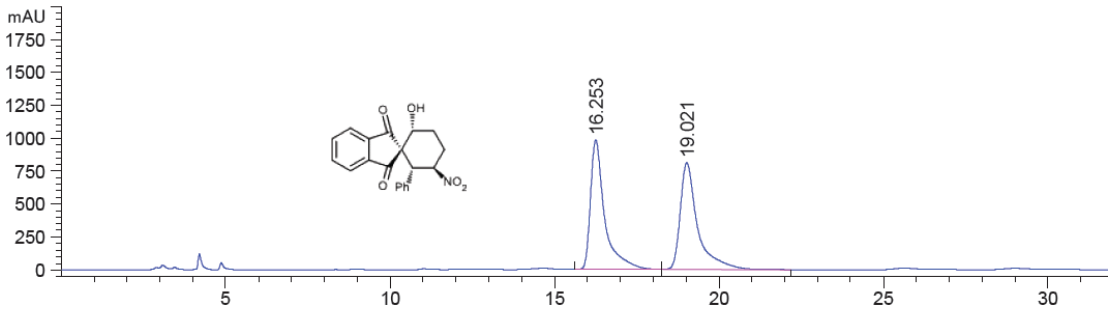


(2R,3R,5R)-5-Hydroxy-3-nitro-2-(3-nitrophenyl)spiro[cyclopentane-1,2'-indene]-1',3'-dione(3gb)

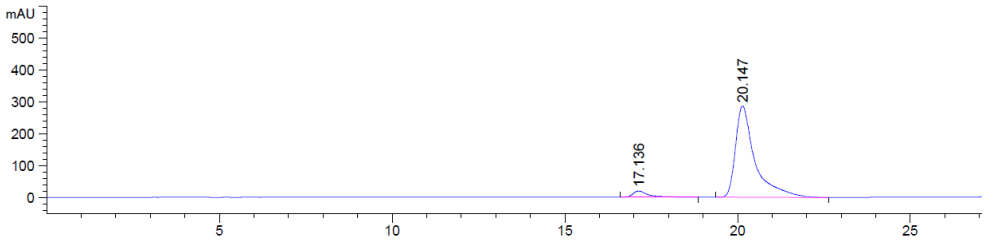


HPLC chromatograms

(2R,3R,6R)-6-Hydroxy-3-nitro-2-phenylspiro[cyclohexane-1,2'-indene]-1',3'-dione(3aa)

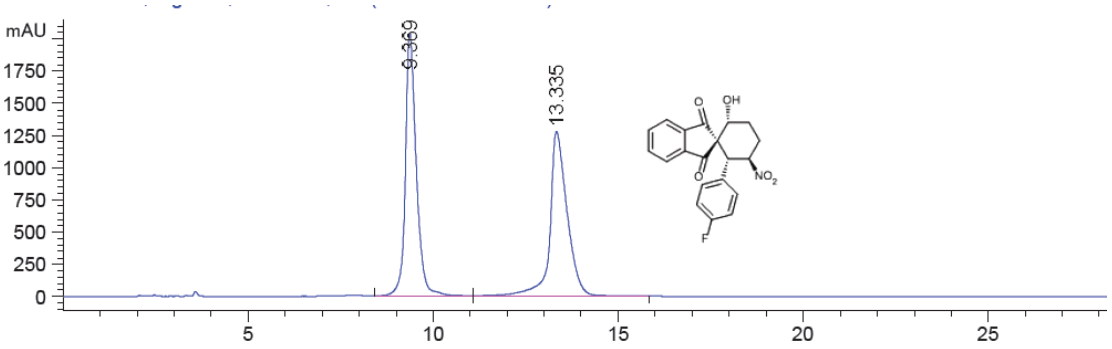


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.253	BB	0.4368	2.55332e4	853.97699	49.7900
2	19.021	BB	0.5346	2.57486e4	704.13849	50.2100

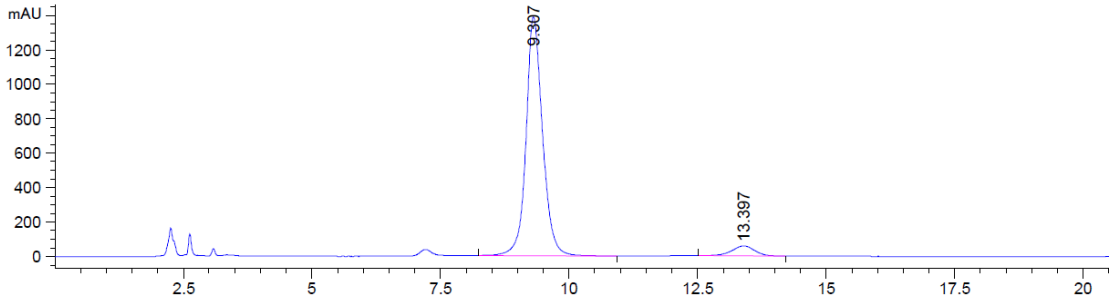


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.136	BB	0.4625	1438.18164	45.53844	5.0921
2	20.148	BB	0.5718	2.68051e4	680.17822	94.9079

(2R,3R,6R)-2-(4-Fluorophenyl)-6-hydroxy-3-nitrospiro[cyclohexane-1,2'-indene]-1',3'-dione(3ba)

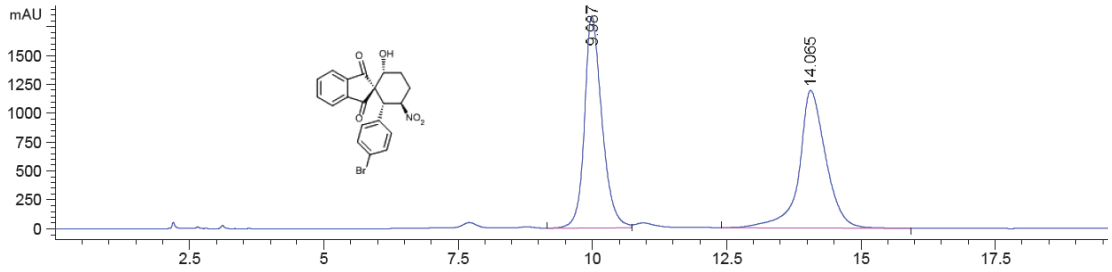


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.369	BB	0.3033	4.18816e4	2042.25781	50.2670
2	13.335	BB	0.4758	4.14367e4	1279.43555	49.7330

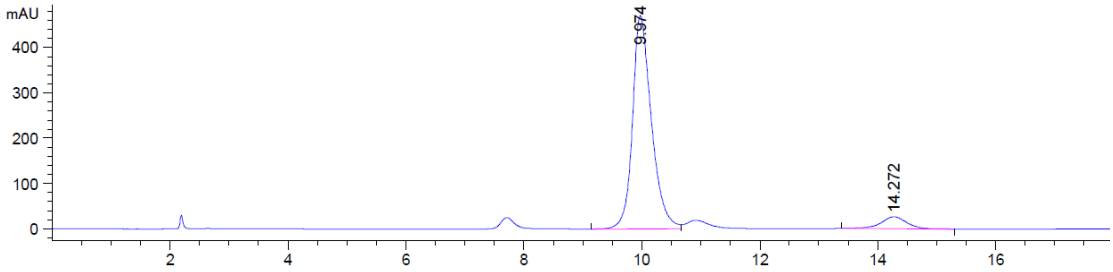


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.307	BB	0.3345	3.09855e4	1387.46765	94.4788
2	13.397	BB	0.4774	1810.75903	57.81847	5.5212

(2R,3R,6R)-2-(4-Bromophenyl)-6-hydroxy-3-nitrospiro[cyclohexane-1,2'-indene]-1',3'-dione(3ca)

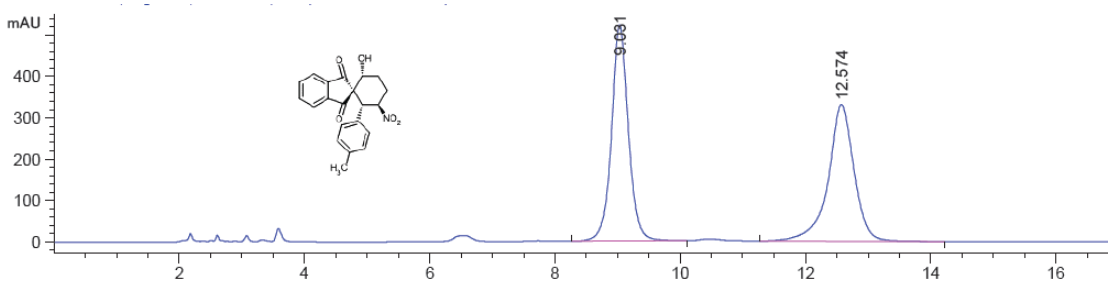


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.987	BV	0.3415	4.18093e4	1837.11255	50.3319
2	14.065	BB	0.5100	4.12579e4	1191.36108	49.6681

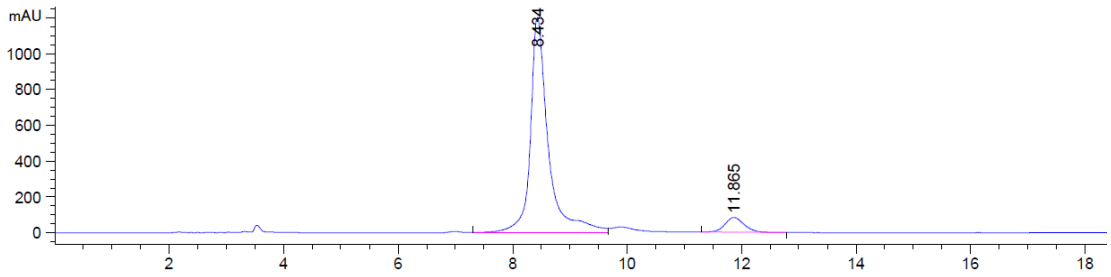


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.974	BV	0.3303	1.04951e4	470.33276	92.9283
2	14.272	BB	0.4374	798.66638	26.21976	7.0717

(2R,3R,6R)-6-Hydroxy-3-nitro-2-(p-tolyl)spiro[cyclohexane-1,2'-indene]-1',3'-dione(3da)

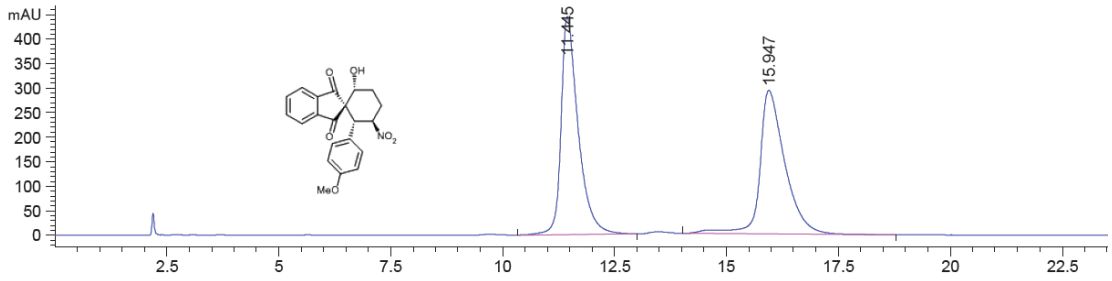


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.031	BB	0.2817	9833.81934	522.24817	50.7584
2	12.574	BB	0.4249	9539.96875	330.36652	49.2416

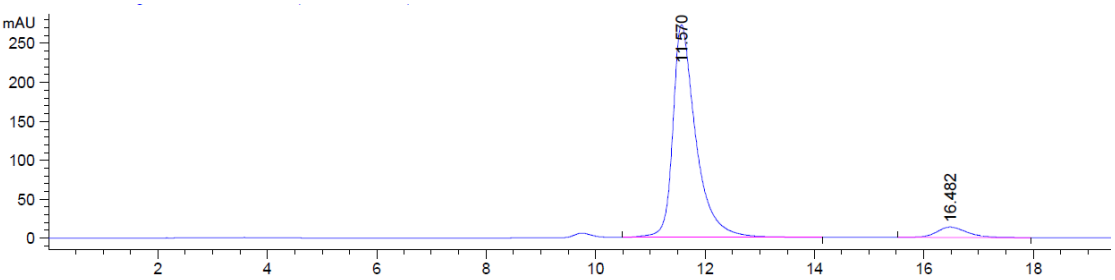


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.434	BV	0.3128	2.59612e4	1198.05847	93.1180
2	11.865	BB	0.3500	1918.68237	82.29803	6.8820

(2R,3R,6R)-6-Hydroxy-2-(4-methoxyphenyl)-3-nitrospiro[cyclohexane-1,2'-indene]-1',3'-dione(3ea)

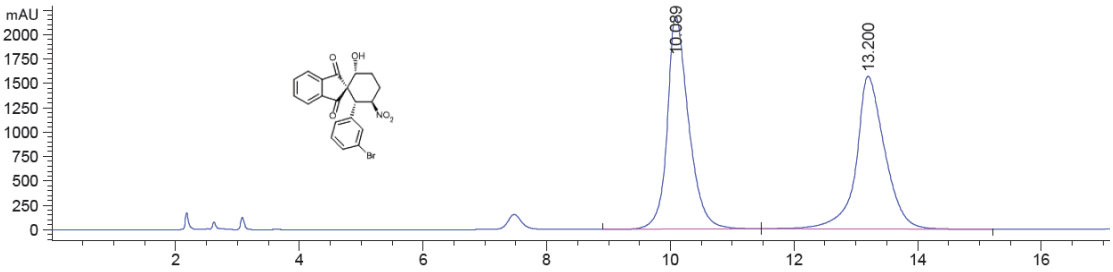


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.445	BB	0.3904	1.18199e4	444.32159	50.8760
2	15.947	BB	0.5723	1.14129e4	293.06638	49.1240

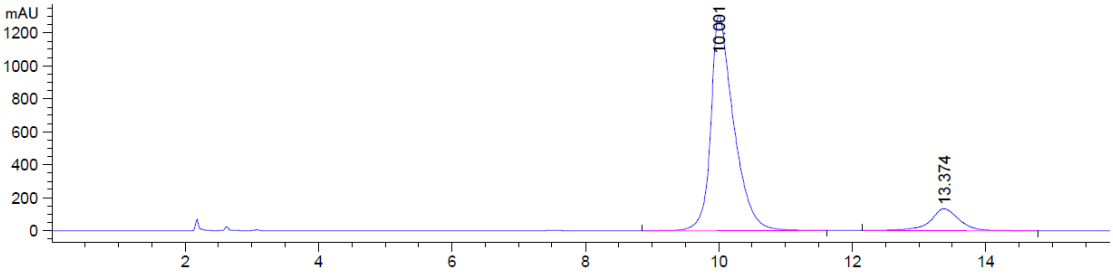


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.570	BB	0.4304	8004.49561	272.70755	93.8807
2	16.482	BB	0.5820	521.75037	13.34822	6.1193

(2R,3R,6R)-2-(3-Bromophenyl)-6-hydroxy-3-nitrospiro[cyclohexane-1,2'-indene]-1',3'-dione(3fa)

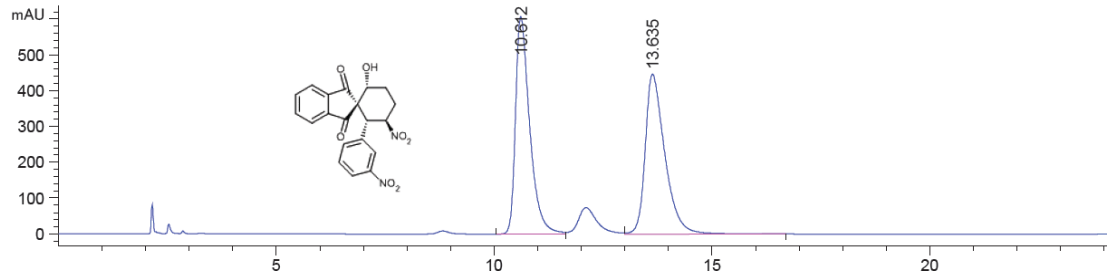


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.089	BB	0.3576	5.26502e4	2181.50879	50.9125
2	13.200	BB	0.4763	5.07629e4	1565.56897	49.0875

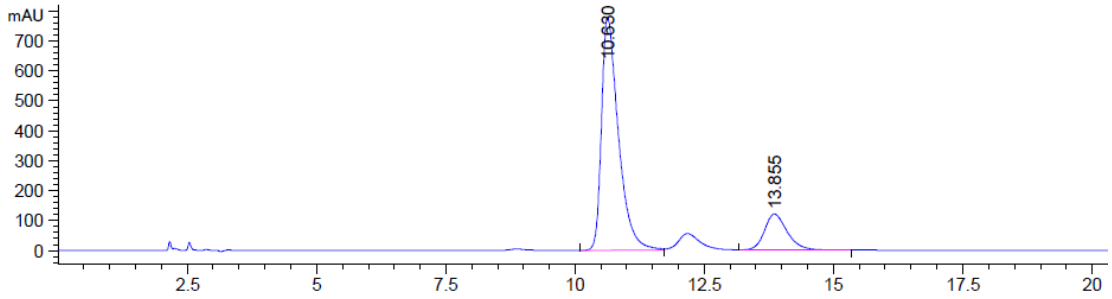


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.001	BB	0.3439	3.11253e4	1306.62756	88.6725
2	13.374	BB	0.4424	3976.11279	132.38905	11.3275

(2R,3R,6R)-6-Hydroxy-3-nitro-2-(3-nitrophenyl)spiro[cyclohexane-1,2'-indene]-1',3'-dione(3ga)

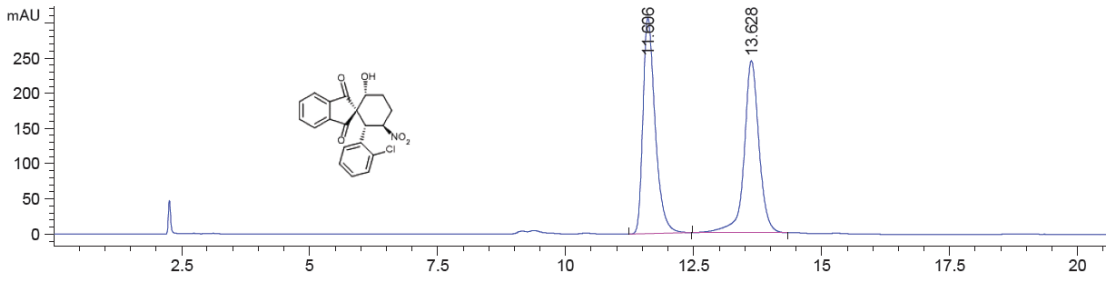


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.612	BV	0.3410	1.38061e4	607.71643	49.6401
2	13.635	VB	0.4697	1.40063e4	446.83270	50.3599

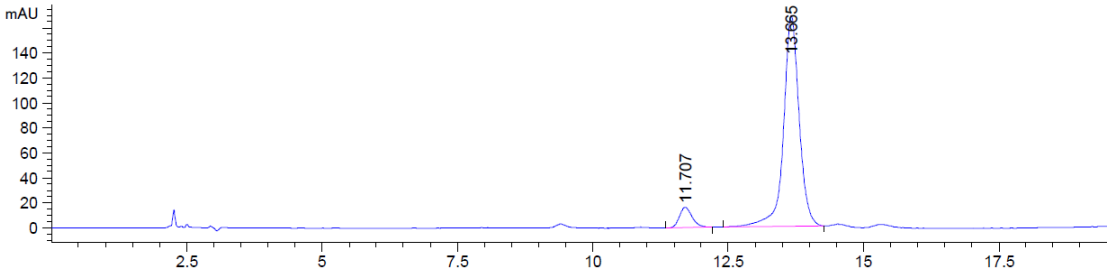


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.630	BV	0.3418	1.77828e4	780.46069	82.9432
2	13.855	BB	0.4627	3656.92969	120.28986	17.0568

(2S,3R,6R)-2-(2-Chlorophenyl)-6-hydroxy-3-nitrospiro[cyclohexane-1,2'-indene]-1',3'-dione(3ha)

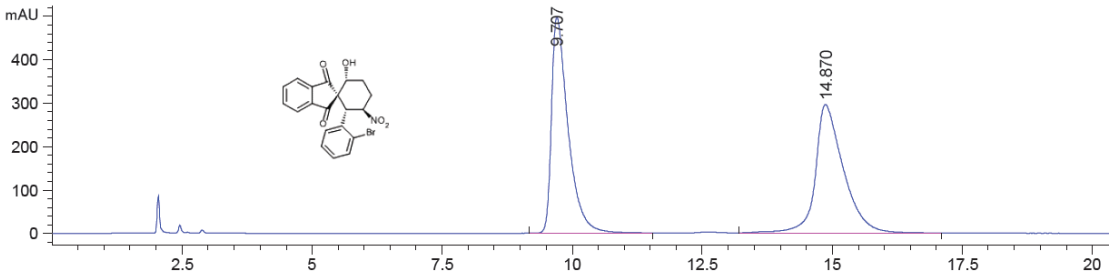


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.606	BB	0.2491	5088.10303	307.38098	50.8394
2	13.628	BB	0.2989	4920.08398	244.37735	49.1606

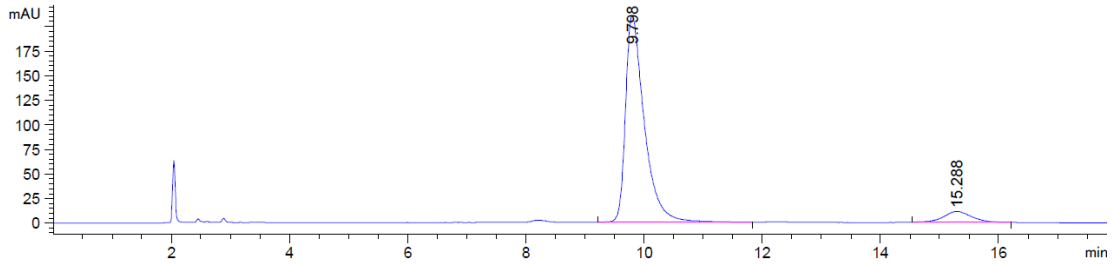


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.707	BB	0.2526	743.25397	45.49549	7.2548
2	13.665	BB	0.3034	9501.74512	470.92419	92.7452

(2S,3R,6R)-2-(2-Bromophenyl)-6-hydroxy-3-nitrospiro[cyclohexane-1,2'-indene]-1',3'-dione(3ia)

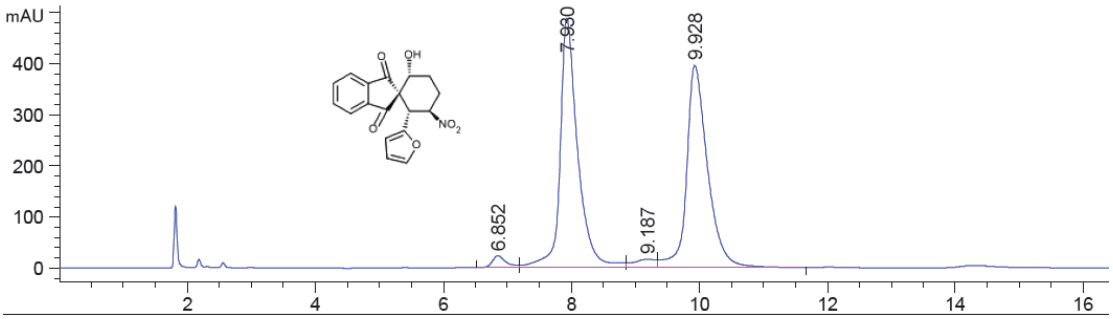


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.707	BB	0.3282	1.10259e4	498.21313	49.8769
2	14.870	BB	0.5441	1.10804e4	295.06595	50.1231

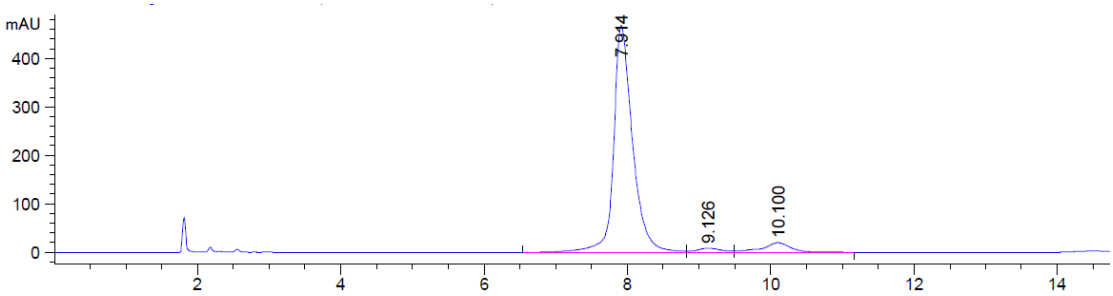


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.798	BB	0.3275	4635.42383	209.99899	92.7230
2	15.288	BB	0.4827	363.79510	10.86412	7.2770

(2R,3R,6R)-2-(Furan-2-yl)-6-hydroxy-3-nitrospiro[cyclohexane-1,2'-indene]-1',3'-dione(3ja)

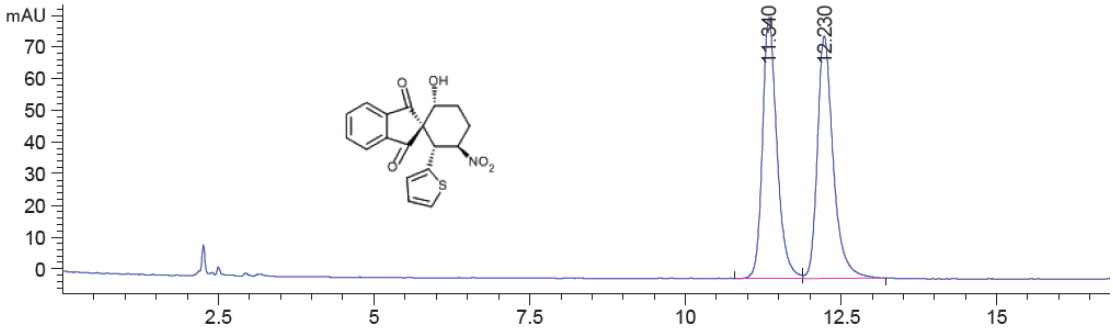


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.852	BV	0.2235	345.51950	22.96283	1.8080
2	7.930	VV	0.2773	9333.17383	487.66599	48.8387
3	9.187	VV	0.3444	390.05984	16.00299	2.0411
4	9.928	VB	0.3370	9041.44238	395.12744	47.3121

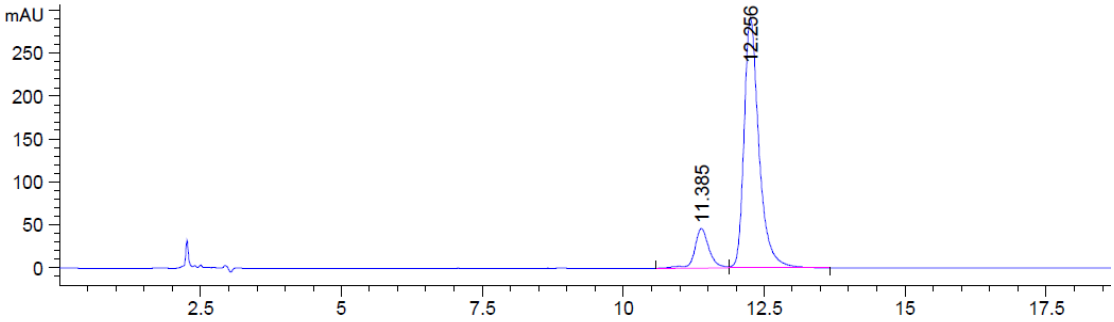


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.914	BV	0.2711	8620.12402	467.59308	92.0836
2	9.126	VV	0.3438	200.45915	8.60523	2.1414
3	10.100	VB	0.3882	540.61438	19.82370	5.7751

(2R,3R,6R)-6-Hydroxy-3-nitro-2-(thiophen-2-yl)spiro[cyclohexane-1,2'-indene]-1',3'-dione(3ka)

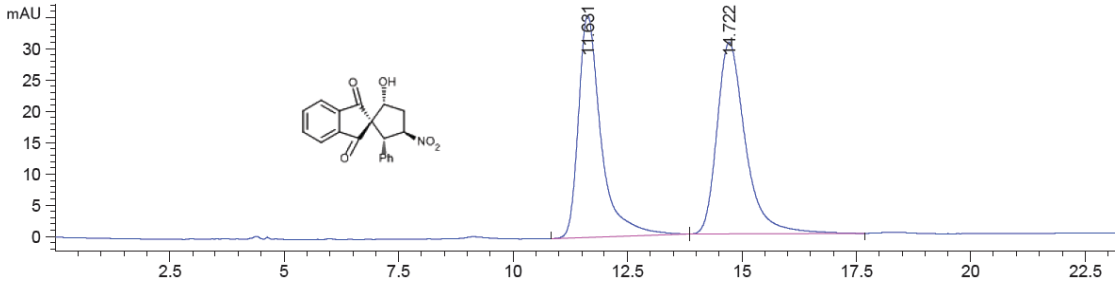


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.340	BV	0.2446	1331.47620	82.36429	49.6108
2	12.230	VB	0.2642	1352.36499	76.52934	50.3892

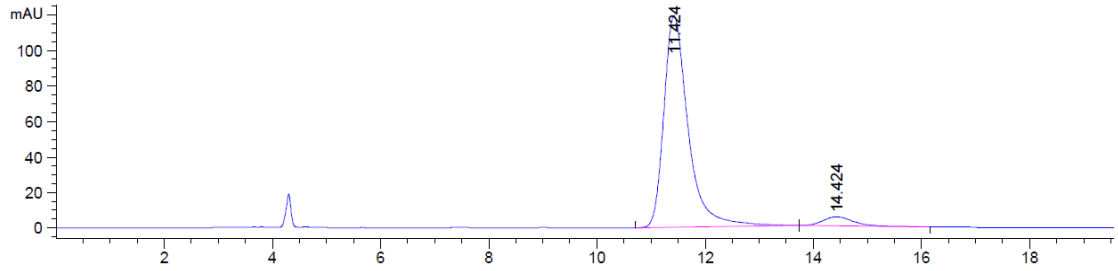


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.385	BV	0.2634	823.66144	46.33184	13.2814
2	12.256	VB	0.2730	5377.94434	291.81488	86.7186

(2R,3R,5R)-5-Hydroxy-3-nitro-2-phenylspiro[cyclopentane-1,2'-indene]-1',3'-dione(3ab)

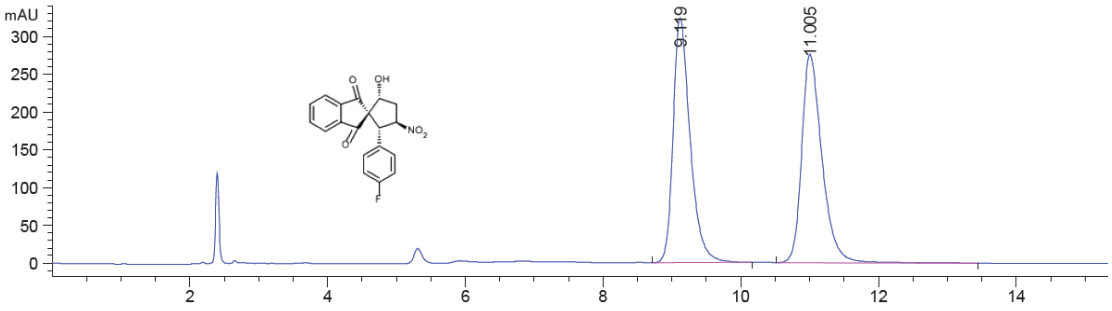


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.631	BB	0.5133	1220.81396	35.49238	48.0308
2	14.722	BB	0.6557	1320.91846	30.59381	51.9692

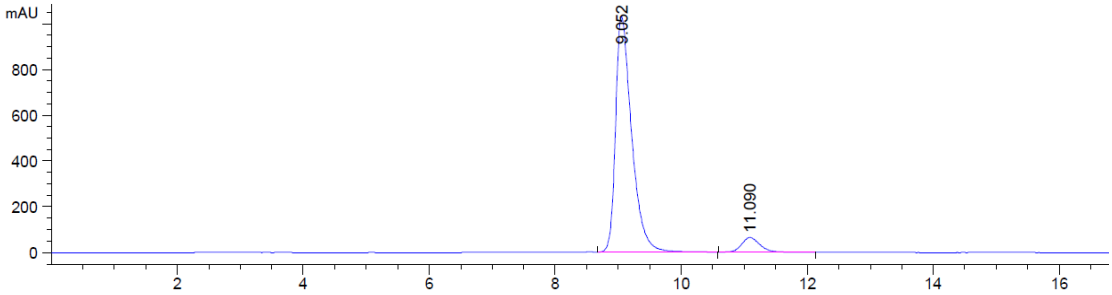


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.424	BB	0.4703	3730.86743	119.47281	94.9220
2	14.424	BB	0.6020	199.58965	5.08446	5.0780

(2R,3R,5R)-2-(4-Fluorophenyl)-5-hydroxy-3-nitrospiro[cyclopentane-1,2'-indene]-1',3'-dione(3bb)

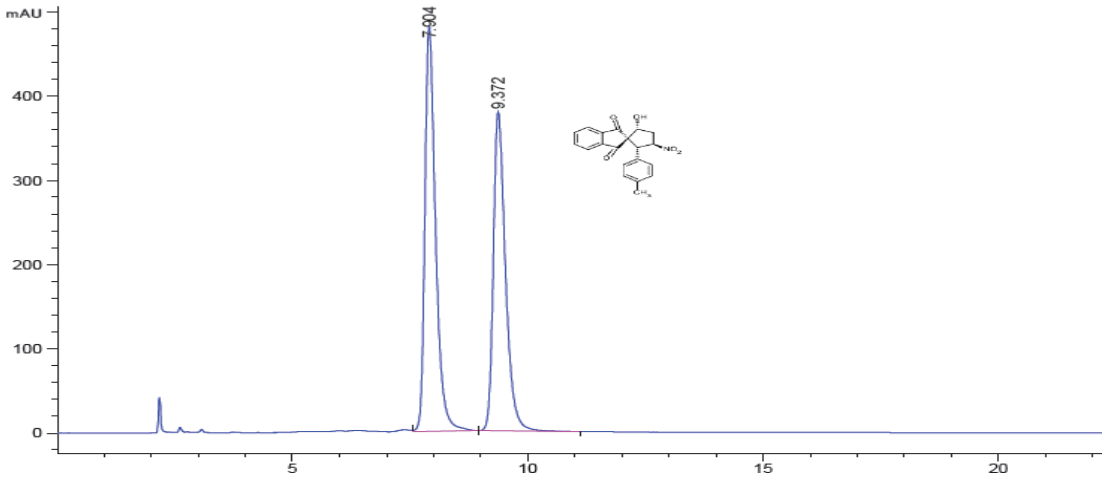


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.119	BB	0.2607	5562.17725	323.38464	49.7330
2	11.005	BB	0.3080	5621.88965	275.62732	50.2670

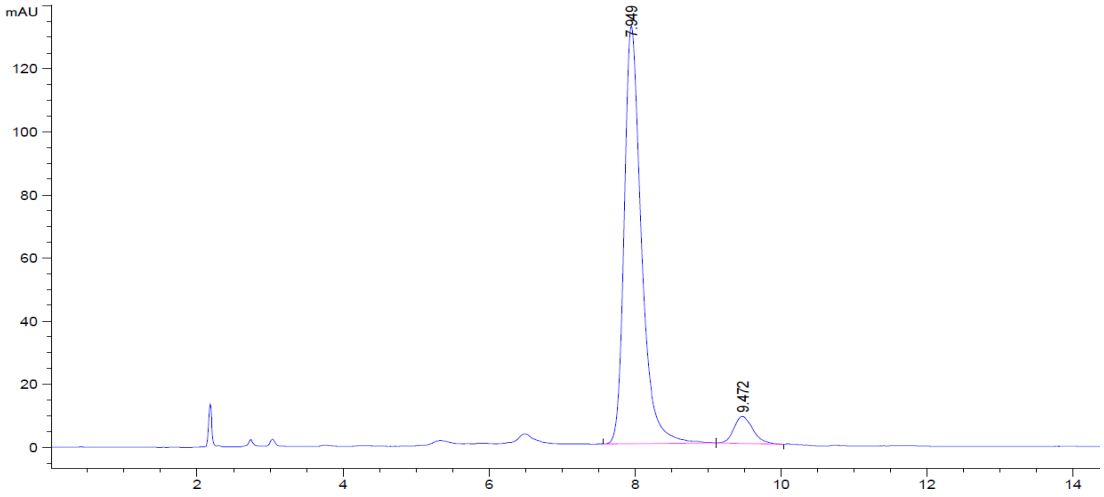


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.052	VB	0.2670	1.83256e4	1032.84497	93.3636
2	11.090	BB	0.3061	1302.61731	64.36866	6.6364

(2R,3R,5R)-5-Hydroxy-3-nitro-2-(p-tolyl)spiro[cyclopentane-1,2'-indene]-1',3'-dione(3db)

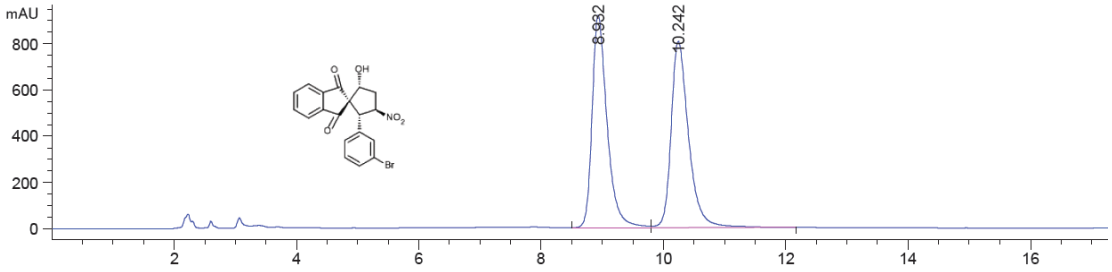


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.904	VB	0.2379	7574.25684	480.55981	52.7329
2	9.372	BB	0.2693	6789.18750	378.37341	47.2671

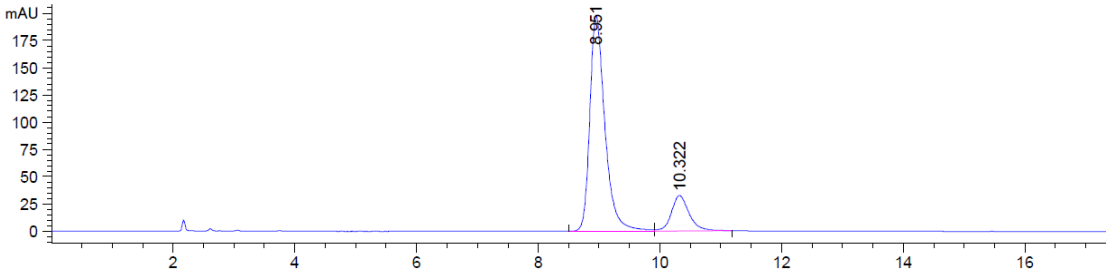


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.949	BB	0.2449	2144.45166	132.42311	93.2734
2	9.472	BB	0.2617	154.65190	8.60287	6.7266

(2R,3R,5R)-2-(3-Bromophenyl)-5-hydroxy-3-nitrospiro[cyclopentane-1,2'-indene]-1',3'-dione(3fb)

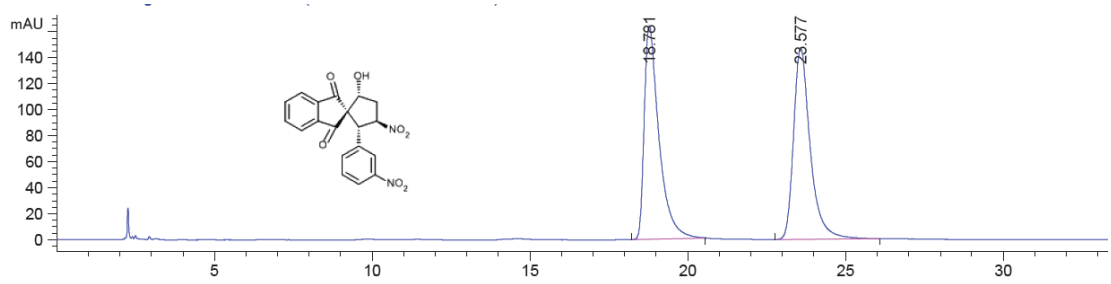


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.932	BV	0.2565	1.56476e4	919.64313	49.4185
2	10.242	VB	0.2999	1.60158e4	805.80792	50.5815

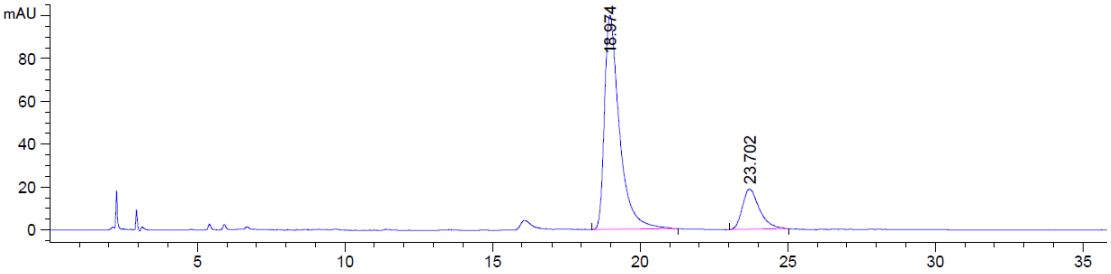


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.951	BV	0.2588	3412.71875	198.23868	83.9084
2	10.322	VB	0.3038	654.47711	32.38340	16.0916

(2R,3R,5R)-5-Hydroxy-3-nitro-2-(3-nitrophenyl)spiro[cyclopentane-1,2'-indene]-1',3'-dione(3gb)

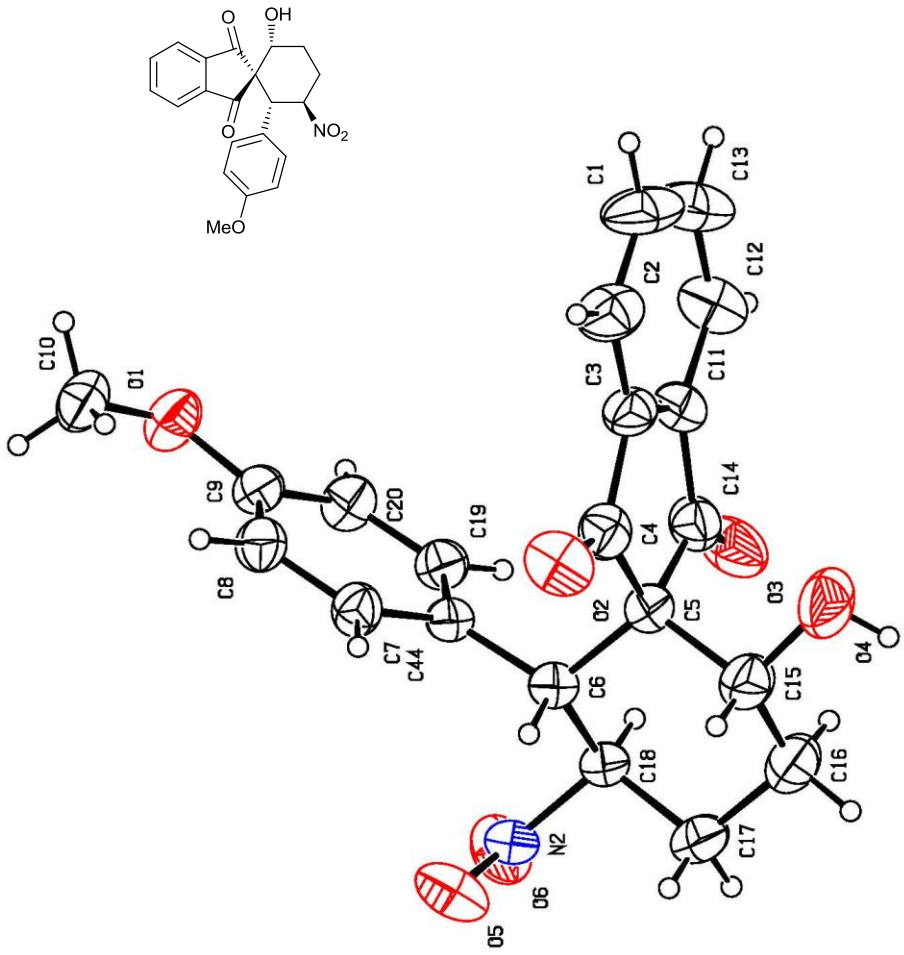


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.781	BB	0.4790	5332.33301	164.12785	49.6093
2	23.577	BB	0.5527	5416.32568	147.38565	50.3907



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.974	BB	0.5208	3514.56592	99.80968	82.2950
2	23.702	BB	0.5238	756.12445	18.69752	17.7050

Crystal Structure and data for compound 3ea



Crystal data and structure refinement for compound **3ea**

Identification code	shelx	
Empirical formula	C21 H19 N O6	
Formula weight	381.37	
Temperature	293(2) K	
Wavelength	1.54187 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 10.85690(10) Å	α= 90 °.
	b = 14.9130(2) Å	β= 90 °.
	c = 23.1808(16) Å	γ = 90 °.
Volume	3753.2(3) $Å^3$	
Z	8	
Density (calculated)	1.350 Mg/m^3	
Absorption coefficient	0.831 mm^{-1}	
F(000)	1600	
Crystal size	0.20 x 0.20 x 0.20 mm^3	
Theta range for data collection	7.034 to 68.581 °.	
Index ranges	-12<=h<=13, -17<=k<=17, -27<=l<=27	
Reflections collected	52124	
Independent reflections	6840 [R(int) = 0.0484]	
Completeness to theta = 67.687 °	99.5 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.861 and 0.684	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6840 / 1 / 512	
Goodness-of-fit on F^2	1.097	
Final R indices [I>2sigma(I)]	R1 = 0.0978, wR2 = 0.2475	
R indices (all data)	R1 = 0.1036, wR2 = 0.2574	
Absolute structure parameter	0.03(7)	
Extinction coefficient	0.0016(6)	
Largest diff. peak and hole	0.735 and -0.302 e.$Å^{-3}$	