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Dearomative Michael addition involving enals and 2-nitrobenzofurans realized under NHC-catalysis

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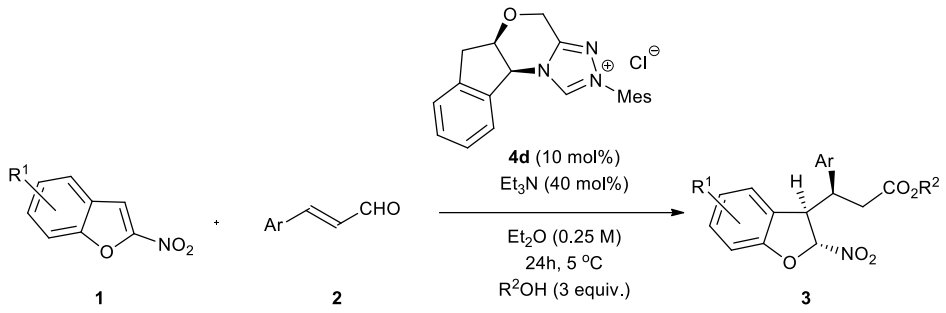
1. General methods

NMR spectra were acquired on a Bruker Ultra Shield 700 instrument, running at 700 MHz for ^{1}H and 176 MHz for ^{13}C, respectively. Chemical shifts (δ) are reported in ppm relative to residual solvent signals ($CDCl_3$: 7.26 ppm for ^{1}H NMR, 77.16 ppm for ^{13}C NMR). Mass spectra were recorded on a Bruker Maxis Impact spectrometer using chemical ionization (APCI) and electrospray (ESI) referenced to the mass of the charged species. Optical rotations were measured on a Perkin-Elmer 241 polarimeter and $[\alpha]_D$ values are given in deg•cm•g^{-1}•dm^{-1}; concentration *c* is listed in g•(100 mL)$^{-1}$. Analytical thin layer chromatography (TLC) was performed using pre-coated aluminum-backed plates (Merck Kieselgel 60 F254) and visualized by ultraviolet irradiation or Hanessian's stain. The enantiomeric ratio (er) of the products was determined by chiral stationary phase HPLC (Daicel Chiralpak IA, IB, IC and IF columns). Unless otherwise noted, analytical grade solvents and commercially available reagents were used without further purification. For flash chromatography (FC) silica gel (60, 35-70 μm, Merck KGaA). 2-Nitrobenzofurans **1a**-**h** and cinnamaldehydes **2e**-**h** and **2j**-**k** were obtained using literature procedures.[1-3] The racemic samples of products **3** for chiral HPLC separation studies were prepared using 2-mesityl-2,5,6,7-tetrahydropyrrolo[2,1-*c*][1,2,4]triazol-4-ium chloride **4e** under the general reaction condition.

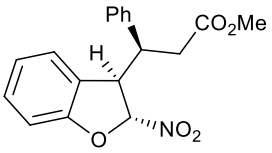
[1] S.-C. Lu, P.-R. Zheng and G. Liu, *J. Org. Chem*. 2012, **77**, 7711–7717.
[2] L. Lei, H.-Y. Niu, D.-C. Wang, X.-H. Yang, G.-R. Qu and H.-M. Guo, *Chem. Commun.* 2019, **55**, 553-556.
[3] N. Daubresse, C. Francesch and C. Rolando, *Tetrahedron* 1998, **54***,* 10761-10770.

2. Organocatalytic synthesis of 3 – general procedure



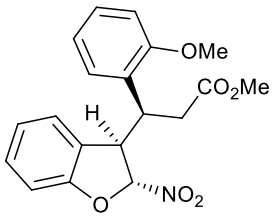
To a flame-dried 4 mL glass vial, equipped with a Teflon-coated magnetic stirring bar and a screw cap was charged triazolium salt **4d** (3.9 mg, 0.01 mmol), 2-nitrobenzofuran **1** (1 equiv., 0.1 mmol), cinnamaldehyde **2** (1.5 equiv., 0.15 mmol) and Et_3N (0.4 equiv., 0.04 mmol) in a dry Et_2O (0.4 mL) and stirred for 15 minutes in 5 °C. After this time the corresponding alcohol (3 equiv., 0.3 mmol) was added. The reaction mixture was stirred at 5 °C for 24 h and the residue was purified by column chromatography on silica gel (hexanes/diethyl ether as the eluent, typically 100:0 to 95:5) to furnish the corresponding products **3**.

(*S*)-Methyl 3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate 3a



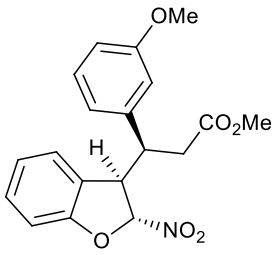
Following the general procedure, product **3a** (>20:1 dr in a crude reaction mixture) was isolated after 24 h by flash chromatography in 92% (28 mg) yield as a light-red oil. ^{1}H NMR (700MHz, $CDCl_3$) δ 7.37 – 7.33 (m, 2H), 7.33 – 7.27 (m, 2H), 7.22-7.20 (m, 1H), 7.20 – 7.17 (m, 2H), 7.08 – 7.03 (m, 2H), 5.77 (d, *J* = 1.2 Hz, 1H), 4.10-4.07 (m, 1H), 3.56 (s, 3H), 3.45-3.40 (m, 1H), 2.92 (dd, *J* = 15.8, 5.8 Hz, 1H), 2.81 (dd, *J* = 15.8, 8.9 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 171.7, 158.4, 139.0, 130.1, 129.1 (2C), 128.2 (2C), 128.1, 125.7, 124.8, 123.3, 111.2, 108.9, 54.61, 52.0, 45.1, 37.2. The er was determined by HPLC using a chiral Chiralpack IC column [hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major}=14.8 min; τ_{minor}=17.1 min (96.5:3.5 er). $[\alpha]_D^{20} = -43.2$ (c=1.0, $CHCl_3$). HRMS calculated for $[C_{18}H_{15}NO_5]^{-\bullet}$: 325.0955; found: 325.0941.

(*S*)-Methyl 3-(2-methoxyphenyl)-3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl)propanoate 3b



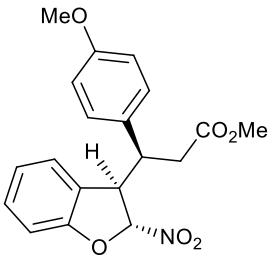
Following the general procedure, product **3b** (>20:1 dr in a crude reaction mixture) was isolated after 24 h by flash chromatography in 98% (35.0 mg) yield as a light-yellow oil. ^{1}H NMR (700MHz, $CDCl_3$) δ 7.32 – 7.28 (m, 2H), 7.14 – 7.11 (m, 2H), 7.10 – 7.07 (m, 1H), 7.03-6.99 (m, 1H), 6.96 – 6.94 (m, 2H), 5.81 (d, *J* = 1.2 Hz, 1H), 4.32 – 4.28 (m, 1H), 3.89 (s, 3H), 3.69 – 3.63 (m, 1H), 3.51 (s, 3H), 2.90 (dd, *J* = 15.8, 9.2 Hz, 1H), 2.80 (dd, *J* = 15.8, 5.4 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 172.1, 158.5, 157.5, 129.8, 129.8, 129.2, 127.3, 125.9, 125.2, 123.0, 120.9, 111.4, 111.0, 109.8, 55.5, 52.8, 51.7, 41.1, 35.3. The er was determined by HPLC using a chiral Chiralpack IB column [hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major}= 9.2 min; τ_{minor}=16.6 min (93:7 er). $[\alpha]_D^{20} = -30.8$ (c=1.0, $CHCl_3$). HRMS calculated for $[C_{19}H_{17}NO_6]^{-\bullet}$: 355.1061 found: 355.1060.

(*S*)-Methyl 3-(3-methoxyphenyl)-3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl)propanoate 3c



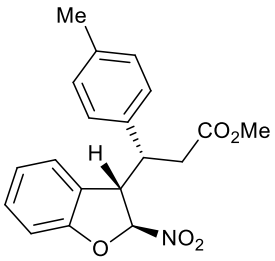
Following the general procedure, product **3c** (>20:1 dr in a crude reaction mixture) was isolated after 24 h by flash chromatography in 74% (26.5 mg) yield as a light-yellow oil. ^{1}H NMR (700MHz, $CDCl_3$) δ 7.32 – 7.28 (m, 1H), 7.25 – 7.21 (m, 2H), 7.07 – 7.03 (m, 2H), 6.83 – 6.81 (m, 1H), 6.79 – 6.76 (m, 1H), 6.69 – 6.66 (m, 1H), 5.77 (d, *J* = 1.3 Hz, 1H), 4.10-4.06 (m, 1H), 3.73 (s, 3H) 3.56 (s, 3H), 3.41-3.36 (m, 1H), 2.90 (dd, *J* = 15.9, 5.8 Hz, 1H), 2.80 (dd, *J* = 15.9, 8.7 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 171.7, 160.0, 158.4, 140.5, 130.1 (2C), 125.7, 124.9, 123.3, 120.3, 114.0, 113.6, 111.2, 108.9, 55.3, 54.5, 52.0, 45.0, 37.2. The er was determined by HPLC using a chiral Chiralpack IC column [hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major}= 18.9 min; τ_{minor}=23.4 min (94.5:5.5 er). $[\alpha]_D^{20} = -37.5$ (c=1.0, $CHCl_3$). HRMS calculated for $[C_{19}H_{17}NO_6]^{-\bullet}$: 355.1061; found: 355.1067.

(*S*)-Methyl 3-(4-methoxyphenyl)-3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl) propanoate 3d



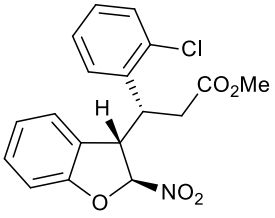
Following the general procedure, product **3d** (>20:1 dr in a crude reaction mixture) was isolated after 24 h by flash chromatography in 79% (28.2 mg) yield as a light-yellow oil. ^{1}H NMR (700MHz, $CDCl_3$) δ 7.36 – 7.28 (m, 1H), 7.24 – 7.20 (m, 1H), 7.14 – 7.08 (m, 2H), 7.08 – 7.02 (m, 2H), 6.90 – 6.84 (m, 2H), 5.76 (d, *J* = 1.3 Hz, 1H), 4.04-4.02 (m, 1H), 3.80 (s, 3H), 3.56 (s, 3H), 3.38-3.35 (m, 1H), 2.90 (dd, *J* = 15.7, 5.6 Hz, 1H), 2.77 (dd, *J* = 15.7, 9.0 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 171.8, 159.3, 158.4, 130.9, 130.1, 129.2 (2C), 125.7, 125.0, 123.2, 114.5 (2C), 111.2, 108.9, 55.4, 54.8, 51.9, 44.4, 37.4. The er was determined by HPLC using a Chiralpak IB column [hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major}=16.9 min; τ_{minor}=15.1 min (96.5:3.5 er). $[\alpha]_D^{20} = -35.3$ (c=1.0, $CHCl_3$). HRMS calculated for $[C_{19}H_{17}NO_6]^{\bullet\bullet}$: 355.1061; found: 355.1054.

(*R*)-Methyl 3-((2*S*,3*S*)-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-(p-tolyl)propanoate 3e



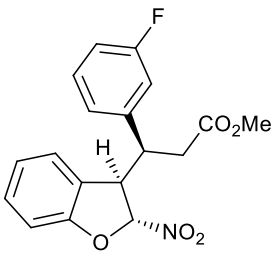
Following the general procedure, product **3e** (>20:1 dr in a crude reaction mixture) was isolated after 24 h by flash chromatography in 78% (26.6 mg) yield as a red oil. Catalyst *ent*-**4d** (5a*S*,10b*R* configuration) was used in the reaction. ^{1}H NMR (700MHz, $CDCl_3$) δ 7.33 – 7.28 (m, 1H), 7.23-7.21 (m, 1H), 7.16 – 7.12 (m, 2H), 7.09 – 7.02 (m, 4H), 5.76 (d, *J* = 1.2 Hz, 1H), 4.07 – 4.03 (m, 1H), 3.56 (s, 3H), 3.39-3.35 (m, 1H), 2.90 (dd, *J* = 15.8, 5.7 Hz, 1H), 2.79 (dd, *J* = 15.8, 8.9 Hz, 1H), 2.33 (m, 3H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 171.8, 158.3, 137.7, 135.9, 130.1, 129.8 (2C), 128.0 (2C), 125.7, 125.0, 123.2, 111.2, 109.0, 54.6, 51.9, 44.7, 37.3, 21.2. The er was determined by HPLC using a Chiralpak IA column [hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major} = 12.2 min; τ_{minor} =13.8 min (94.5:5.5 er). $[\alpha]_D^{20} = 45.6$ (c=1.0, $CHCl_3$). HRMS calculated for $[C_{19}H_{17}NO_5]^{\bullet\bullet}$: 339.1112; found: 339.1115.

(*R*)-Methyl 3-(2-chlorophenyl)-3-((2*S*,3*S*)-2-nitro-2,3-dihydrobenzofuran-3-yl) propanoate 3f



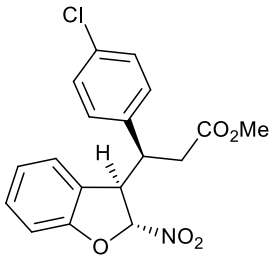
Following the general procedure, product **3f** (>20:1 dr in a crude reaction mixture) was isolated after 24 h by flash chromatography in 74% (26.56 mg) yield as a red oil. Catalyst *ent*-**4d** (5a*S*,10b*R* configuration) was used in the reaction. ^{1}H NMR (700MHz, $CDCl_3$) δ 7.47 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.37 – 7.30 (m, 3H), 7.30-7.27 (m, 1H), 7.15 – 7.12 (m, 1H), 7.07 – 7.01 (m, 2H), 5.80 (d, *J* = 1.1 Hz, 1H), 4.22-4.20 (m, 1H), 4.04-3.98 (m, 1H), 3.54 (s, 3H), 2.79 (dd, *J* = 16.0, 5.5 Hz, 1H), 2.75 (dd, *J* = 16.0, 8.6 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 171.4, 158.6, 137.0, 134.6, 130.6, 130.3, 129.2, 128.9, 127.5, 126.1, 123.9, 123.2, 111.3, 109.4, 53.2, 51.9, 40.9, 35.4. The er was determined by HPLC using a Chiralpak IC column [hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major} = 14.9 min; τ_{minor} = 13.9 min (94.5:5.5 er). $[\alpha]_D^{20} = 47.0$ (c=1.0, $CHCl_3$). HRMS calculated for $[C_{18}H_{14}ClNO_5]^{-\bullet}$: 359.0566; found: 359.0570.

(*S*)-Methyl 3-(3-fluorophenyl)-3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl) propanoate 3g



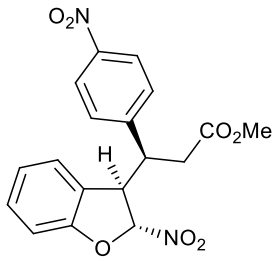
Following the general procedure, product **3g** (>20:1 dr in a crude reaction mixture) was isolated after 24 h by flash chromatography in 83% (28.6 mg) yield as a light-red oil. ^{1}H NMR (700MHz, $CDCl_3$) δ 7.34 – 7.29 (m, 2H), 7.22 – 7.20 (m, 1H), 7.10 – 7.04 (m, 2H), 7.02 – 6.97 (m, 2H), 6.90-6.88 (m, 1H), 5.76 (d, *J* = 1.3 Hz, 1H), 4.08 – 4.04 (m, 1H), 3.58 (s, 3H), 3.47-3.42 (m, 1H), 2.91 (dd, *J* = 16.0, 5.7 Hz, 1H), 2.79 (dd, *J* = 16.0, 8.9 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 171.5, 163.1 (d, *J* = 247.5 Hz), 158.3, 141.5 (d, *J* = 7.6 Hz), 130.7 (d, *J* = 7.8 Hz), 130.3, 125.6, 124.4, 123.9 (d, *J* = 3.2 Hz), 123.40, 115.3 (d, *J* = 21.2 Hz), 115.1 (d, *J* = 21.2 Hz), 111.3, 108.6, 54.4, 52.1, 44.7, 36.9. The er was determined by HPLC using a Chiralpak IC column [hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major} = 16.9 min; τ_{minor} = 15.5 min; (95:5 er). $[\alpha]_D^{20} = -33.7$ (c=1.0, $CHCl_3$). HRMS calculated for $[C_{18}H_{14}FNO_5]^{-\bullet}$: 343.0861; found: 343.0865.

(*S*)-Methyl 3-(4-chlorophenyl)-3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl) propanoate 3h



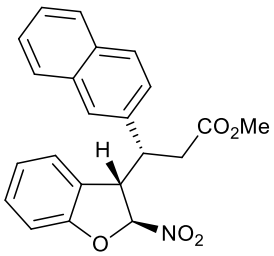
Following the general procedure product **3h** (>20:1 dr in a crude reaction mixture) was isolated after 24 h by flash chromatography in 77% (27.8 mg) yield as a light-red oil. ^{1}H NMR (700MHz, $CDCl_3$) δ 7.34 – 7.28 (m, 3H), 7.22 – 7.17 (m, 1H), 7.16 – 7.10 (m, 2H), 7.09 – 7.04 (m, 2H), 5.73 (d, *J* = 1.2 Hz, 1H), 4.15 – 3.98 (m, 1H), 3.57 (s, 3H), 3.44-3.40 (m, 1H), 2.91 (dd, *J* = 16.0, 5.6 Hz, 1H), 2.78 (dd, *J* = 16.0, 9.1 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 171.5, 158.3, 137.5, 134.0, 130.3, 129.6 (2C), 129.3 (2C), 125.6, 124.5, 123.4, 111.3, 108.6, 54.4, 52.0, 44.5, 37.1. The er was determined by HPLC using a Chiralpak IB column [hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major} = 16.8 min; τ_{minor} = 15.7 min; (95:5 er). $[\alpha]_D^{20} = -40.3$ (c=1.0, $CHCl_3$). HRMS calculated for $[C_{18}H_{14}ClNO_5]^{-\bullet}$: 359.0566; found: 359.0569.

(*S*)-Methyl 3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-(4-nitrophenyl)propanoate 3i



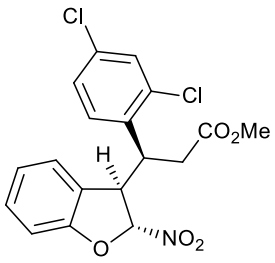
Following the general procedure product **3i** (>20:1 dr in a crude reaction mixture) was isolated after 24 h by flash chromatography in 74% (27.5mg) yield as a light-red oil. ^{1}H NMR (700MHz, $CDCl_3$) δ 8.20 – 8.18 (m, 2H), 7.38 – 7.36 (m, 2H), 7.35-7.31 (m, 1H), 7.22-7.19 (m, 1H), 7.10-7.07 (m, 1H), 7.06-7.03 (m, 1H), 5.72 (d, *J* = 1.3 Hz, 1H), 4.12-4.10 (m, 1H), 3.62 – 3.60 (m, 1H), 3.59 (s, 3H), 2.98 (dd, *J* = 16.3, 5.6 Hz, 1H), 2.86 (dd, *J* = 16.3, 9.0 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 171.1, 158.2, 147.7, 146.4, 130.6, 129.3 (2C), 125.5, 124.2 (2C), 123.8, 123.6, 111.4, 108.1, 54.1, 52.2, 44.8, 36.7. The er was determined by HPLC using a Chiralpak IA column [hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major} = 3.3 min; τ_{minor} = 4.0 min (85:15 er). $[\alpha]_D^{20} = -28.1$ (c=1.0, $CHCl_3$). HRMS calculated for $[C_{18}H_{14}N_2O_7]^{-\bullet}$: 370.0806; found: 370.0799.

(*R*)-Methyl 3-(naphthalen-2-yl)-3-((2*S*,3*S*)-2-nitro-2,3-dihydrobenzofuran-3-yl) propanoate 3j



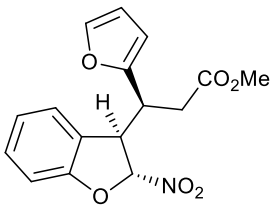
Following the general procedure product **3j** (>20:1 dr in a crude reaction mixture) was isolated after 24 h by flash chromatography in 69% (26.0 mg) yield as a white solid (mp.=94-96 ^{o}C after recrystalization from hexane/diethyl ether mixture). Catalyst *ent*-**4d** (5a*S*,10b*R* configuration) was used in the reaction. ^{1}H NMR (700MHz, $CDCl_3$) δ 7.93 – 7.82 (m, 2H), 7.82 – 7.77 (m, 1H), 7.67-7.66 (m, 1H), 7.53 – 7.48 (m, 2H), 7.35 – 7.30 (m, 2H), 7.24-7.22 (m, 1H), 7.09 – 7.04 (m, 2H), 5.81 (d, *J* = 1.2 Hz, 1H), 4.20-4.18 (m, 1H), 3.61-3.57 (m, 1H), 3.53 (s, 3H), 3.00 (dd, *J* = 15.9, 5.6 Hz, 1H), 2.92 (dd, *J* = 15.9, 9.0 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 171.7, 158.4, 136.5, 133.5, 133.0, 130.2, 129.1, 128.0, 127.9, 127.4, 126.6, 126.4, 125.8, 125.8, 124.8, 123.3, 111.3, 108.9, 54.5, 52.0, 45.2, 37.2. The er was determined by HPLC using a Chiralpak IF column [hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major}=13.6 min; τ_{minor} = 16.7 min (80.5:19.5 er, after recrystallization 99.9:0.1 er). $[\alpha]_D^{20} = 34.1$ (c= 1.0, $CHCl_3$). HRMS calculated for $[C_{22}H_{17}NO_5]^{\bullet-}$: 375.1112 found: 375.1108.

(*S*)-Methyl 3-(2,4-dichlorophenyl)-3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl) propanoate 3k



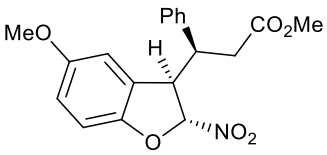
Following the general procedure product **3k** (19:1 dr in a crude reaction mixture) was isolated after 24 h by flash chromatography in 71% (28.0 mg) yield as a light-red oil. ^{1}H NMR (700MHz, $CDCl_3$) δ 7.49 (d, *J* = 2.2 Hz, 1H), 7.37 – 7.31 (m, 2H), 7.29 – 7.23 (m, 1H), 7.16 – 7.12 (m, 1H), 7.07 – 7.01 (m, 2H), 5.77 (d, *J* = 1.1 Hz, 1H), 4.19-4.17 (m, 1H), 3.98-3.93 (m, 1H), 3.55 (s, 3H), 2.77 (dd, *J* = 16.2, 5.2 Hz, 1H), 2.71 (dd, *J* = 16.2, 8.9 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 171.2, 158.5, 135.6, 135.4, 134.5, 130.4, 130.4, 129.8, 127.9, 126.0, 123.6, 123.3, 111.5, 109.1, 53.0, 52.1, 40.5, 35.2. The er was determined by HPLC using a Chiralpak IC column [hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major}=13.3 min; τ_{minor}=12.3 min (94:6 er). $[\alpha]_D^{20} = -47.1$ (c=1.0, $CHCl_3$). HRMS calculated for $[C_{18}H_{13}Cl_2NO_5]^{\bullet-}$: 393.0176; found: 393.0174.

(*S*)-Methyl 3-(furan-2-yl)-3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl) propanoate 3l



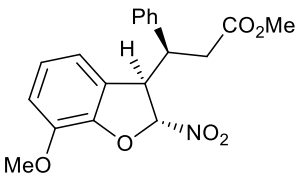
Following the general procedure product **3l** (>20:1 dr in a crude reaction mixture) was isolated after 24 h by flash chromatography in 87% (27.5 mg) yield as a light-red oil. ^{1}H NMR (700MHz, $CDCl_3$) δ 7.36-7.35 (m, 1H), 7.30-7.27 (m, 1H), 7.09-7.07 (m, 1H), 7.05 – 7.00 (m, 2H), 6.26 (dd, *J* = 3.3, 1.8 Hz, 1H), 6.06 (d, *J* = 1.8 Hz, 1H), 5.99-5.98 (m, 1H), 4.14-4.12 (m, 1H), 3.75-3.71 (m, 1H), 3.66 (s, 3H), 2.80 (d, *J* = 0.8 Hz, 1H), 2.79 (d, *J* = 1.6 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 171.6, 158.4, 152.2, 142.7, 130.1, 125.3, 124.2, 123.3, 110.9, 110.5, 108.6, 108.0, 53.2, 52.2, 38.8, 34.8. The er was determined by HPLC using a Chiralpak IC column [hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major} = 13.3 min; τ_{minor} = 15.4 min (94.5:5.5 er). $[\alpha]_D^{20} = -40.7$ (c=1.0, $CHCl_3$). HRMS calculated for $[C_{16}H_{13}NO_6]^{-\bullet}$: 315.0748; found: 315.0743.

(*S*)-Methyl 3-((2*R*,3*R*)-5-methoxy-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate 3m



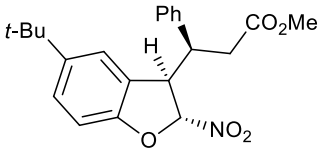
Following the general procedure product **3m** (16:1 dr in a crude reaction mixture) was isolated after 24 h by flash chromatography in 66% (23.6 mg) yield as a light-green oil. ^{1}H NMR (700MHz, $CDCl_3$) δ 7.38 – 7.32 (m, 2H), 7.31 – 7.27 (m, 1H), 7.21 – 7.18 (m, 2H), 7.07 (d, *J* = 8.3 Hz, 1H), 6.63 (d, *J* = 2.3 Hz, 1H), 6.59 (dd, *J* = 8.3, 2.3 Hz, 1H), 5.76 (d, *J* = 1.2 Hz, 1H), 4.00-3.98 (m, 1H), 3.81 (s, 3H), 3.55 (s, 3H), 3.41-3.36 (m, 1H),2.88 (dd, *J* = 15.8, 5.6 Hz, 1H), 2.78 (dd, *J* = 15.8, 9.0 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 171.8, 161.8, 159.7, 139.2, 129.1 (2C), 128.2 (2C), 128.0, 125.8, 116.5, 109.6, 109.3, 97.6, 55.8, 54.2, 51.9, 45.3, 37.1. The er was determined by HPLC using a Chiralpak IC column [hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major} = 23.0 min; τ_{minor} = 21.4 min (94.5:5.5 er). $[\alpha]_D^{20} = -14.9$ (c=1.0, $CHCl_3$). HRMS calculated for $[C_{19}H_{17}NO_6]^{-\bullet}$: 355.1061; found: 355.1066.

(*S*)-Methyl 3-((2*R*,3*R*)-7-methoxy-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate 3n



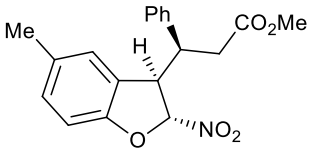
Following the general procedure product **3n** (>20:1 dr in a crude reaction mixture) was isolated after 24 h by flash chromatography in 76% (27.2 mg) yield as a red oil. ^{1}H NMR (700MHz, $CDCl_3$) δ 7.44 – 7.31 (m, 2H), 7.31 – 7.27 (m, 1H), 7.23 – 7.14 (m, 2H), 7.01 (dd, *J* = 8.2, 7.5 Hz, 1H), 6.91 (dd, *J* = 8.2, 1.1 Hz, 1H), 6.87 – 6.69 (m, 1H), 5.77 (d, *J* = 1.3 Hz, 1H), 4.10-4.07 (m, 1H), 3.93 (s, 3H), 3.55 (s, 3H), 3.43-3.37 (m, 1H), 2.92 (dd, *J* = 15.8, 5.5 Hz, 1H), 2.80 (dd, *J* = 15.8, 9.1 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 171.7, 146.6, 145.2, 139.1, 129.1 9 (2C), 128.2 (2C), 128.1, 126.3, 124.2, 117.6, 113.8, 109.0, 56.6, 55.1, 51.9, 45.1, 37.3. The er was determined by HPLC using a Chiralpak IC column [hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major} = 10.6 min; τ_{minor} = 13.3 min (97:3 er). $[\alpha]_D^{20} = -22.9$ (c=1.0, $CHCl_3$). HRMS calculated for $[C_{19}H_{17}NO_6]^{\bullet-}$: 355.1061; found: 355.1063.

(*S*)-Methyl 3-((2*R*,3*R*)-5-(*tert*-butyl)-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate 3o



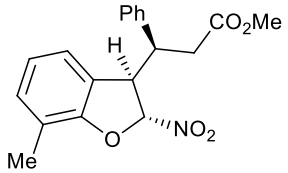
Following the general procedure product **3o** (>20:1 dr in a crude reaction mixture) was isolated after 24 h by flash chromatography in 66% (25.3 mg) yield as a colorless oil. ^{1}H NMR (700MHz, $CDCl_3$) δ 7.37 – 7.32 (m, 2H), 7.31 – 7.27 (m, 2H), 7.21 – 7.15 (m, 2H), 7.11-7.10 (m, 1H), 6.95 (d, *J* = 8.5 Hz, 1H), 5.79 (d, *J* = 1.2 Hz, 1H), 4.05-4.04 (m, 1H), 3.56 (s, 3H), 3.53 – 3.47 (m, 1H), 2.86 (dd, *J* = 15.9, 5.8 Hz, 1H), 2.78 (dd, *J* = 15.9, 9.0 Hz, 1H), 1.30 (s, 9H). ^{13}C NMR (176 MHz, $CDCl_3$) δ171.9, 156.2, 146.4, 139.1, 129.0 (2C), 128.2 (2C), 128.0, 126.9, 124.1, 122.8, 110.2, 109.3, 54. 9, 51.9, 44.9, 36.7, 34.6, 31.7 (3C). The er was determined by HPLC using a Chiralpak IC column [hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major} = 10.0 min; τ_{minor} = 13.6 min (94.5:5.5 er). $[\alpha]_D^{20} = -13.4$ (c=1.0, $CHCl_3$). HRMS calculated for $[C_{22}H_{23}NO_5]^{\bullet-}$: 381.1581; found: 381.1576.

(*S*)-Methyl 3-((2*R*,3*R*)-5-methyl-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate 3p



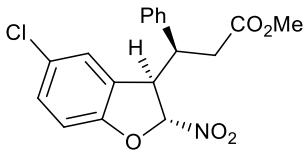
Following the general procedure product **3p** (>20:1 dr in a crude reaction mixture) was isolated after 24 h by flash chromatography in 74% (25.2 mg) yield as an orange oil. ^{1}H NMR (700MHz, $CDCl_3$) δ 7.38 – 7.32 (m, 2H), 7.32 – 7.27 (m, 1H), 7.22 – 7.17 (m, 2H), 7.12 – 7.08 (m, 1H), 7.02 – 7.00 (m, 1H), 6.94 (d, *J* = 8.2 Hz, 1H), 5.72 (d, *J* = 1.2 Hz, 1H), 4.05 – 3.98 (m, 1H), 3.55 (s, 3H), 3.41-3.37 (m, 1H), 2.93 (dd, *J* = 15.8, 5.7 Hz, 1H), 2.81 (dd, *J* = 15.8, 9.0 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 171.8, 156.4, 139.2, 132.8, 130.6, 129.1 (2C), 128.2 (2C), 128.0, 126.1, 124.8, 110.7, 109.2, 54.7, 51.9, 45.1, 37.4, 21.1. The er was determined by HPLC using a Chiralpak IC column [hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major}=13.5 min; τ_{minor}=19.0 min (95:5 er). $[\alpha]_D^{20} = -22.9$ (c=1.0, $CHCl_3$). HRMS calculated for $[C_{19}H_{17}NO_5]^{-\bullet}$: 339.1112; found: 339.1115.

(*S*)-Methyl 3-((2*R*,3*R*)-7-methyl-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate 3q



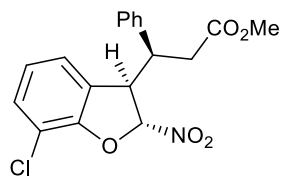
Following the general procedure product **3q** (>20:1 dr in a crude reaction mixture) was isolated after 24 h by flash chromatography in 64% (22.1 mg) yield as red oil. ^{1}H NMR (700MHz, $CDCl_3$) δ 7.40 – 7.33 (m, 2H), 7.33 – 7.28 (m, 1H), 7.24 – 7.19 (m, 2H), 7.12-7.10 (m, 1H), 7.03-7.01 (m, 1H), 6.96-6.93 (m, 1H), 5.73 (d, *J* = 1.2 Hz, 1H), 4.07-4.03 (m, 1H), 3.54 (s, 3H), 3.40-3.35 (m, 1H), 2.91 (dd, *J* = 15.8, 5.5 Hz, 1H), 2.79 (dd, *J* = 15.8, 9.1 Hz, 1H), 2.31 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 171.8, 156.9, 139.3, 131.4, 129.1 (2C), 128.3 (2C), 128.0, 124.1, 123.1, 123.0, 121.7, 108.9, 54.9, 51.9, 45.2, 37.4, 15.0. The er was determined by HPLC using a Chiralpak IA column [hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major}=27.8 min; τ_{minor}=18.1 min (96:4 er). $[\alpha]_D^{20} = -39.2$ (c=1.0, $CHCl_3$). HRMS calculated for $[C_{19}H_{17}NO_5]^{-\bullet}$: 339.1112; found: 339.1117.

(*S*)-Methyl 3-((2*R*,3*R*)-5-chloro-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate 3r



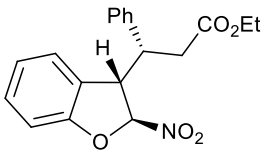
Following the general procedure product **3r** (>20:1 dr in a crude reaction mixture) was isolated after 24 h by flash chromatography in 66% (23.9 mg) yield as an orange oil. ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.37 – 7.33 (m, 2H), 7.32 – 7.29 (m, 1H), 7.28-7.26 (m, 1H), 7.20-7.19 (m, 1H), 7.18 – 7.16 (m, 2H), 6.98-7.96 (m, 1H), 5.78 (d, *J* = 1.3 Hz, 1H), 4.08-4.06 (m, 1H), 3.59 (s, 3H), 3.46-3.41 (m, 1H), 2.90 (dd, J = 15.9, 6.2 Hz, 1H), 2.81 (dd, J = 15.9, 8.4 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 171.6, 157.0, 138.5, 130.1, 129.2 (2C), 128.4, 128.2, 128.1 (2C), 126.8, 125.8, 112.2, 108.9, 54.5, 52.1, 44.8, 37.1. The er was determined by HPLC using a Chiralpak IC column [hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major} = 11.4 min; τ_{minor} = 14.3 min (93:7 er). $[\alpha]_D^{20} = -31.2$ (c=1.0, $CHCl_3$). HRMS calculated for $[C_{18}H_{14}ClNO_5]^{\bullet\bullet}$: 359.0566; found: 359.0561.

(*S*)-Methyl 3-((2*R*,3*R*)-7-chloro-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate 3s



Following the general procedure product **3s** (>20:1 dr in a crude reaction mixture) was isolated after 24 h by flash chromatography in 83% (30.2 mg) yield as red oil. ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.38 – 7.33 (m, 2H), 7.33 – 7.29 (m, 2H), 7.21 – 7.15 (m, 2H), 7.12-7.10 (m, 1H), 7.02-6.99 (m, 1H), 5.83 (d, *J* = 1.3 Hz, 1H), 4.25 – 3.98 (m, 1H), 3.57 (s, 3H), 3.46-3.42 (m, 1H), 2.88 (dd, *J* = 15.8, 5.8 Hz, 1H), 2.80 (dd, *J* = 15.8, 8.6 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 171.6, 154.4, 138.6, 130.5, 129.3 (2C), 128.3, 128.1 (2C), 126.7, 124.3, 123.9, 116.9, 108.4, 55.2, 52.0, 45.0, 37.1.The er was determined by HPLC using a Chiralpak IC column [hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major} = 8.6 min; τ_{minor} = 9.9min (94:6 er). $[\alpha]_D^{20} = -41.1$ (c=1.0, $CHCl_3$). HRMS calculated for $[C_{18}H_{14}ClNO_5]^{\bullet\bullet}$: 359.0566; found: 359.0567.

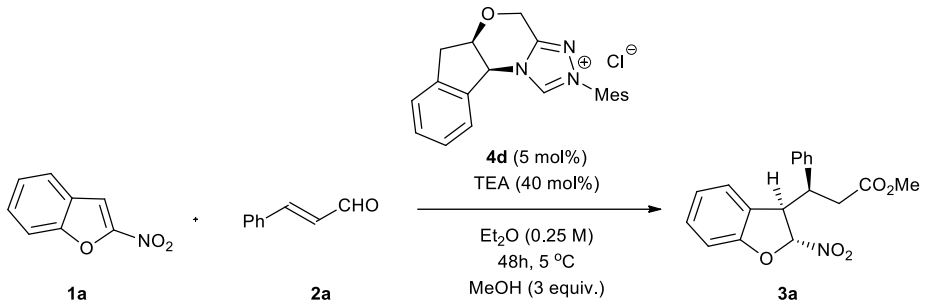
(*R*)-Ethyl 3-((2*S*,3*S*)-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate 3t



Following the general procedure product **3t** (>20:1 dr in a crude reaction mixture) was isolated after 24 h by flash chromatography in 89% (30.4 mg) yield as a light-yellow oil. Catalyst *ent*-**4d** (5a*S*,10b*R* configuration) was used in the reaction. ^{1}H NMR (700 MHz, $CDCl_3$) δ

7.36 – 7.32 (m, 2H), 7.32 – 7.27 (m, 2H), 7.22-7.20 (m, 1H), 7.20-7.18 (m, 2H), 7.07 – 7.03 (m, 2H), 5.78 (d, *J* = 1.3 Hz, 1H), 4.08-4.06 (m, 1H), 4.05 – 4.01 (m, 1H), 4.01 – 3.96 (m, 1H), 3.44-3.40 (m, 1H), 2.90 (dd, *J* = 15.7, 5.8 Hz, 1H), 2.79 (dd, *J* = 15.7, 9.0 Hz, 1H), 1.10 (t, *J* = 7.1 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 171.3, 158.4, 138.9, 130.1, 129.1 (2C), 128.3 (2C), 128.0, 125.7, 124.8, 123.3, 111.2, 108.9, 60.9, 54.7, 45.1, 37.4, 14.2. The er was determined by HPLC using a Chiralpak IC column [hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; τ_{major} = 14.4 min; τ_{minor} = 12.2 min (94.5:5.5 er). $[\alpha]_D^{20} = 43.2$ (c=1.0, $CHCl_3$). HRMS calculated for $[C_{18}H_{17}NO_5]^{\bullet-}$: 339.1112 found: 339.1117.

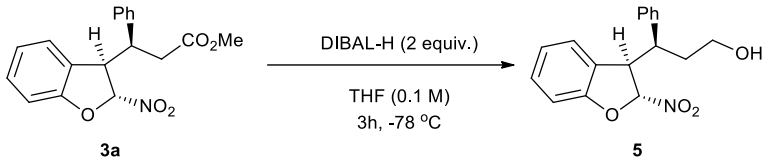
3. Enantioselective synthesis of (*S*)-methyl 3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate 3a on 1 mmol scale



To a flame-dried 10 mL glass vial, equipped with a Teflon-coated magnetic stirring bar and a screw cap was charged triazolium salt **4d** (19.3 mg, 0.05 mmol), 2-nitrobenzofurane **1a** (1equiv., 1 mmol), cinnamaldehyde **2a** (1.5 equiv., 1.5 mmol) and Et_3N (0.4 equiv., 0.4 mmol) in a dry Et_2O (4 mL) and stirred for 15 minutes in 5 °C. After this time, methanol (3 equiv., 3 mmol) was added. The reaction mixture was stirred at 5 °C for 48 h and the residue was purified by column chromatography on silica gel (hexanes/diethyl ether100:0 to 95:5) to furnish the corresponding product **3a** in 84% yield as a light-red oil. NMR and HPLC data were in accordance with previously obtained results.

4. Transformations of 3a

4.1 Synthesis of (*S*)-3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropan-1-ol 5

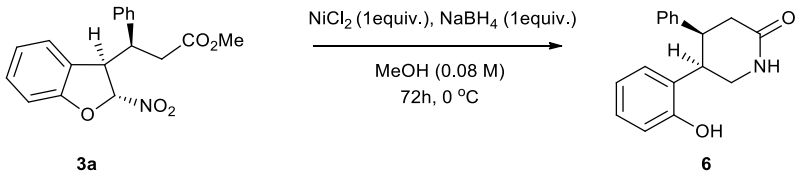


3a **5**

To a stirred solution of **3a** (1.0 equiv., 0.1 mmol, 32 mg) in freshly distilled THF (1 mL) diisobutylaluminum hydride solution (1 M in toluene) (2.0 equiv., 0.2 mmol) under inert atmosphere at -78 °C was added. The reaction mixture was stirred for 3 h at -78 °C and subsequently purified by flash chromatography on silica gel (eluent hexanes/ethyl acetate 10:1) to obtain product **5** as single diastereoisomer (>20:1) in 68% yield (20.3 mg).

(*S*)-3-((2*R*,3*R*)-2-Nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropan-1-ol 5: ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.41 – 7.36 (m, 2H), 7.33 – 7.28 (m, 3H), 7.24 – 7.21 (m, 2H), 7.08 – 7.04 (m, 2H), 5.71 (d, *J* = 1.2 Hz, 1H), 3.98 (dd, *J* = 9.2, 1.2 Hz, 1H), 3.60-3.55 (m, 1H), 3.43-3.38 (m, 1H), 3.00-2.97 (m, 1H), 2.27-2.21 (m, 1H), 2.04-1.94 (m, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 158.3, 139.71, 129.9, 129.2 (2C), 128.5 (2C), 127.9, 126.1, 125.5, 123.1, 111.1, 109.3, 60.4, 55.5, 45.9, 35.0. $[\alpha]_D^{20}$ = +21.1 (c = 1.0, $CHCl_3$). HRMS calculated for $[C_{17}H_{15}NO_4]^{\bullet-}$: 297.1006 found: 297.1003.

4.2 Synthesis of (4*S*,5*R*)-5-(2-hydroxyphenyl)-4-phenylpiperidin-2-one 6



3a **6**

To a stirred solution of **3a** (1.0 equiv., 0.08 mmol, 25.0 mg) in methanol (1 mL), nickel chloride (1.0 equiv., 0.08 mmol) and $NaBH_4$ (1.0 equiv., 0.08 mmol) in 0 °C were added. The reaction mixture was stirred for 72 h at 0 °C, and H_2O (3 mL) was added. After stirring for 5 minutes saturated NaCl aq. solution (10 mL) was added and resulting mixture was extracted with dichloromethane (3 x 10 mL). Combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure to obtain crude product, which was purified by flash chromatography on silica gel (eluent dichloromethane/methanol 100:0 to 95:5) to obtain product **6** as single diastereoisomer (>20:1) in 83% yield (17.0 mg).

(4*S*,5*R*)-5-(2-Hydroxyphenyl)-4-phenylpiperidin-2-one 6: ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.21 – 7.15 (m, 3H), 7.1-7.08 (m, 1H), 6.81 (dd, *J* = 8.0, 1.2 Hz, 1H), 6.77-6.74 (m, 2H), 6.69-6.66 (m, 1H), 6.40 (dd, *J* = 7.7, 1.6 Hz, 1H), 6.18 (bs, 1H), 5.76 (bs, 1H), 3.91-3.87 (m, 1H), 3.68-3.65 (m, 1H), 3.58 – 3.54 (m, 1H), 3.42-3.39 (m, 1H), 2.99 (dd, *J* = 18.0, 6.5 Hz, 1H), 2.80 (dd, *J* = 18.0, 3.8 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 172.6, 153.7, 139.9, 128.6 (2C), 128.1 (3C), 127.9, 127.1, 126.2, 120.5, 115.6, 43.0, 40.8, 36.3, 36.2. $[\alpha]_D^{19}$= +12.1 (c = 1.0, $CHCl_3$). HRMS (ES+) calculated for $[C_{17}H_{17}NO_2+H]^+$: 268.1338; found: 268.1338.

5. Crystal and X-ray data for (*R*)-methyl 3-(naphthalen-2-yl)-3-((2*S*,3*S*)-2-nitro-2,3-dihydrobenzofuran-3-yl) propanoate 3j

The crystal structure of the compound **3j** (99.9:0.1 er) $C_{22}H_{19}NO_5$, was established by single-crystal X-ray diffraction at 100 K. The compound crystallizes in the non-centrosymmetric orthorhombic space group $P2_12_12_1$ (Z = 4) and the crystal structure consists of one crystallographically independent formula unit in the unit cell (Figure 1).

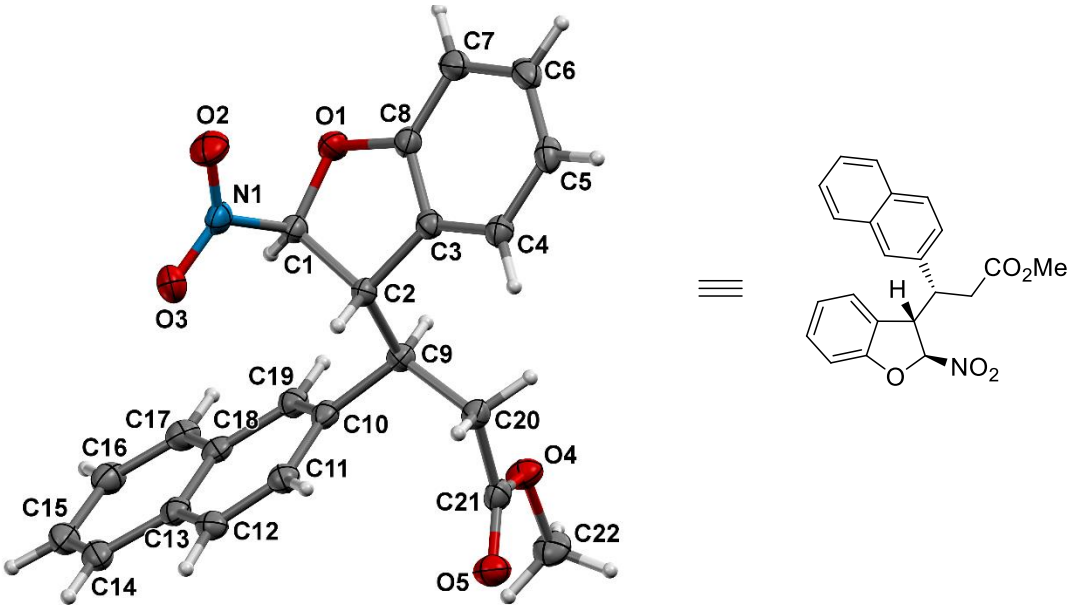


Figure 1. The molecular structure of the compound **3j** at 100 K, with the atom labeling scheme, showing 50% probability displacement ellipsoids. Hydrogen atoms are drawn with an arbitrary radius.

Single crystal X-ray diffraction data were collected at 100 K by the ω-scan technique using a RIGAKU XtaLAB Synergy, Dualflex, Pilatus 300K diffractometer[4] with PhotonJet micro-focus X-ray Source Cu-Kα (λ = 1.54184 Å). Data collection, cell refinement, data reduction and absorption correction were performed using CrysAlis PRO software.[4] The crystal structure was solved by using direct methods with the SHELXT 2018/2 program.[5] Atomic scattering factors were taken from the International Tables for X-ray Crystallography. Positional parameters of non-H-atoms were refined by a full-matrix least-squares method on F^2 with anisotropic thermal parameters by using the SHELXL 2018/3 program.[6] All hydrogen atoms were found from the difference Fourier maps and for further calculations they were positioned geometrically in calculated positions (C–H = 0.95–1.00 Å) and constrained to ride

on their parent atoms with isotropic displacement parameters set to 1.2-1.5 times the U_{eq} of the parent atom.

3j: Formula $C_{22}H_{19}NO_5$, orthorhombic, space group $P2_12_12_1$, Z = 4, unit cell constants a = 8.6297(1), b = 10.2148(1), c = 20.5342(3) Å, V = 1810.10(4) Å^3. The integration of the data yielded a total of 49500 reflections with θ angles in the range of 4.31 to 66.54°, of which 3197 were independent (R_{int} = 3.92%), and 3164 were greater than 2σ(F^2). The final anisotropic full-matrix least-squares refinement on F^2 with 255 parameters converged at R_1 = 2.94% and wR_2 = 7.54% for all data. The largest peak in the final difference electron density synthesis was 0.264 e Å^{-3} and the largest hole was -0.205 e Å^{-3}. The goodness-of-fit was 1.051. The absolute configuration was unambiguously established from anomalous scattering, by calculating the *x* Flack parameter[7] of -0.06(5) using 1321 quotients.

CCDC 2105519 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures

[4] Rigaku OD. CrysAlis PRO. Rigaku Oxford Diffraction Ltd, Yarnton, Oxfordshire, England, 2019.

[5] G. M. Sheldrick, *Acta Cryst.* 2015, **A71**, 3-8.

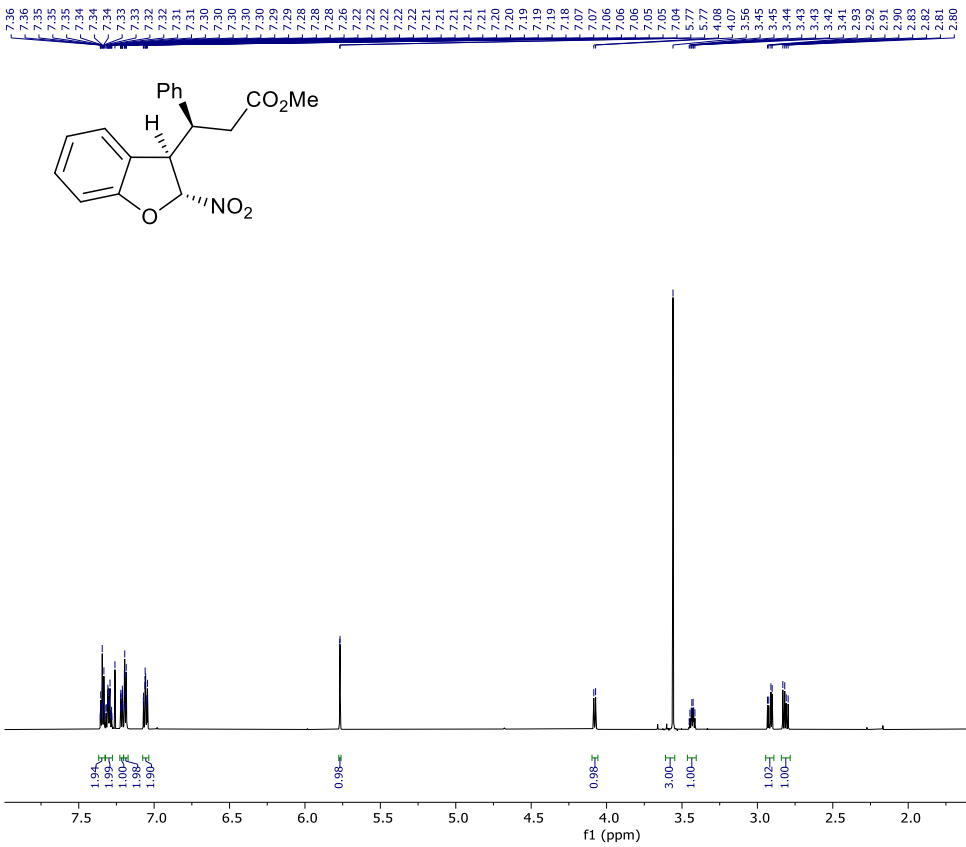
[6] G. M. Sheldrick, *Acta Cryst.* 2015, **C71**, 3-8.

[7] S. Parsons, H. D. Flack, and T. Wagner, *Acta Cryst.* 2013, **B69**, 249-259.

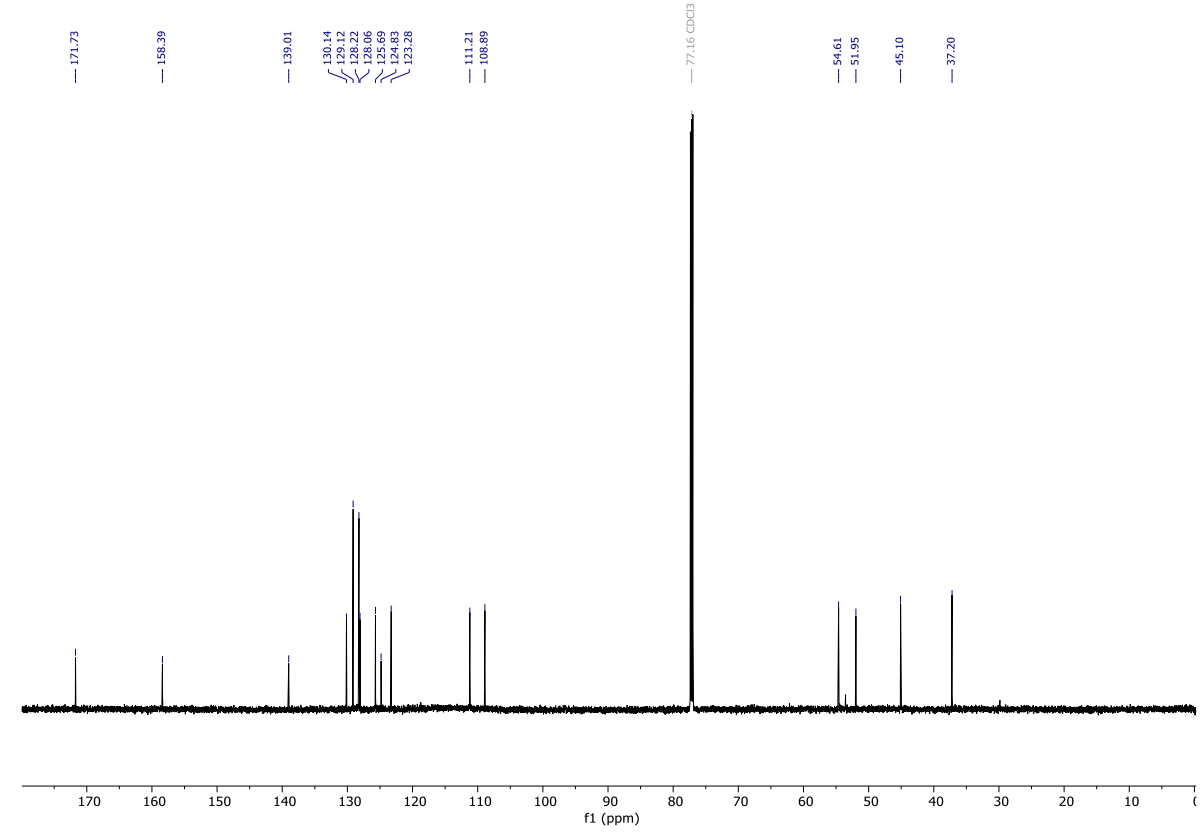
6. NMR spectra

(*S*)-Methyl 3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate 3a

^{1}H NMR

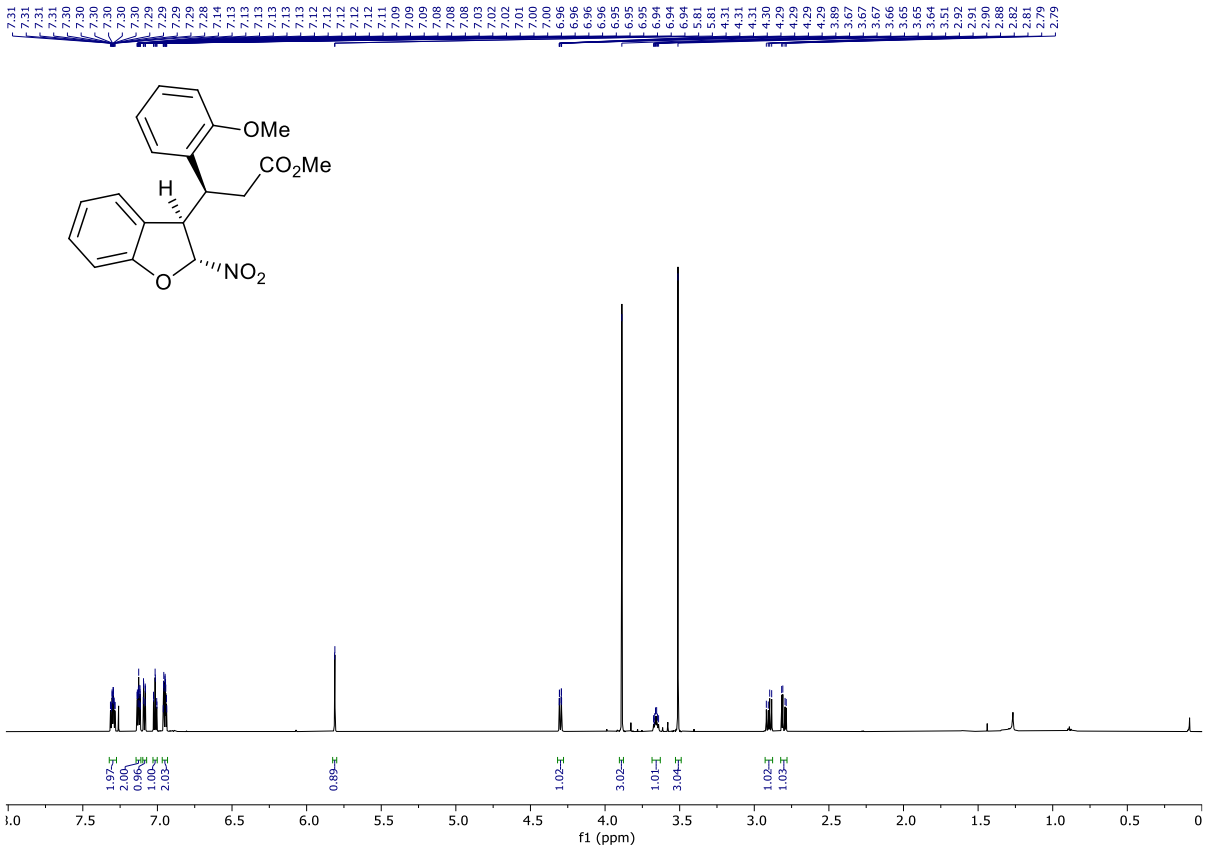


^{13}C NMR

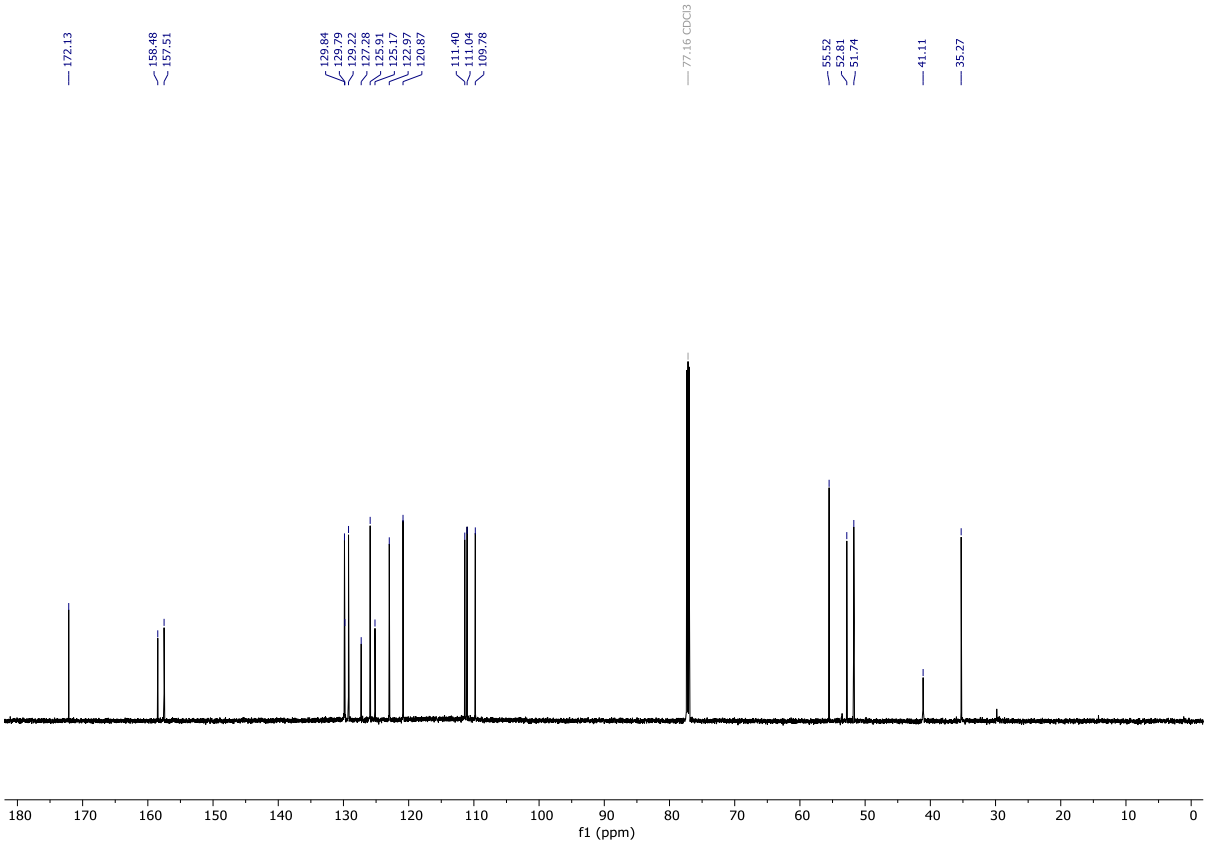


(*S*)-Methyl 3-(2-methoxyphenyl)-3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl)propanoate 3b

^{1}H NMR

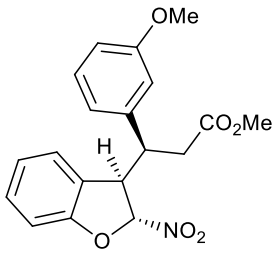


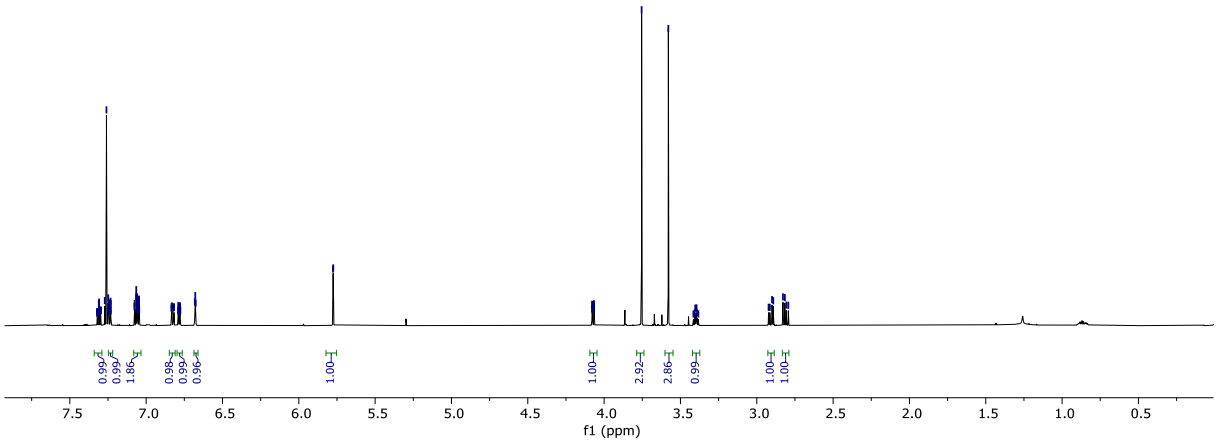
^{13}C NMR



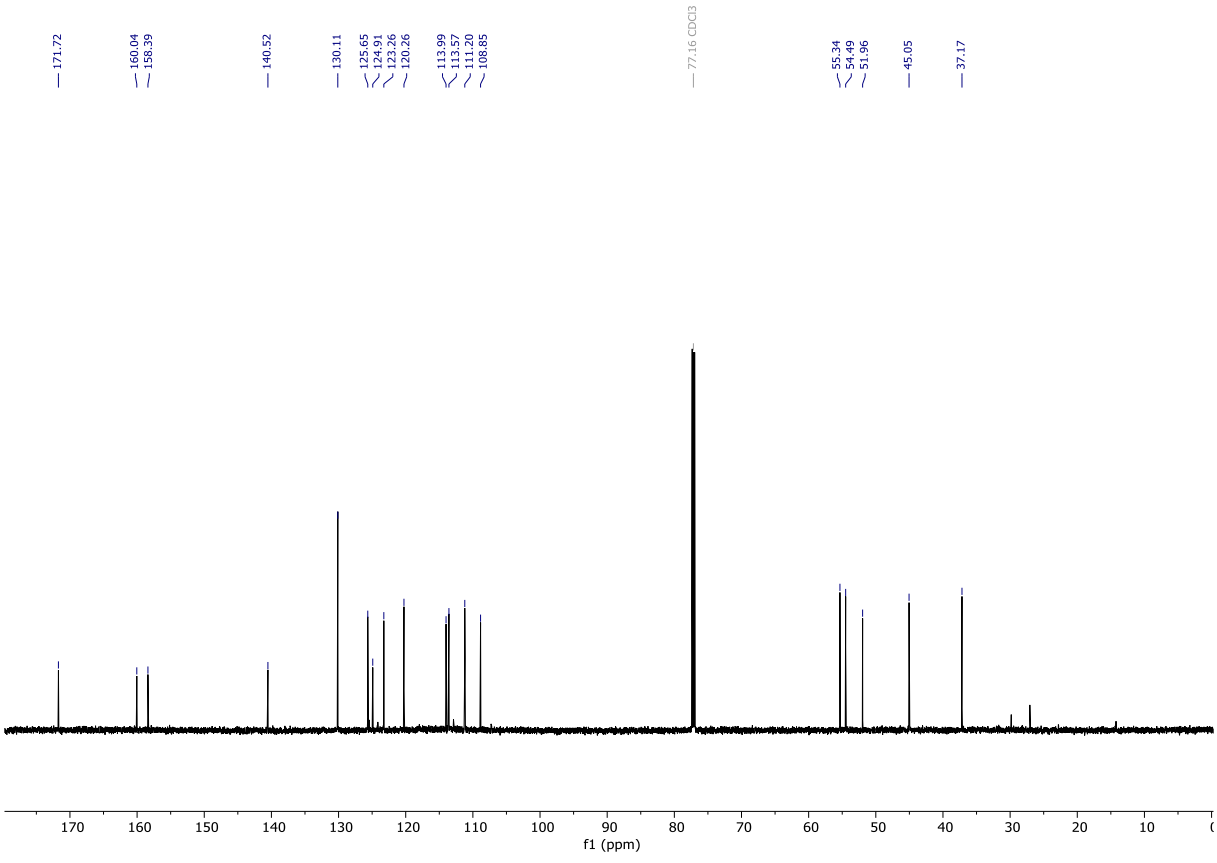
(*S*)-Methyl 3-(3-methoxyphenyl)-3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl)propanoate 3c

^{1}H NMR



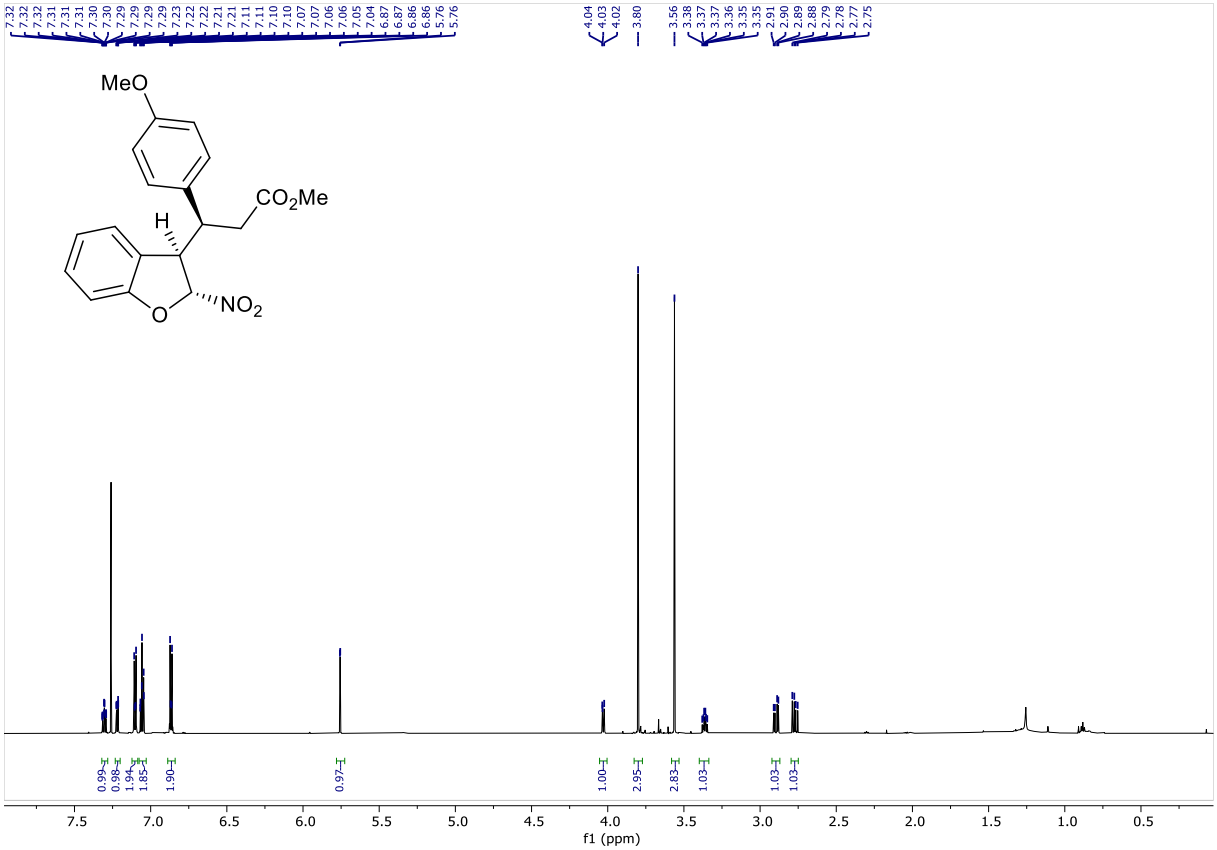


^{13}C NMR

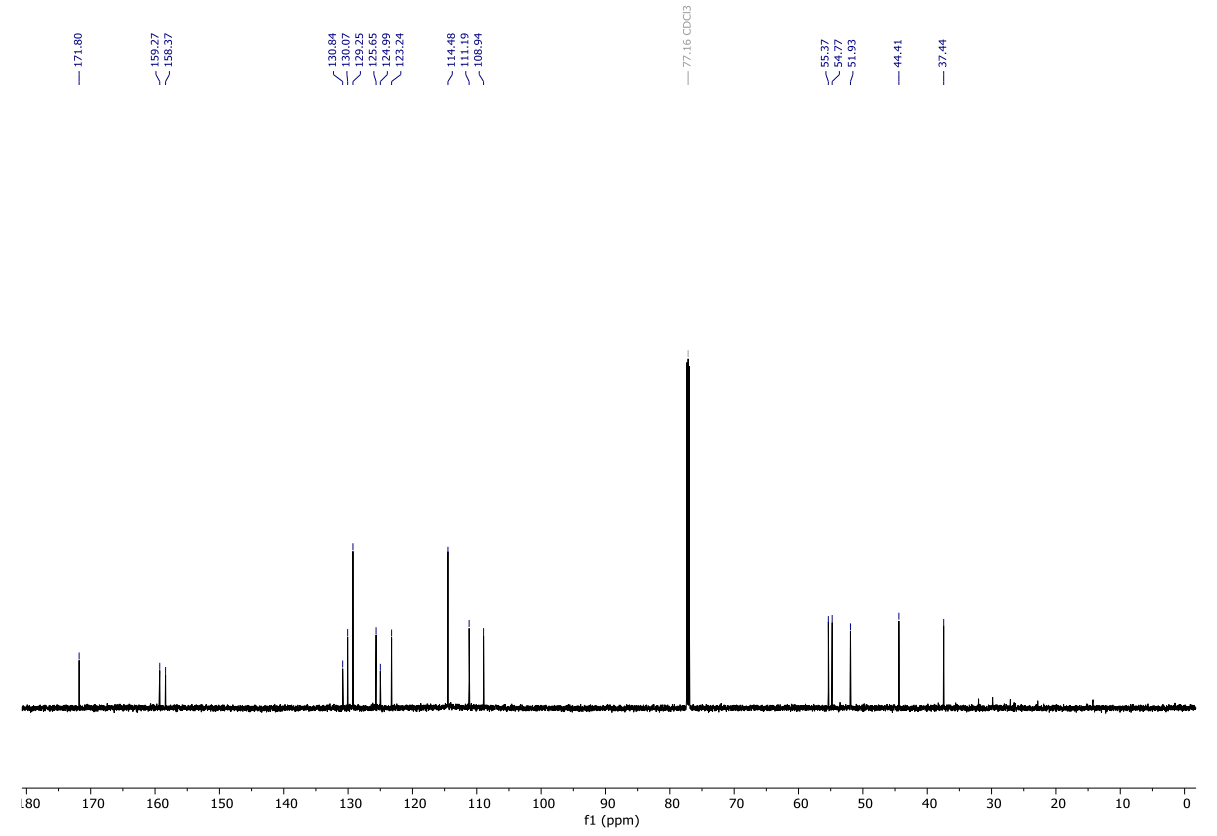


(*S*)-Methyl 3-(4-methoxyphenyl)-3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl) propanoate 3d

^{1}H NMR

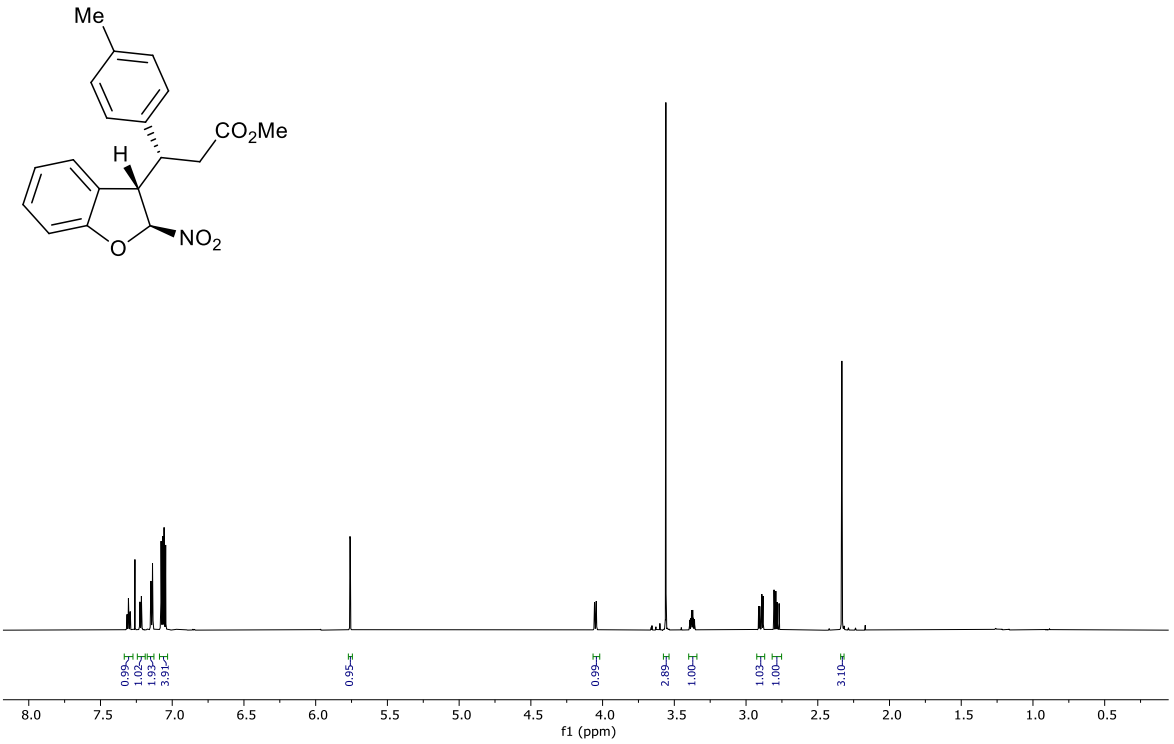


^{13}C NMR

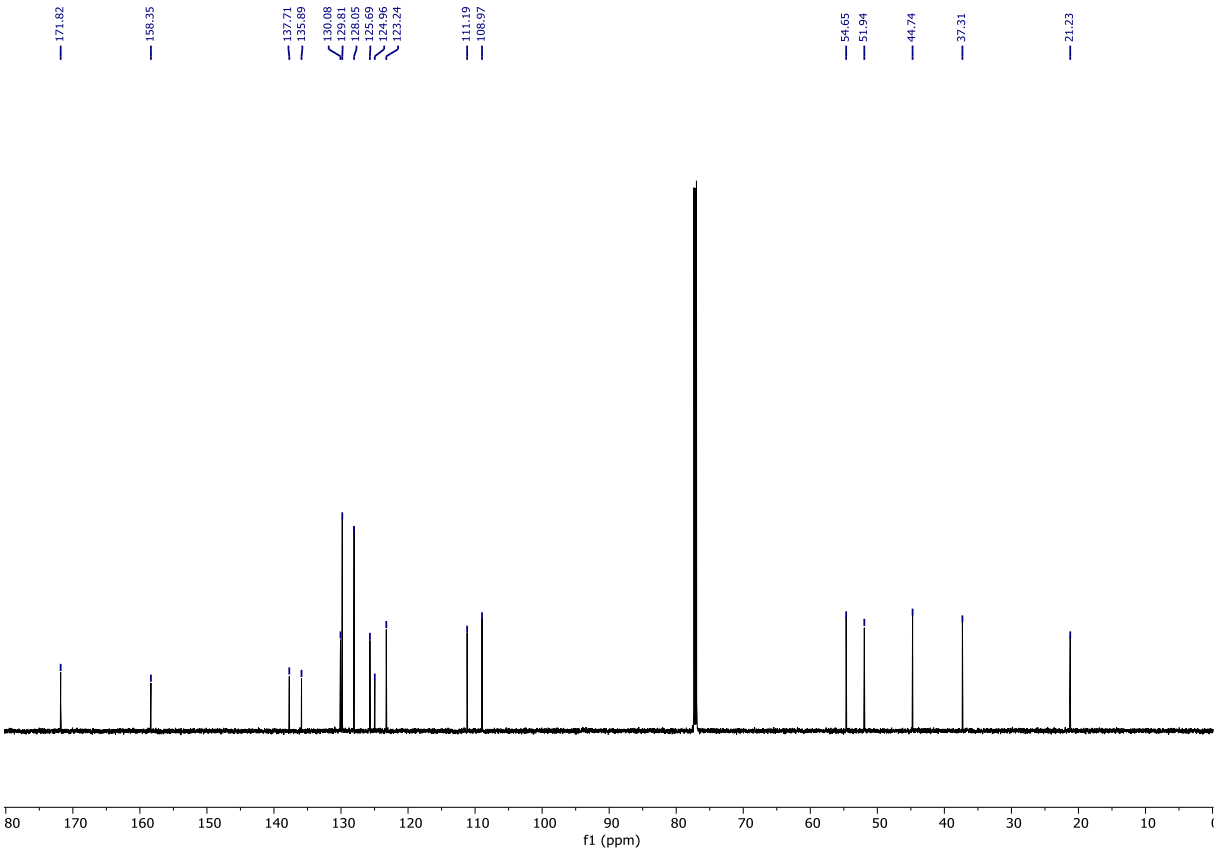


(*R*)-Methyl 3-((2*S*,3*S*)-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-(p-tolyl)propanoate 3e

^{1}H NMR



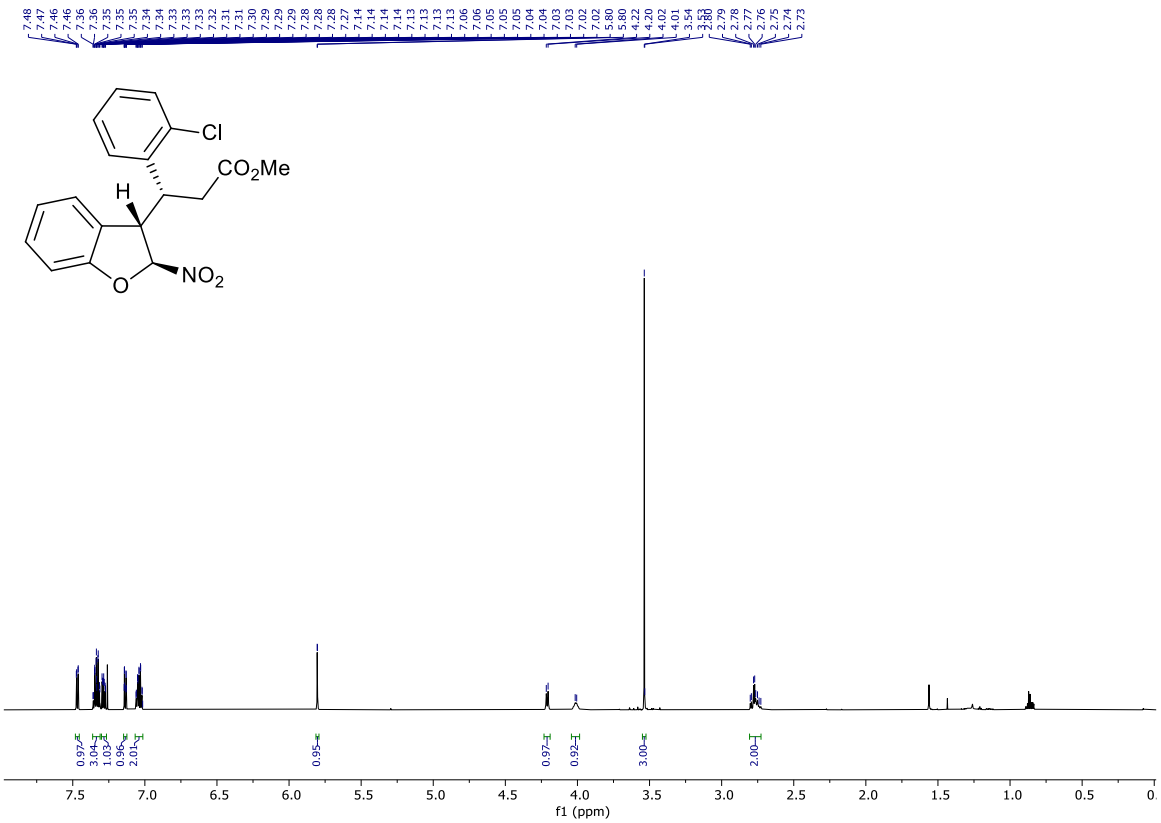
^{13}C NMR



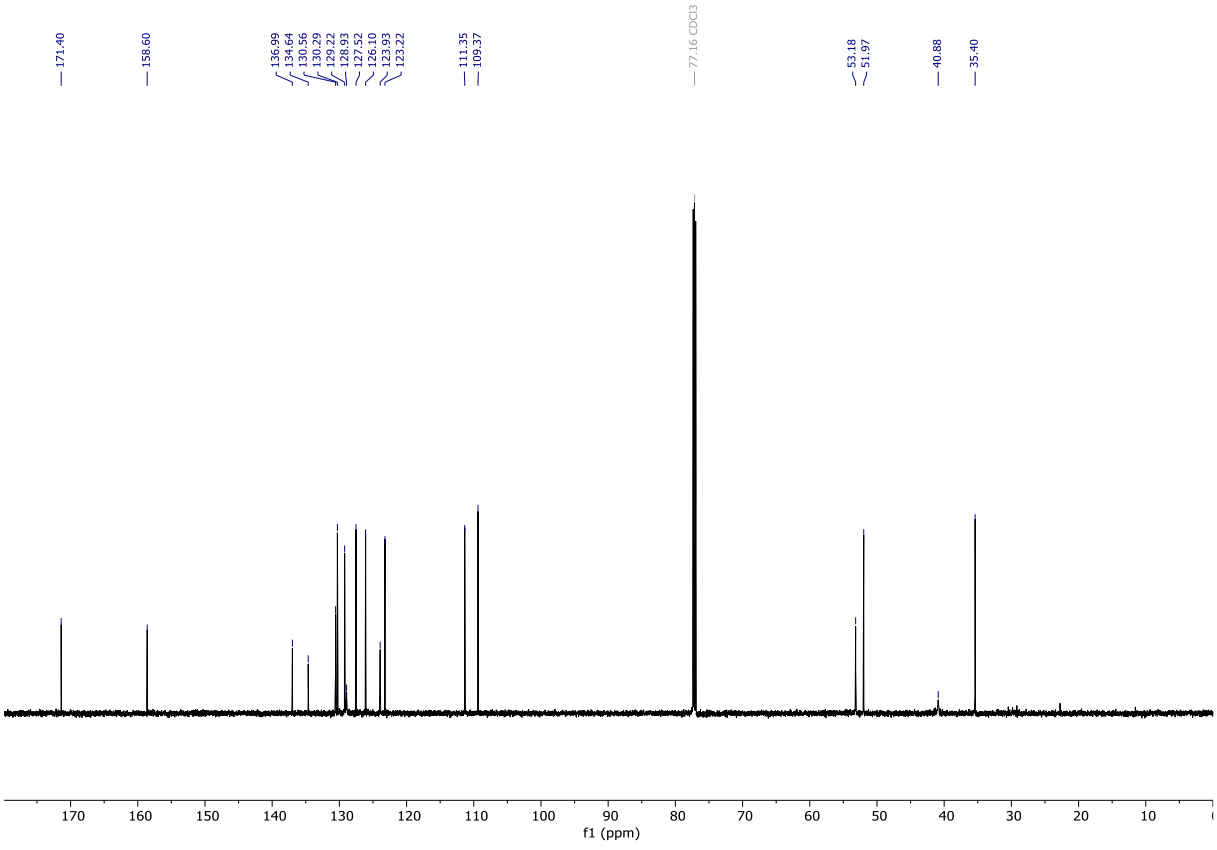
(*R*)-Methyl 3-(2-chlorophenyl)-3-((2*S*,3*S*)-2-nitro-2,3-dihydrobenzofuran-3-yl) propanoate

3f

^{1}H NMR



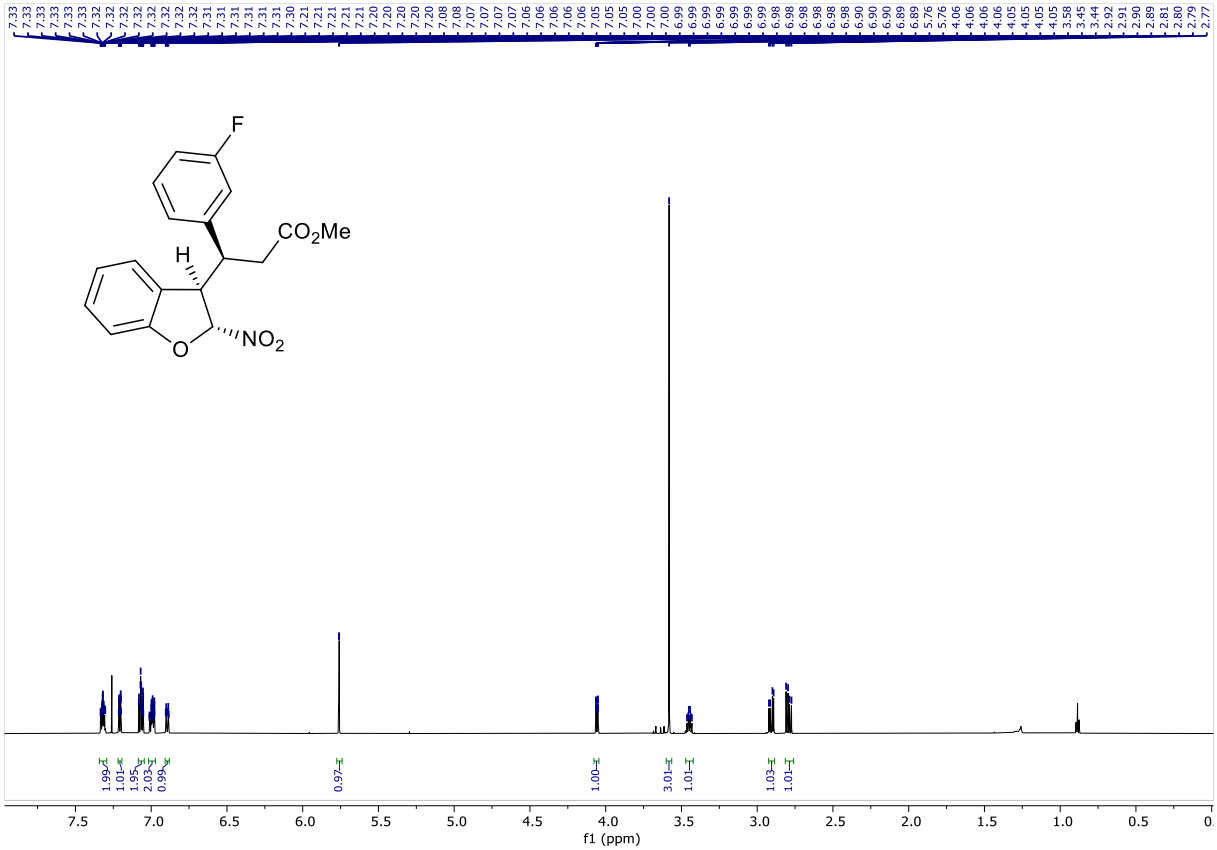
^{13}C NMR



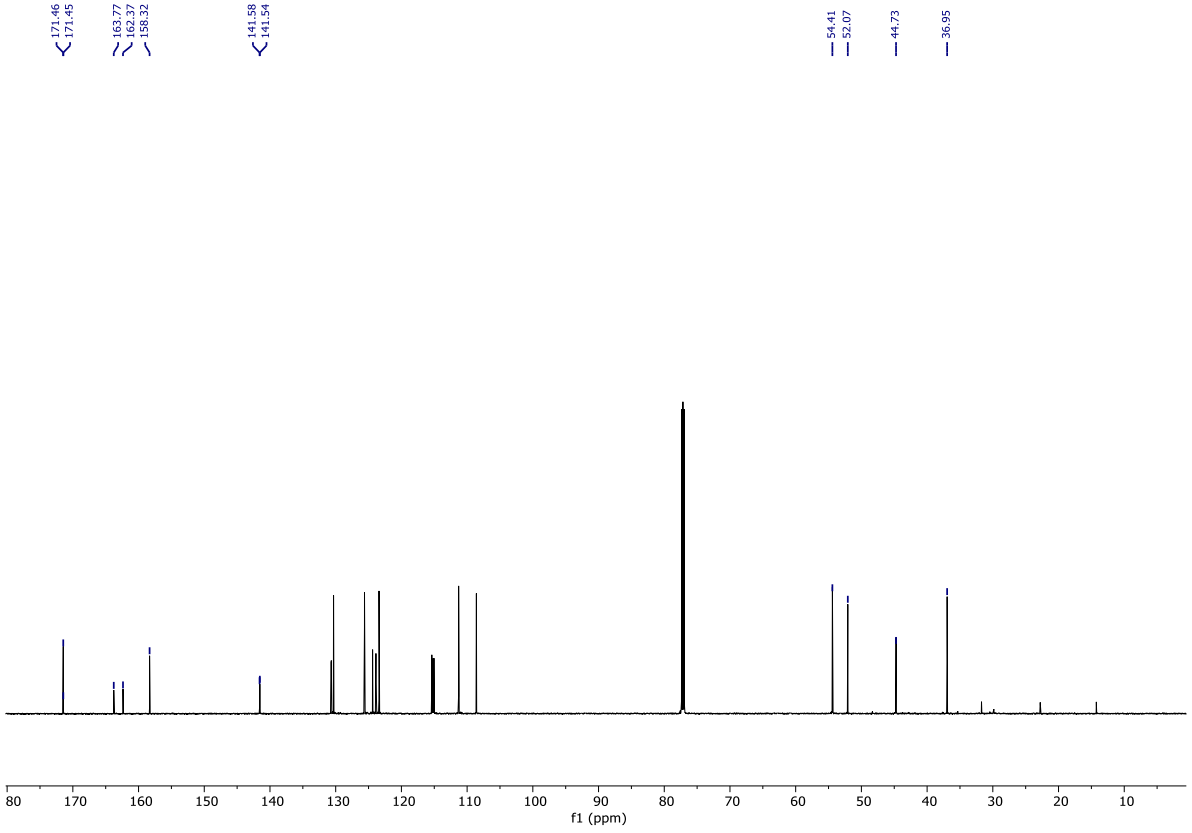
(*S*)-Methyl 3-(3-fluorophenyl)-3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl) propanoate

3g

^{1}H NMR



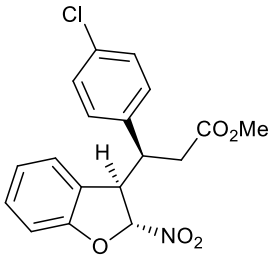
^{13}C NMR

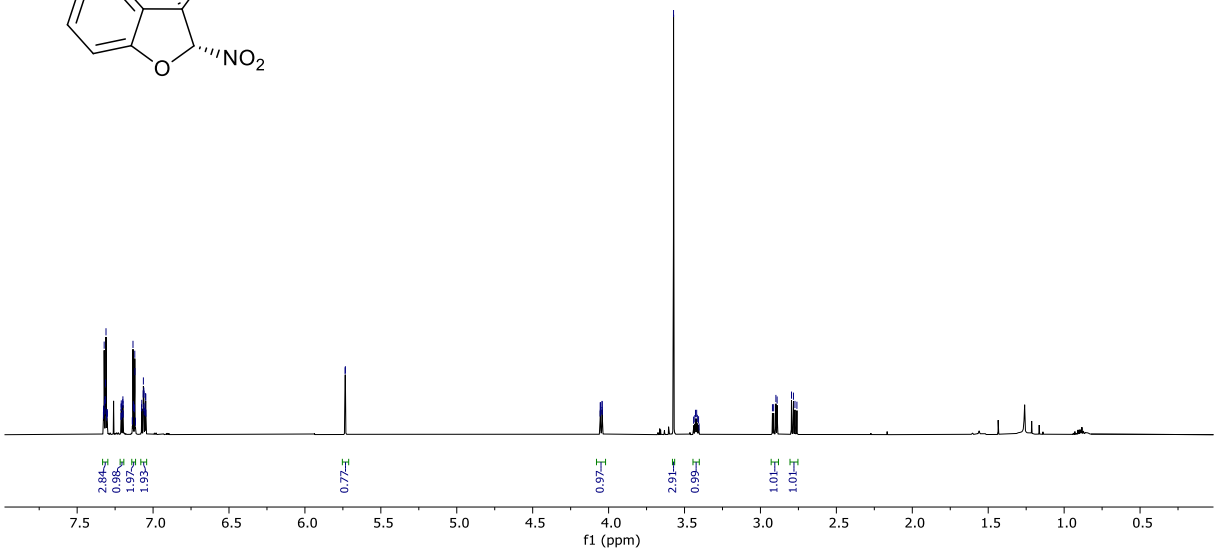


(*S*)-Methyl 3-(4-chlorophenyl)-3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl) propanoate

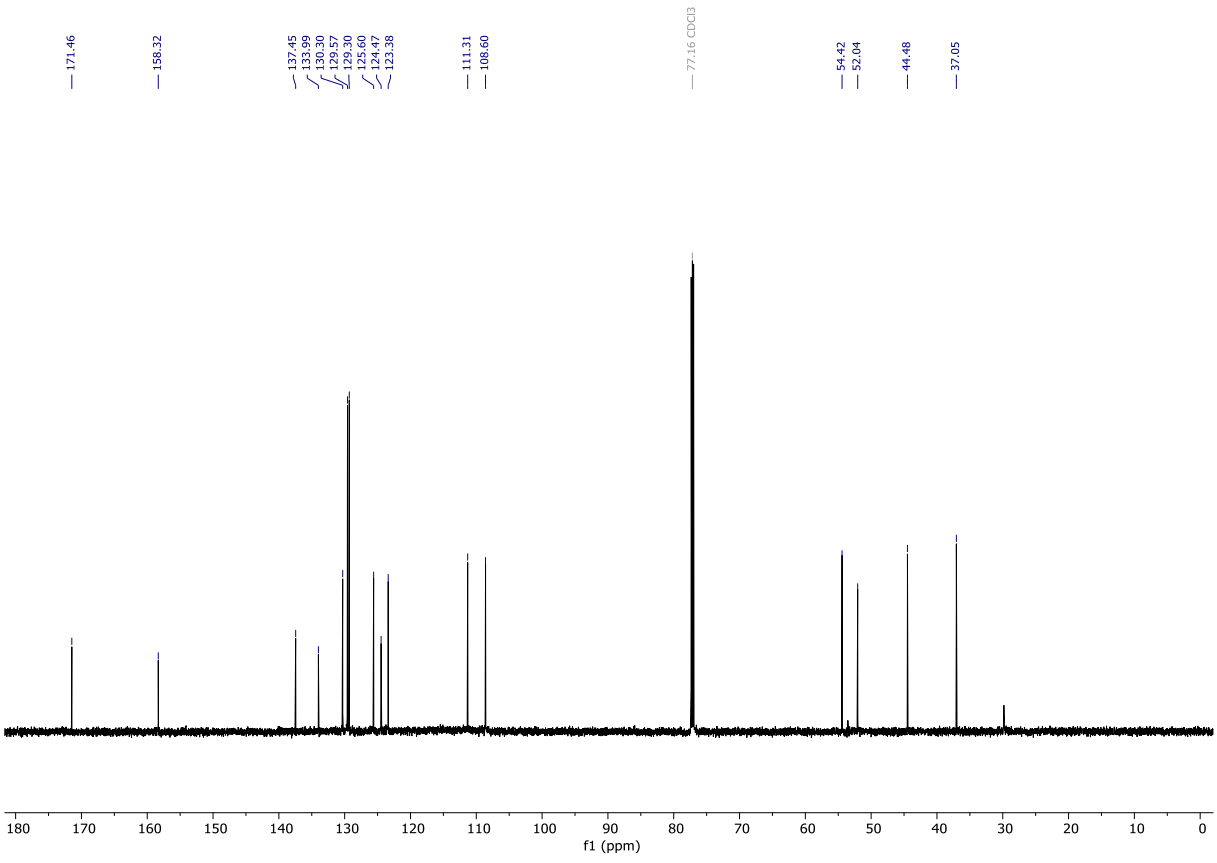
3h

^{1}H NMR



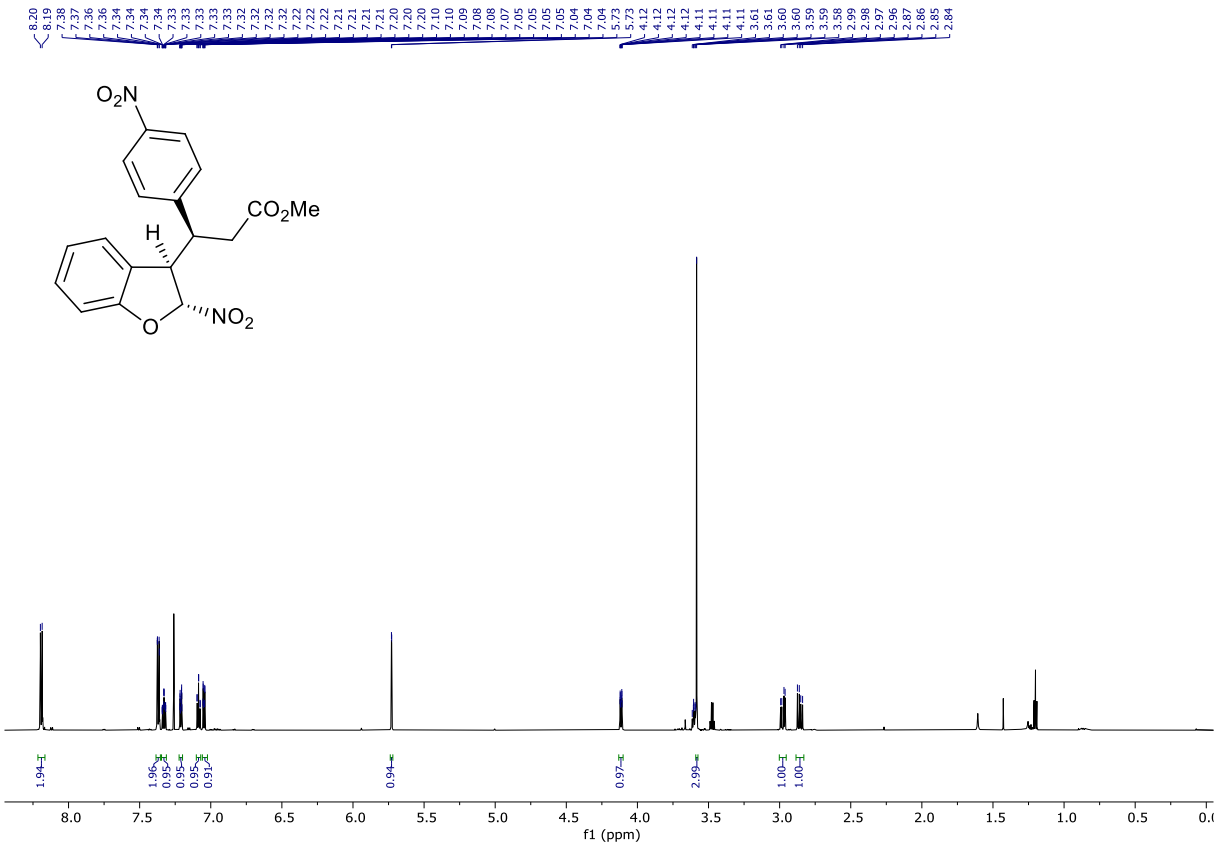


^{13}C NMR

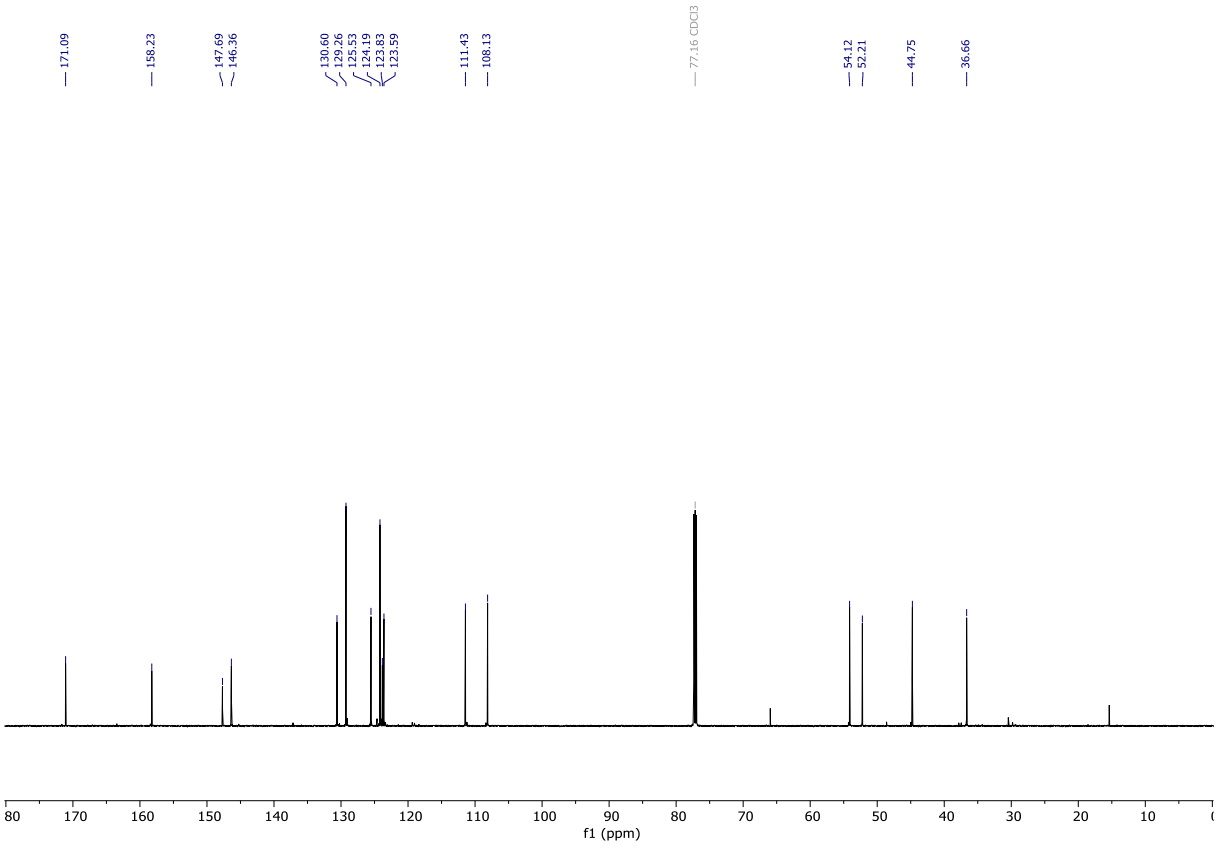


(*S*)-Methyl 3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-(4-nitrophenyl)propanoate 3i

^{1}H NMR



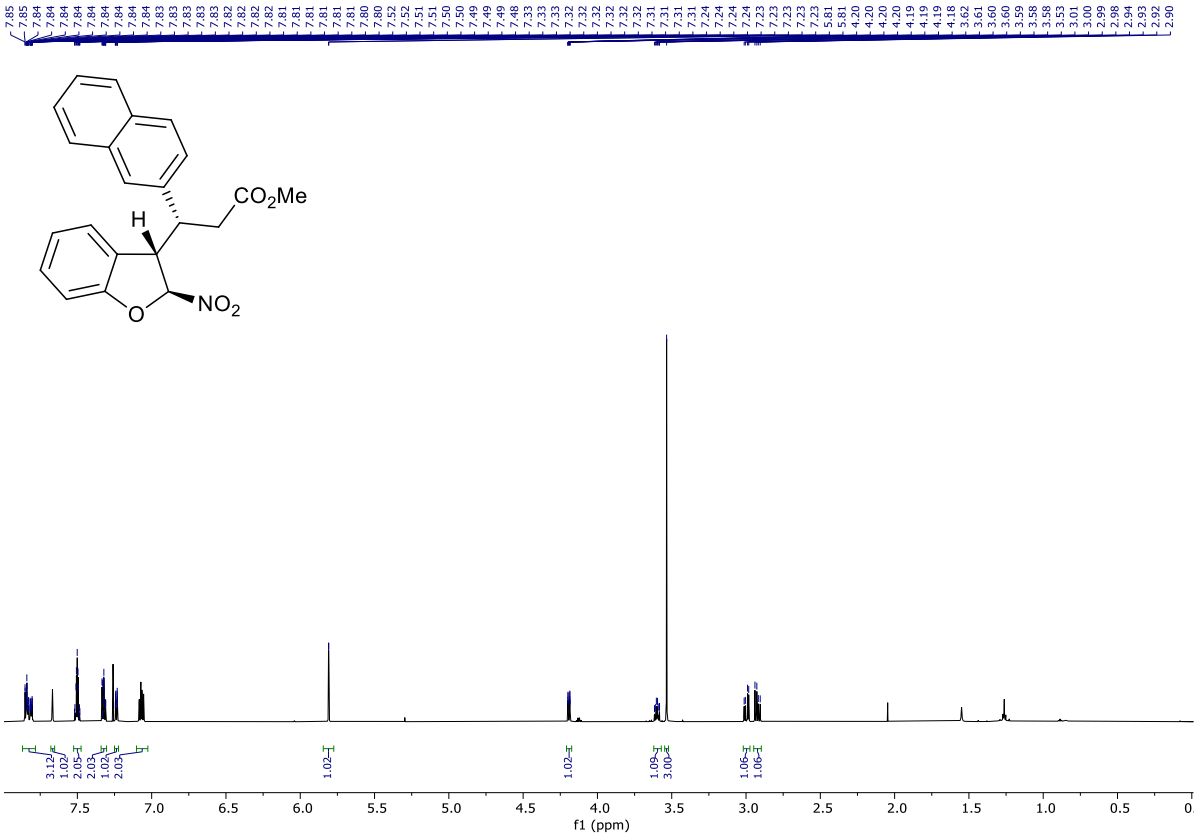
^{13}C NMR



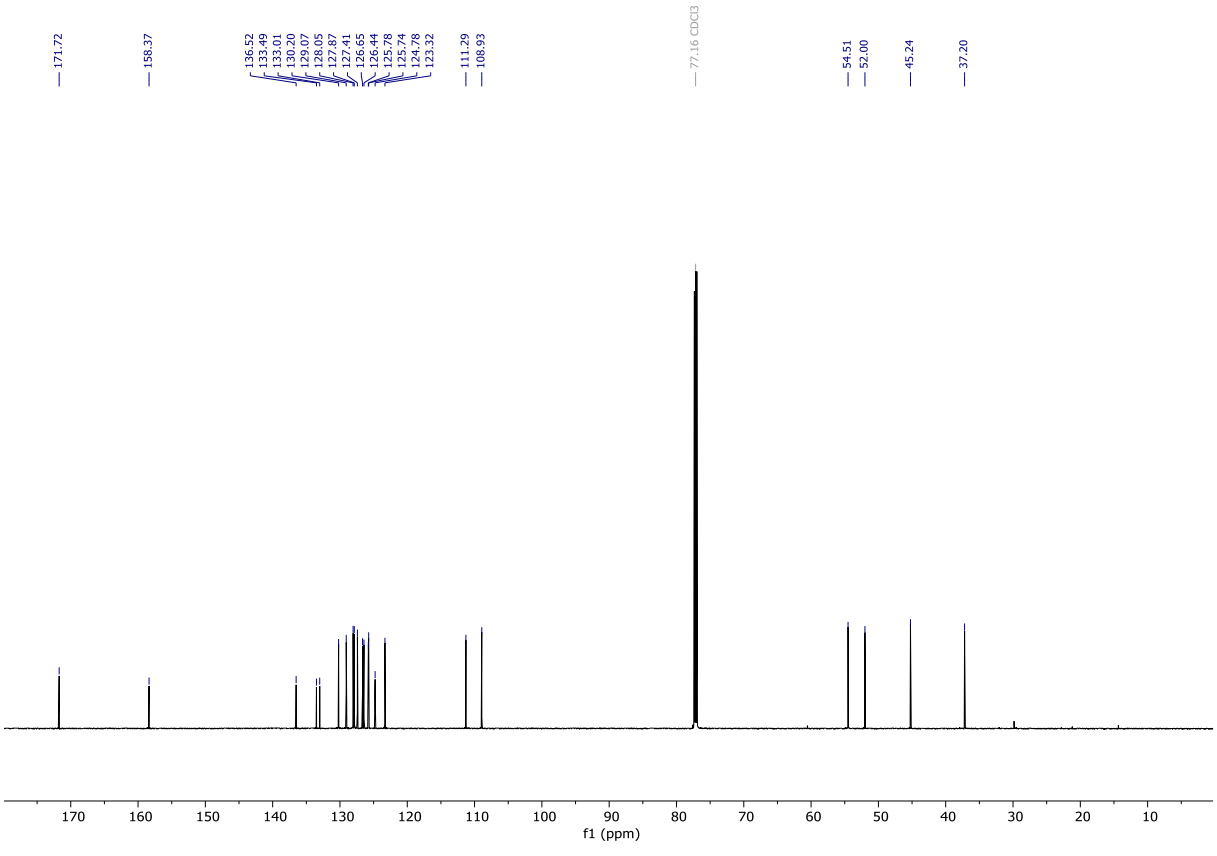
(*R*)-Methyl 3-(naphthalen-2-yl)-3-((2*S*,3*S*)-2-nitro-2,3-dihydrobenzofuran-3-yl) propanoate

3j

^{1}H NMR

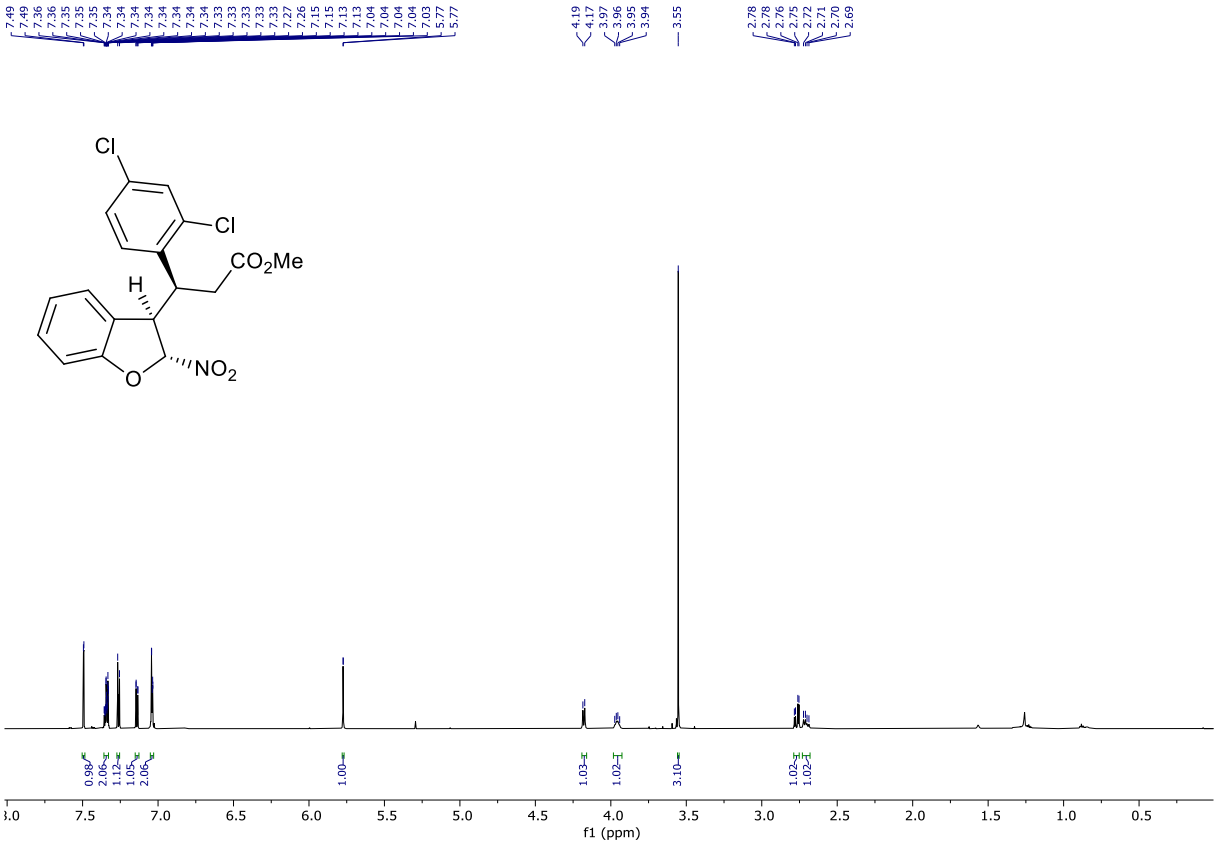


^{13}C NMR

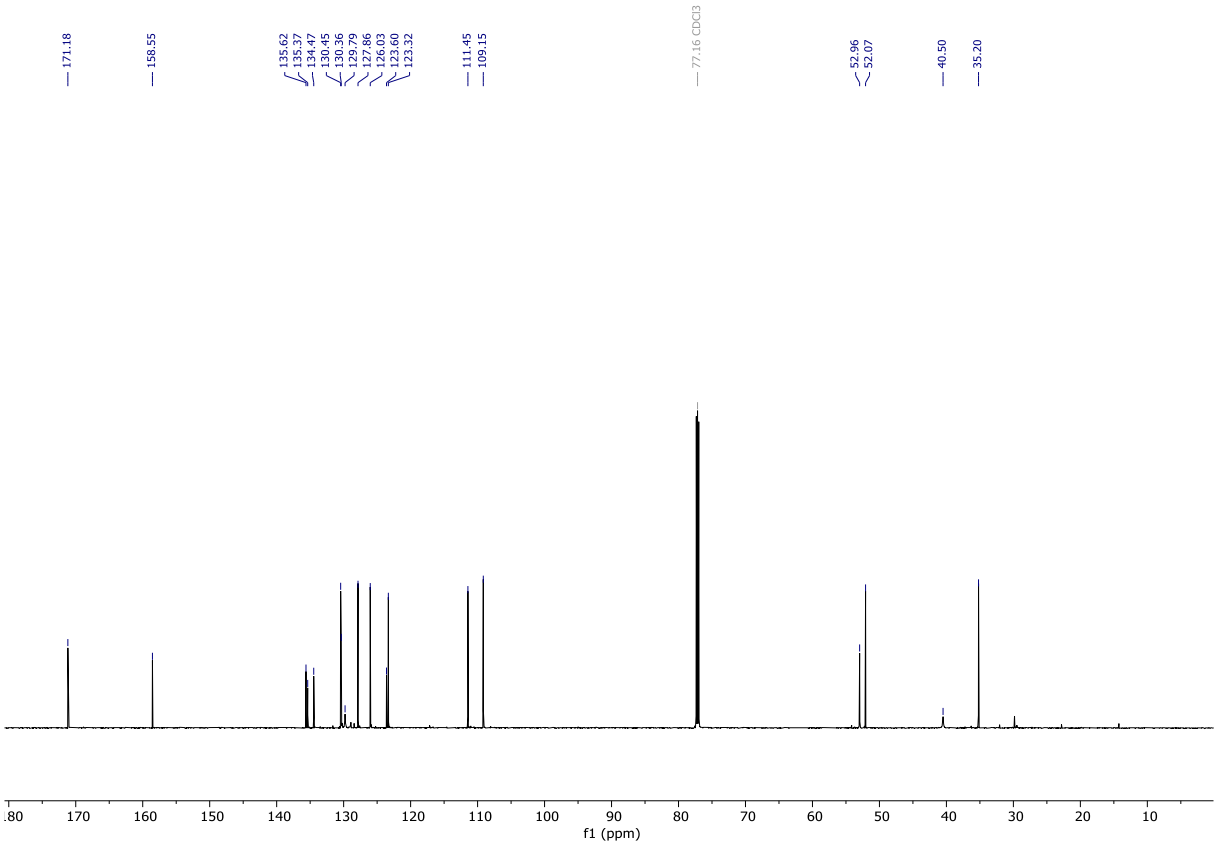


(*S*)-Methyl 3-(2,4-dichlorophenyl)-3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl) propanoate 3k

^{1}H NMR

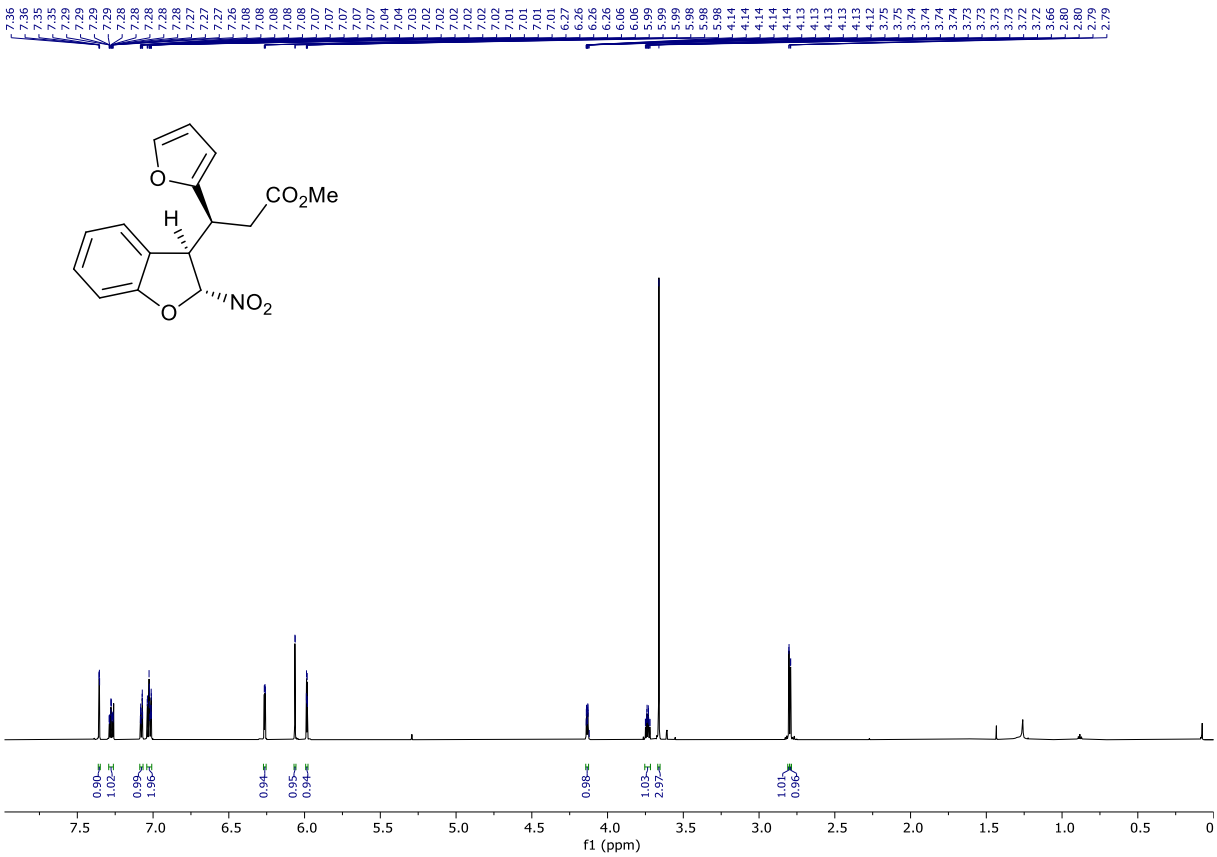


^{13}C NMR



(*S*)-Methyl 3-(furan-2-yl)-3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl) propanoate 3l

^{1}H NMR



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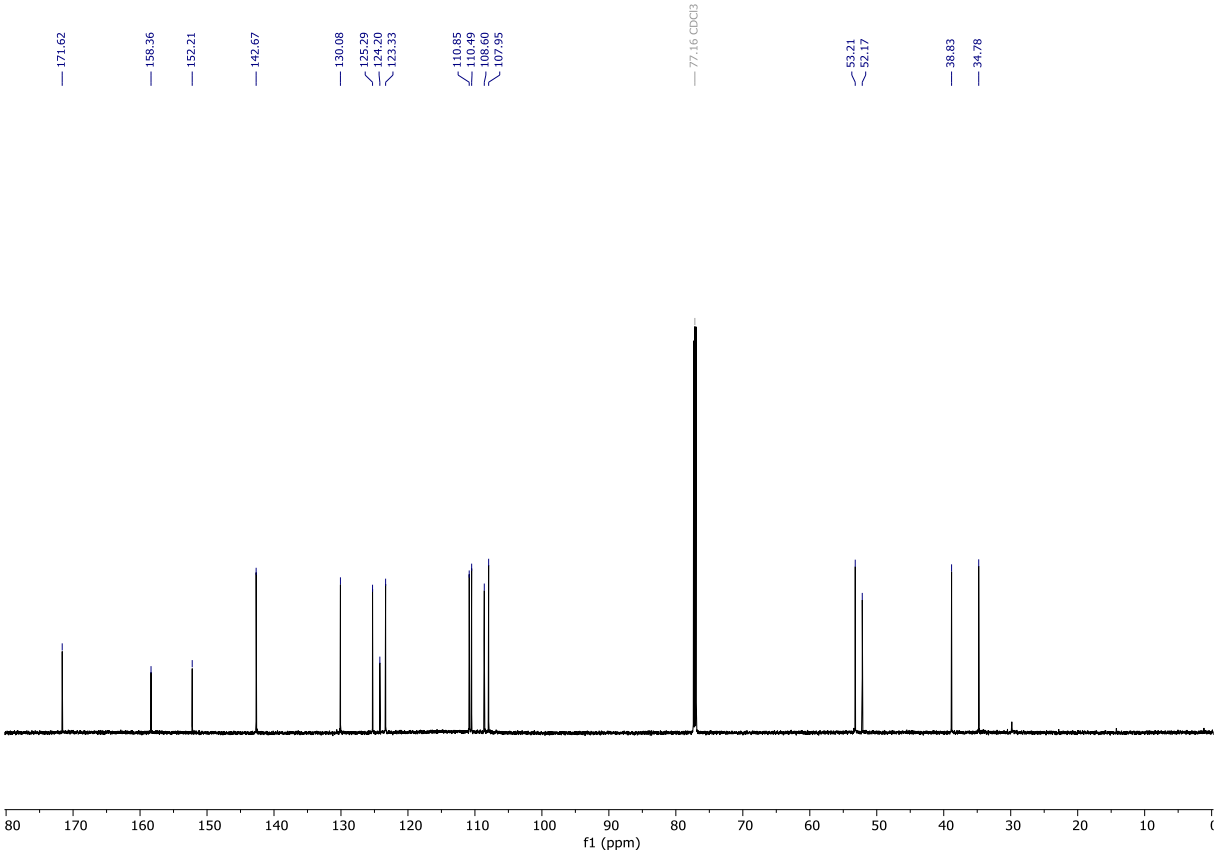
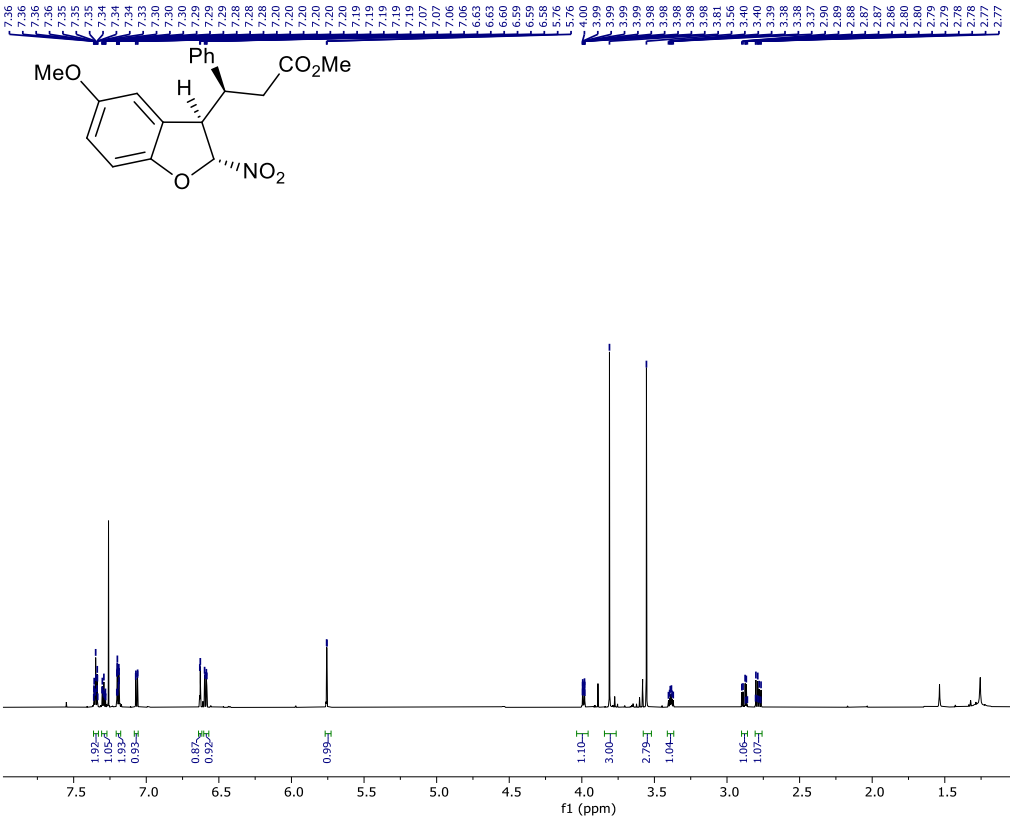


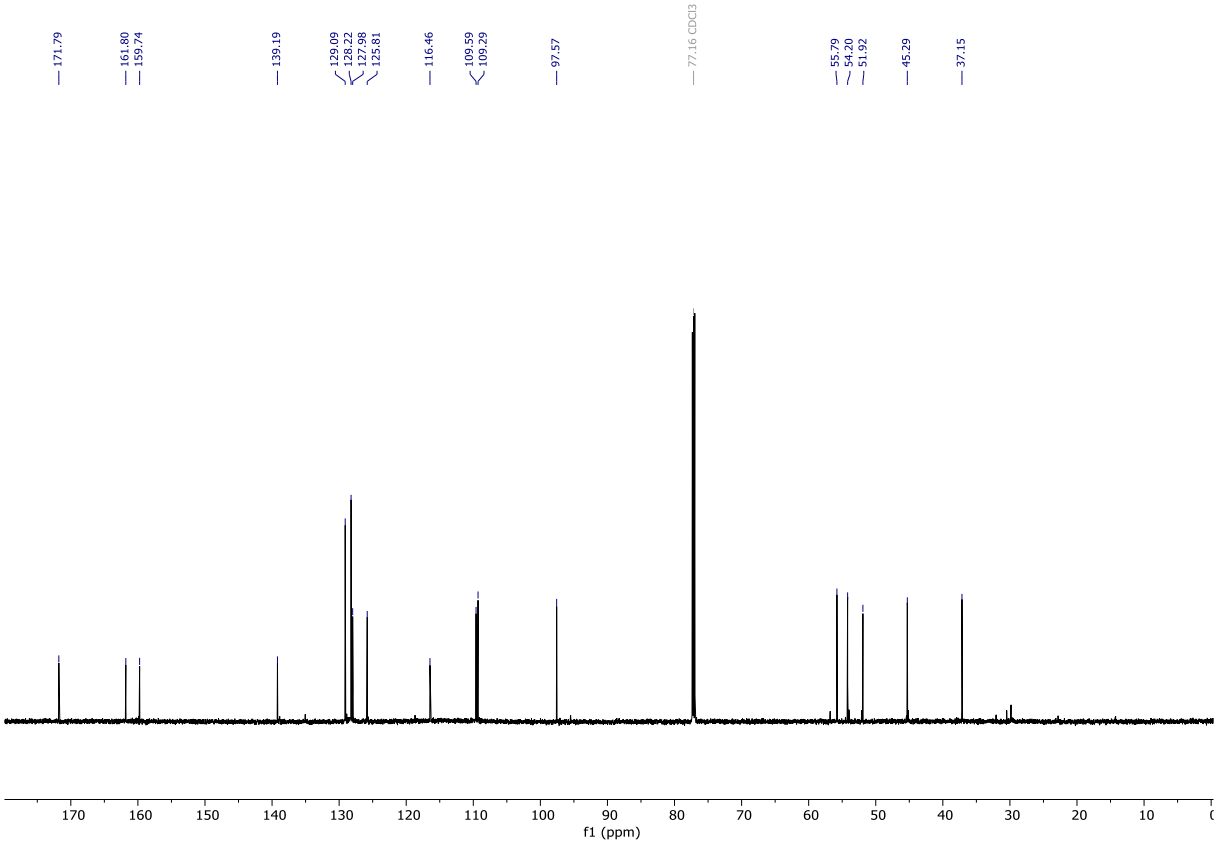
(*S*)-Methyl 3-((2*R*,3*R*)-5-methoxy-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate

3m

^{1}H NMR



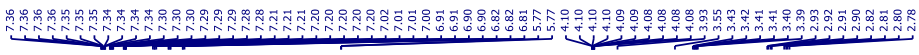
^{13}C NMR

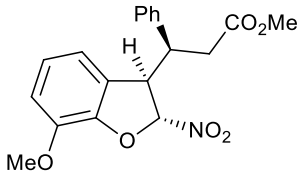


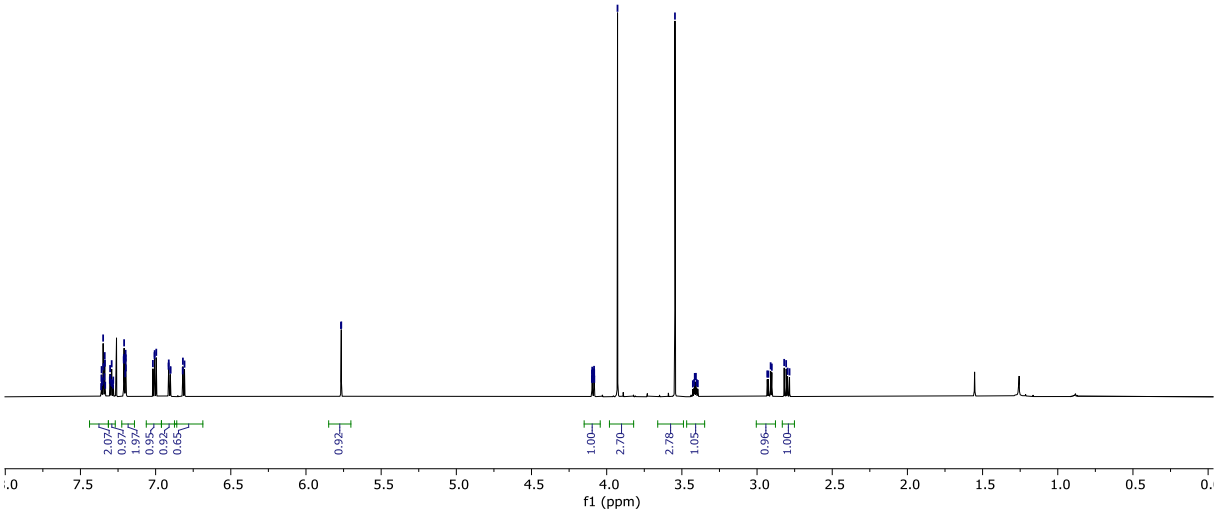
(*S*)-Methyl 3-((2*R*,3*R*)-7-methoxy-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate

3n

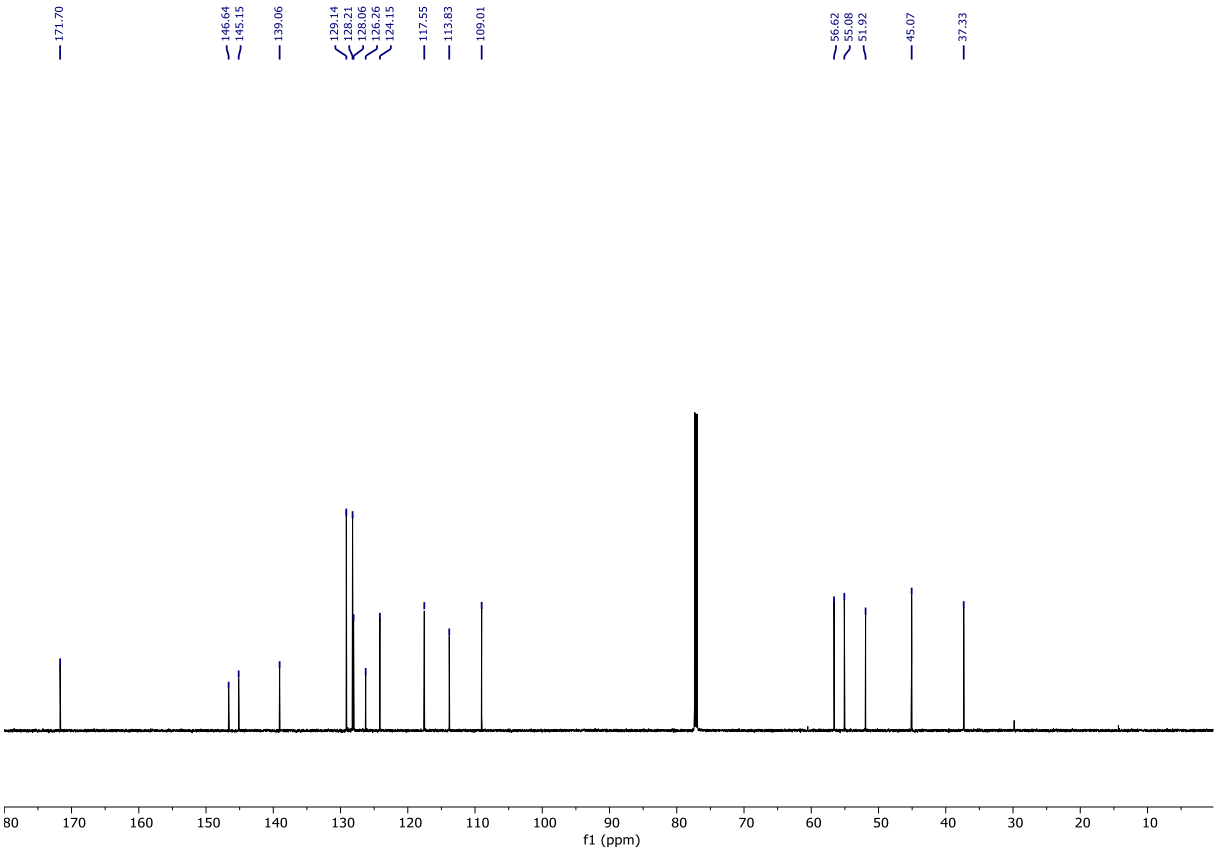
^{1}H NMR





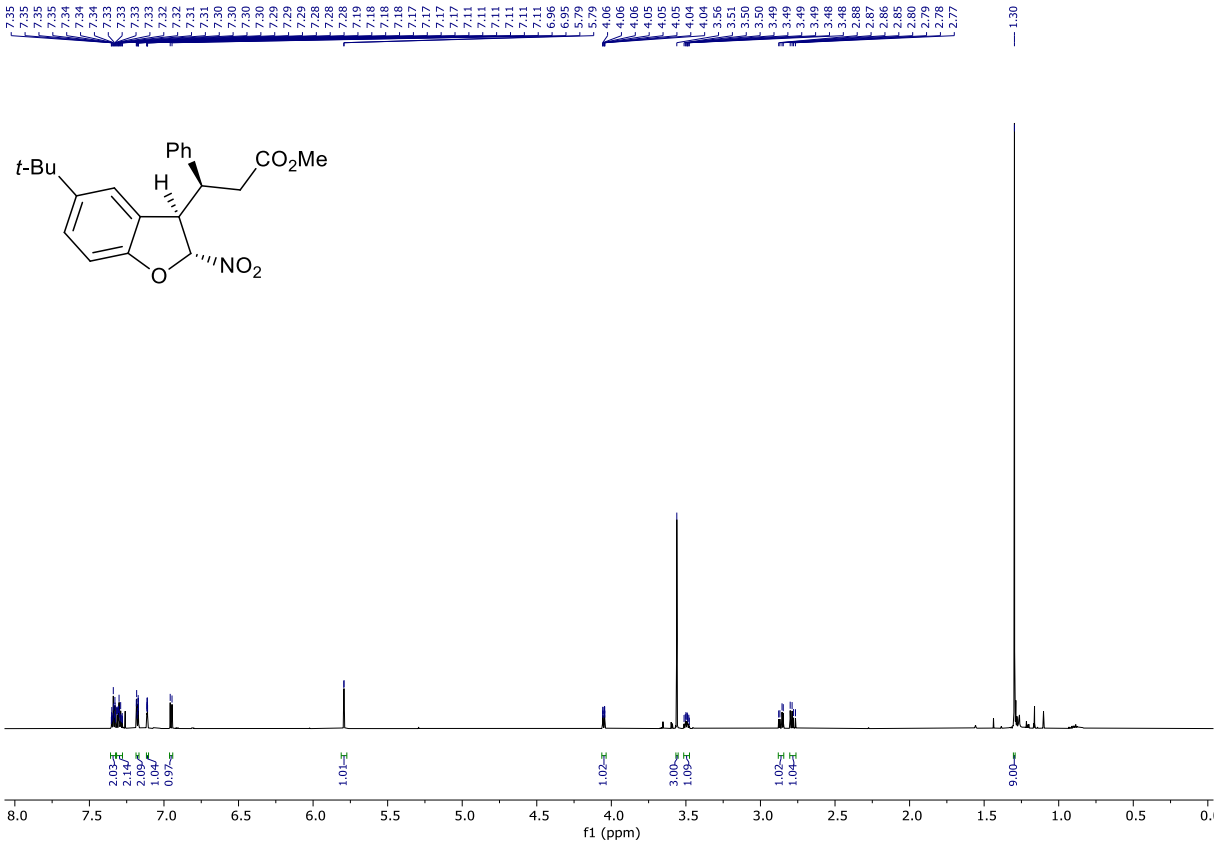


^{13}C NMR

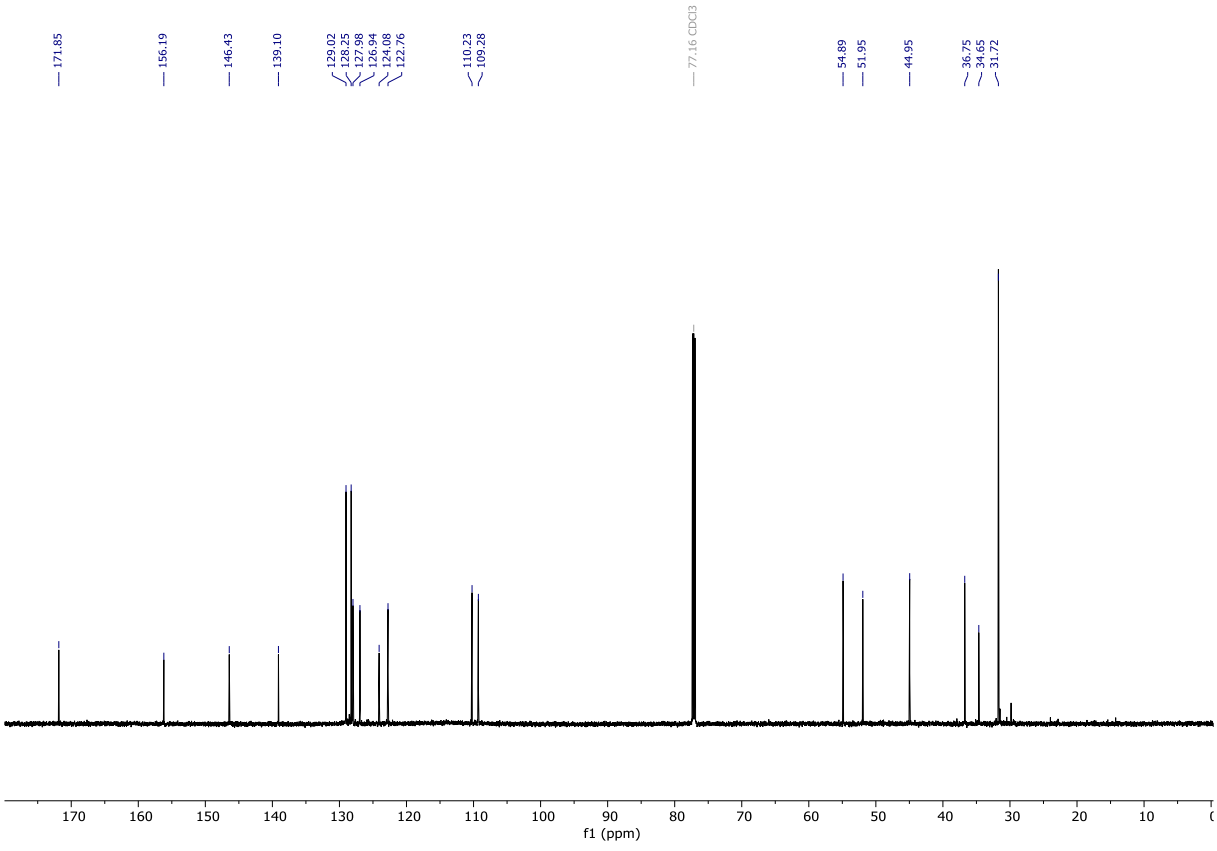


(*S*)-Methyl 3-((2*R*,3*R*)-5-(*tert*-butyl)-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate 3o

^{1}H NMR



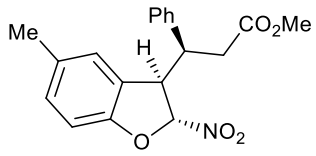
^{13}C NMR



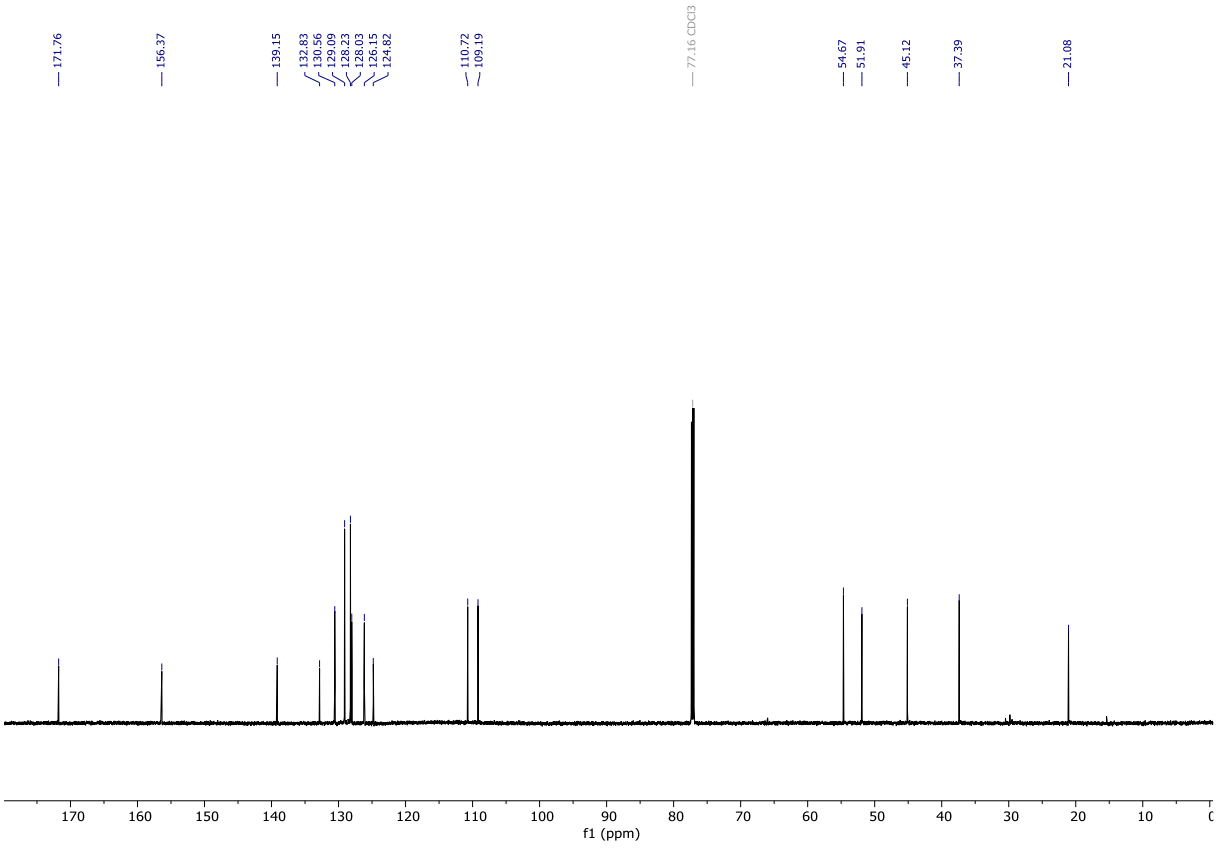
(*S*)-Methyl 3-((2*R*,3*R*)-5-methyl-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate

3p

^{1}H NMR



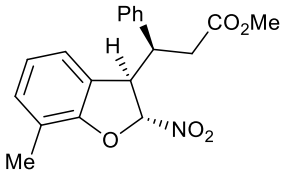
^{13}C NMR

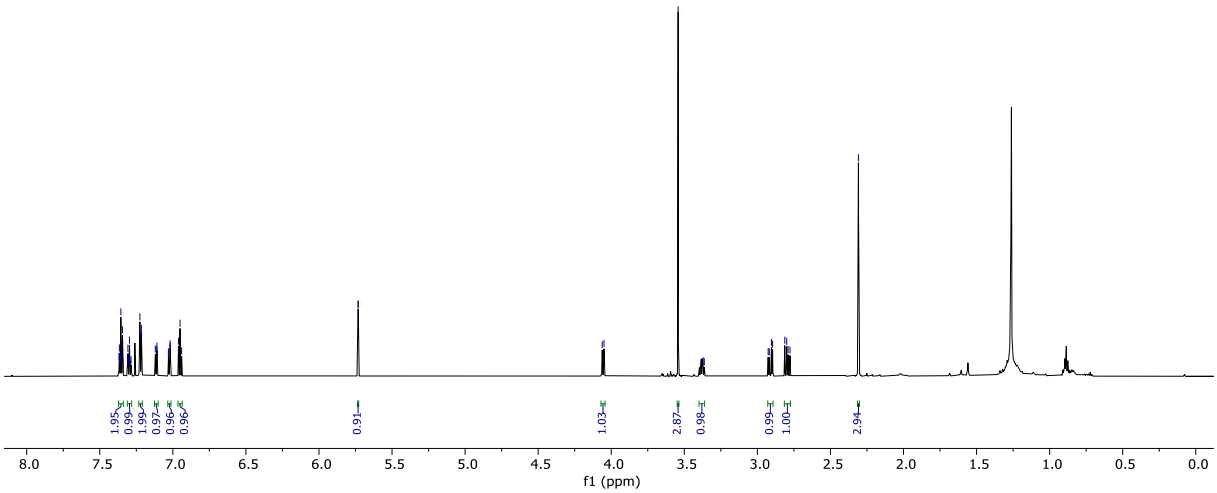


(*S*)-Methyl 3-((2*R*,3*R*)-7-methyl-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate

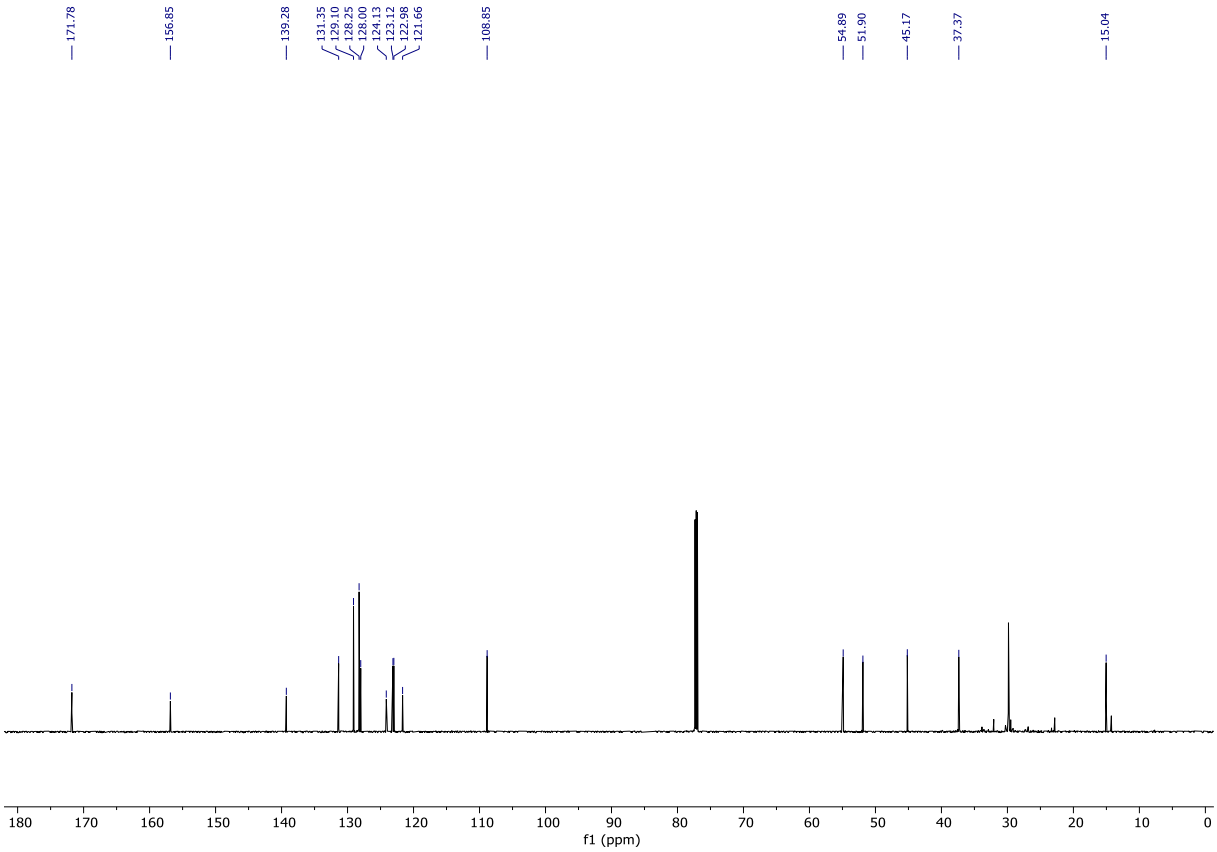
3q

^{1}HNMR



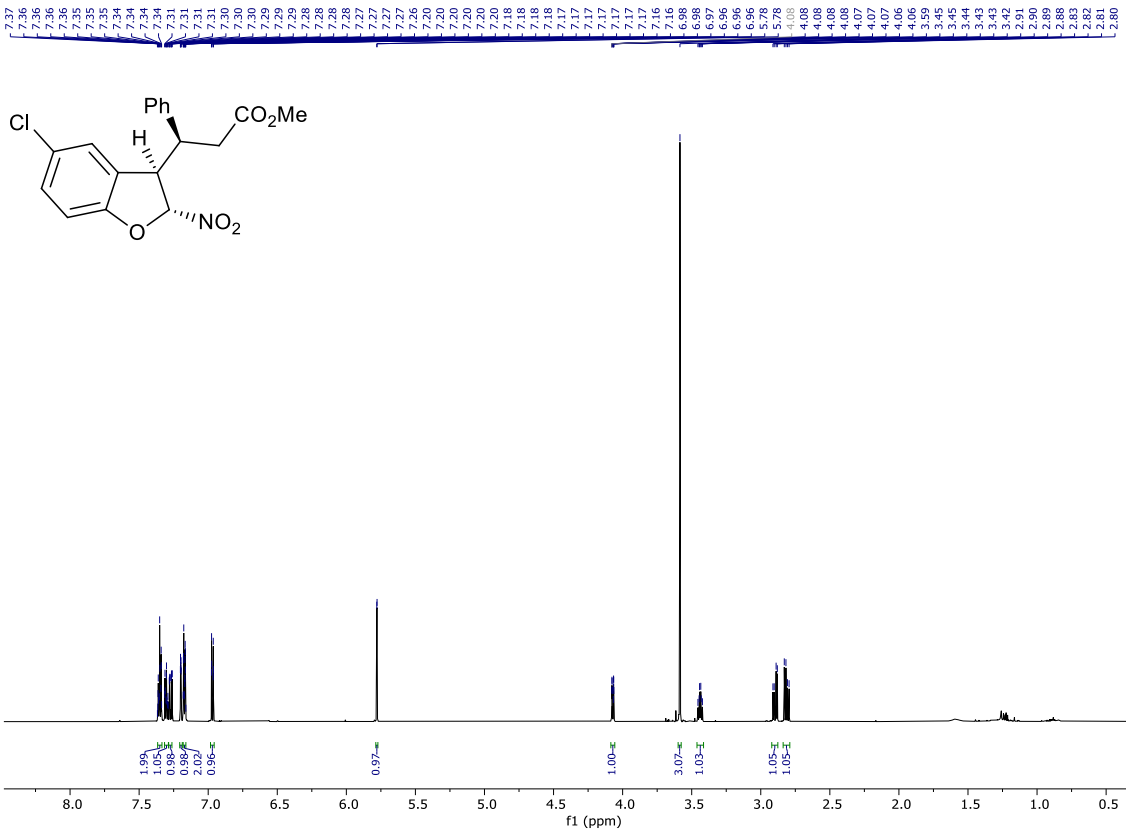


^{13}C NMR

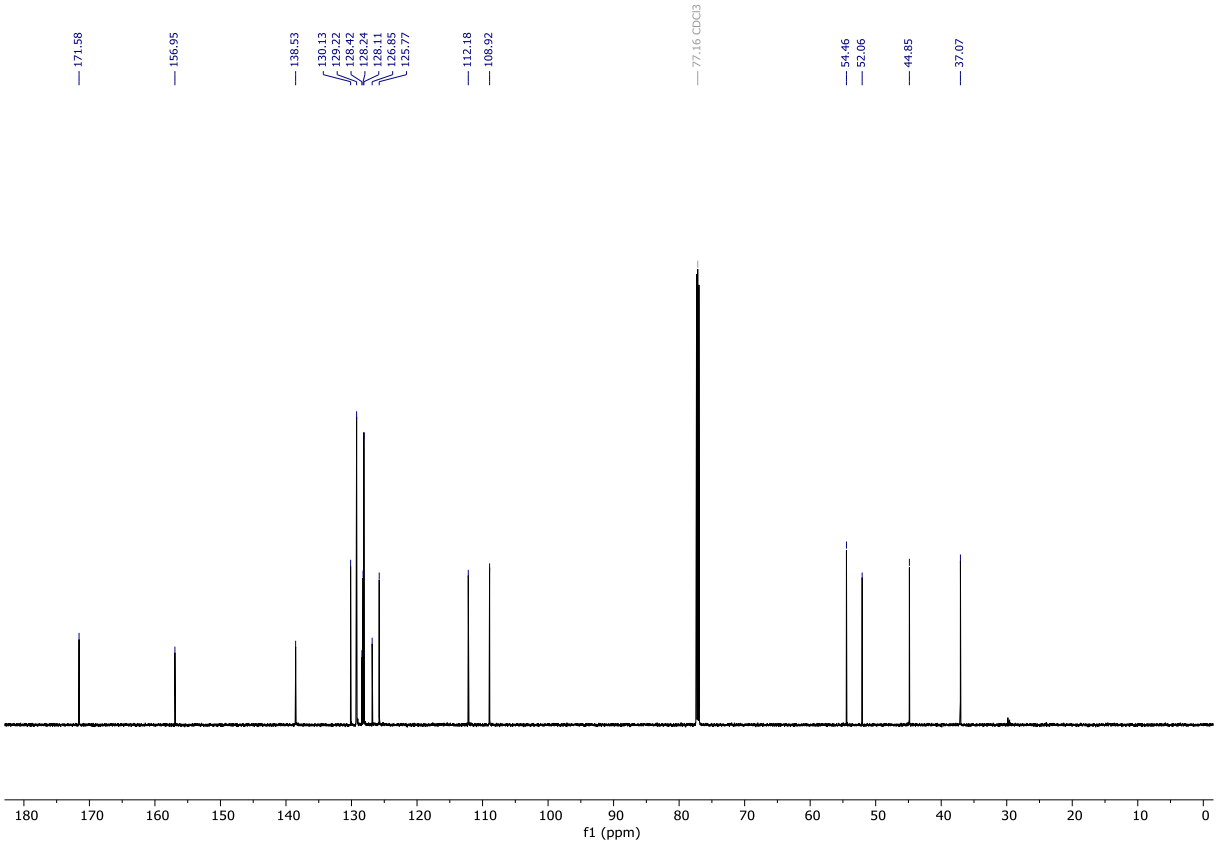


(*S*)-Methyl 3-((2*R*,3*R*)-5-chloro-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate 3r

^{1}H NMR

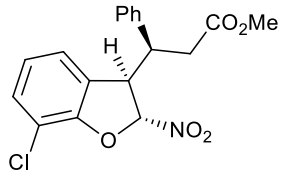


^{13}C NMR

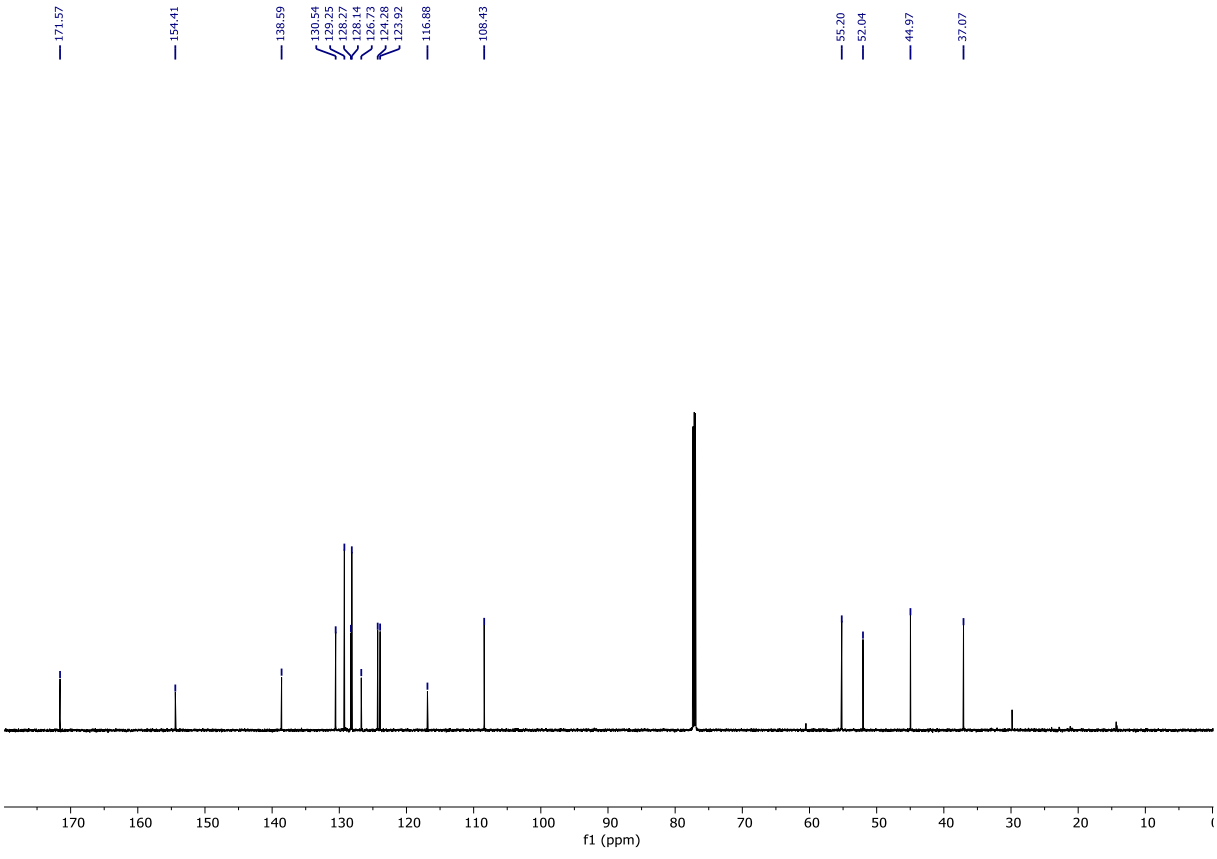


(*S*)-Methyl 3-((2*R*,3*R*)-7-chloro-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate 3s

^{1}H NMR

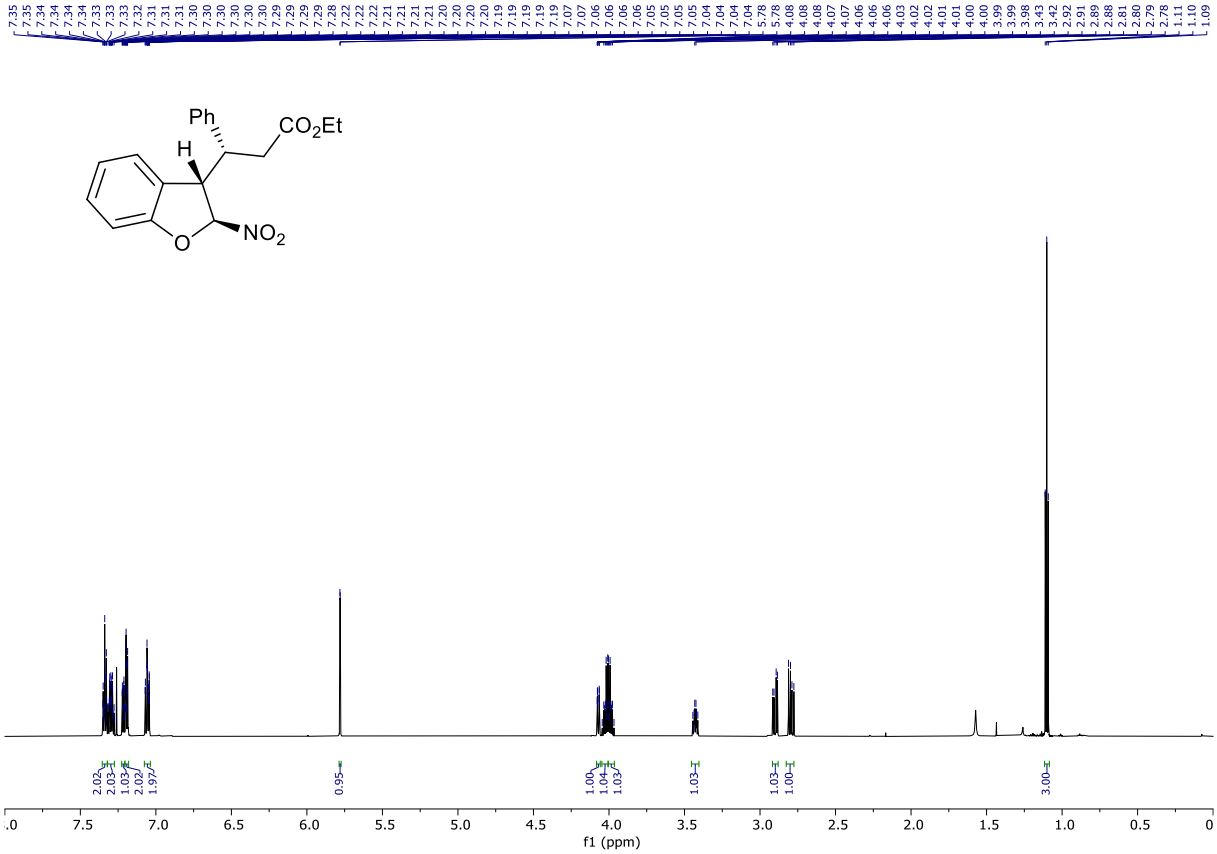


^{13}C NMR

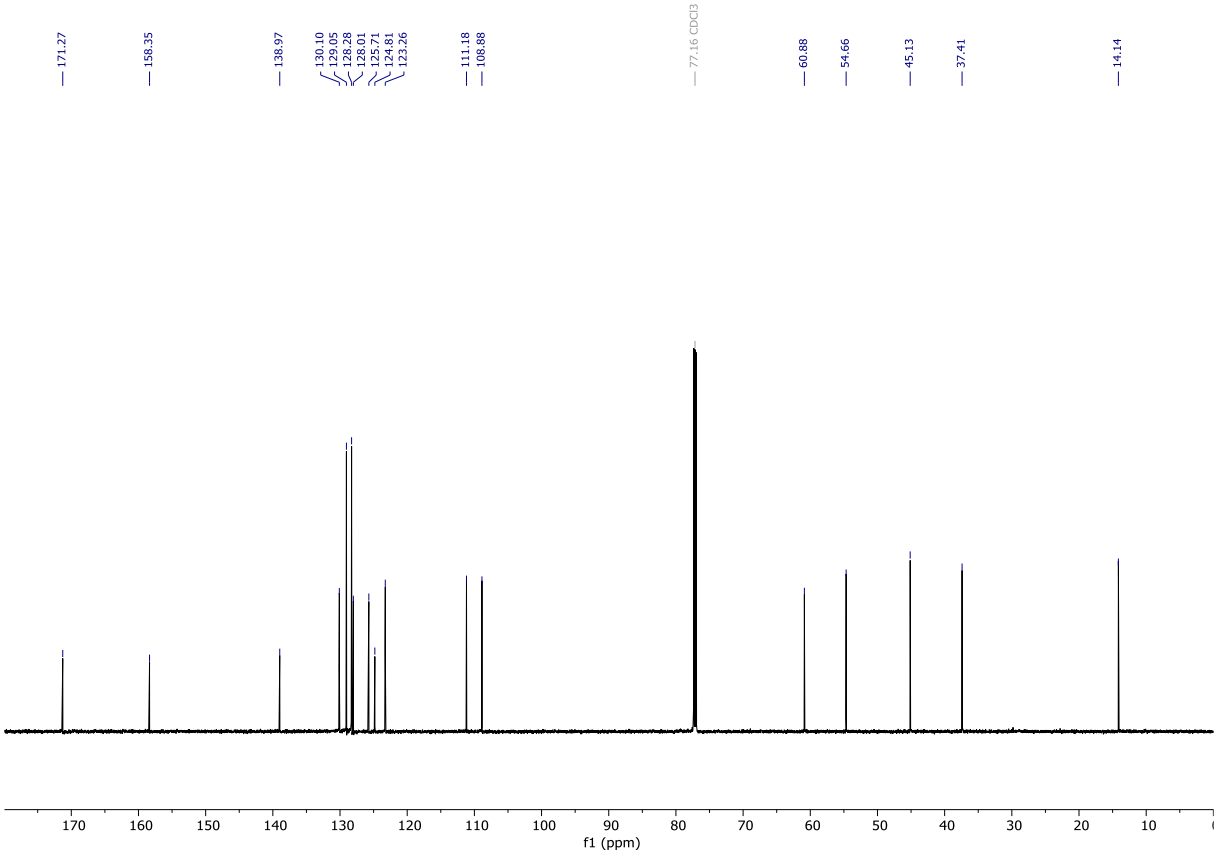


(*R*)-Ethyl 3-((2*S*,3*S*)-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate 3t

^{1}H NMR

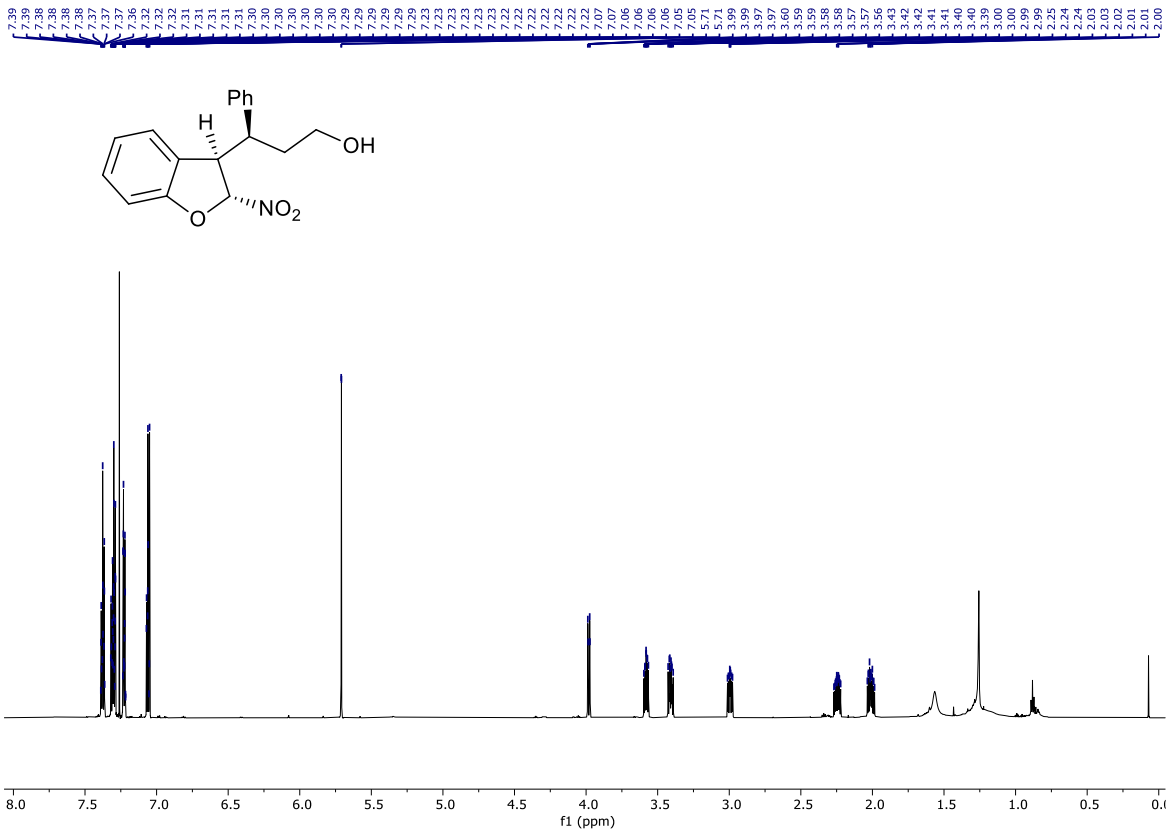


^{13}C NMR

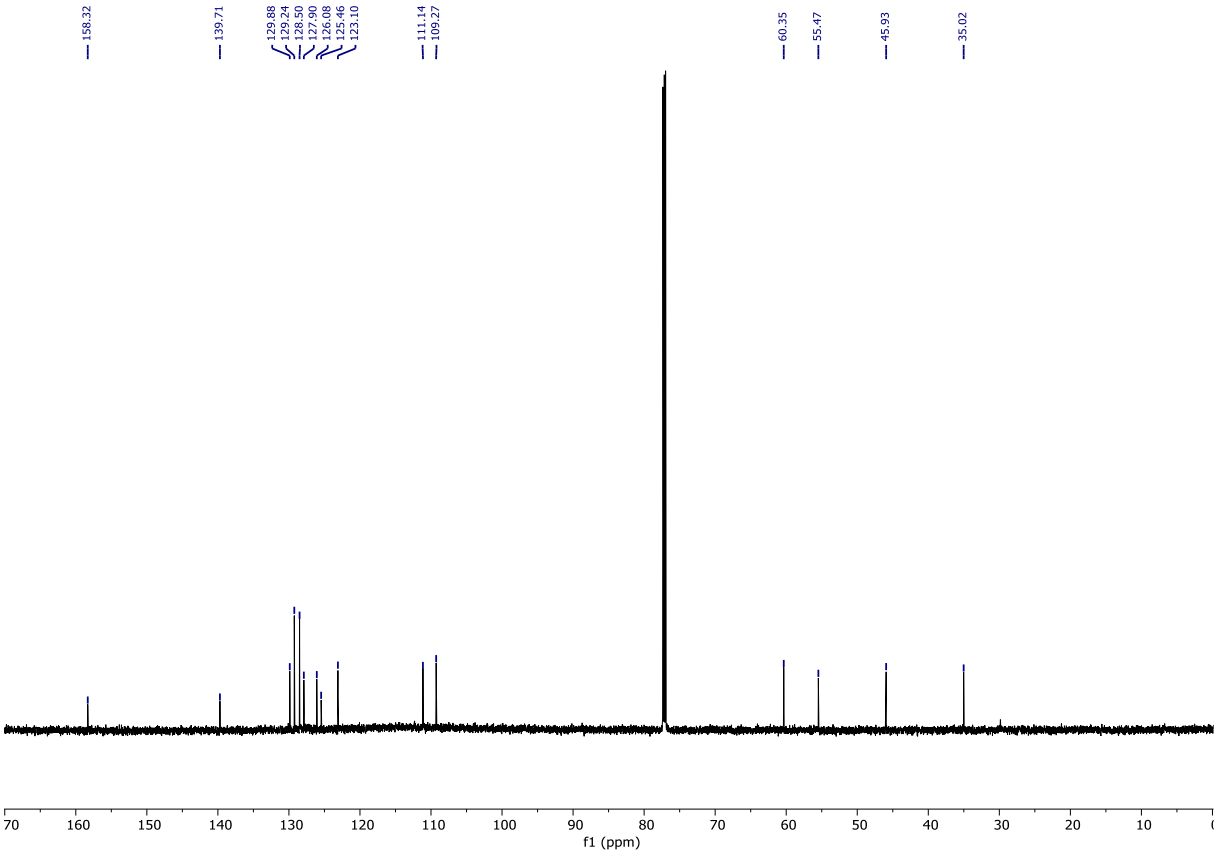


(*S*)-3-((2*R*,3*R*)-2-Nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropan-1-ol 5

^{1}H NMR

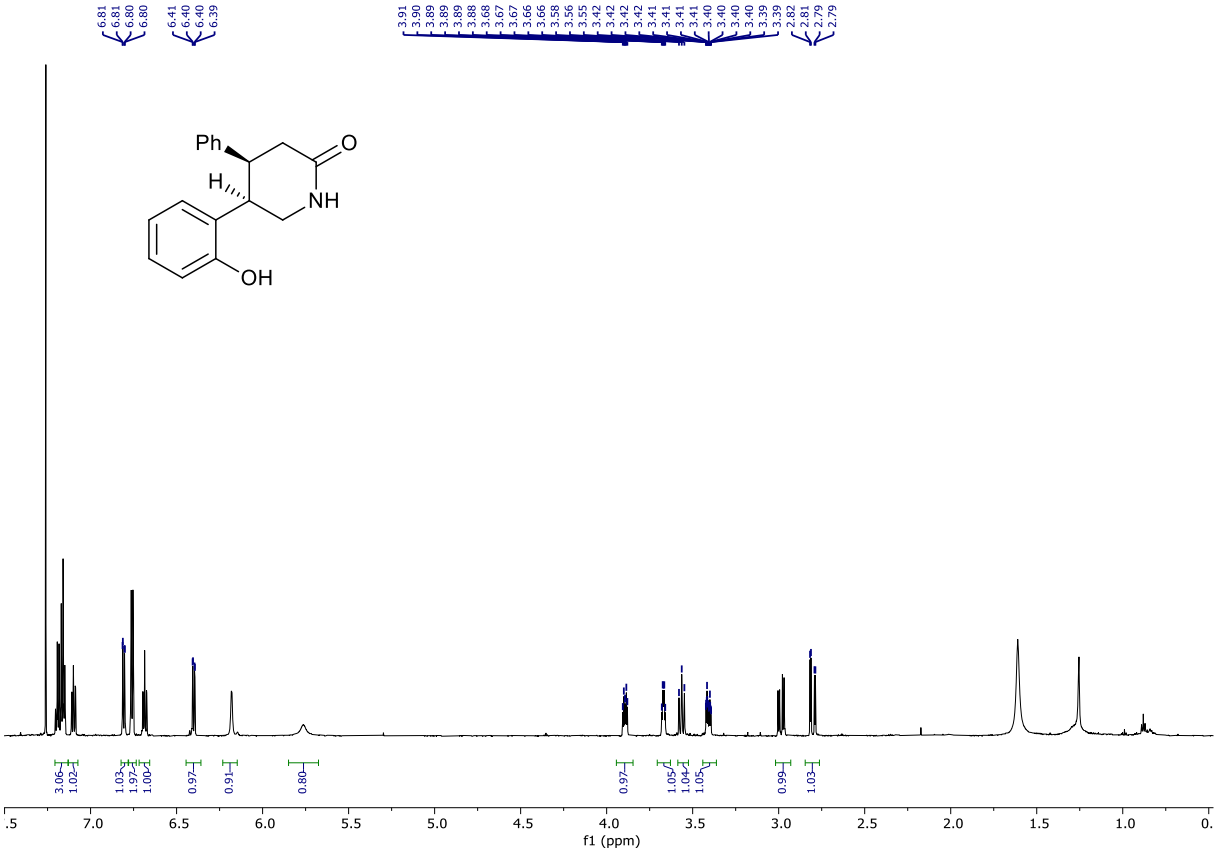


^{13}C NMR

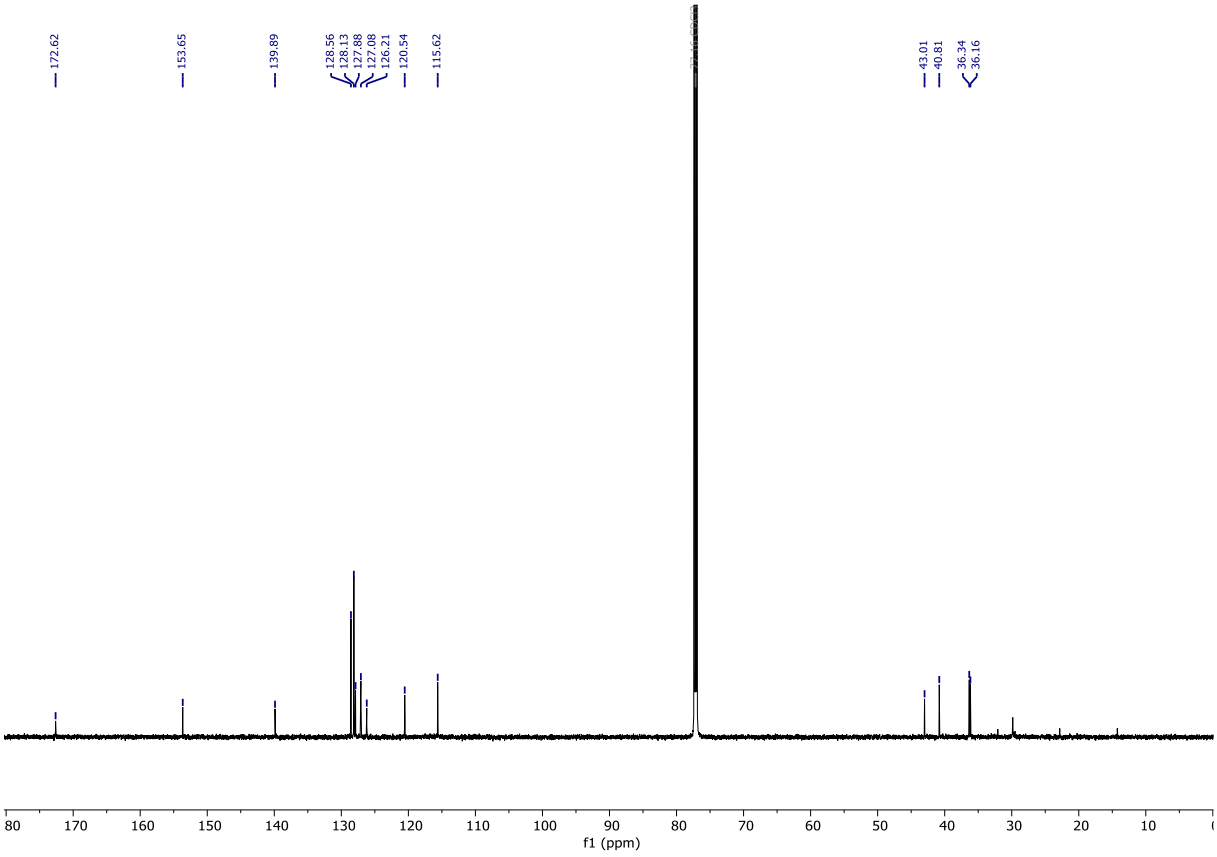


(4*S*,5*R*)-5-(2-Hydroxyphenyl)-4-phenylpiperidin-2-one 6

^{1}H NMR



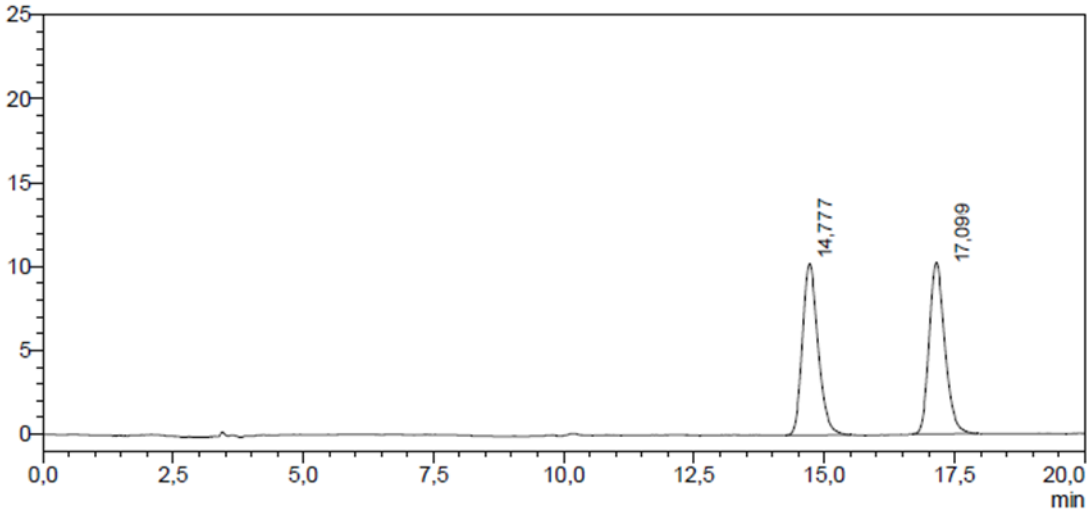
^{13}C NMR



7. HPLC data

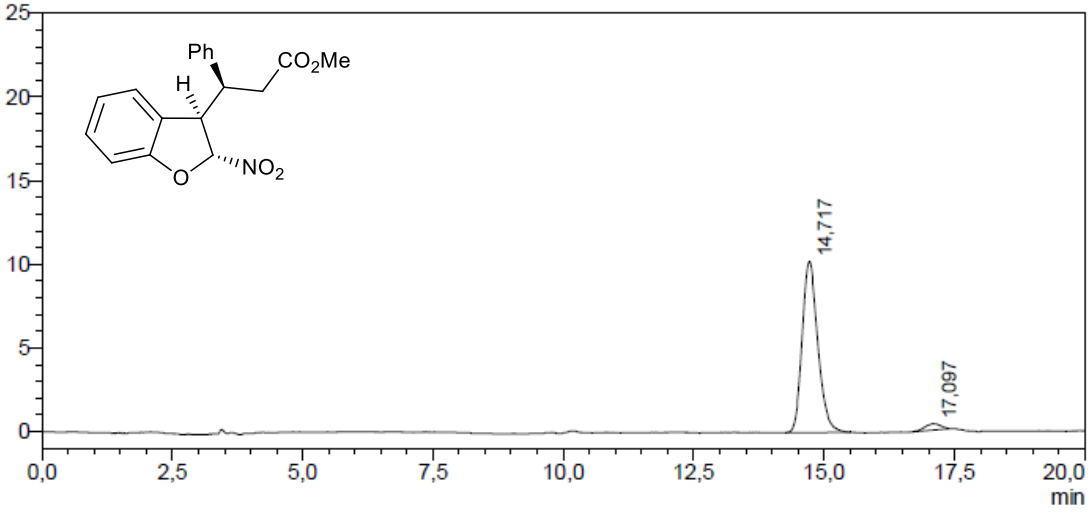
(*S*)-Methyl 3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate 3a

Racemic sample



Peak#	Ret. Time	Area%
1	14,777	49,530
2	17,099	50,470
Total		100,000

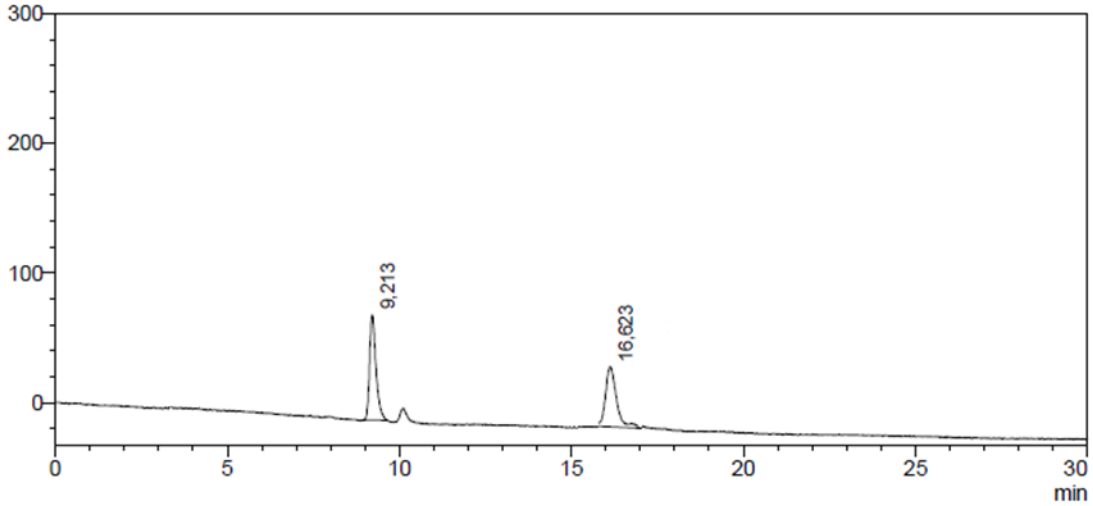
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	14,717	96,656
2	17,097	3,344
Total		100,000

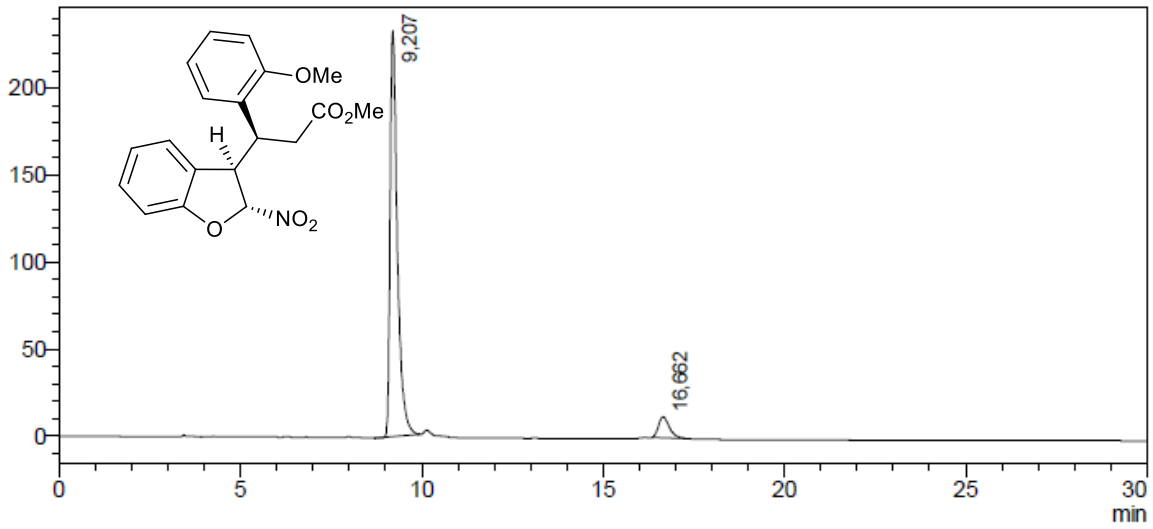
(*S*)-Methyl 3-(2-methoxyphenyl)-3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl)propanoate 3b

Racemic sample



Peak#	Ret. Time	Area%
1	9,213	48,562
2	16,623	51,438
Total		100,000

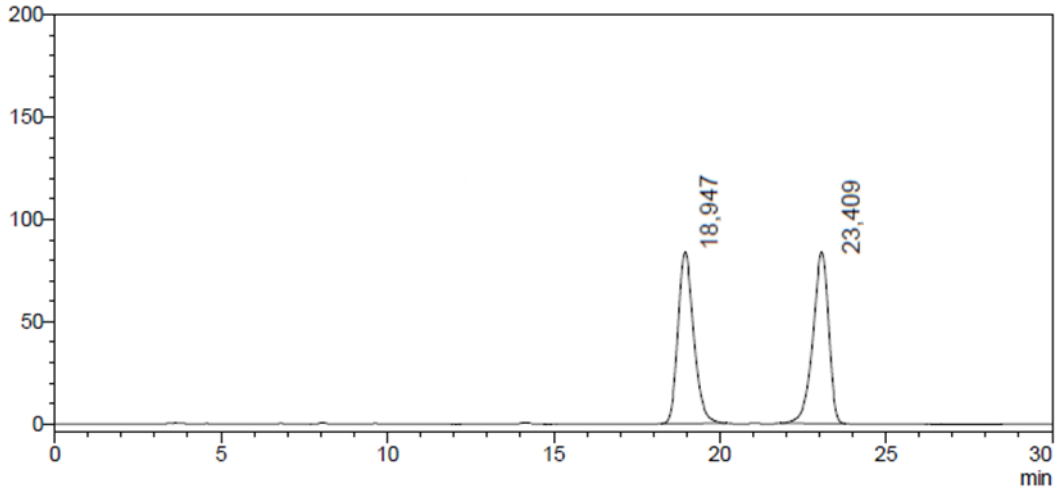
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	9,207	92,889
2	16,662	7,111
Total		100,000

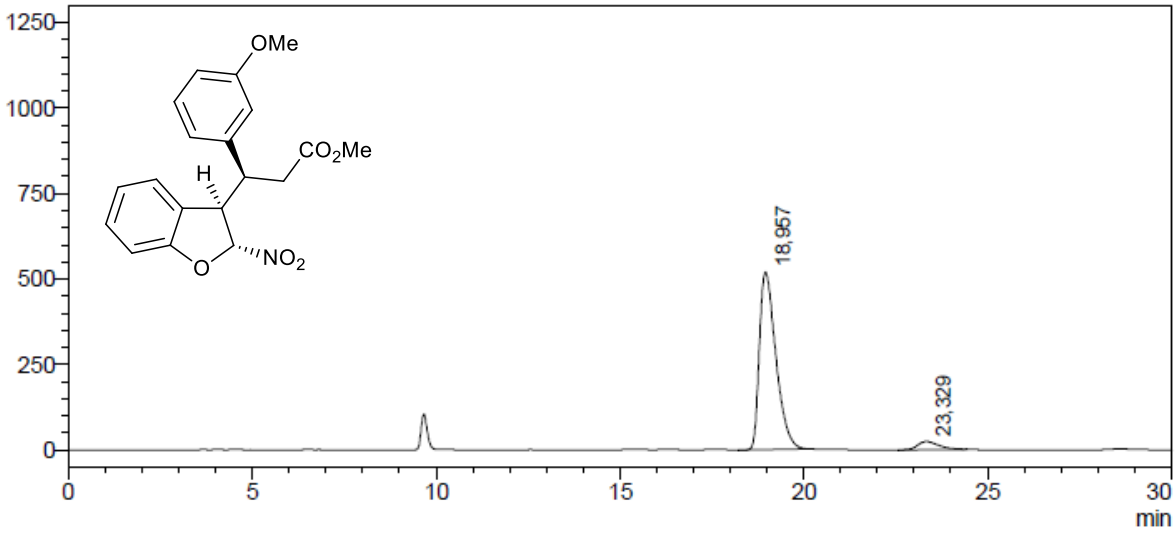
(*S*)-Methyl 3-(3-methoxyphenyl)-3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl)propanoate 3c

Racemic sample



Peak#	Ret. Time	Area%
1	18,947	49,530
2	23,409	50,470
Total		100,000

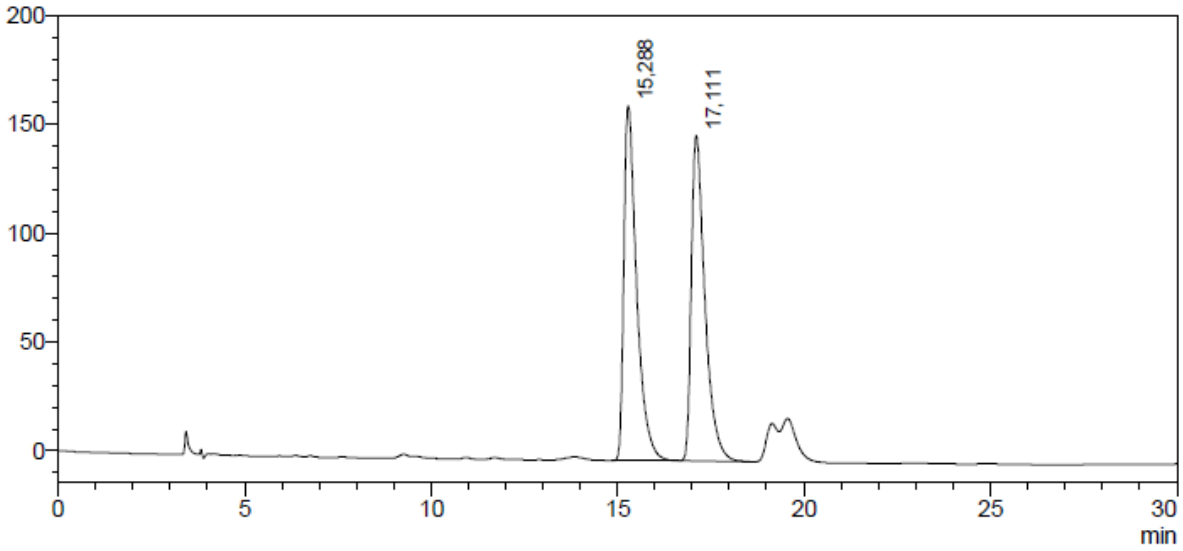
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	18,957	94,406
2	23,329	5,594
Total		100,000

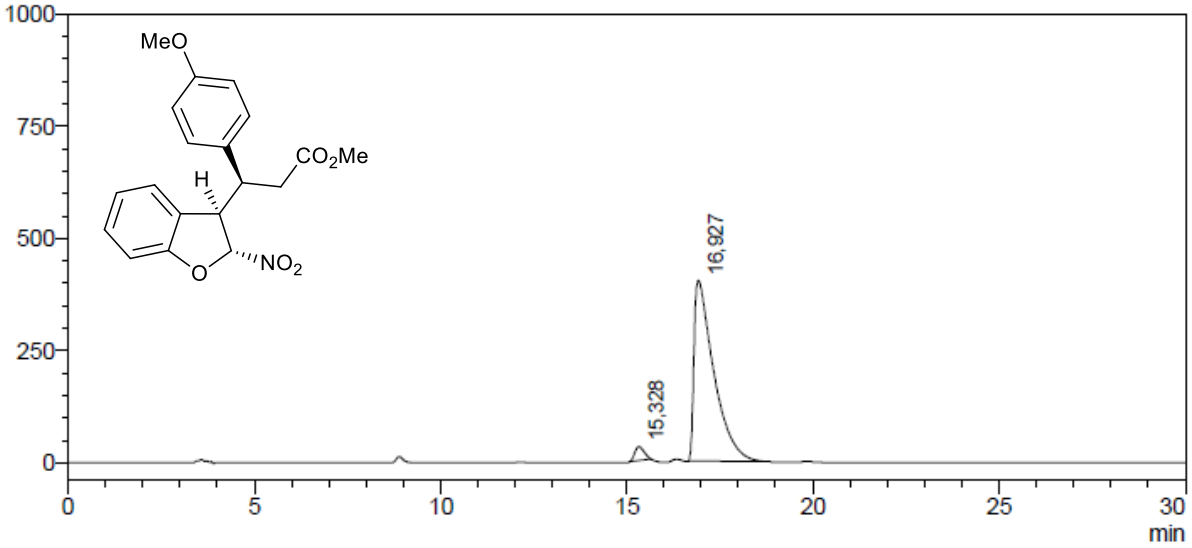
(*S*)-Methyl 3-(4-methoxyphenyl)-3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl) propanoate 3d

Racemic sample



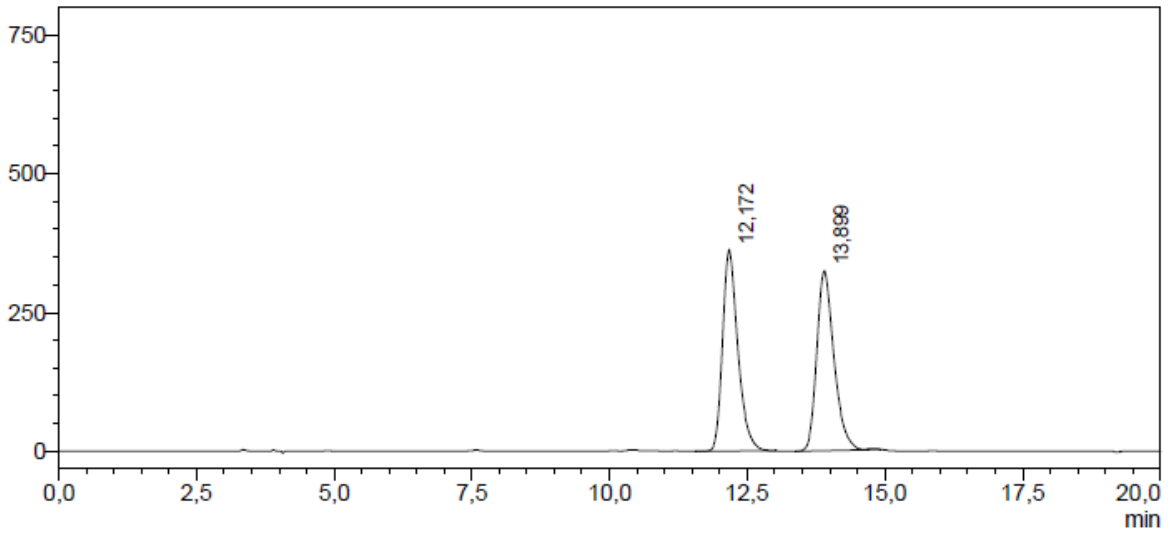
Peak#	Ret. Time	Area%
1	15,288	50,693
2	17,111	49,307
Total		100,000

Enantiomerically enriched sample



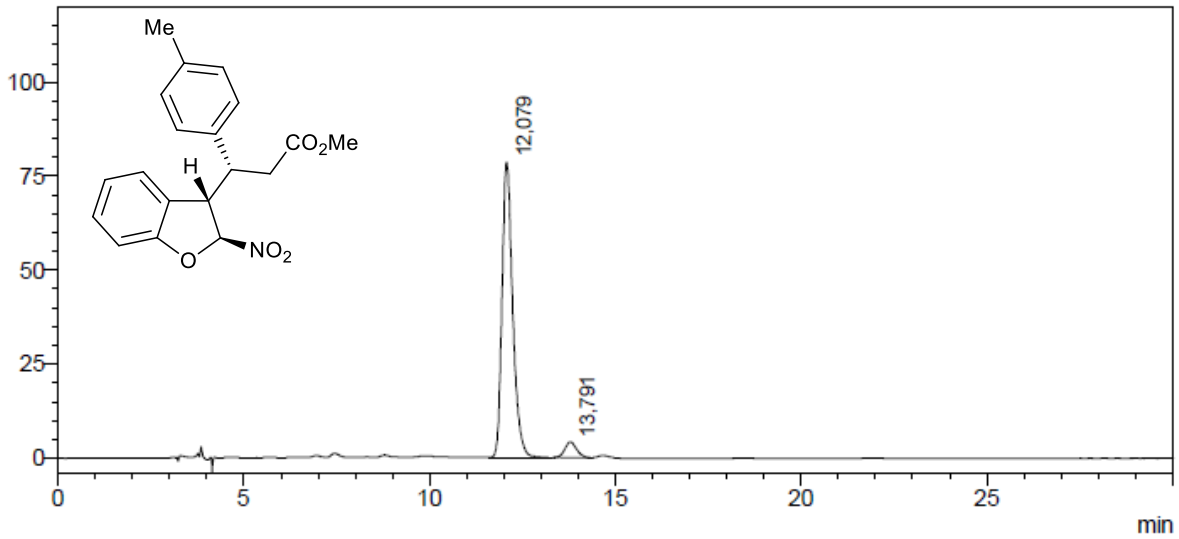
Peak#	Ret. Time	Area%
1	15,328	3,517
2	16,927	96,483
Total		100,000

(*R*)-Methyl 3-((2*S*,3*S*)-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-(p-tolyl)propanoate 3e
Racemic sample



Peak#	Ret. Time	Area%
1	12,172	49,908
2	13,899	50,092
Total		100,000

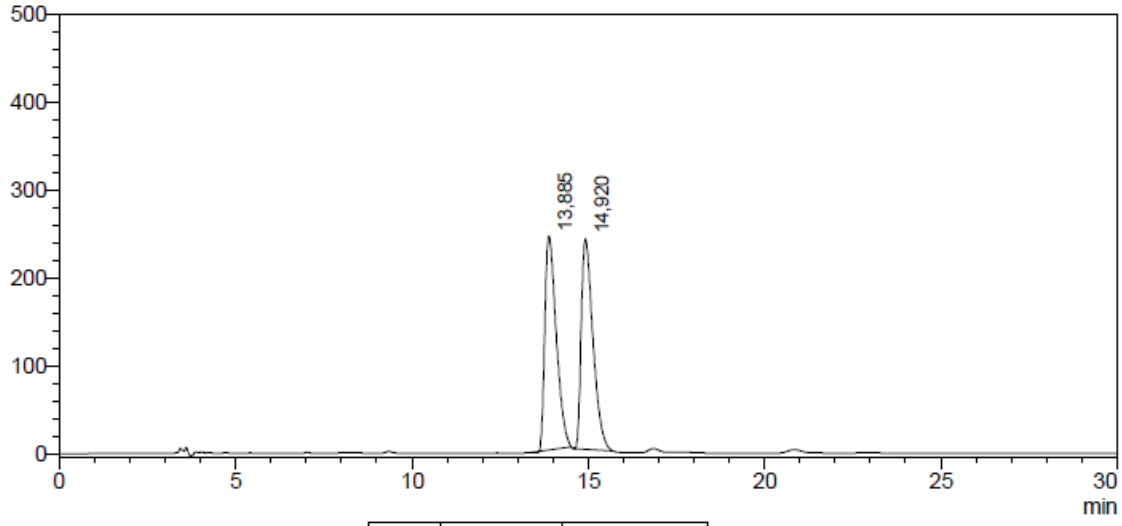
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	12,079	94,433
2	13,791	5,567
Total		100,000

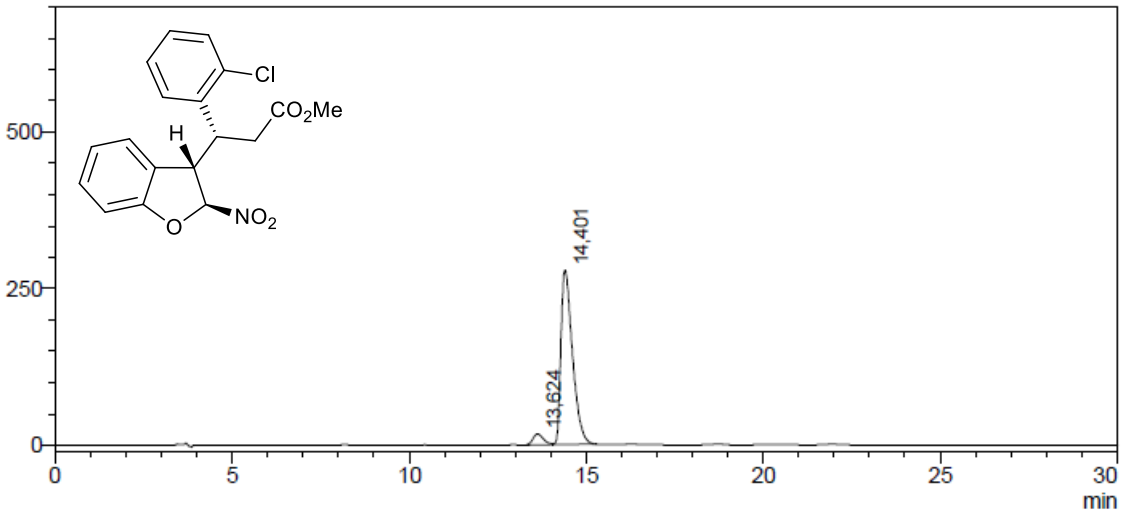
(*R*)-Methyl 3-(2-chlorophenyl)-3-((2*S*,3*S*)-2-nitro-2,3-dihydrobenzofuran-3-yl) propanoate
3f

Racemic sample



Peak#	Ret. Time	Area%
1	13,885	49,530
2	14,920	50,470
Total		100,000

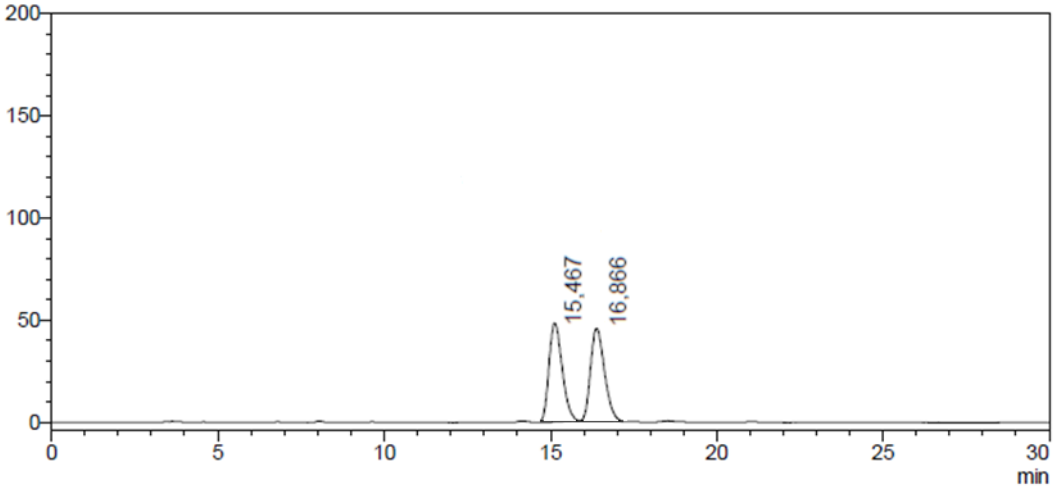
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	13,624	5,477
2	14,401	94,523
Total		100,000

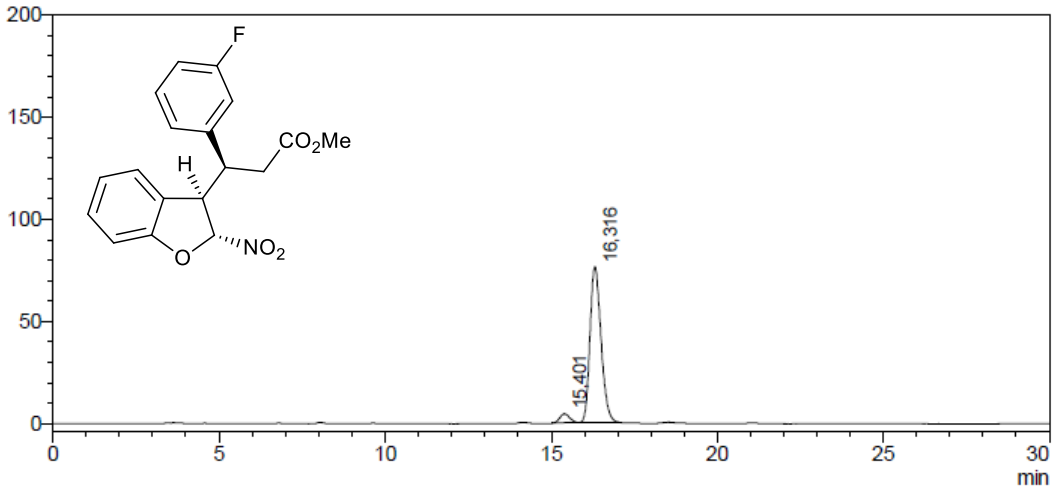
(*S*)-Methyl 3-(3-fluorophenyl)-3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl) propanoate 3g

Racemic sample



Peak#	Ret. Time	Area%
1	15,467	50,076
2	16,866	49,924
Total		100,000

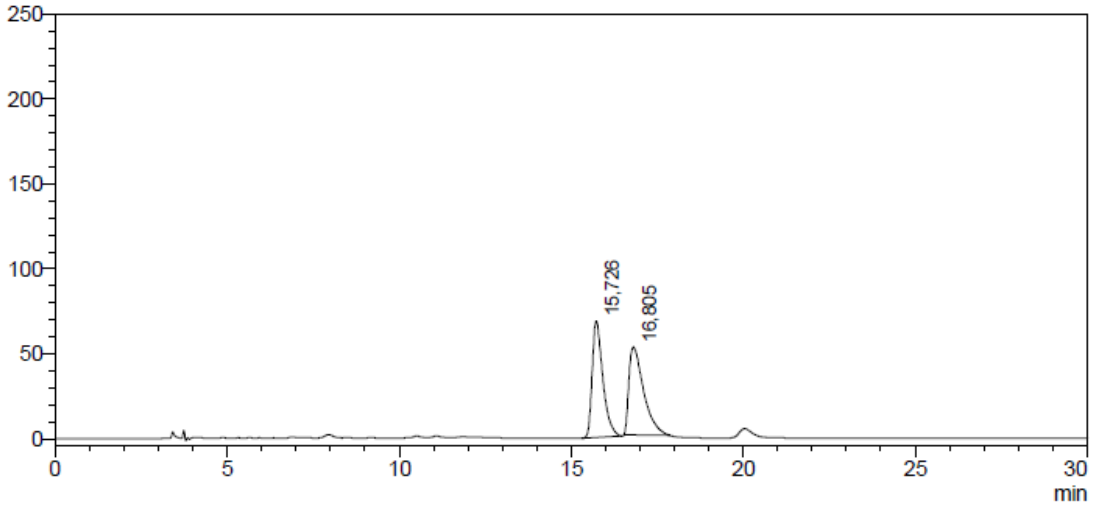
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	15,401	4,867
2	16,316	95,133
Total		100,000

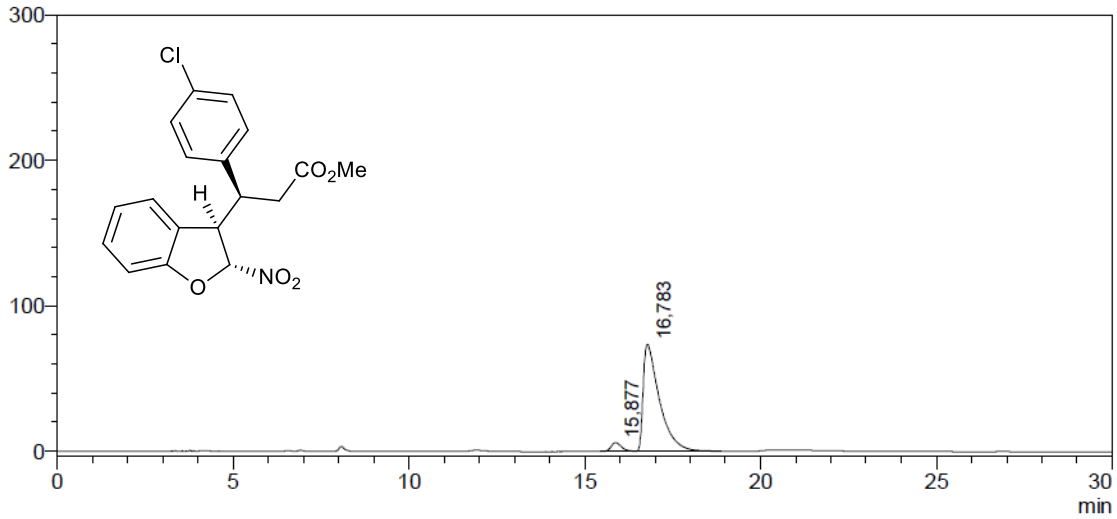
(*S*)-Methyl 3-(4-chlorophenyl)-3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl) propanoate 3h

Racemic sample



Peak#	Ret. Time	Area%
1	15,726	49,098
2	16,805	50,902
Total		100,000

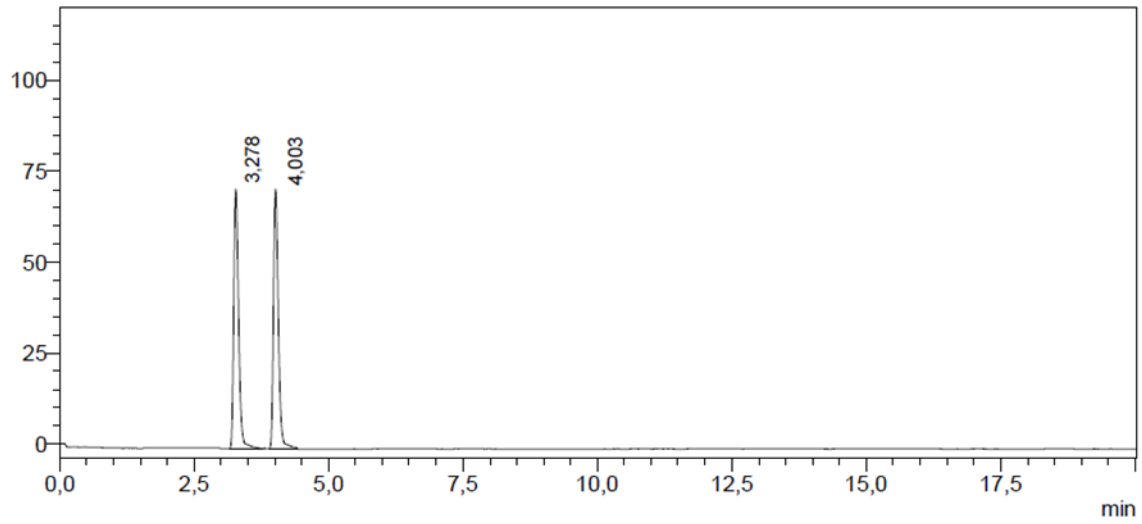
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	15,877	5,140
2	16,783	94,860
Total		100,000

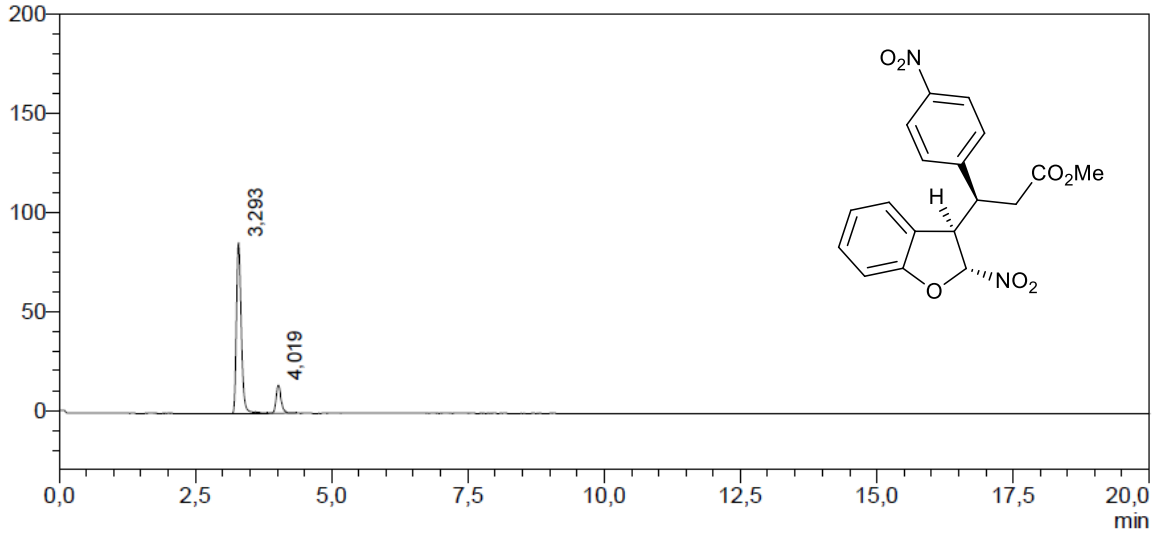
(*S*)-Methyl 3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-(4-nitrophenyl)propanoate 3i

Racemic sample



Peak#	Ret. Time	Area%
1	3,278	49,908
2	4,003	50,092
Total		100,000

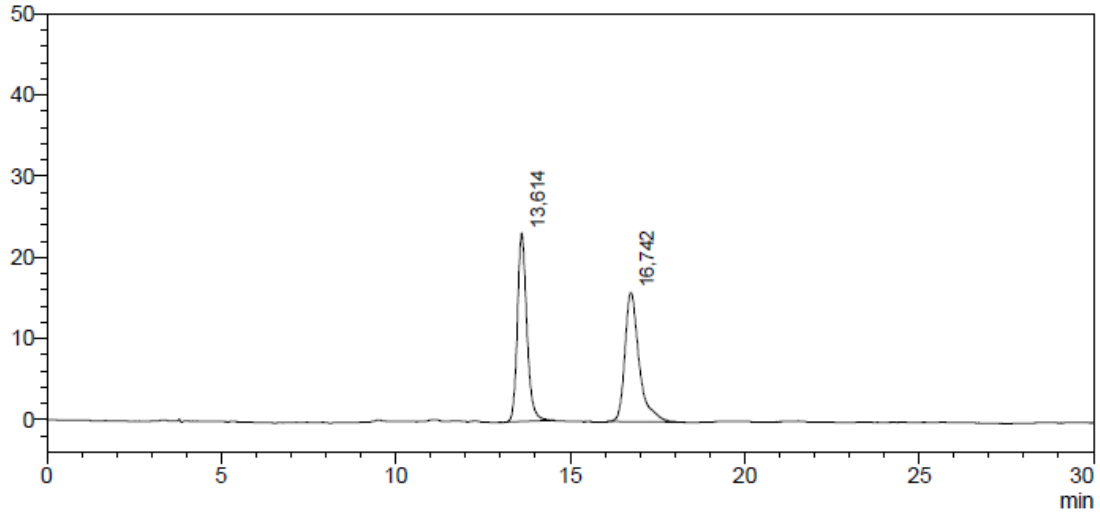
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	3,293	84,806
2	4,019	15,194
Total		100,000

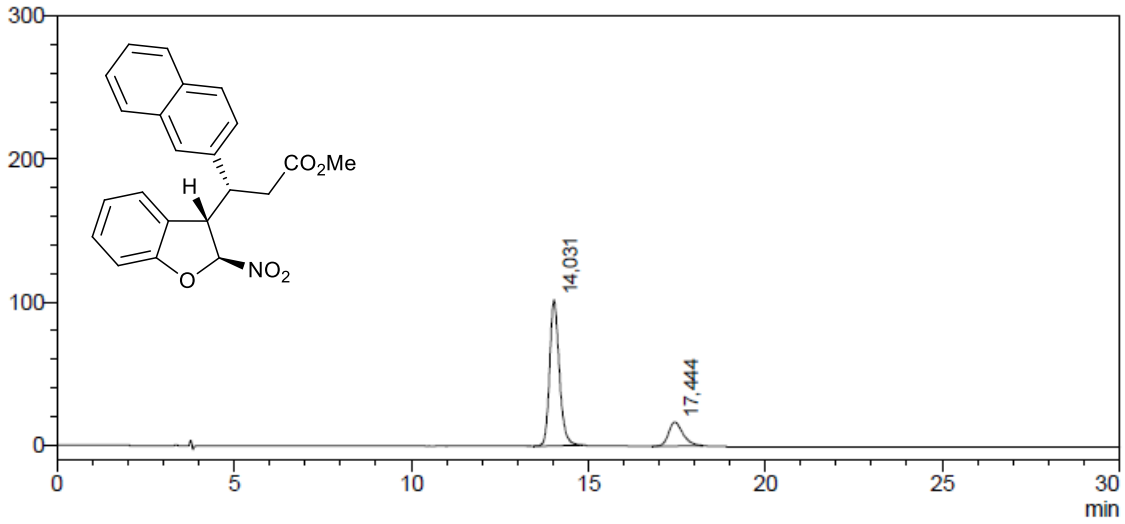
(*R*)-Methyl 3-(naphthalen-2-yl)-3-((2*S*,3*S*)-2-nitro-2,3-dihydrobenzofuran-3-yl) propanoate 3j

Racemic sample



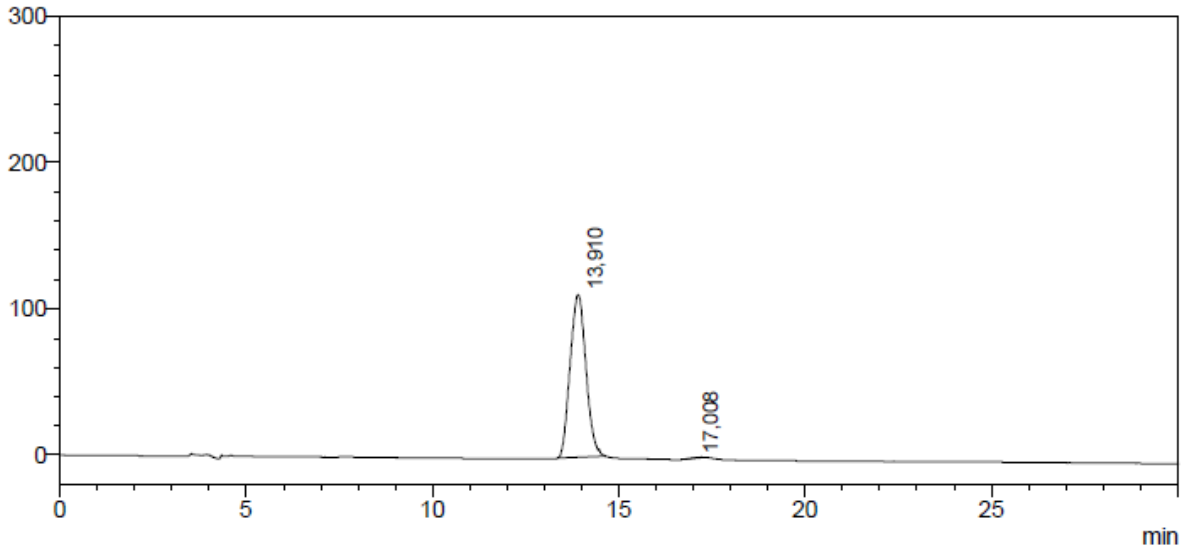
Peak#	Ret. Time	Area%
1	13,614	49,279
2	16,742	50,721
Total		100,000

Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	14,031	80,613
2	17,444	19,387
Total		100,000

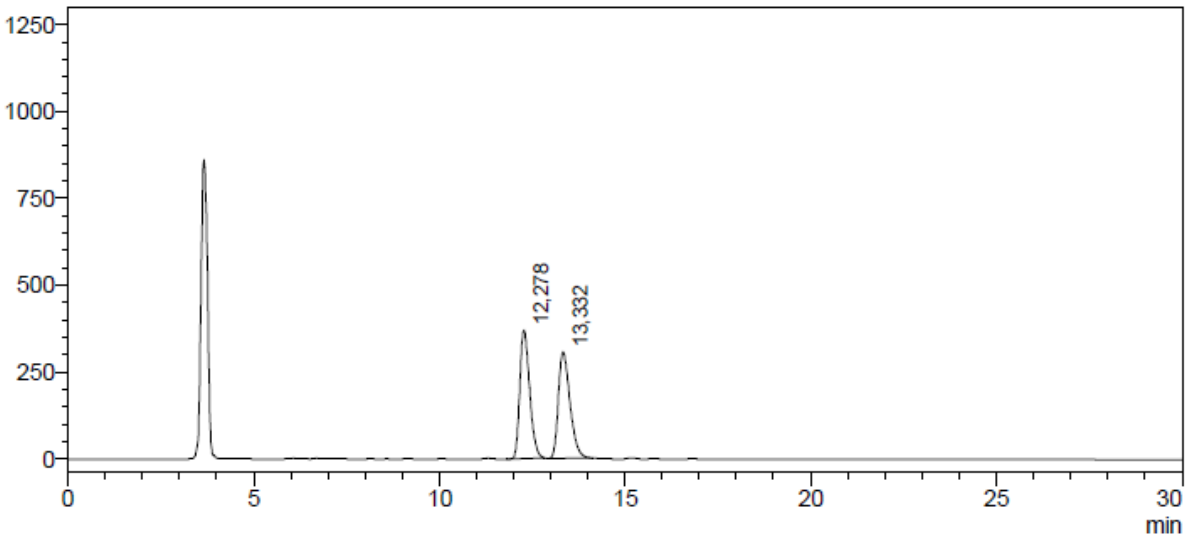
After recrystallization



Peak#	Ret. Time	Area%
1	13,910	99,869
2	17,008	0,131
Total		100,000

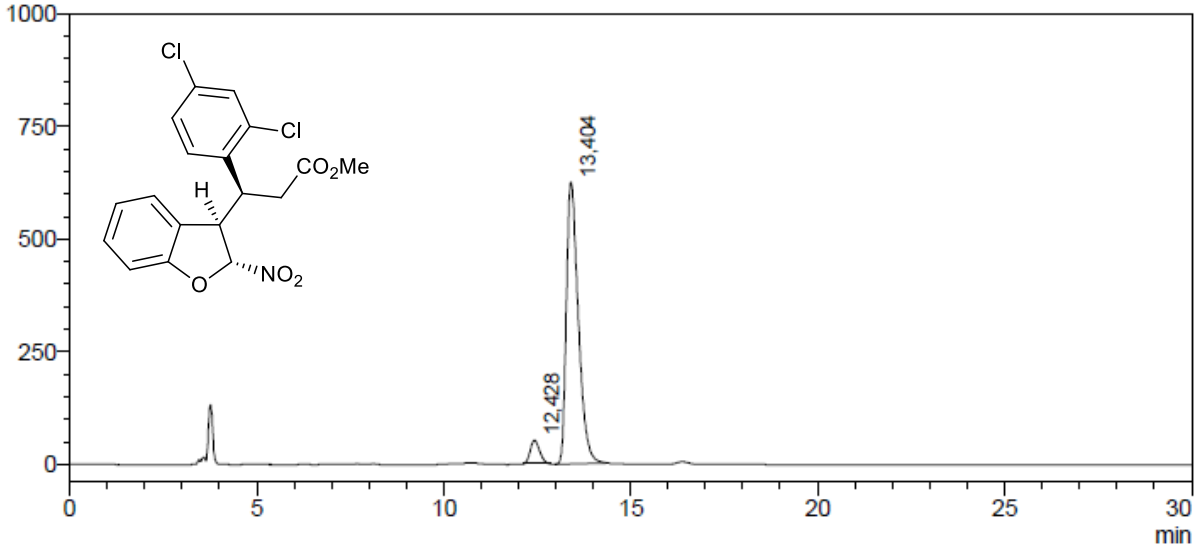
(*S*)-Methyl 3-(2,4-dichlorophenyl)-3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl) propanoate 3k

Racemic sample



Peak#	Ret. Time	Area%
1	12,278	50,401
2	13,332	49,599
Total		100,000

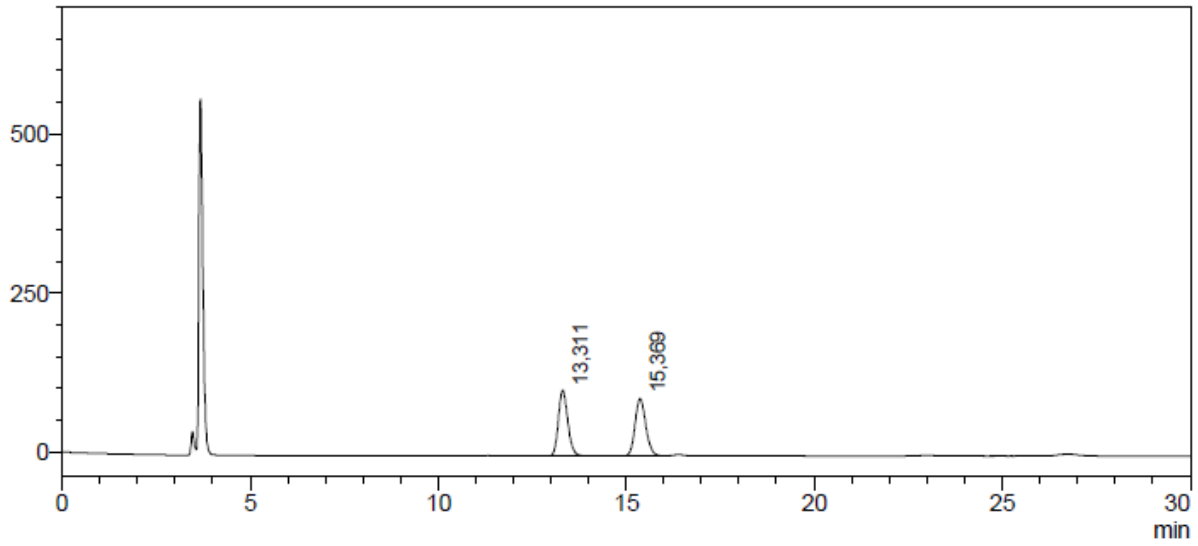
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	12,428	6,176
2	13,404	93,824
Total		100,000

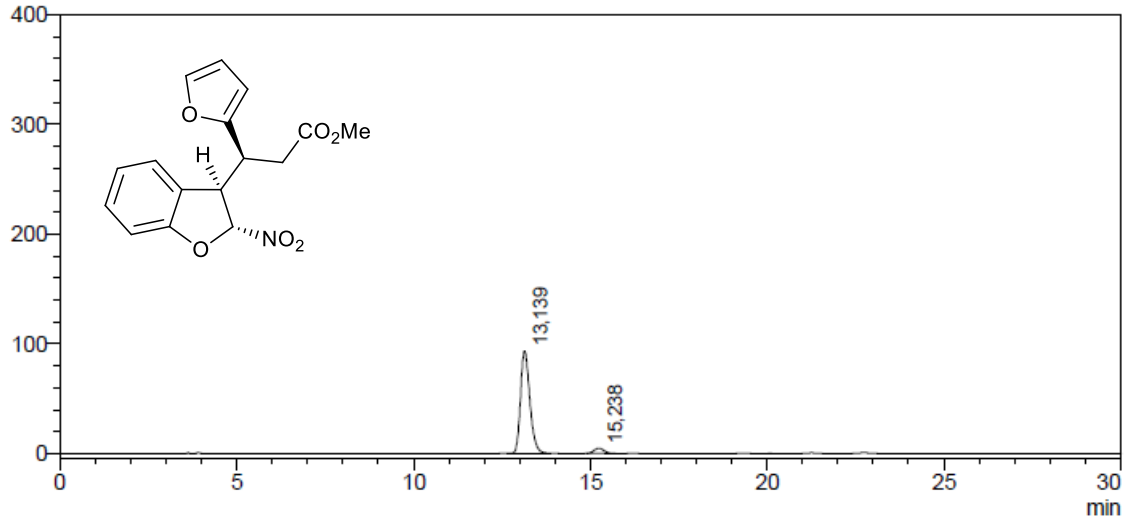
(*S*)-Methyl 3-(furan-2-yl)-3-((2*R*,3*R*)-2-nitro-2,3-dihydrobenzofuran-3-yl) propanoate 3l

Racemic sample



Peak#	Ret. Time	Area%
1	13,311	50,758
2	15,369	49,242
Total		100,000

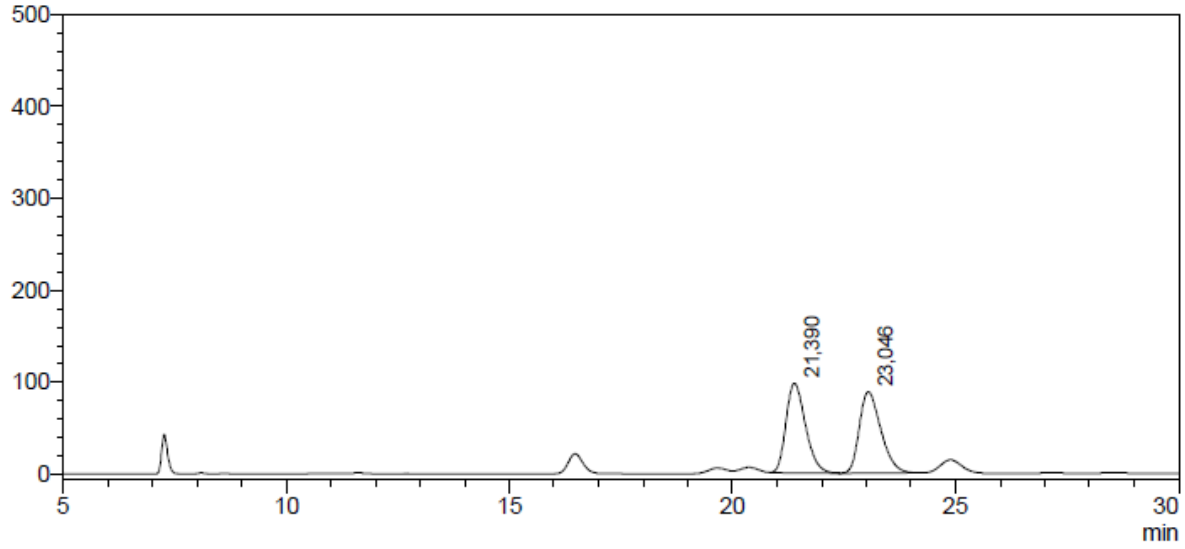
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	13,139	94,701
2	15,238	5,299
Total		100,000

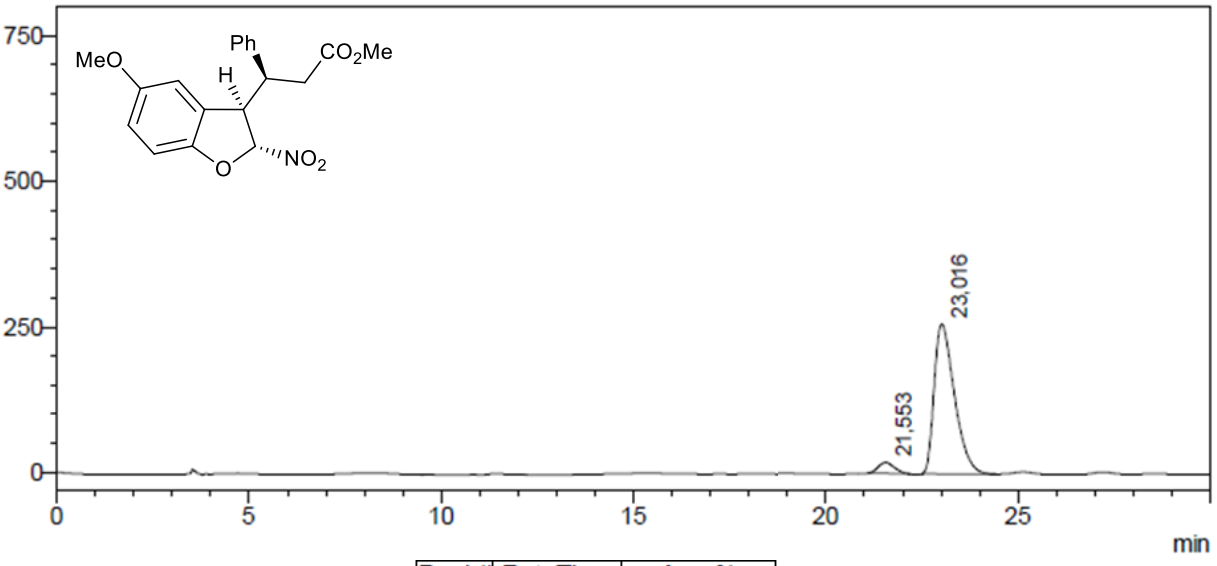
(*S*)-Methyl 3-((2*R*,3*R*)-5-methoxy-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate 3m

Racemic sample



Peak#	Ret. Time	Area%
1	21,390	49,781
2	23,046	50,219
Total		100,000

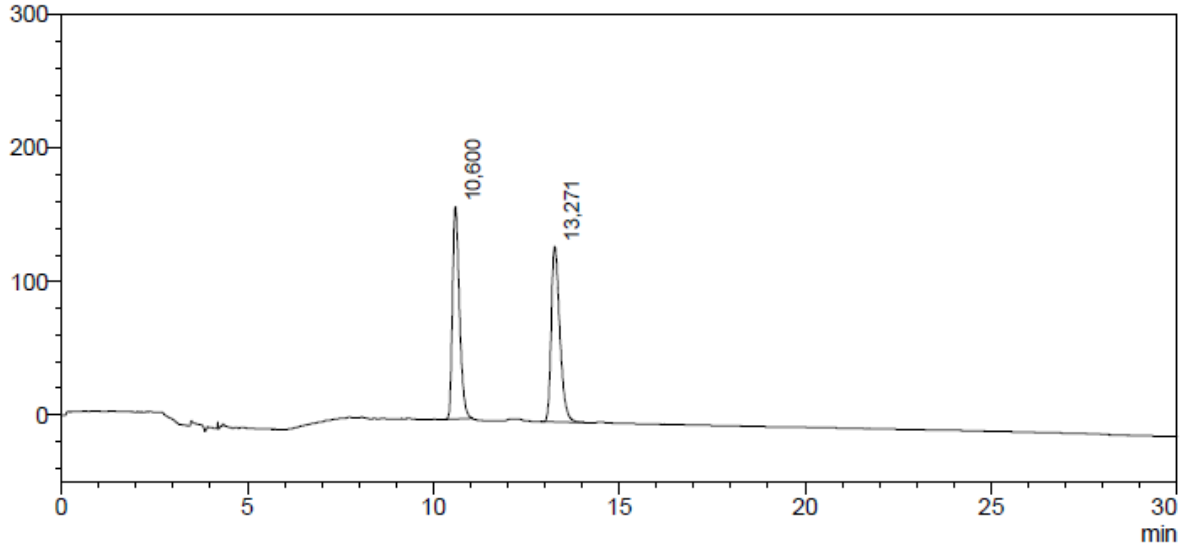
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	21,553	5,478
2	23,016	94,522
Total		100,000

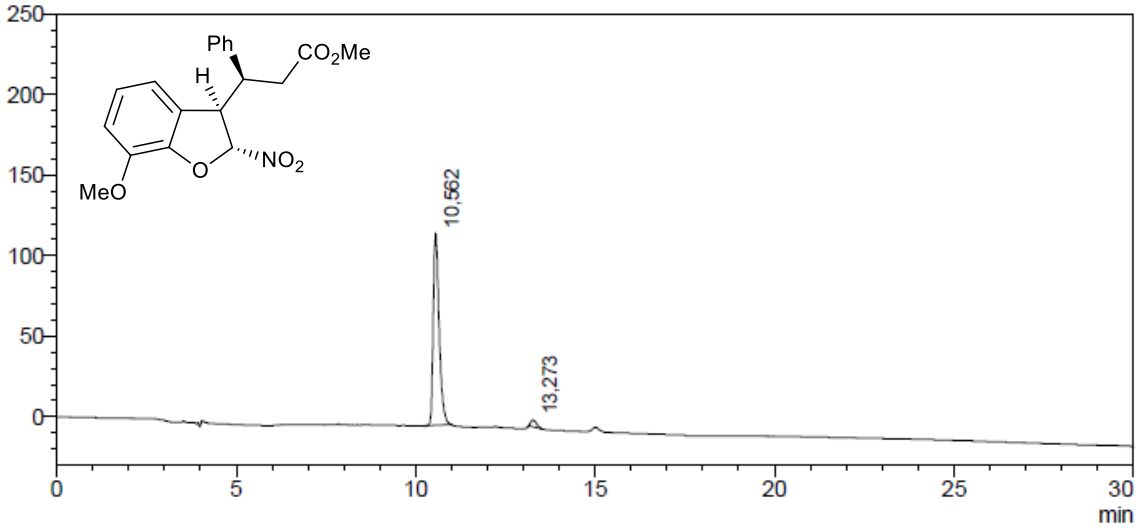
(*S*)-Methyl 3-((2*R*,3*R*)-7-methoxy-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate 3n

Racemic sample



Peak#	Ret. Time	Area%
1	10,600	49,539
2	13,271	50,461
Total		100,000

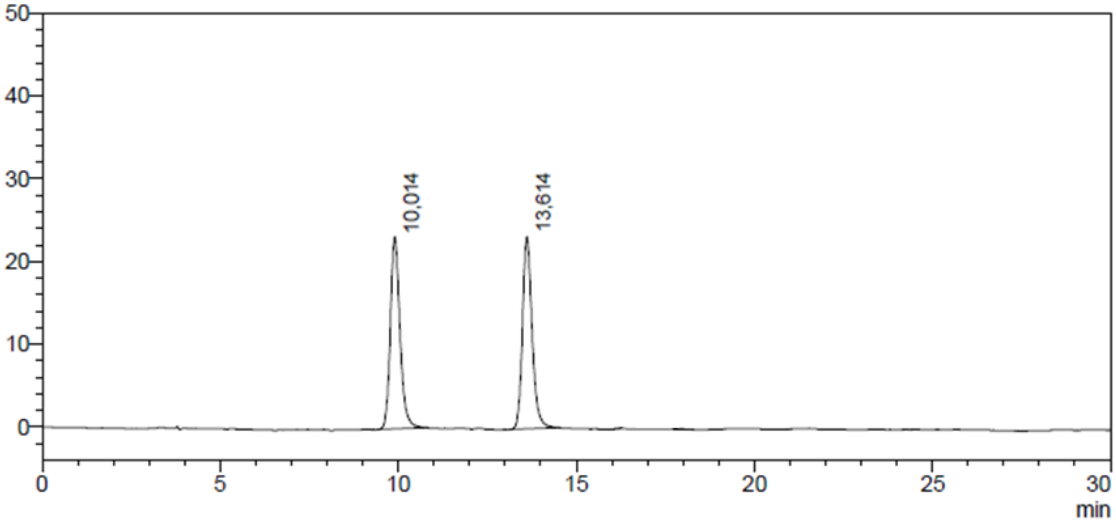
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	10,562	96,668
2	13,273	3,332
Total		100,000

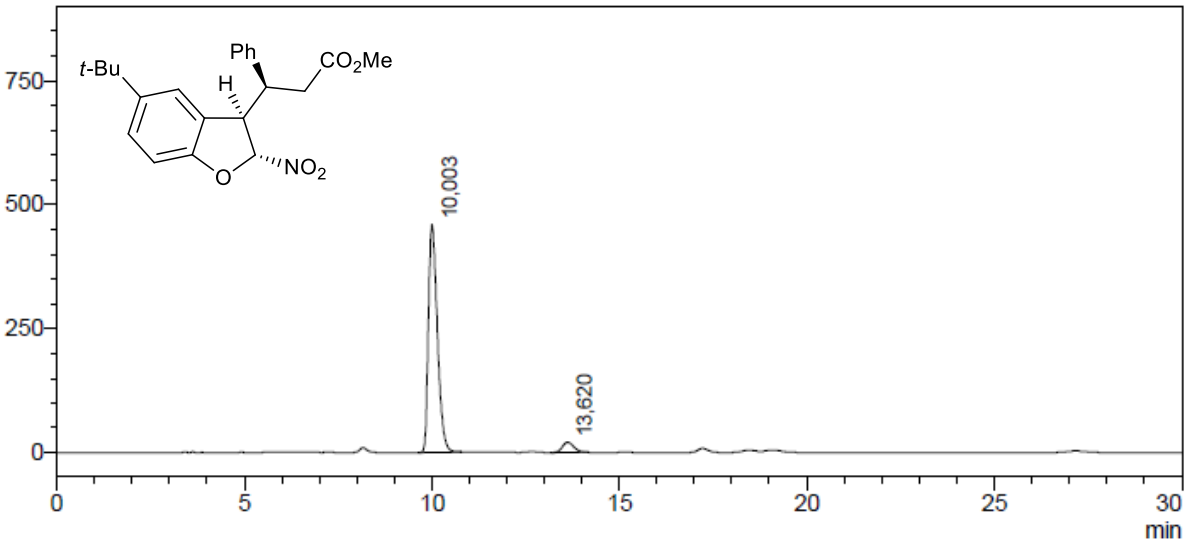
(*S*)-Methyl 3-((2*R*,3*R*)-5-(*tert*-butyl)-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate 3o

Racemic sample



Peak#	Ret. Time	Area%
1	10,014	49,279
2	13,614	50,721
Total		100,000

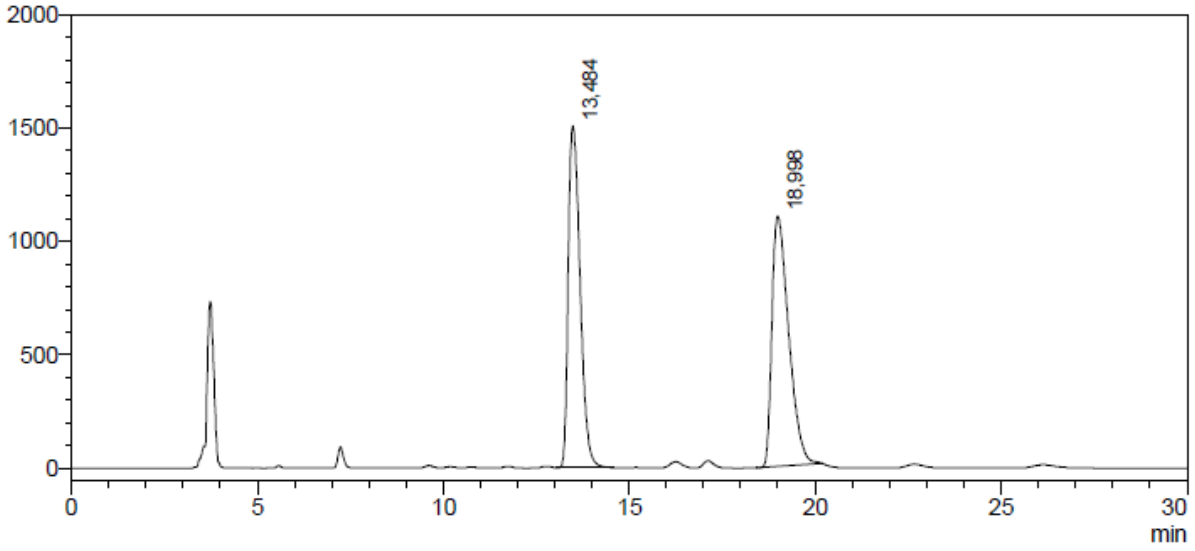
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	10,003	94,602
2	13,620	5,398
Total		100,000

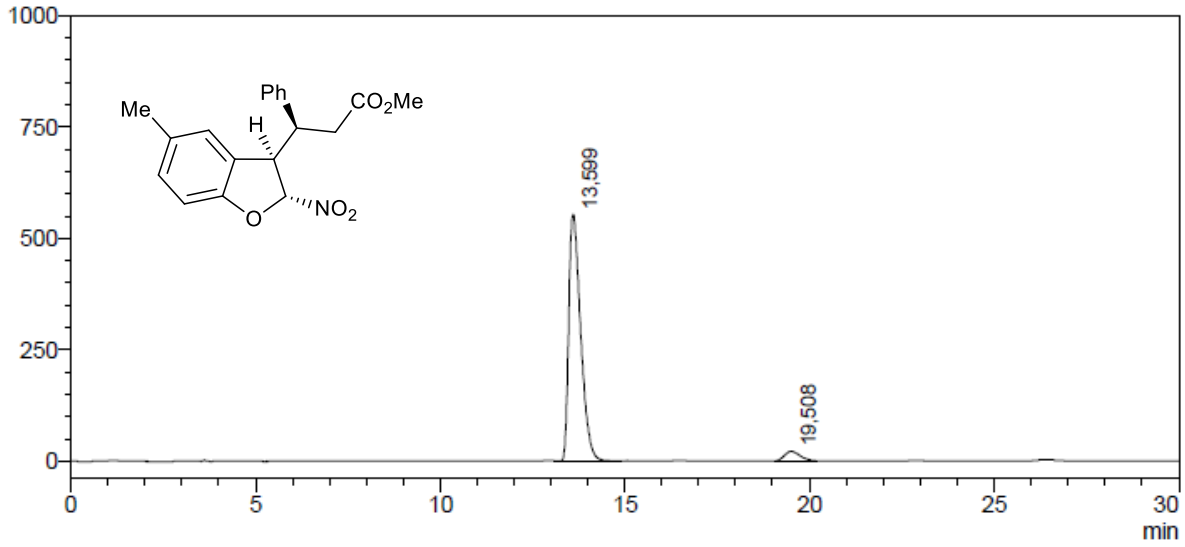
(*S*)-Methyl 3-((2*R*,3*R*)-5-methyl-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate 3p

Racemic sample



Peak#	Ret. Time	Area%
1	13,485	49,219
2	18,998	50,781
Total		100,000

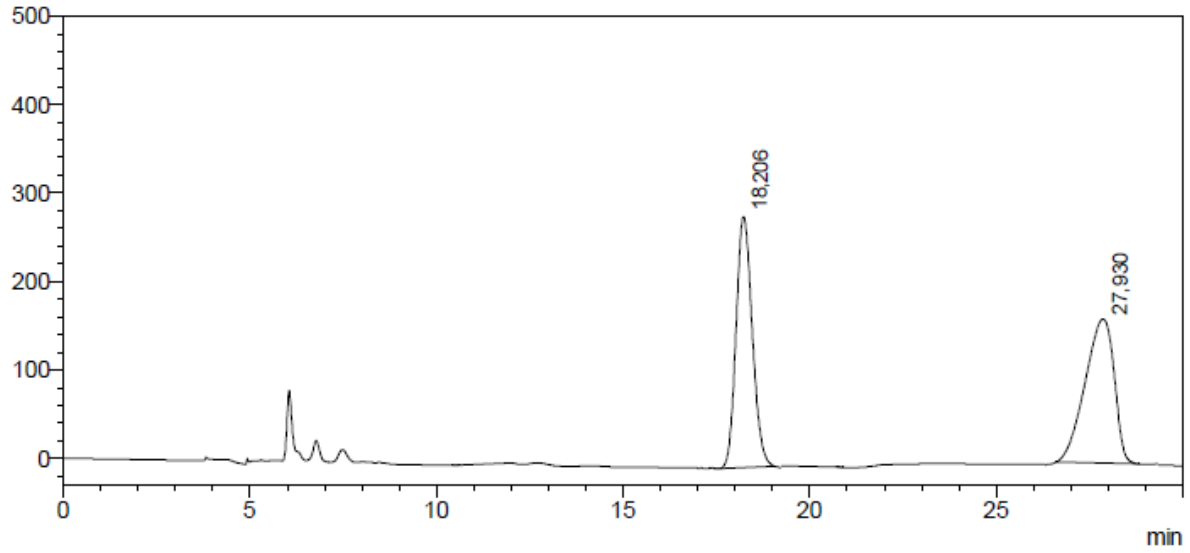
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	13,599	95,087
2	19,508	4,913
Total		100,000

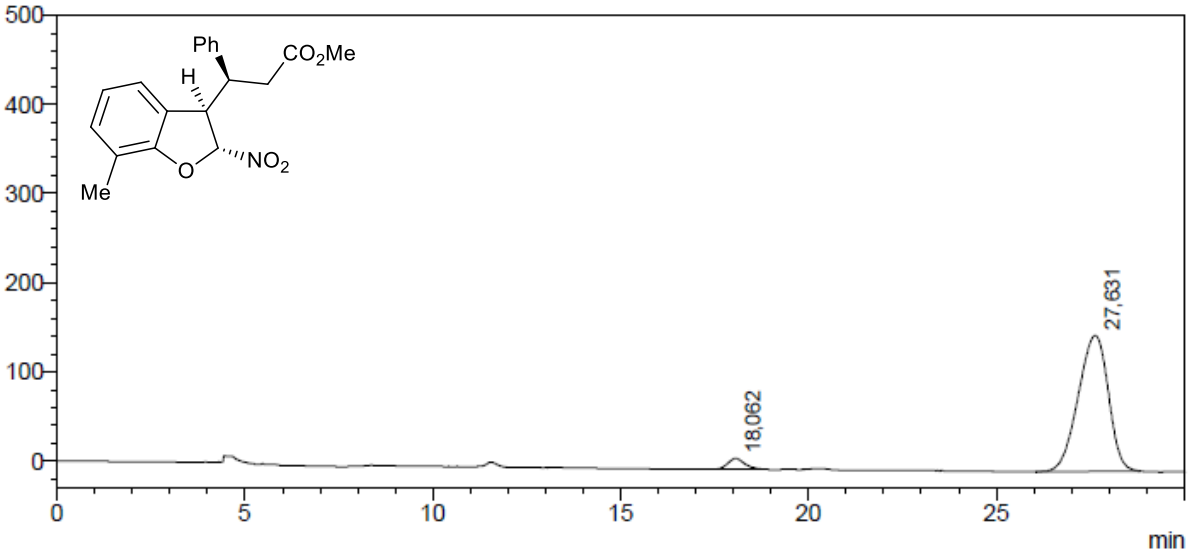
(*S*)-Methyl 3-((2*R*,3*R*)-7-methyl-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate 3q

Racemic sample



Peak#	Ret. Time	Area%
1	18,206	49,118
2	27,930	50,882
Total		100,000

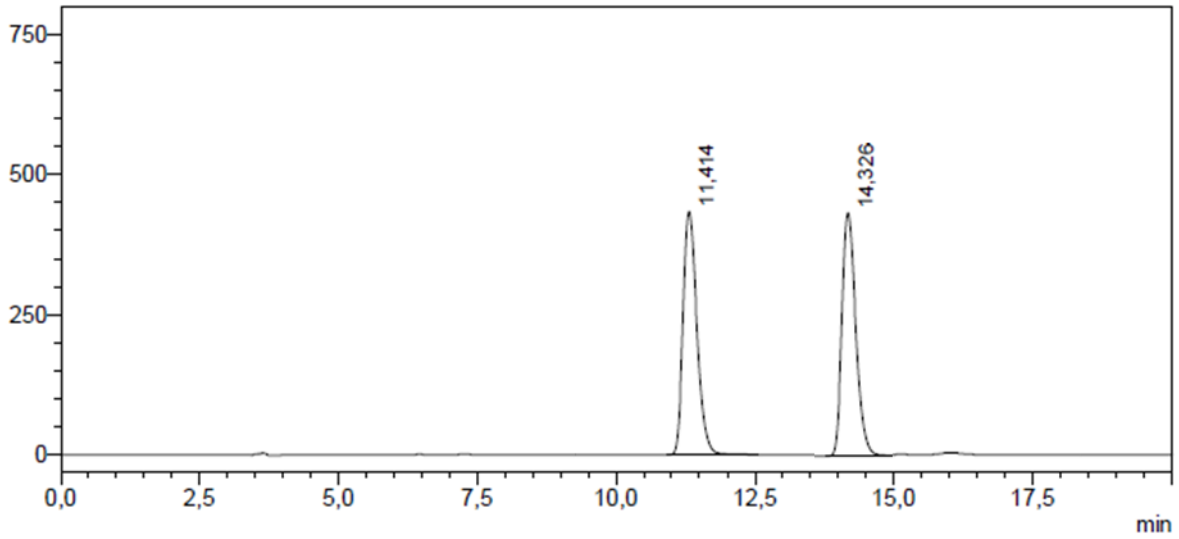
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	18,062	4,238
2	27,631	95,762
Total		100,000

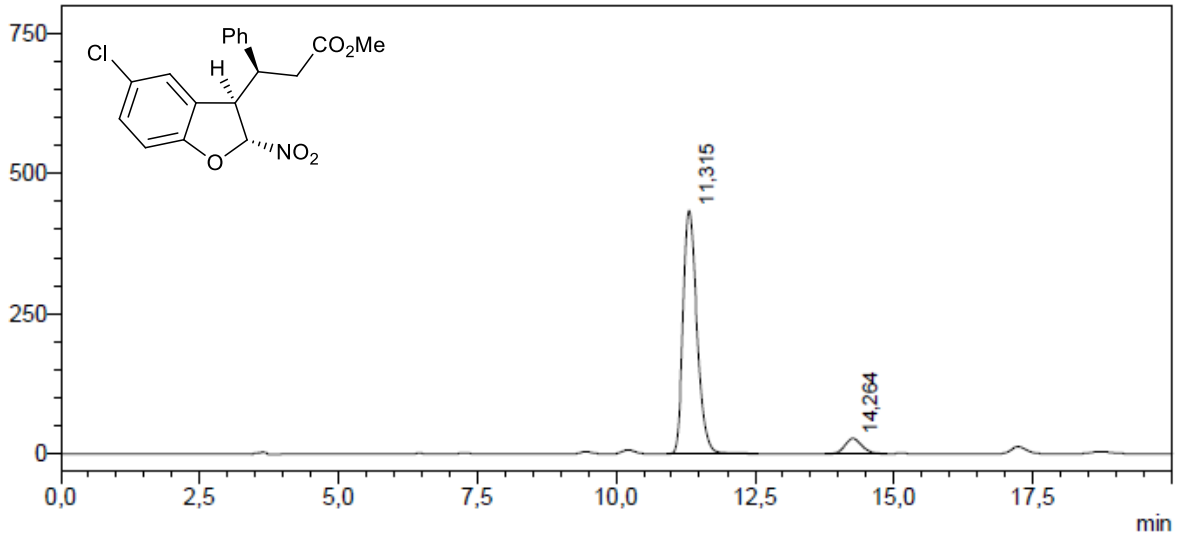
(*S*)-Methyl 3-((2*R*,3*R*)-5-chloro-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate 3r

Racemic sample



Peak#	Ret. Time	Area%
1	11,414	49,781
2	14,364	50,219
Total		100,000

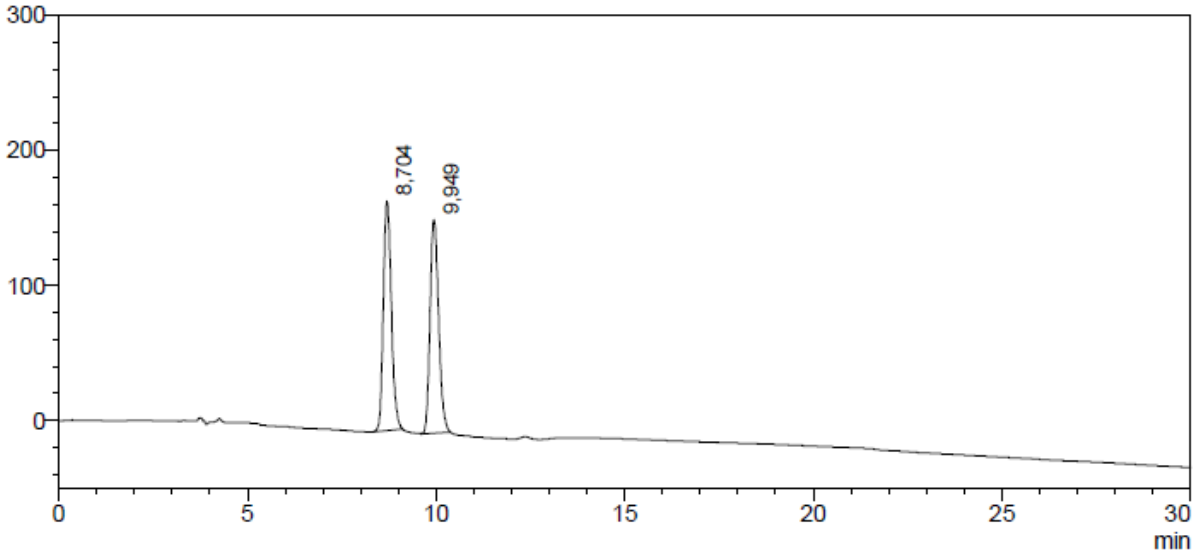
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	11,315	92,904
2	14,264	7,096
Total		100,000

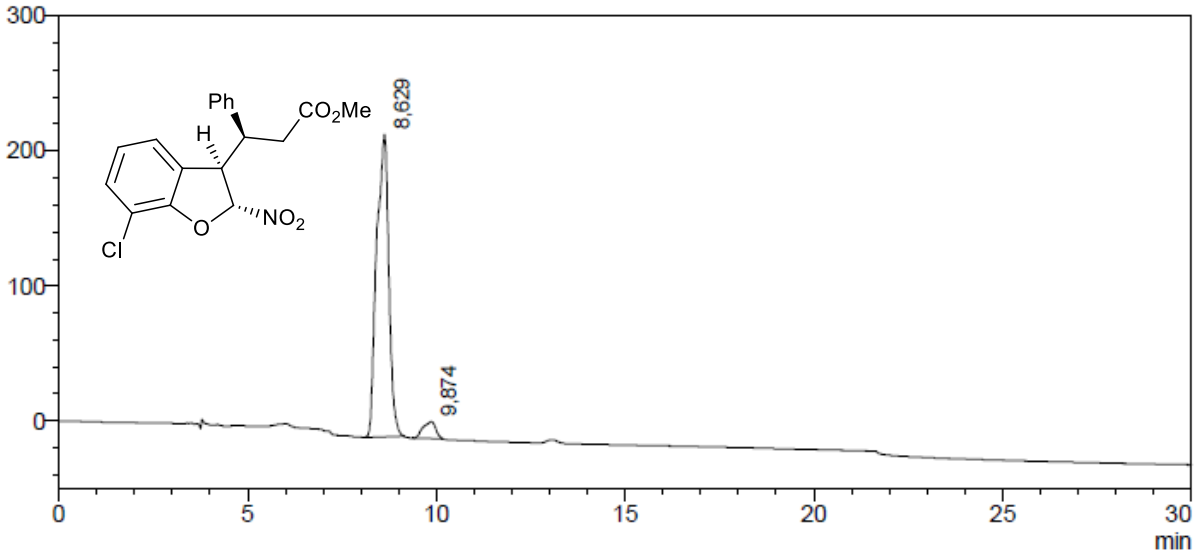
(*S*)-Methyl 3-((2*R*,3*R*)-7-chloro-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate 3s

Racemic sample



Peak#	Ret. Time	Area%
1	8,704	50,170
2	9,949	49,830
Total		100,000

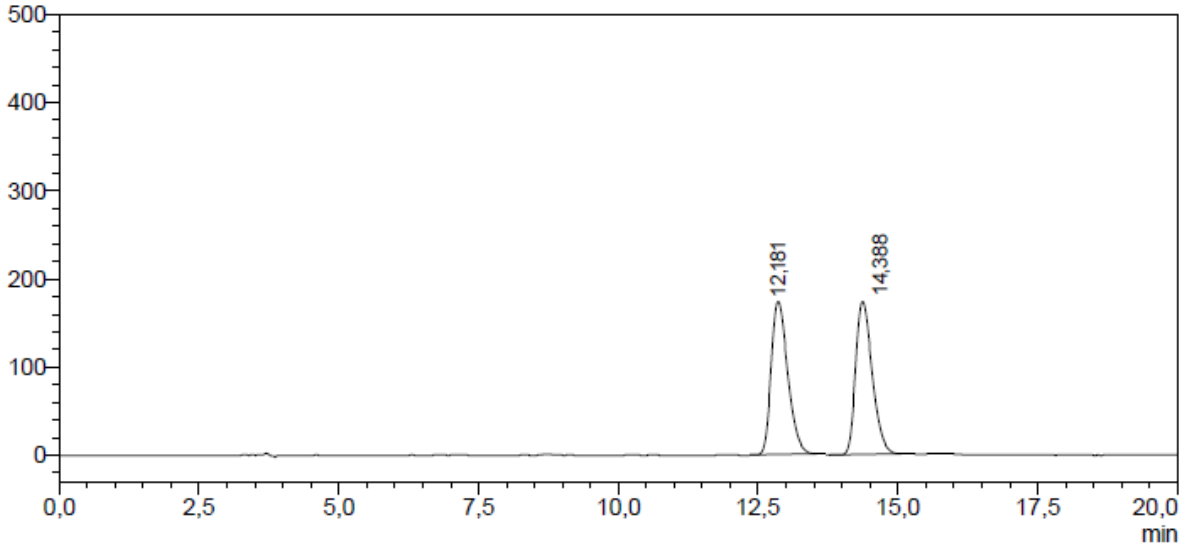
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	8,629	94,594
2	9,874	5,406
Total		100,000

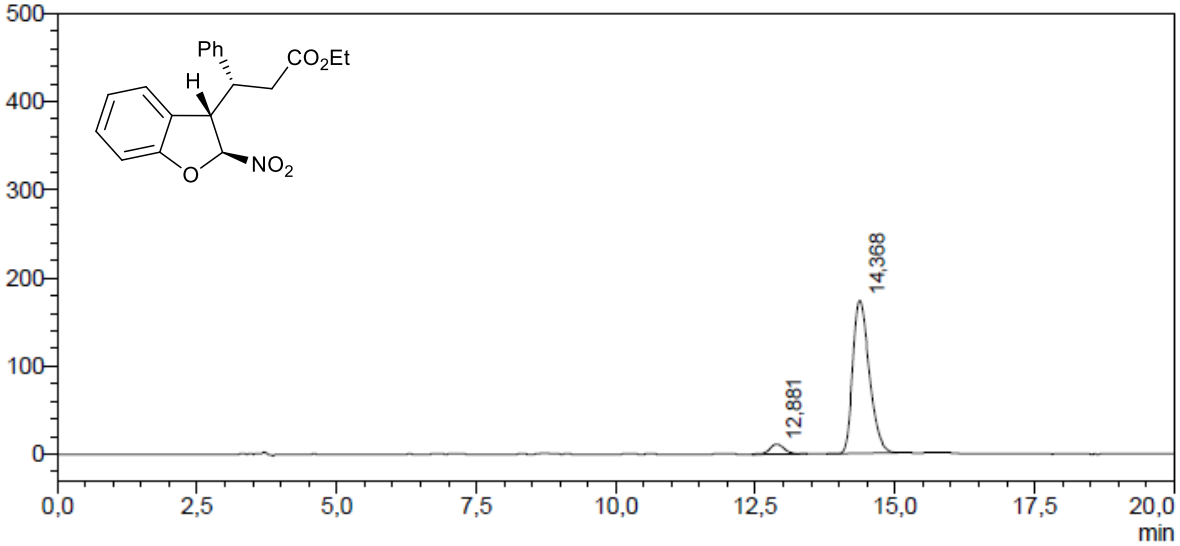
(*R*)-Ethyl 3-((2*S*,3*S*)-2-nitro-2,3-dihydrobenzofuran-3-yl)-3-phenylpropanoate 3t

Racemic sample



Peak#	Ret. Time	Area%
1	12,181	50,693
2	14,388	49,307
Total		100,000

Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	12,881	5,309
2	14,368	94,691
Total		100,000