Electronic Supplementary Material (ESI) for Chemical Communications

Organocatalytic asymmetric domino Michael- Henry reaction for the synthesis of substituted bicyclo[3.2.1]octan-2-ones

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Supporting Information

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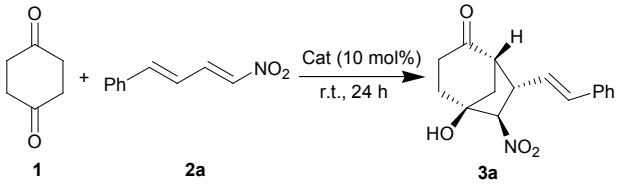
General Remarks

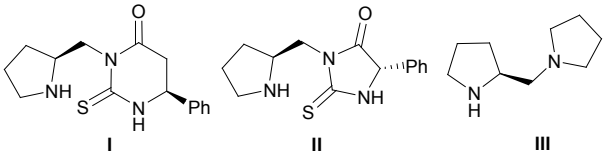
Chromatographic purification of products was accomplished using forced-flow chromatography on Merck Kieselgel 60 F_{254} 230-400 mesh. Thin-layer chromatography (TLC) was performed on aluminum backed silica plates (0.2 mm, 60 F_{254}). Visualization of the developed chromatogram was performed by fluorescence quenching using phosphomolybdic acid stains. Optical rotations were measured on a Perkin Elmer 343 polarimeter. Melting points were determined on a Buchi 530 hot stage apparatus and are uncorrected. IR spectra were recorded on a Nicolet 6700 FT-IR spectrometer and are reported in terms of frequency of absorption (cm^{-1}). ^{1}H spectra were recorded on Varian Mercury (600 MHz, 300 MHz or 200 MHz) and are internally referenced to residual protio solvent signals (acetone-d_6). Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quadruplet, m = multiplet, bs = broad signal, bs m = broad signal multiplet), coupling constant and assignment. ^{13}C NMR spectra were recorded on Varian Mercury (75 MHz or 50 MHz) and are internally referenced to residual protio solvent signals (acetone-d_6). Data for ^{13}C NMR are reported in terms of chemical shift (δ ppm). Mass spectra were recorded on a Finnigan Surveyor MSQ Plus, with only molecular ions and major peaks being reported with intensities quoted as percentages of the base peak. Chiral High Performance Liquid Chromatography (HPLC) analyses were performed using an Agilent 1100 Series apparatus and Chiralpak® AD-H and OD-H columns.

Optimization studies

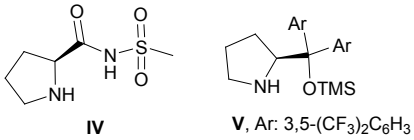
Table 1. Screening of bifunctional catalysts used in the model reaction[a]



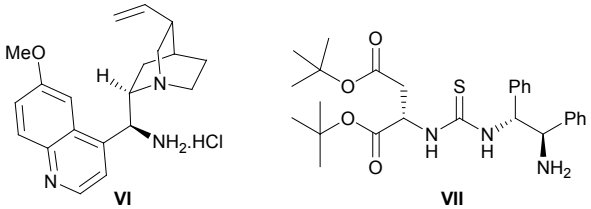
1 **2a** **3a**



I **II** **III**



IV **V**, Ar: 3,5-$(CF_3)_2C_6H_3$

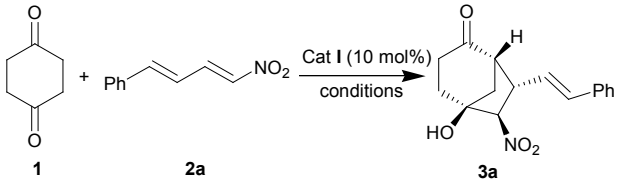


VI **VII**

Entry	Catalyst	Solvent	Additives (10 mol%)	Yield (%)[b]	*ee* (%)[c]
1	L-Proline	DMSO	-	94	19
2	**I**	THF	4-NBA, H_2O[d]	91	96
3	**II**	THF	4-NBA, H_2O[d]	22	90
4	**III**	THF	-	92	75
5	**IV**	THF	-	Traces	-
6	**V**	THF	-	-	-
8	**VI**	THF	Na_2CO_3	10	-52
9	**VII**	THF	Benzoic acid	-	-

[a] Reactions were performed using **1** (0.2) mmol, **2a** (0.1 mmol), catalyst (10 mol%) and additive (10 mol%) in solvent (0.25 ml) at room temperature for 24 hours. [b] Isolated yield. [c] The enantiomeric excess (*ee*) was determined by chiral HPLC. [d] 50 μL of H_2O were used. 4-NBA: 4-Nitrobenzoic acid.

Table 2. Optimization of the reaction conditions using catalyst **I**[a]



1 **2a** **3a**

Entry	Solvent	Additives (10 mol%)	Yield (%)[b]	*ee* (%)[c]
1	THF	4-NBA, H_2O[d]	95 (91)	96
2	Toluene	4-NBA, H_2O[d]	48	90
3	$CHCl_3$	4-NBA, H_2O[d]	50	92
4	CH_2Cl_2	4-NBA, H_2O[d]	58	90
5	CH_3CN	4-NBA, H_2O[d]	62	93
6	Et_2O	4-NBA, H_2O[d]	72	94
7	Dioxane	4-NBA, H_2O[d]	65	90
8	MeOH	4-NBA, H_2O[d]	-	-
9	THF	4-CBA, H_2O[d]	58	89
10	THF	Acetic acid, H_2O[d]	34	87
11	THF	Benzoic acid, H_2O[d]	Traces	-
12	THF	4-NBA	Traces	-
13[e]	THF	4-NBA, H_2O[d]	74(72)	96
14[f]	THF	4-NBA, H_2O[d]	76(75)	96

[a] Reactions were performed using **1** (0.2) mmol, **2a** (0.1 mmol), catalyst **I** (10 mol%) and additive (10 mol%) in solvent (0.25 ml) at room temperature for 24 hours. [b] Yields were determined by ^{1}H NMR analysis of the crude reaction mixture, isolated yield in parenthesis. [c] The enantiomeric excess (*ee*) was determined by chiral HPLC. [d] 50 μL of H_2O were used. [e] 5 mol% of catalyst **I** was used. [f] 1.1 equiv. of **1** was used. 4-NBA: 4-Nitrobenzoic acid, 4-CBA: 4-Cyanobenzoic acid.

General procedure for the domino Michael-Henry reaction between 1,4-cyclohexanedione and nitrodienes

A solution of catalyst **I** (3 mg, 0.01 mmol), nitrodiene (0.1 mmol), diketone **1** (22 mg, 0.2 mmol), 4-NBA (1.7 mg, 0.01 mmol) and H_2O (50 μL) in dry THF (0.25 mL) was stirred for 24 hours. The solvent was evaporated and the crude product was purified using flash column chromatography eluting with 1:1 mixture of petroleum ether (40-60 ^oC)/ethyl acetate to afford the desired bicyclic product.

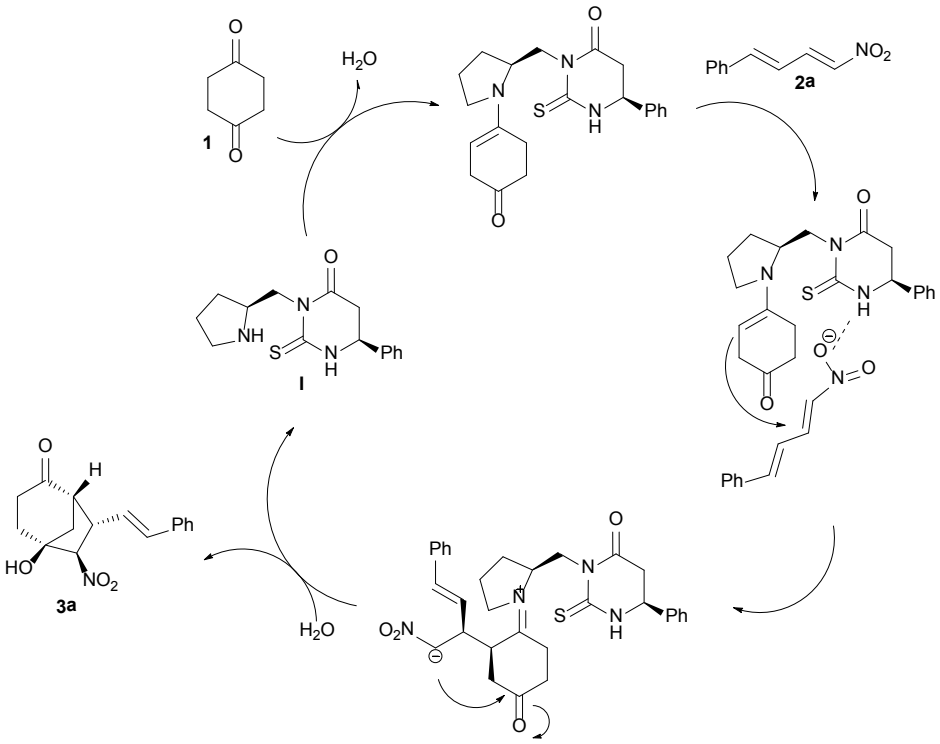
Racemic compounds were prepared following the general procedure using racemic proline (10 mol%) as catalyst, no additives and DMSO as the reaction solvent.

General procedure for the domino Michael-Henry reaction between 1,4-cyclohexanedione and nitrostyrenes

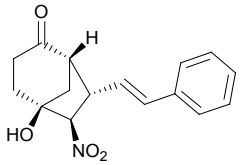
A solution of catalyst **I** (6 mg, 0.02 mmol), nitrostyrene (0.1 mmol), diketone **1** (22 mg, 0.2 mmol), 4-NBA (3.4 mg, 0.02 mmol) and H_2O (50 μL) in dry THF (0.25 mL) was stirred for 24 hours. The solvent was evaporated and the crude product was purified using flash column chromatography eluting with 1:1 mixture of petroleum ether (40-60 ^oC)/ethyl acetate to afford the desired bicyclic product.

Racemic compounds were prepared following the general procedure using racemic proline (20 mol%) as catalyst, no additives and DMSO as the reaction solvent.

Figure 1 Proposed mechanistic pathway for the organocatalytic domino Michael- Henry reaction between 1,4-cyclohexanedione and nitroalkenes.

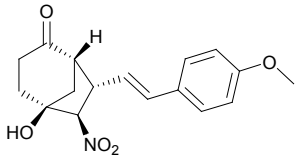


(1*S*, 5*S*, 6*R*, 7*S*, *E*)-5-Hydroxy-6-nitro-7-styrylbicyclo[3.2.1]octan-2-one (3a)



White solid (91%); $[\alpha]_D^{20}$ = -18.4 (*c* 0.25, CH_3OH); mp 142-144 °C; **^{1}H NMR** (200 MHz, acetone-d_6) δ 7.42-7.23 (5H, m, Ph), 6.66 (1H, d, *J* = 16.1 Hz, =CHPh), 6.32 (1H, dd, *J* = 16.1 and 6.8 Hz, =CH), 5.30 (1H, d, *J* = 5.9 Hz, $CHNO_2$), 5.19 (1H, s, OH), 4.15-4.01 (1H, m, C**H**$CHNO_2$), 3.04-2.93 (1H, m, COCH), 2.65-2.42 (3H, m, 3 x CH**H**), 2.37-2.15 (3H, m, 3 x CH**H**); **^{13}C NMR** (75 MHz, acetone-d_6) δ 208.4, 137.3, 133.9, 129.3, 128.6, 127.2, 125.7, 95.5, 79.0, 54.7, 50.3, 41.0, 38.1, 35.3; **IR** 3437, 2067, 1637, 1555, 1494, 1449, 1134, 968, 747 (film) cm^{-1}; **MS** (ESI) *m/z* (%): 286 [M-H, (100)]$^-$; **HRMS** exact mass calculated for $[M-H]^-$ ($C_{16}H_{16}NO_4$) requires *m/z* 286.1085, found *m/z* 286.1082; HPLC analysis: 96% ee, Daicel Chiralpak AD-H, hexane/*i*-PrOH (90/10), 0.7 mL/min, t_R = 24.58 min (major), 29.60 min (minor).

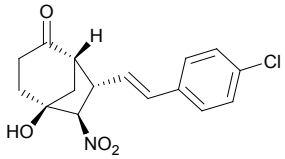
(1*S*, 5*S*, 6*R*, 7*S*, *E*)-7-(4-Methoxystyryl)-5-hydroxy-6-nitrobicyclo[3.2.1]octan-2-one (3b)



White solid (56%); $[\alpha]_D^{20}$ = +18.2 (*c* 0.5, acetone); mp 143-145 °C; **^{1}H NMR** (200 MHz, acetone-d_6) δ 7.33 (2H, d, *J* = 8.8 Hz, Ar), 6.86 (2H, d, *J* = 8.8 Hz, Ar), 6.58 (1H, d, *J* = 16.2 Hz, =CHAr), 6.15 (1H, dd, *J* = 16.2 and 7.0 Hz, =CH), 5.26 (1H, d, *J* = 5.9 Hz, $CHNO_2$), 5.21 (1H, s, OH), 4.08-3.98 (1H, m, C**H**$CHNO_2$), 3.77 (3H, s, OCH_3), 2.99-2.84 (1H, m, COCH), 2.67-2.57 (1H, m, CH**H**), 2.55-2.48 (1H, m, CH**H**), 2.46-2.39 (1H, m, CH**H**), 2.34-2.24 (1H, m, CH**H**), 2.22-2.08 (2H, m, CH_2); **^{13}C NMR** (50 MHz, acetone-d_6) δ 208.5, 160.5, 133.5, 130.0, 128.5, 123.2, 114.8, 95.7, 79.0, 55.5, 54.9, 50.6, 41.1, 38.2, 35.4; **IR** (film) 3381, 2962, 2358, 1708, 1554, 1511, 1368, 1293, 1248, 1175, 1030, 806, 778 cm^{-1}; **MS** (ESI) *m/z* (%): 316 [M-H, (15)]$^-$; **HRMS** exact mass calculated

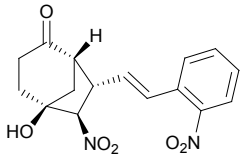
for $[M-H]^-$ ($C_{17}H_{18}NO_5$) requires *m/z* 316.1190, found *m/z* 316.1184; HPLC analysis: 94% ee, Daicel Chiralpak AD-H, hexane/*i*-PrOH (90/10), 1.0 mL/min, t_R = 25.71 min (major), 34.35 min (minor).

(1*S*, 5*S*, 6*R*, 7*S*, *E*)-7-(4-Chlorostyryl)-5-hydroxy-6-nitrobicyclo[3.2.1]octan-2-one (3c)



White solid (72%); $[\alpha]_D^{20}$ = +10.3 (*c* 1.0, acetone); mp 151-154 °C; **^{1}H NMR** (600 MHz, acetone-d_6) δ 7.41 (2H, d, *J* = 8.4 Hz, ArH), 7.32 (2H, d, *J* = 8.4 Hz, ArH), 6.64 (1H, d, *J* = 16.2 Hz, =CHAr), 6.35 (1H, dd, *J* = 16.2 and 6.9 Hz, =CH), 5.28 (1H, d, *J* = 5.8 Hz, $CHNO_2$), 5.20 (1H, s, OH), 4.07 (1H, *pseudo* q, *J* = 5.8 Hz, C**H**$CHNO_2$), 2.97 (1H, t, *J* = 5.8 Hz, COCH), 2.61-2.56 (1H, m, CH**H**), 2.52-2.46 (1H, m, C**H**H), 2.40 (1H, dd, *J* = 17.6 and 7.7 Hz, CH**H**), 2.30 (1H, ddd, *J* = 12.6, 8.9 and 3.8 Hz, CH**H**), 2.21-2.14 (1H, m, CH**H**), 2.10-2.05 (1H, m, CH**H**); **^{13}C NMR** (50 MHz, acetone-d_6) δ 208.4, 136.2, 133.7, 132.6, 129.4, 128.8, 126.8, 95.3, 79.0, 54.7, 50.3, 41.0, 38.1, 35.4; **IR** (film) 3416, 2964, 1709, 1555, 1491, 1369, 1090, 971, 804, 775 cm^{-1}; **MS** (ESI) *m/z* (%): 320 [M-H, (75)]$^-$; **HRMS** exact mass calculated for $[M-H]^-$ ($C_{16}H_{15}NO_4Cl$) requires *m/z* 320.0695, found *m/z* 320.0687; HPLC analysis: 91% ee, Daicel Chiralpak AD-H, hexane/*i*-PrOH (90/10), 1.0 mL/min, t_R = 27.63 min (major), 33.82 min (minor).

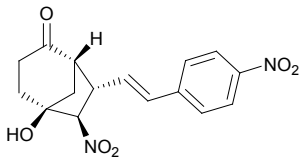
(1*S*, 5*S*, 6*R*, 7*S*, *E*)-7-(2-Nitrostyryl)-5-hydroxy-6-nitrobicyclo[3.2.1]octan-2-one (3d)



White solid (89%); $[\alpha]_D^{20}$ = -6.6 (*c* 0.5, CH_3OH); mp 126-129 °C; **^{1}H NMR** (200 MHz, acetone-d_6) δ 7.99-7.91 (1H, m, ArH), 7.74-7.62 (2H, m, ArH), 7.60-7.47 (1H, m, ArH), 7.04 (1H, d, *J* = 16.0 Hz, =CHAr), 6.37 (1H, dd, *J* = 16.0 and 6.6 Hz, =CH), 5.35 (1H, d, *J* = 5.9 Hz, $CHNO_2$), 5.29 (1H, s, OH), 4.25-4.11 (1H, m, C**H**$CHNO_2$), 3.09-2.99 (1H, m, COCH), 2.68-2.50 (2H, m, 2 x CH**H**), 2.49-2.40 (1H, m, CH**H**), 2.35-2.17 (2H, m, 2 x

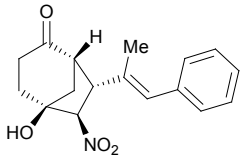
CH**H**), 2.14-2.07 (1H, m, CH**H**); **^{13}C NMR** (50 MHz, acetone-d_6) δ 208.3, 148.9, 134.2, 132.5, 131.3, 129.7, 129.6, 128.9, 125.2, 95.0, 79.1, 54.6, 50.2, 41.0, 38.1, 35.4; **IR** (film) 3402, 2966, 2360, 2337, 1711, 1553, 1522, 1345, 1056, 669 cm^{-1}; **MS** (ESI) *m/z* (%): 331 [M-H, (30)]$^-$; **HRMS** exact mass calculated for [M-H]$^-$ ($C_{16}H_{15}N_2O_6$) requires *m/z* 331.0936, found *m/z* 331.0930; HPLC analysis: 86% ee, Daicel Chiralpak AD-H, hexane/*i*-PrOH (80/20), 1.0 mL/min, t_R = 16.75 min (major), 32.66 min (minor).

(1*S*, 5*S*, 6*R*, 7*S*, *E*)-7-(4-Nitrostyryl)-5-hydroxy-6-nitrobicyclo[3.2.1]octan-2-one (3e)



Yellow solid (73%); $[\alpha]_D^{20}$ = +9.5 (*c* 1.0, acetone); mp 138-140 ^{o}C; **^{1}H NMR** (200 MHz, acetone-d_6) δ 8.19 (2H, d, *J* = 8.5 Hz, ArH), 7.69 (2H, d, *J* = 8.5 Hz, ArH), 6.83 (1H, d, *J* = 16.1 Hz, =CHAr), 6.65 (1H, dd, *J* = 16.1 and 6.6 Hz, =CH), 5.36 (1H, d, *J* = 5.9 Hz, $CHNO_2$), 5.31 (1H, s, OH), 4.23-4.11 (1H, m, C**H**$CHNO_2$), 3.09-2.99 (1H, m, COCH), 2.65-2.50 (2H, m, 2 x CH**H**), 2.47-2.43 (1H, m, CH**H**), 2.40-2.27 (1H, m, CH**H**), 2.25-2.11 (2H, m, 2 x CH**H**); **^{13}C NMR** (75 MHz, acetone-d_6) δ 208.3, 148.0, 144.0, 132.0, 131.2, 128.1, 124.7, 95.1, 79.1, 54.6, 50.3, 41.1, 38.1, 35.4; **IR** (film) 3408, 2968, 2357, 1711, 1596, 1555, 1515, 1343, 1137, 1110, 975, 863, 777, 745 cm^{-1}; **MS** (ESI) *m/z* (%): 331 [M-H, (85)]$^-$; **HRMS** exact mass calculated for [M-H]$^-$ ($C_{16}H_{15}N_2O_6$) requires *m/z* 331.0936, found *m/z* 331.0926; HPLC analysis: 97% ee, Daicel Chiralpak AD-H, hexane/*i*-PrOH (80/20), 1.0 mL/min, t_R = 31.62 min (major), 40.42 min (minor).

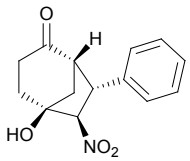
(1*S*, 5*S*, 6*R*, 7*R*, *E*)-5-Hydroxy-6-nitro-7-(1-phenylprop-1-en-2-yl) bicyclo[3.2.1]octan-2-one (3f)



White solid (70%); $[\alpha]_D^{20}$ = +4.6 (*c* 0.5, acetone); mp 111-114 ^{o}C; **^{1}H NMR** (200 MHz, acetone-d_6) δ 7.40-7.15 (5H, m, Ph), 6.59 (1H, s, =CHPh), 5.58 (1H, d, *J* = 6.5 Hz, $CHNO_2$), 5.26 (1H, s, OH), 4.13-4.00 (1H, m, C**H**$CHNO_2$), 3.21 (1H, t, *J* = 5.7 Hz,

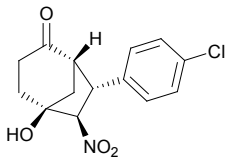
COCH), 2.70-2.54 (1H, m, CH**H**), 2.45-2.27 (3H, m, 3 x CH**H**), 2.24-2.10 (2H, m, 2 x CH**H**), 1.85 (3H, s, CH_3); **^{13}C NMR** (50 MHz, acetone-d_6) δ 209.1, 138.1, 134.6, 129.8, 127.4, 126.1, 125.4, 92.8, 78.6, 55.2, 53.2, 41.3, 38.3, 35.3, 17.8; **IR** (film) 3406, 2970, 1710, 1556, 1447, 1369, 1132, 1086, 979, 778, 750, 702 cm^{-1}; **MS** (ESI) *m/z* (%): 300 [M-H, (75)]$^-$; **HRMS** exact mass calculated for [M-H]$^-$ ($C_{17}H_{18}NO_4$) requires *m/z* 300.1241, found *m/z* 300.1235; HPLC analysis: 95% ee, Daicel Chiralpak AD-H, hexane/*i*-PrOH (90/10), 1.0 mL/min, t_R = 10.83 min (major), 15.23 min (minor).

(1*S*, 5*S*, 6*R*, 7*R*)5-Hydroxy-6-nitro-7-phenylbicyclo[3.2.1]octan-2-one (5a)



White solid (86%); $[\alpha]_D^{20}$ = +3.6 (*c* 0.5, acetone); mp 117-120 ^{o}C; **^{1}H NMR** (200 MHz, acetone-d_6) δ 7.42-7.19 (5H, m, Ph), 5.62 (1H, d, *J* = 6.2 Hz, $CHNO_2$), 5.31 (1H, s, OH), 4.61 (1H, *pseudo* t, *J* = 6.2 Hz, C**H**$CHNO_2$), 3.40 (1H, *pseudo* t, *J* = 6.2 Hz, COCH), 2.77-2.65 (1H, m, CH**H**), 2.41-2.30 (1H, m, CH**H**), 2.27-2.14 (3H, m, 3 x CH**H**), 2.10-2.05 (1H, m, CH**H**); **^{13}C NMR** (50 MHz, acetone-d_6) δ 208.7, 138.0, 129.7, 128.1, 127.5, 95.4, 79.0, 54.0, 51.6, 41.6, 38.5, 35.7; **IR** (film) 3396, 2916, 1702, 1550, 1446, 1372, 1335, 1131, 1080, 779, 745, 698 cm^{-1}; **MS** (ESI) *m/z* (%): 260 [M-H, (100)]$^-$; **HRMS** exact mass calculated for [M-H]$^-$ ($C_{14}H_{14}NO_4$) requires *m/z* 260.0928, found *m/z* 260.0926; HPLC analysis: 93% ee, Daicel Chiralpak AD-H, hexane/*i*-PrOH (90/10), 1.0 mL/min, t_R = 16.02 min (major), 20.13 min (minor).

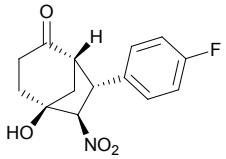
(1*S*, 5*S*, 6*R*, 7*R*)7-(4-Chlorophenyl)-5-hydroxy-6-nitrobicyclo[3.2.1]octan-2-one (5b)



Colourless oil (81%); $[\alpha]_D^{20}$ = -23.8 (*c* 1.0, acetone); **^{1}H NMR** (300 MHz, acetone-d_6) δ 7.44-7.27 (4H, m, ArH), 5.63 (1H, d, *J* = 6.2 Hz, $CHNO_2$), 5.35 (1H, s, OH), 4.62 (1H, *pseudo* t, *J* = 6.2 Hz, C**H**$CHNO_2$), 3.40 (1H, *pseudo* t, *J* = 6.2 Hz, COCH), 2.76-2.66 (1H, m, CH**H**), 2.41-2.23 (2H, m, 2 x CH**H**), 2.21-2.07 (3H, m, 3 x CH**H**); **^{13}C NMR** (75

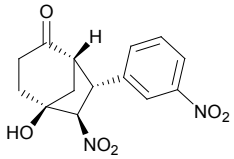
MHz, acetone-d_6) δ 208.5, 136.7, 133.4, 129.6, 129.3, 95.0, 79.0, 54.0, 51.0, 41.4, 38.3, 35.5; **IR** (film) 3413, 2965, 1713, 1556, 1495, 1370, 1229, 1133, 1094, 1013, 981, 813, 776, 507 cm^{-1}; **MS** (ESI) *m/z* (%): 294 [M-H, (65)]$^-$; **HRMS** exact mass calculated for [M-H]$^-$ ($C_{14}H_{13}NO_4Cl$) requires *m/z* 294.0539, found *m/z* 294.0536; HPLC analysis: 95% ee, Daicel Chiralpak AD-H, hexane/*i*-PrOH (90/10), 1.0 mL/min, t_R = 18.06 min (minor), 21.97 min (major).

(1*S*, 5*S*, 6*R*, 7*R*)7-(4-Fluorophenyl)-5-hydroxy-6-nitrobicyclo[3.2.1]octan-2-one (5c)



Colourless oil (75%); $[\alpha]_D^{20}$ = -35.2 (*c* 1.0, acetone); **^{1}H NMR** (300 MHz, acetone-d_6) δ 7.39-7.27 (2H, m, ArH), 7.20-7.06 (2H, m, ArH), 5.62 (1H, d, *J* = 6.3 Hz, $CHNO_2$), 5.34 (1H, s, OH), 4.60 (1H, *pseudo* t, *J* = 6.3 Hz, C**H**$CHNO_2$), 3.39 (1H, *pseudo* t, *J* = 6.3 Hz, COCH), 2.76-2.65 (1H, m, CH**H**), 2.41-2.31 (1H, m, CH**H**), 2.28-2.11 (3H, m, 3 x CH**H**), 2.09-1.96 (1H, m, CH**H**); **^{19}F NMR** (186 MHz, acetone-d_6) δ -117.1 (m, ArF); **^{13}C NMR** (75 MHz, acetone-d_6) δ 208.5, 162.6 (d, *J* = 244 Hz, Ar), 133.8 (d, *J* = 3 Hz, Ar), 129.5 (d, *J* = 8 Hz, Ar), 116.3 (d, *J* = 22 Hz, Ar), 95.2, 79.0, 54.1, 51.0, 41.4, 38.3, 35.5; **IR** (film) 3405, 2966, 1711, 1556, 1513, 1370, 1231, 1165, 1131, 981, 833, 801, 772, 568, 522 cm^{-1}; **MS** (ESI) *m/z* (%): 278 [M-H, (30)]$^-$; **HRMS** exact mass calculated for [M-H]$^-$ ($C_{14}H_{13}FNO_4$) requires *m/z* 278.0834, found *m/z* 278.0829; HPLC analysis: 93% ee, Daicel Chiralpak OD-H, hexane/*i*-PrOH (90/10), 1.0 mL/min, t_R = 25.55 min (minor), 30.50 min (major).

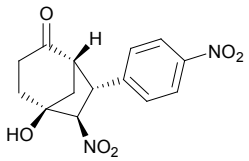
(1*S*, 5*S*, 6*R*, 7*R*)-5-Hydroxy-6-nitro-7-(3-nitrophenyl)bicyclo[3.2.1]octan-2-one (5d)



Light yellow oil (80%); $[\alpha]_D^{20}$ = -5.4 (*c* 1.0, acetone); **^{1}H NMR** (200 MHz, acetone-d_6) δ 8.24-8.10 (2H, m, ArH), 7.83-7.61 (2H, m, ArH), 5.82 (1H, d, *J* = 6.2 Hz, $CHNO_2$), 5.43 (1H, s, OH), 4.80 (1H, *pseudo* t, *J* = 6.2 Hz, C**H**$CHNO_2$), 3.53 (1H, *pseudo* t, *J* = 6.2 Hz,

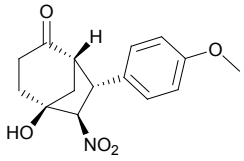
COCH), 2.81-2.71 (1H, m, CH**H**), 2.45-2.10 (5H, m, 5 x CH**H**); **^{13}C NMR** (75 MHz, acetone-d_6) δ 208.9, 139.9, 136.1, 134.1, 130.9, 122.9, 122.4, 94.3, 79.0, 53.9, 51.0, 41.1, 38.0, 35.4; **IR** (film) 3417, 2914, 1711, 1555, 1530, 1416, 1350, 1311, 1138, 963, 808, 736, 692 cm^{-1}; **MS** (ESI) *m/z* (%): 305 [M-H, (35)]$^-$; **HRMS** exact mass calculated for [M-H]$^-$ ($C_{14}H_{13}N_2O_6$) requires *m/z* 305.0779, found *m/z* 305.0775; HPLC analysis: 96% ee, Daicel Chiralpak AD-H, hexane/*i*-PrOH (85/15), 1.0 mL/min, t_R = 31.45 min (major), 52.48 min (minor).

(1*S*, 5*S*, 6*R*, 7*R*)5-Hydroxy-6-nitro-7-(4-nitrophenyl)bicyclo[3.2.1]octan-2-one (5e)



Colourless oil (70%); $[\alpha]_D^{20}$ = -3.1 (*c* 1.0, acetone); **^{1}H NMR** (200 MHz, acetone-d_6) δ 8.23 (2H, d, *J* = 8.8 Hz, ArH), 7.60 (2H, d, *J* = 8.8 Hz, ArH), 5.76 (1H, d, *J* = 6.2 Hz, $CHNO_2$), 5.40 (1H, s, OH), 4.80 (1H, *pseudo* t, *J* = 6.2 Hz, C**H**$CHNO_2$), 3.50 (1H, *pseudo* t, *J* = 6.2 Hz, COCH), 2.79-2.64 (1H, m, CH**H**), 2.43-2.11 (5H, m, 5 x CH**H**); **^{13}C NMR** (75 MHz, acetone-d_6) δ 209.2, 146.4, 132.0, 130.0, 125.6, 95.5, 80.0, 55.1, 52.5, 42.3, 39.1, 36.5; **IR** (film) 3448, 2918, 1713, 1602, 1555, 1520, 1348, 1133, 853, 777, 700 cm^{-1}; **MS** (ESI) *m/z* (%): 305 [M-H, (20)]$^-$; **HRMS** exact mass calculated for [M-H]$^-$ ($C_{14}H_{13}N_2O_6$) requires *m/z* 305.0779, found *m/z* 305.0771; HPLC analysis: 93% ee, Daicel Chiralpak AD-H, hexane/*i*-PrOH (85/15), 1.0 mL/min, t_R = 35.47 min (minor), 42.98 min (major).

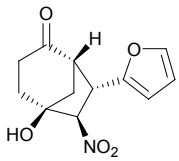
(1*S*, 5*S*, 6*R*, 7*R*)5-Hydroxy-7-(4-methoxyphenyl)-6-nitrobicyclo[3.2.1]octan-2-one (5f)



Colourless oil (83%); $[\alpha]_D^{20}$ = -8.6 (*c* 1.0, acetone); **^{1}H NMR** (200 MHz, acetone-d_6) δ 7.20 (2H, d, *J* = 8.8 Hz, ArH), 6.89 (2H, d, *J* = 8.8 Hz, ArH), 5.56 (1H, d, *J* = 6.3 Hz, $CHNO_2$), 5.25 (1H, s, OH), 4.53 (1H, *pseudo* t, *J* = 6.3 Hz, C**H**$CHNO_2$), 3.76 (3H, s,

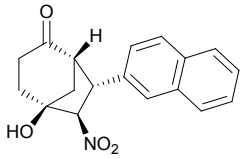
OCH_3), 3.34 (1H, *pseudo* t, J = 6.3 Hz, COCH), 2.80-2.63 (1H, m, CH**H**), 2.39-2.02 (5H, m, 5 x CH**H**); **^{13}C NMR** (50 MHz, acetone-d_6) δ 208.8, 159.8, 129.6, 128.7, 115.0, 95.7, 79.1, 55.6, 54.2, 51.2, 41.6, 38.5, 35.7; **IR** (film) 3409, 2964, 1712, 1613, 1555, 1516, 1446, 1370, 1255, 1185, 1131, 1032, 981, 830, 788 cm^{-1}; **MS** (ESI) *m/z* (%): 290 [M-H, (75)]$^-$; **HRMS** exact mass calculated for [M-H]$^-$ ($C_{15}H_{16}NO_5$) requires *m/z* 290.1034, found *m/z* 290.1026; HPLC analysis: 94% ee, Daicel Chiralpak OD-H, hexane/*i*-PrOH (90/10), 1.0 mL/min, t_R = 35.59 min (minor), 41.06 min (major).

(1*S*, 5*S*, 6*R*, 7*S*)-7-(Furan-2-yl)-5-hydroxy-6-nitrobicyclo[3.2.1]octan-2-one (5g)



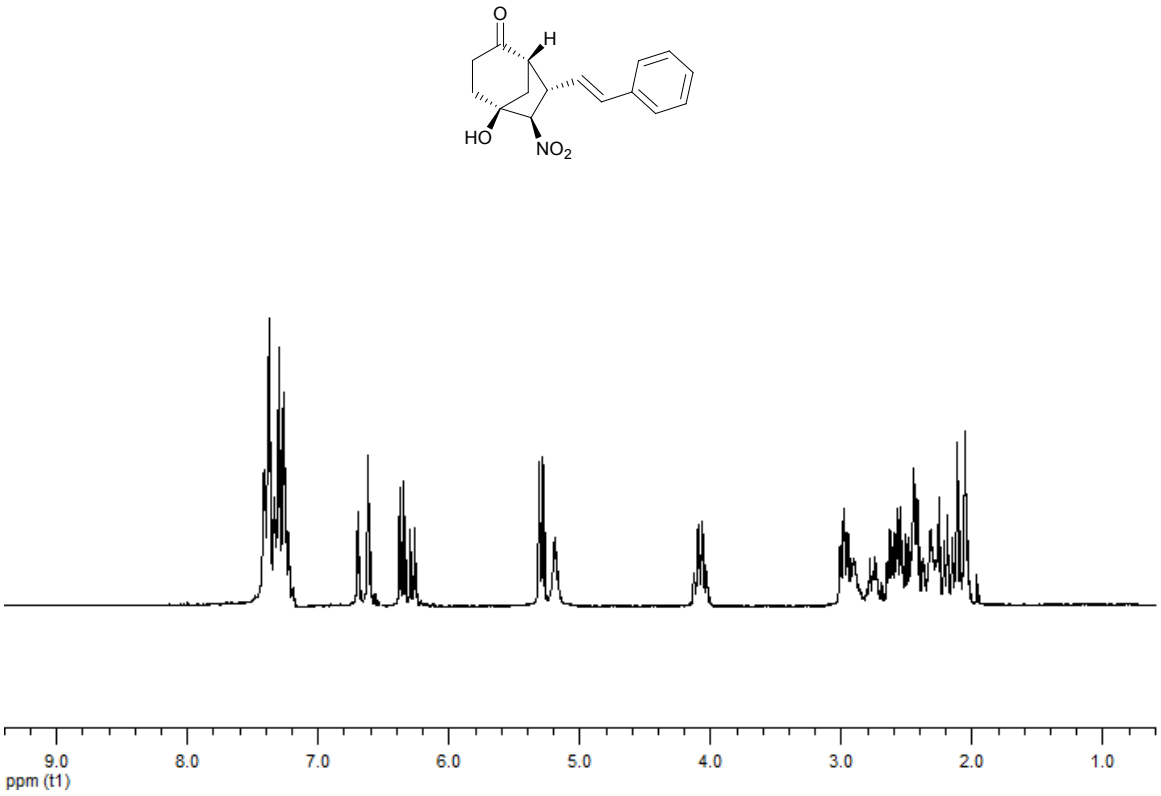
Colourless oil (82%); $[\alpha]_D^{20}$ = -21.2 (*c* 1.0, acetone); **^{1}H NMR** (200 MHz, acetone-d_6) δ 7.52-7.47 (1H, m, ArH), 6.40-6.18 (2H, m, ArH), 5.46 (1H, d, J = 6.2 Hz, $CHNO_2$), 5.33 (1H, s, OH), 4.55 (1H, *pseudo* t, J = 6.2 Hz, C**H**$CHNO_2$), 3.16 (1H, *pseudo* t, J = 6.2 Hz, COCH), 2.68-2.56 (1H, m, CH**H**), 2.44-2.11 (5H, m, 5 x CH**H**); **^{13}C NMR** (75 MHz, acetone-d_6) δ 208.1, 151.3, 143.5, 111.1, 107.3, 94.1, 78.7, 53.0, 46.3, 41.2, 37.9, 35.0; **IR** (film) 2921, 2359, 1711, 1556, 1370, 1251, 1132, 980, 747 cm^{-1}; **MS** (ESI) *m/z* (%): 250 [M-H, (100)]$^-$; **HRMS** exact mass calculated for [M-H]$^-$ ($C_{12}H_{12}NO_5$) requires *m/z* 250.0721, found *m/z* 250.0719; HPLC analysis: 91% ee, Daicel Chiralpak AD-H, hexane/*i*-PrOH (90/10), 1.0 mL/min, t_R = 15.51 min (major), 22.56 min (minor).

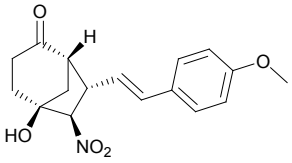
(1*S*, 5*S*, 6*R*, 7*R*)-5-Hydroxy-7-(napthalen-2-yl)-6-nitrobicyclo[3.2.1]octan-2-one (5h)

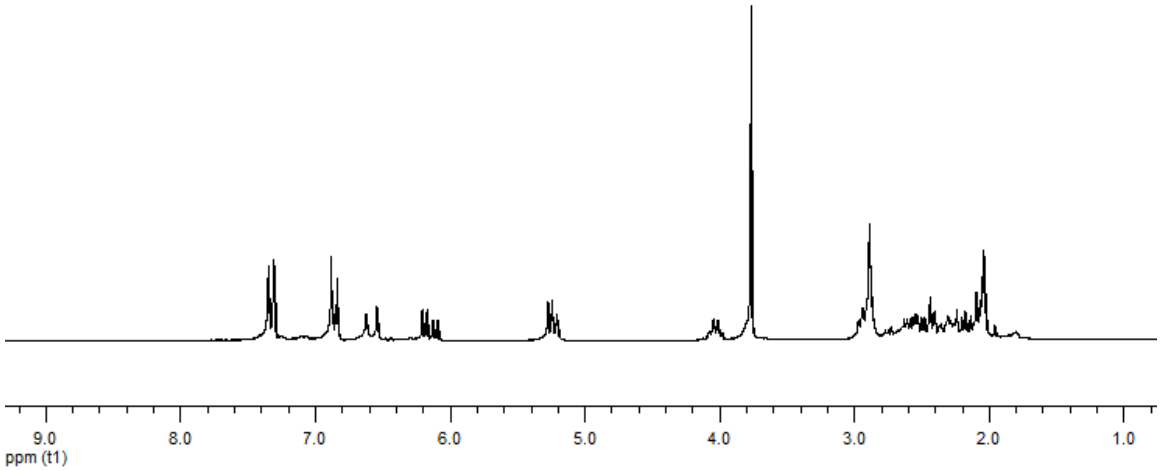


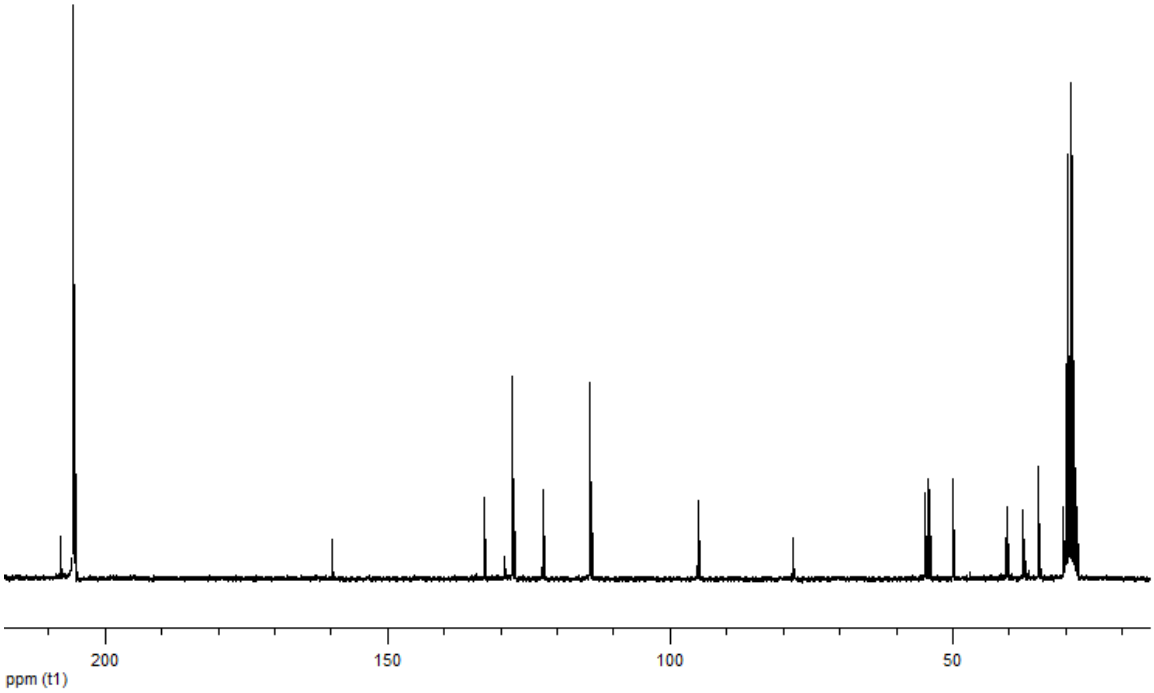
Colourless oil (78%); $[\alpha]_D^{20}$ = +10.2 (*c* 0.5, acetone); **^{1}H NMR** (300 MHz, acetone-d_6) δ 7.93-7.82 (4H, m, ArH), 7.56-7.46 (2H, m, ArH), 7.44-7.38 (1H, m, ArH), 5.82 (1H, d, J = 6.2 Hz, $CHNO_2$), 5.53-5.46 (1H, br s, OH), 4.80 (1H, *pseudo* t, J = 6.2 Hz, C**H**$CHNO_2$), 3.58-3.49 (1H, m, COCH), 2.84-2.73 (1H, m, CH**H**), 2.44-2.34 (1H, m, CH**H**), 2.28-2.10 (4H, m, 4 x CH**H**); **^{13}C NMR** (75 MHz, acetone-d_6) δ 208.6, 135.3,

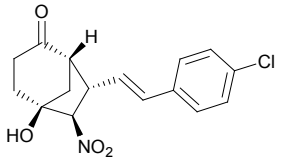
134.2, 133.4, 129.4, 128.7, 128.4, 127.3, 127.0, 126.2, 125.6, 94.9, 79.1, 54.2, 51.8, 41.9, 38.5, 35.7; **IR** (film) 3384, 3058, 2962, 1704, 1555, 1369, 1340, 1250, 1130, 1040, 820, 757, 478 cm^{-1}; **MS** (ESI) *m/z* (%): 310 $[M-H, (100)]^-$; **HRMS** exact mass calculated for $[M-H]^-$ ($C_{18}H_{16}NO_4$) requires *m/z* 310.1085, found *m/z* 310.1079; HPLC analysis: 90% ee, Daicel Chiralpak OD-H, hexane/*i*-PrOH (90/10), 1.0 mL/min, t_R = 33.28 min (minor), 46.18 min (major).

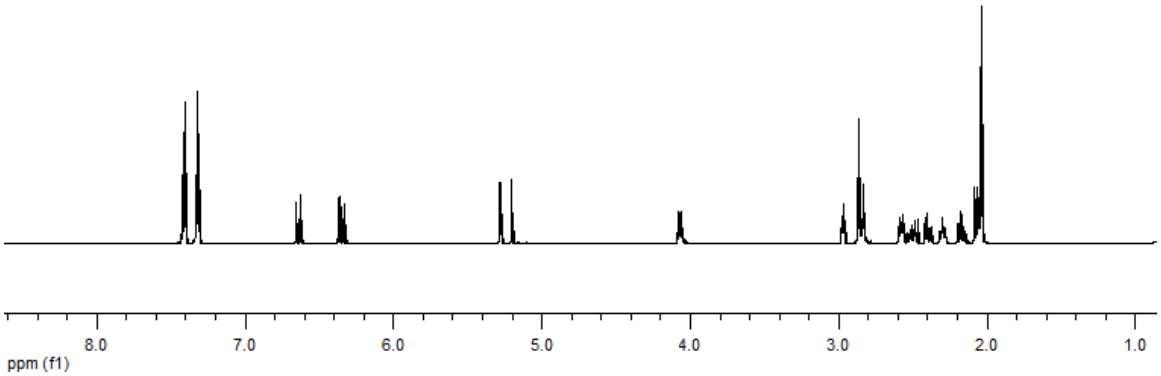


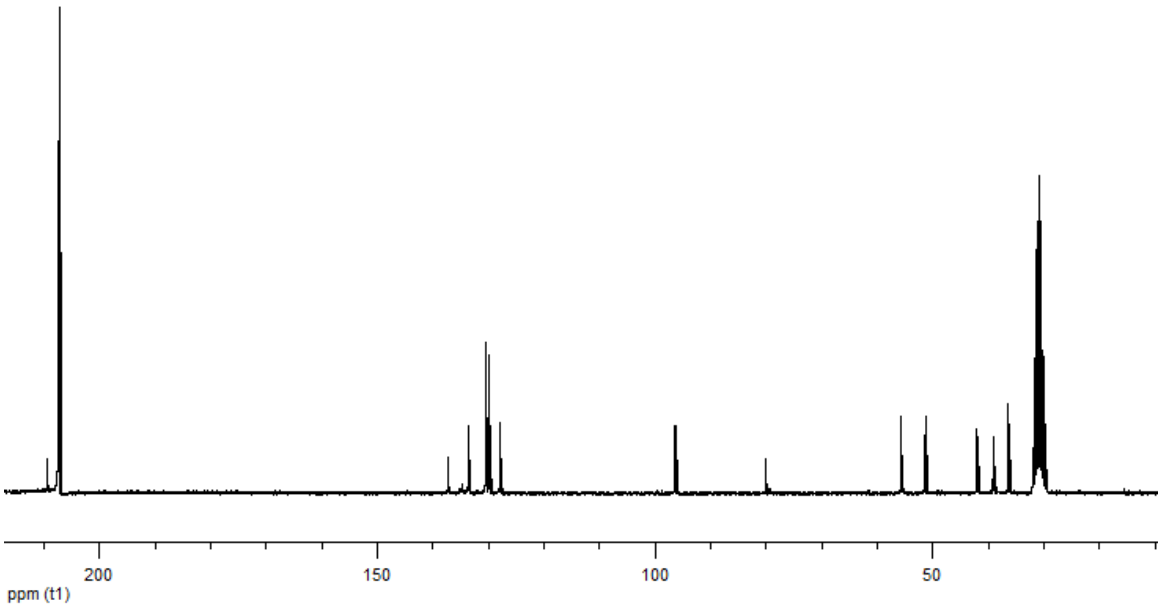


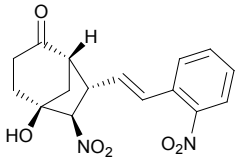


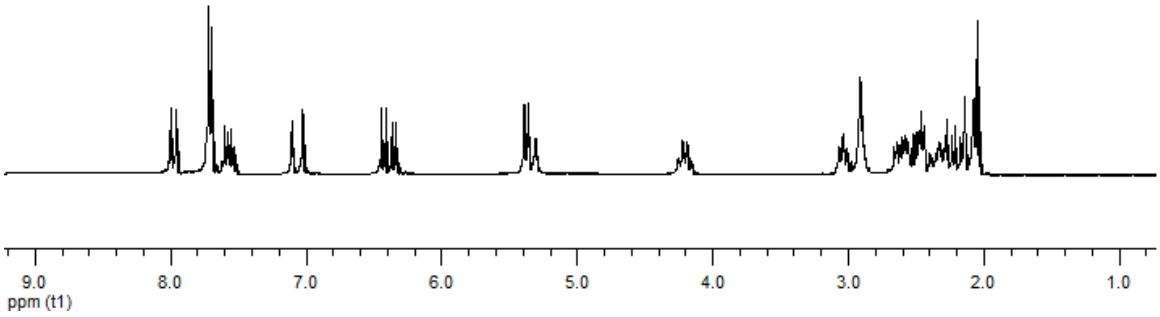


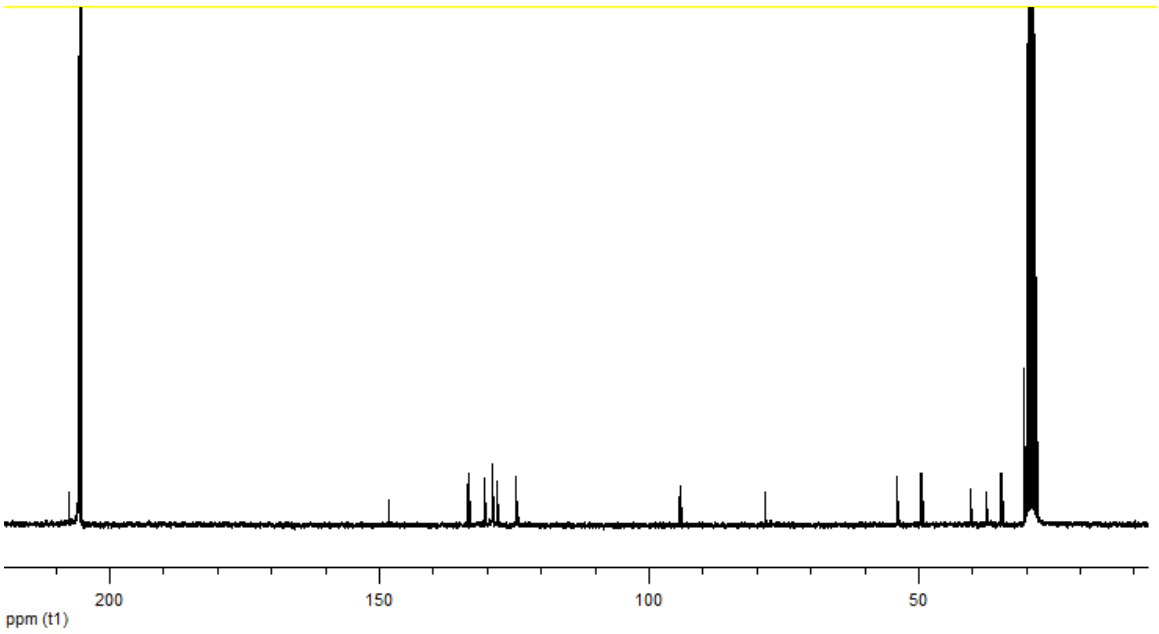


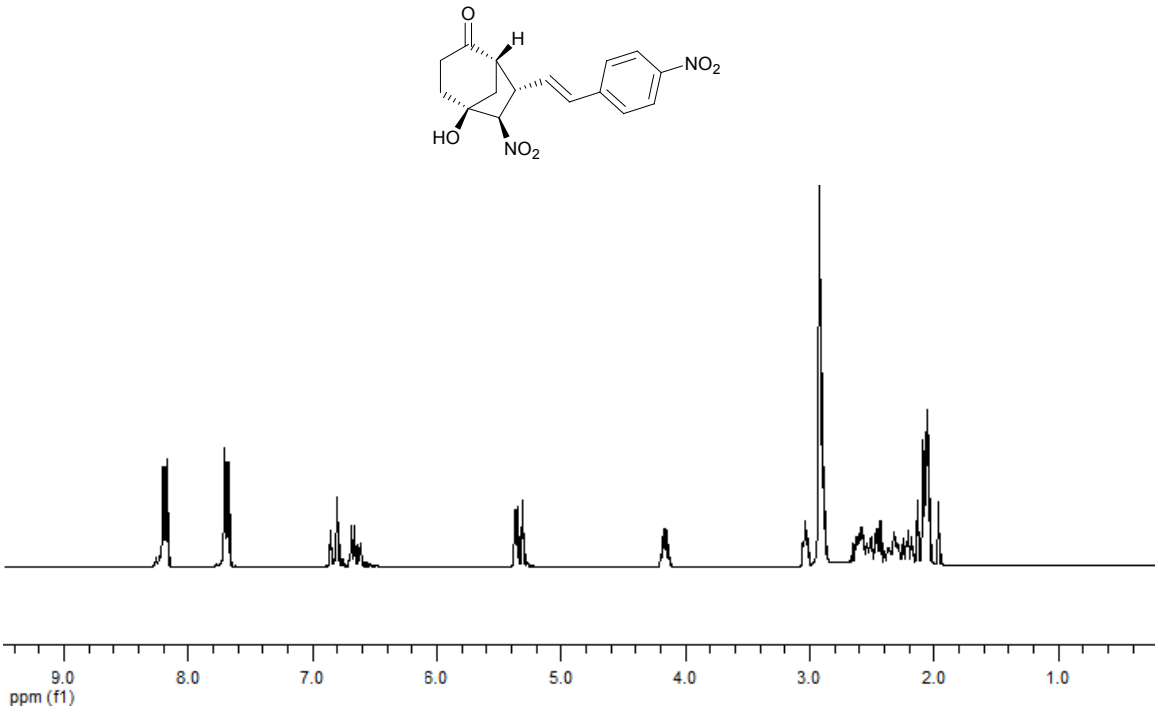


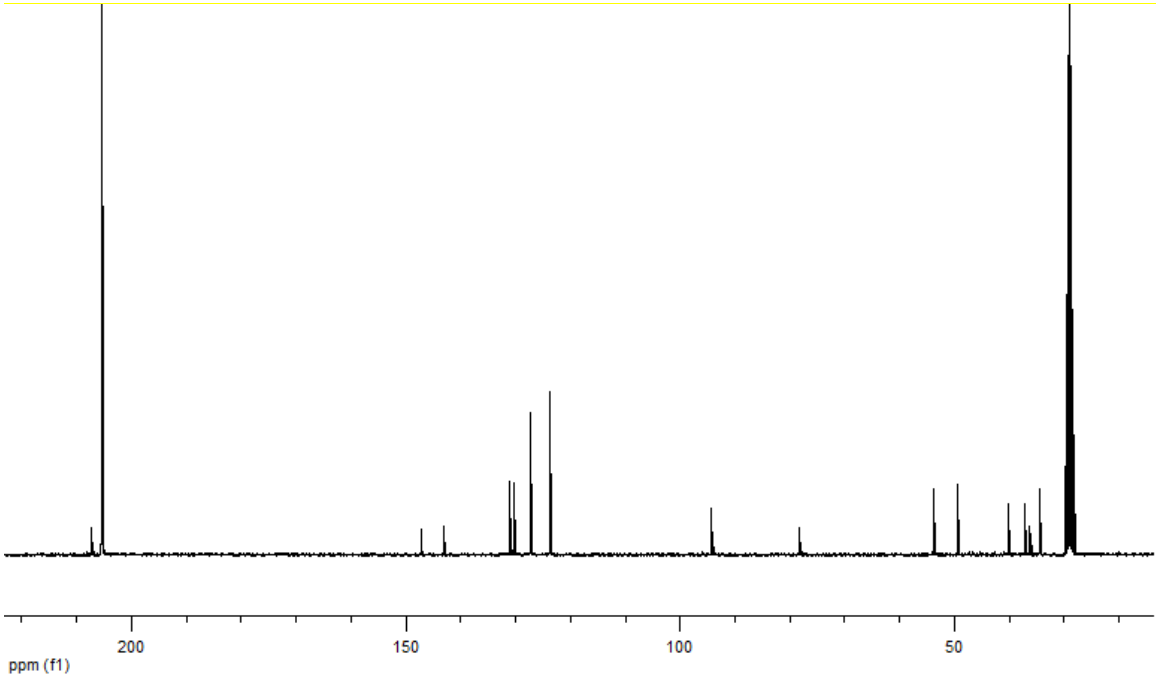


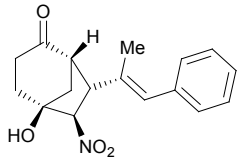


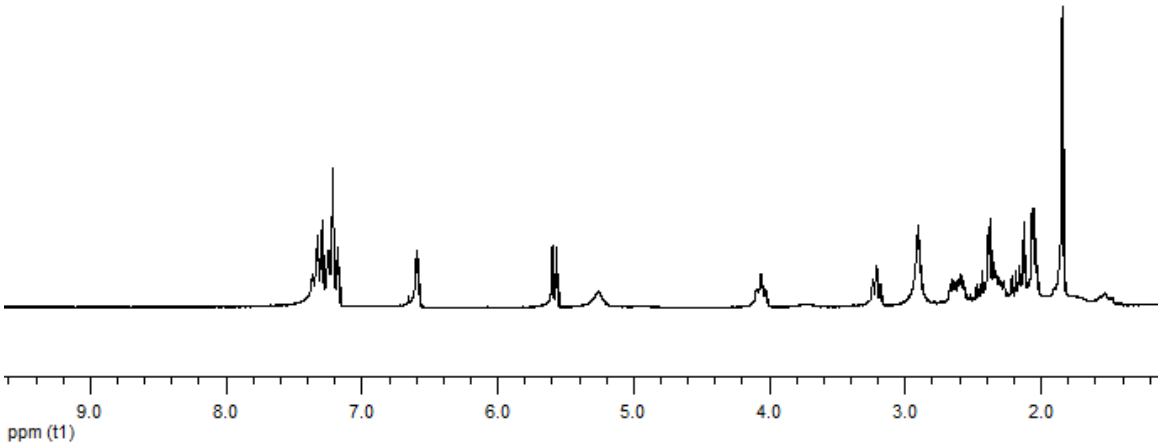


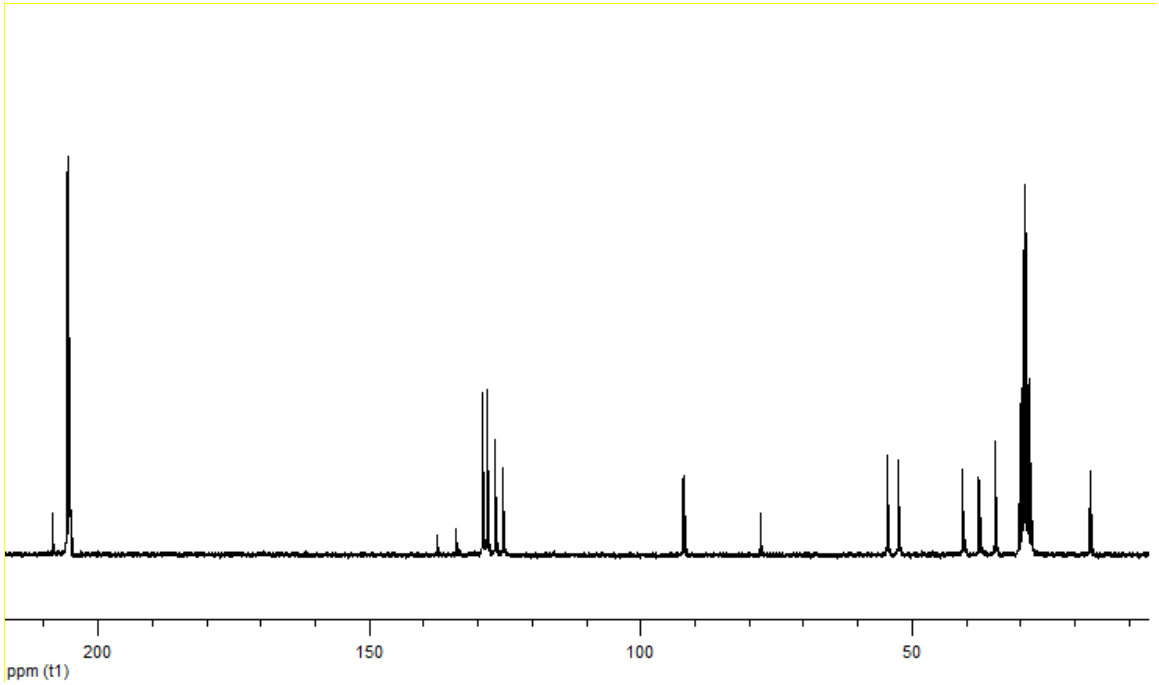


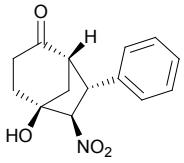


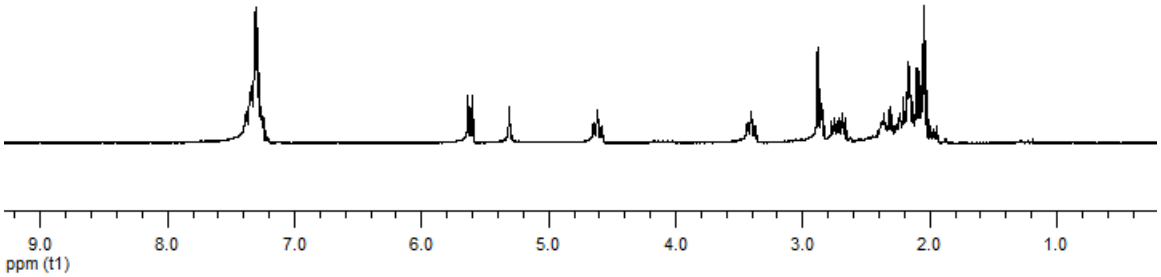


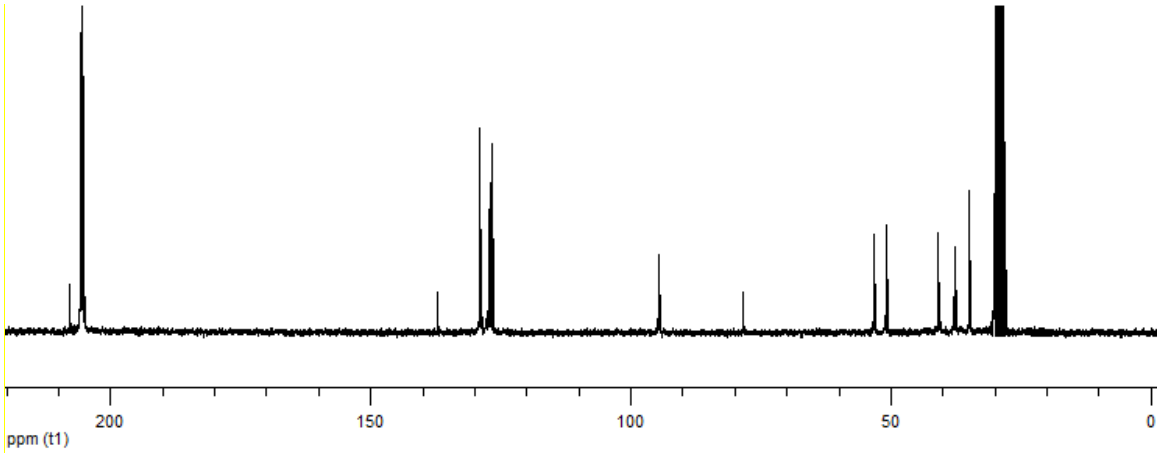


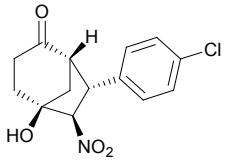


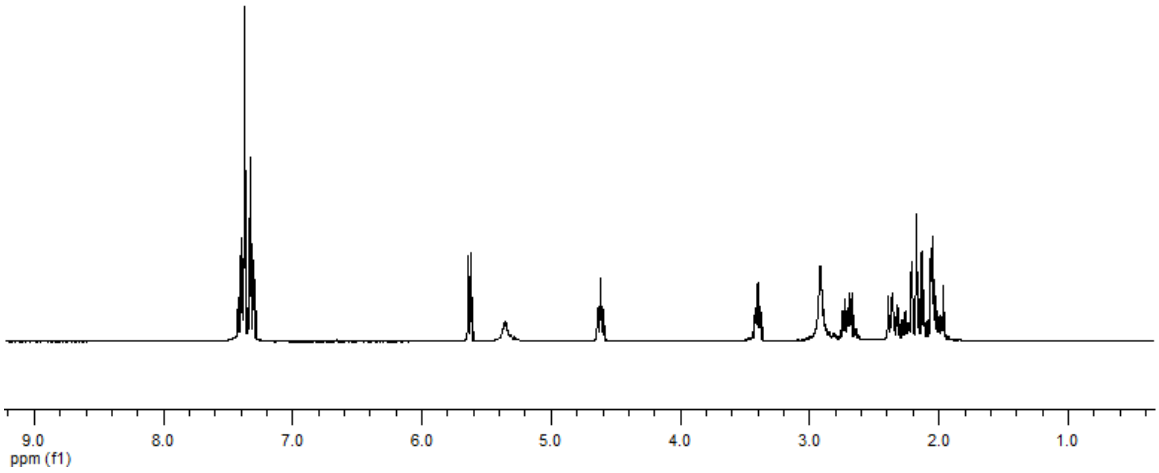


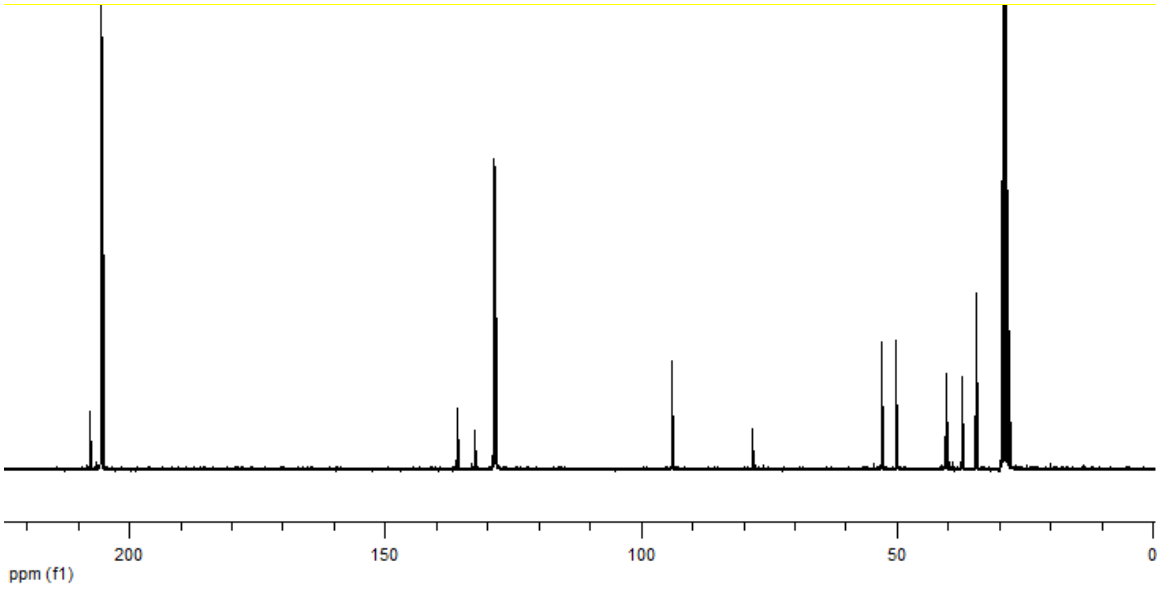


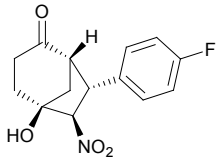


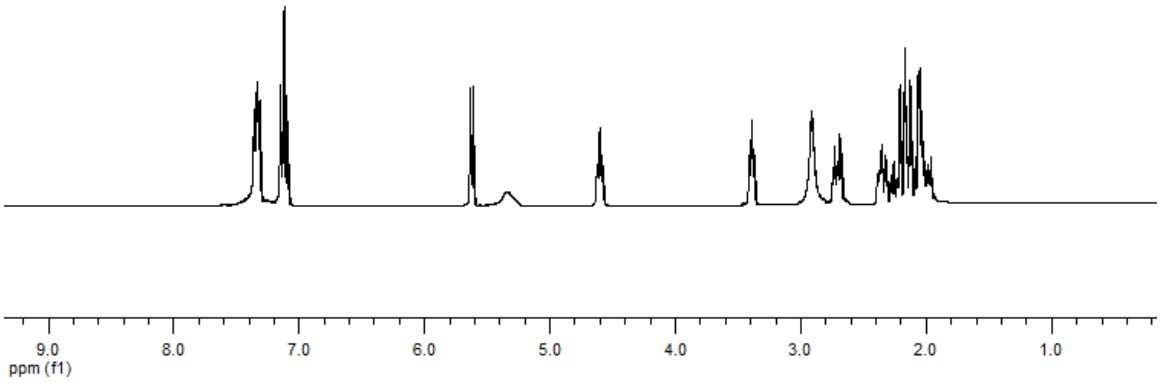


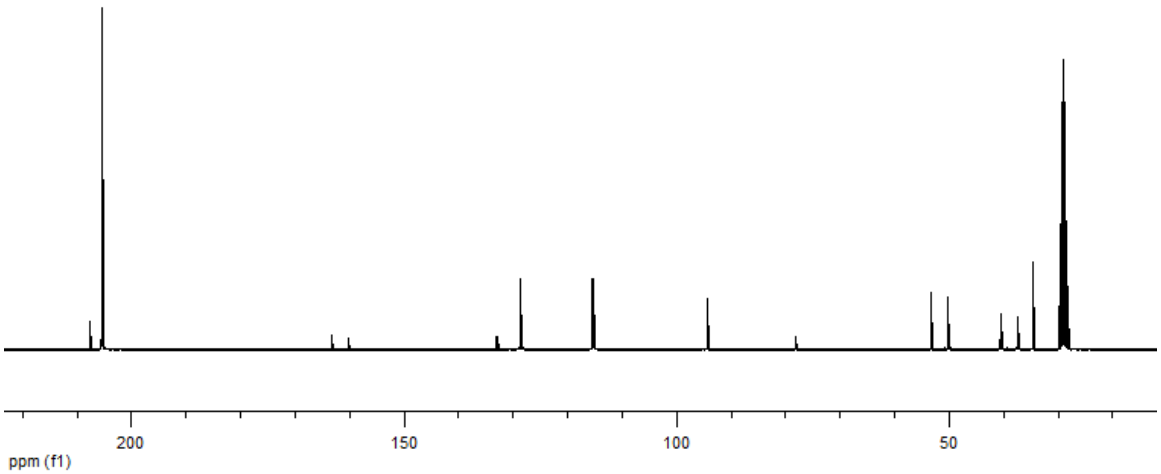


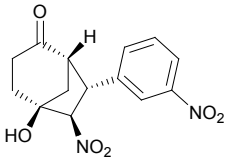


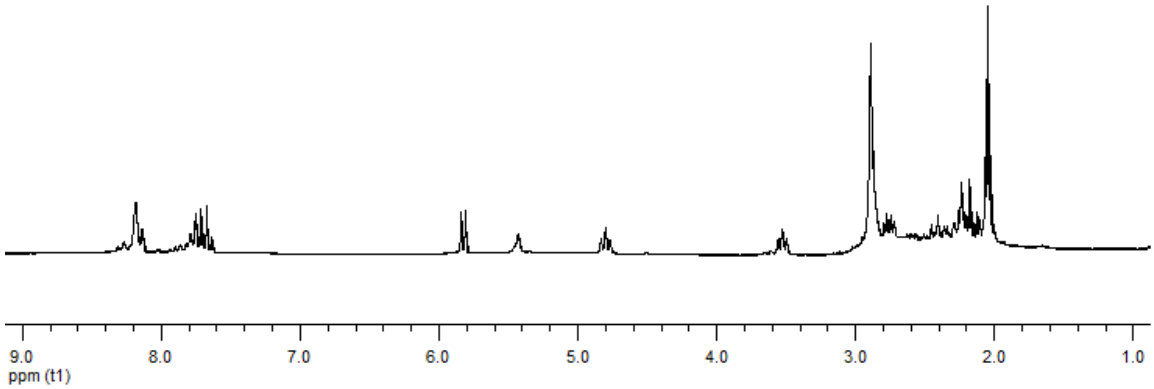


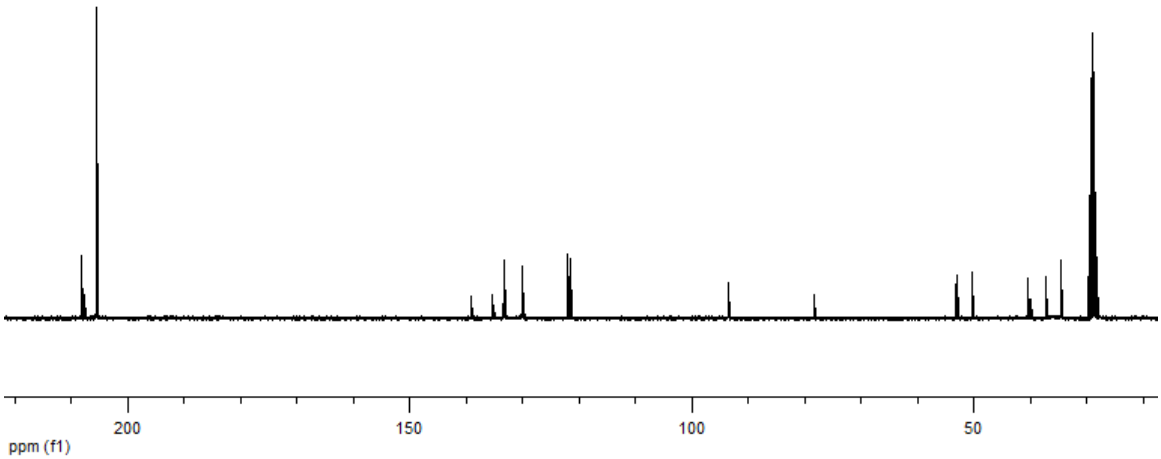


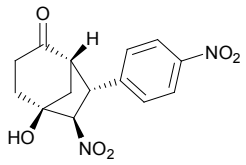


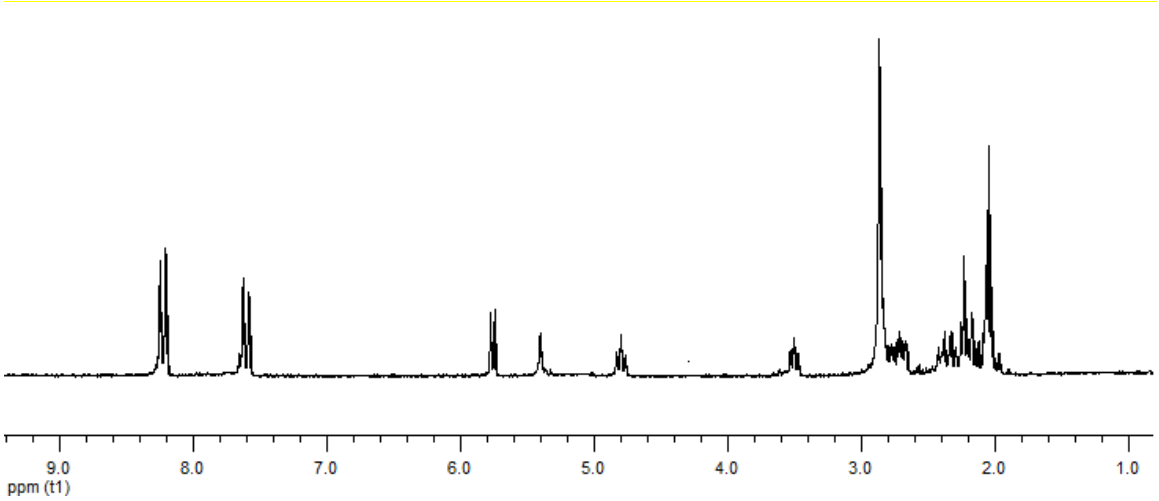


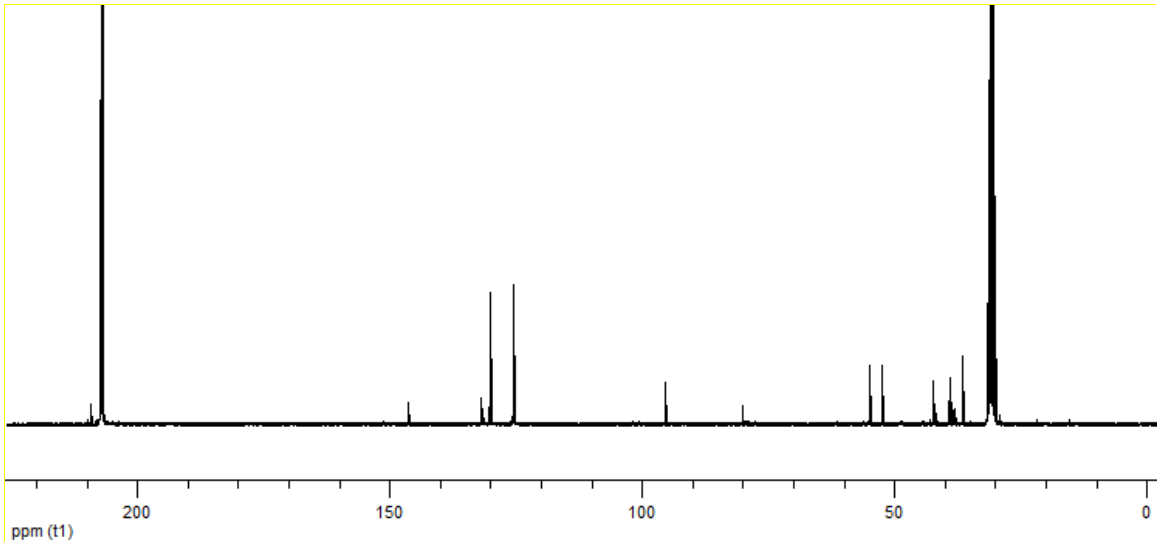


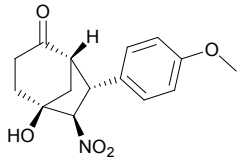


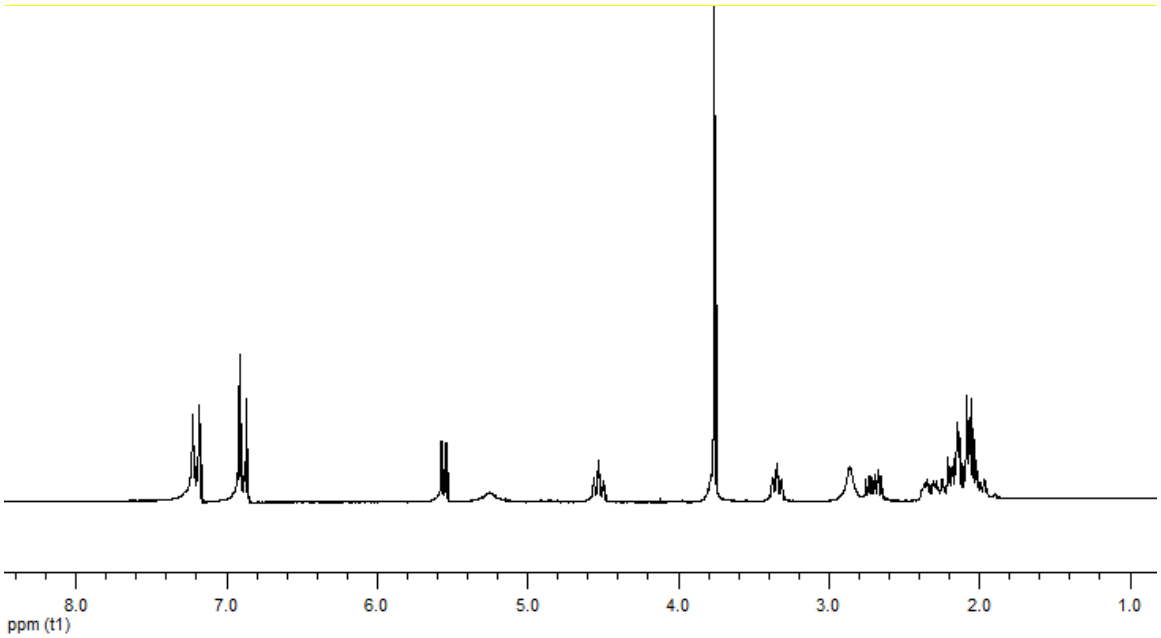


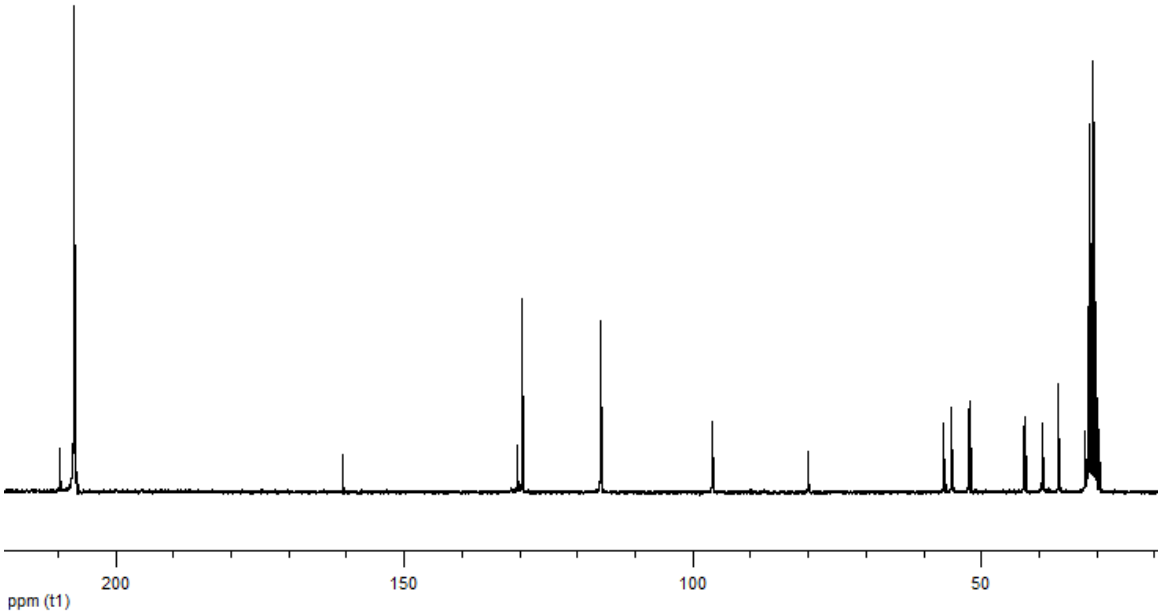


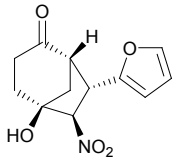


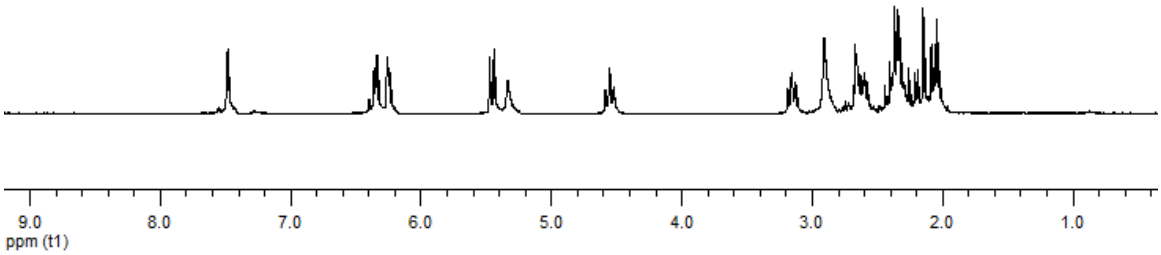


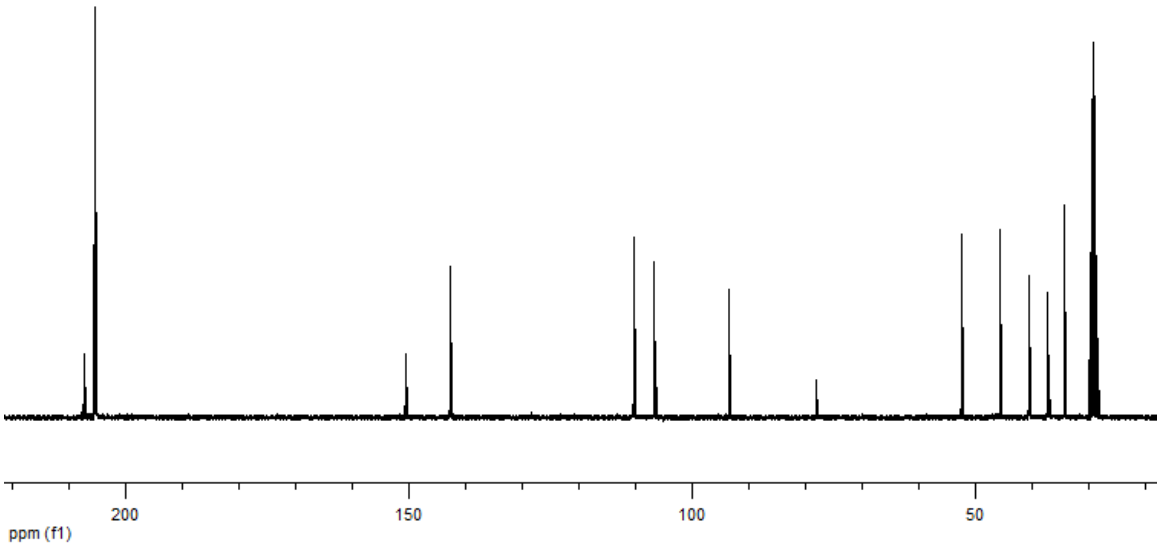


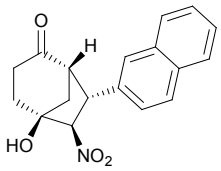


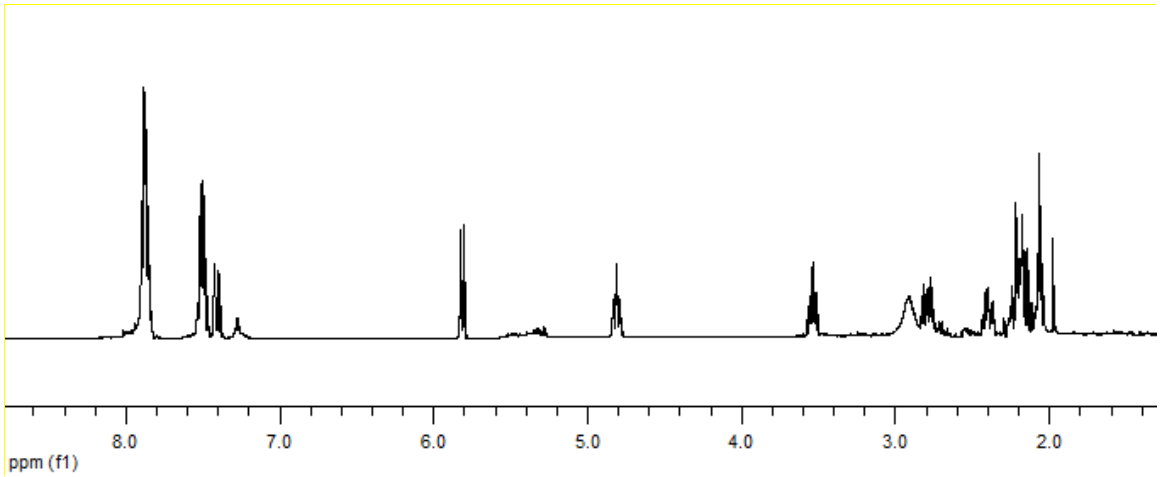


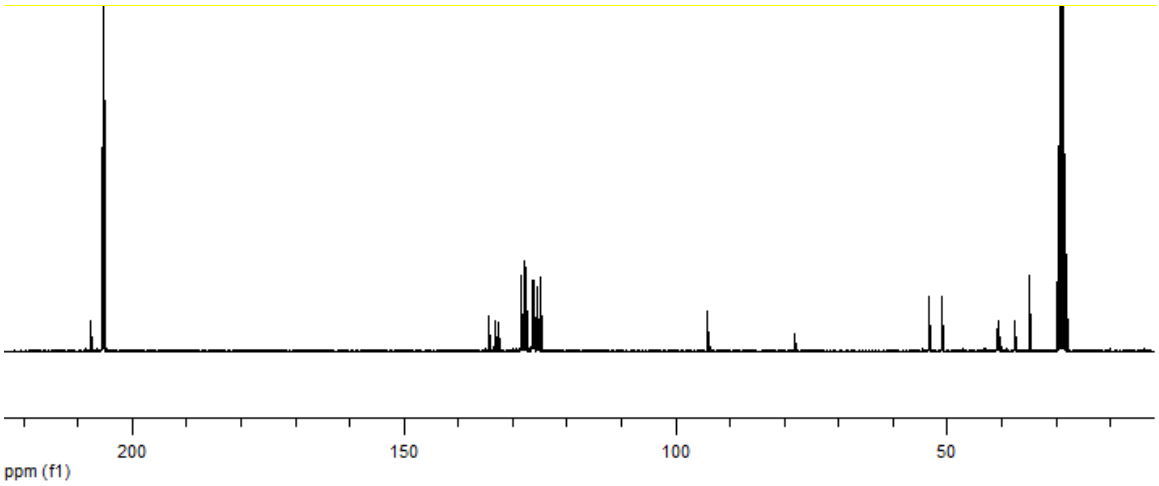


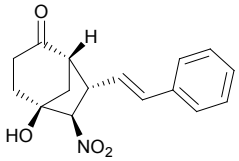




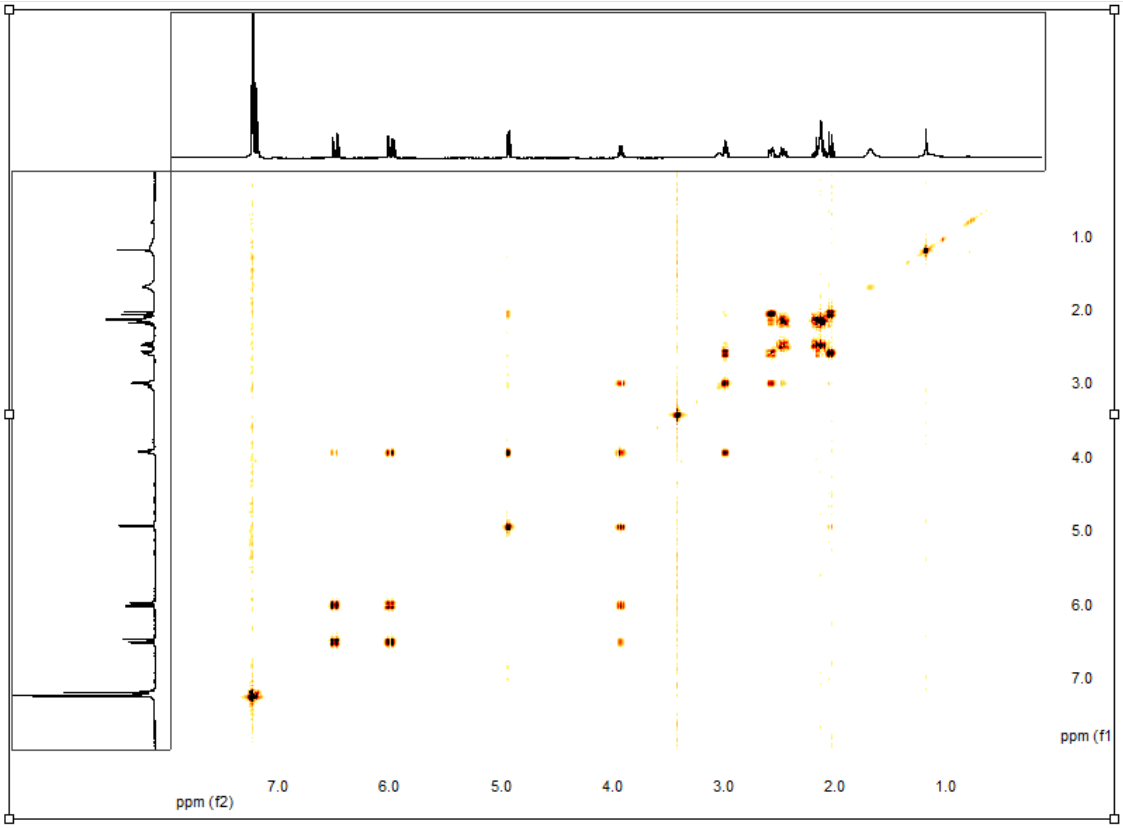


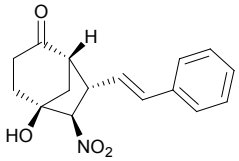




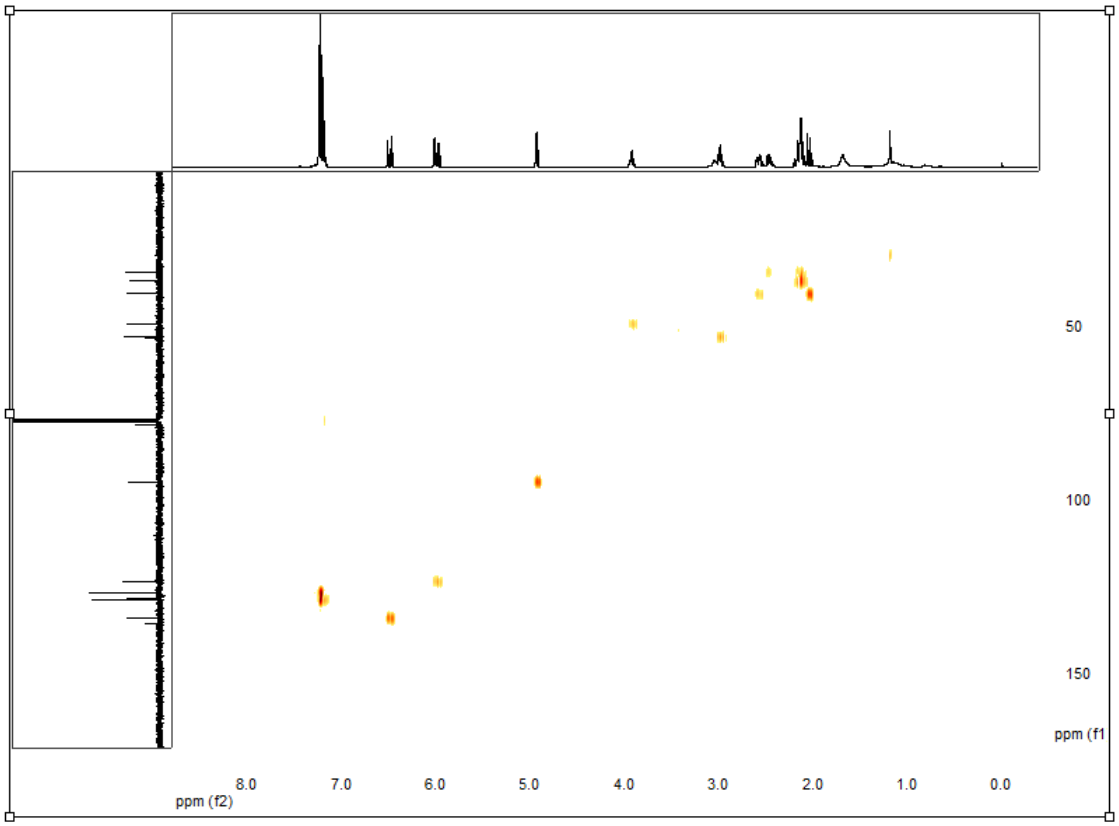


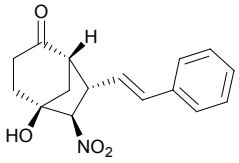
COSY (600 MHz, $CDCl_3$)



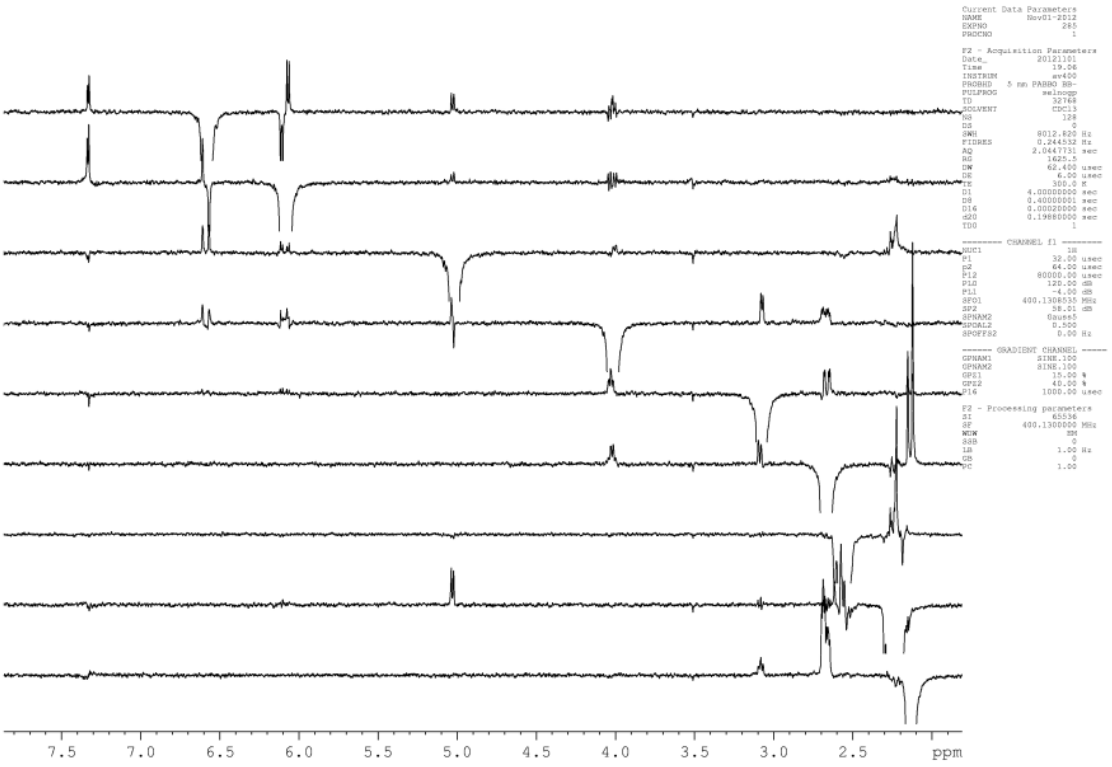


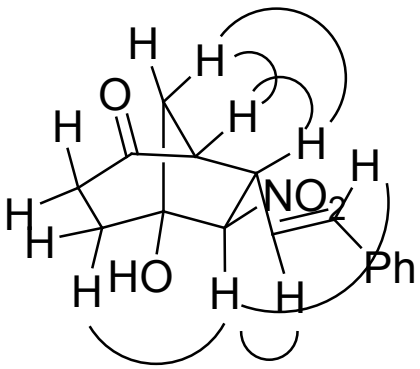
HMQC (600 MHz, $CDCl_3$)

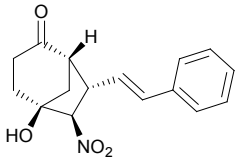


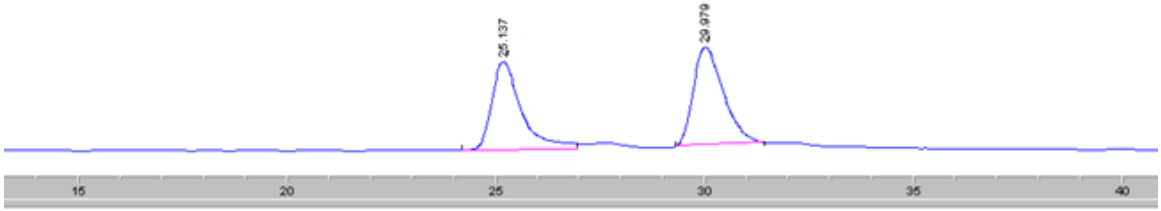


Selective 1D NOESY (600 MHz, $CDCl_3$)

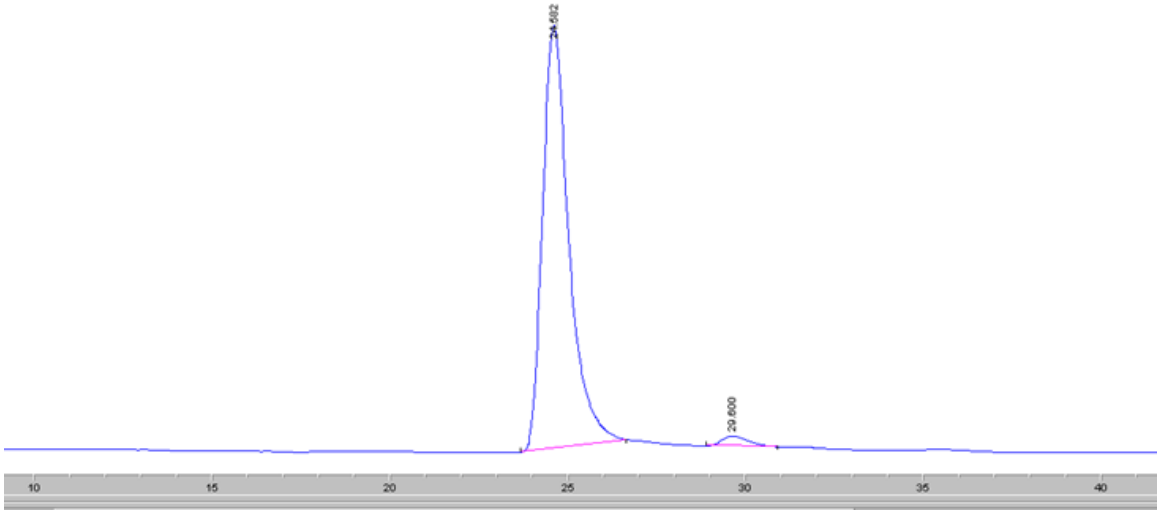




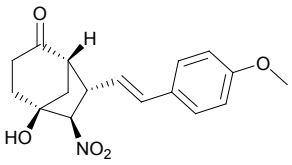


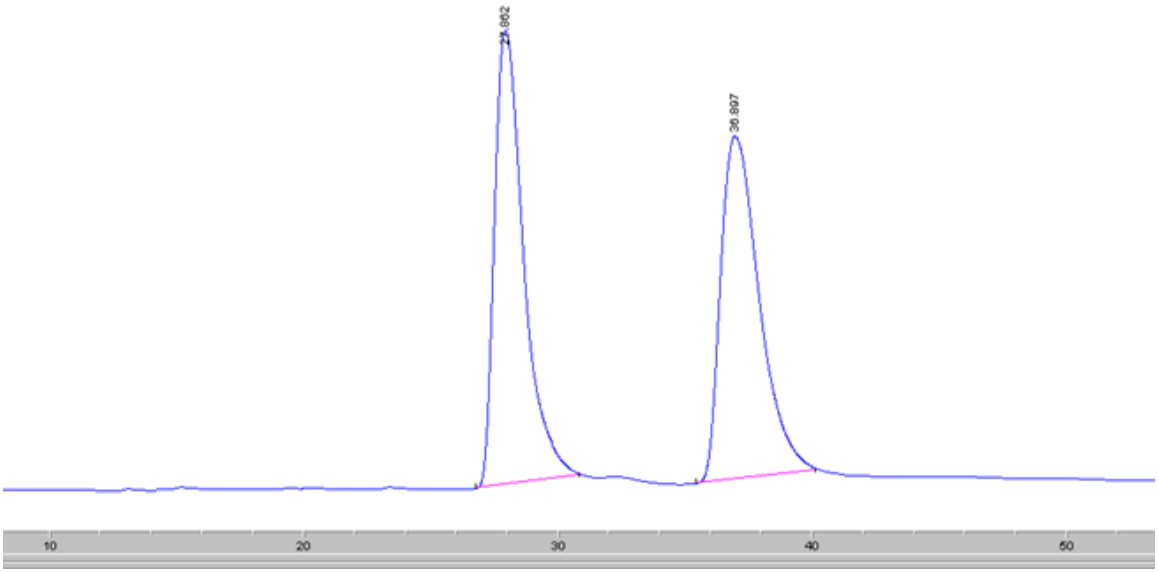


#	Time	Area	Height	Width	Area%	Symmetry
1	25.137	7108.5	142	0.8342	47.787	0.602
2	29.979	7766.8	155.8	0.8309	52.213	0.639

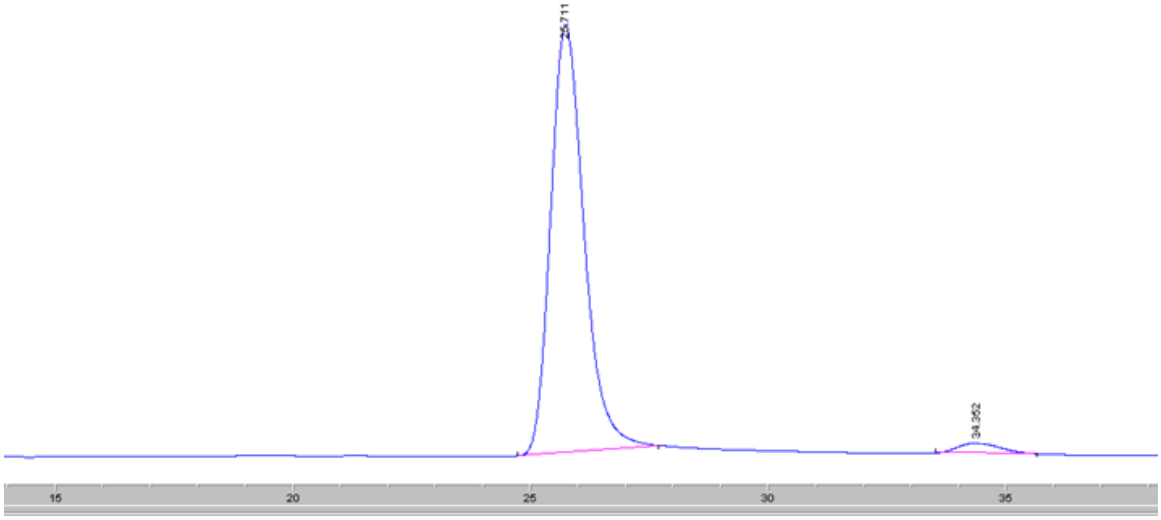


#	Time	Area	Height	Width	Area%	Symmetry
1	24.582	20082.6	389.2	0.78	97.706	0.69
2	29.6	471.5	9.1	0.7309	2.294	0.677

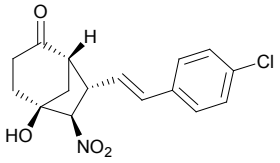


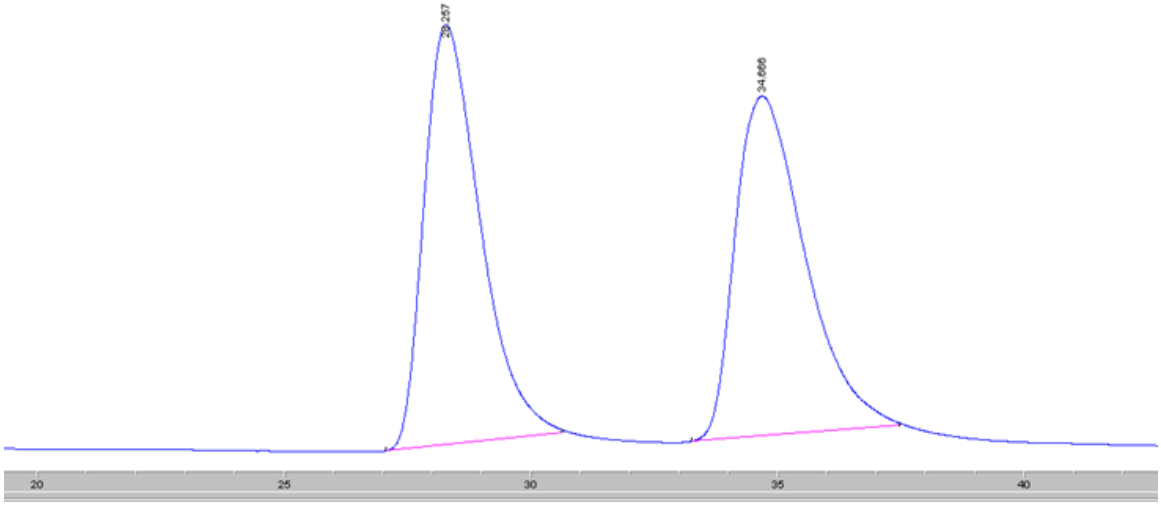


#	Time	Area	Height	Width	Area%	Symmetry
1	27.862	16349.5	205.2	1.2516	50.159	0.553
2	36.897	16245.6	154.8	1.598	49.841	0.559

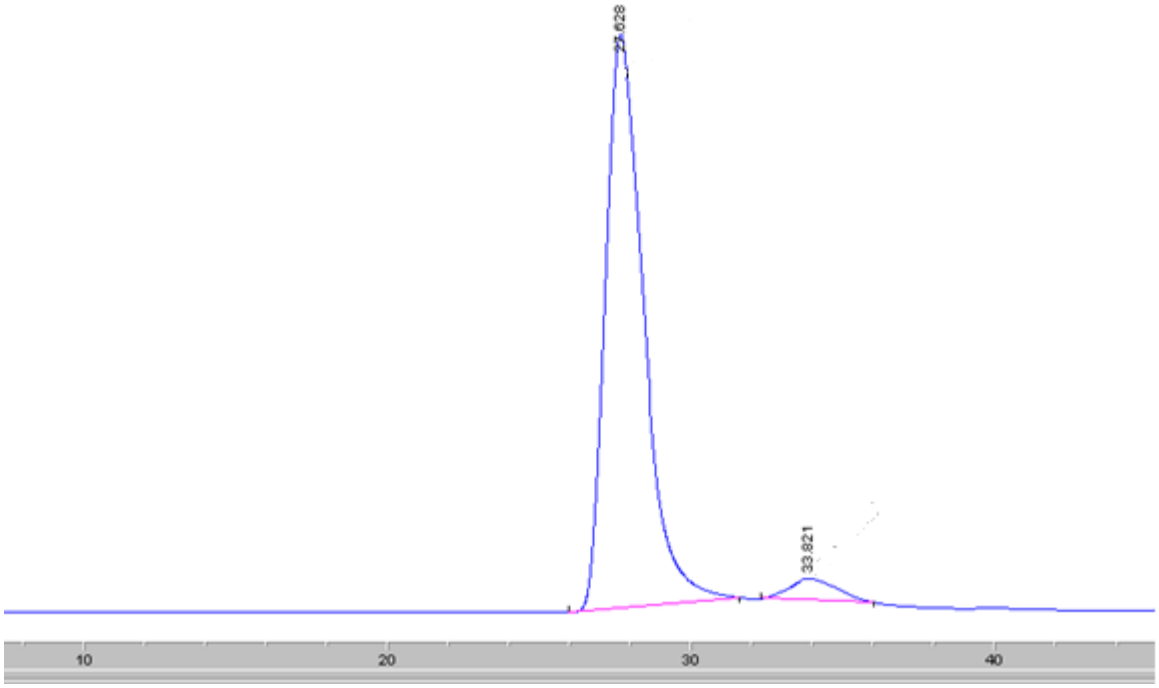


#	Time	Area	Height	Width	Area%	Symmetry
1	25.711	24049.6	491	0.7515	96.981	0.749
2	34.352	748.6	12	1.0405	3.019	0.723

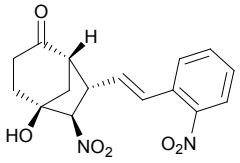


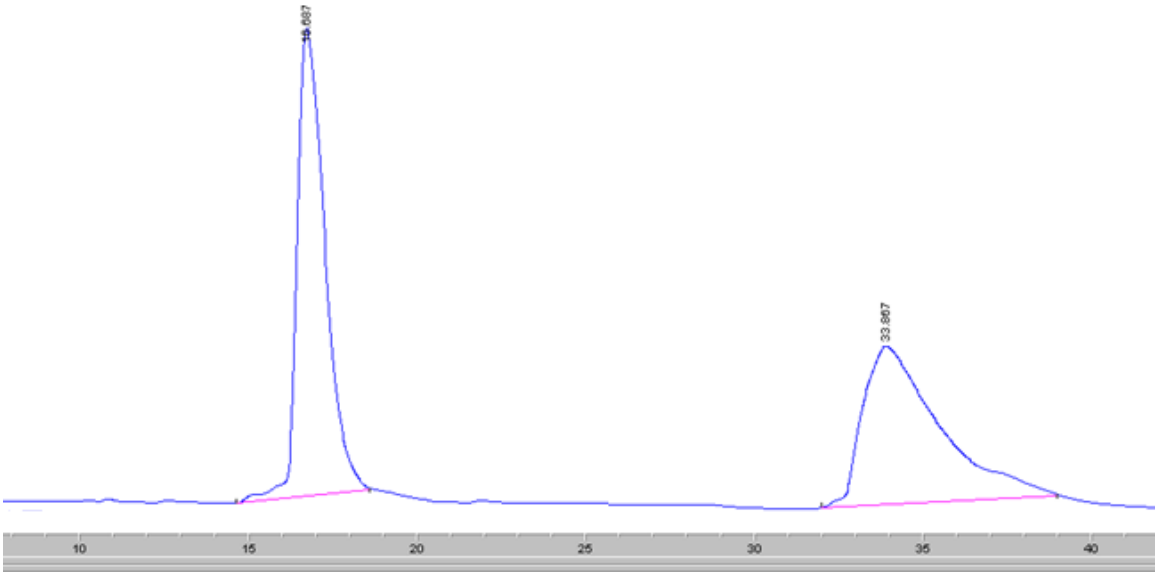


#	Time	Area	Height	Width	Area%	Symmetry
1	28.257	8663.5	109.7	1.1955	49.800	0.602
2	34.666	8733	88.8	1.4254	50.200	0.592

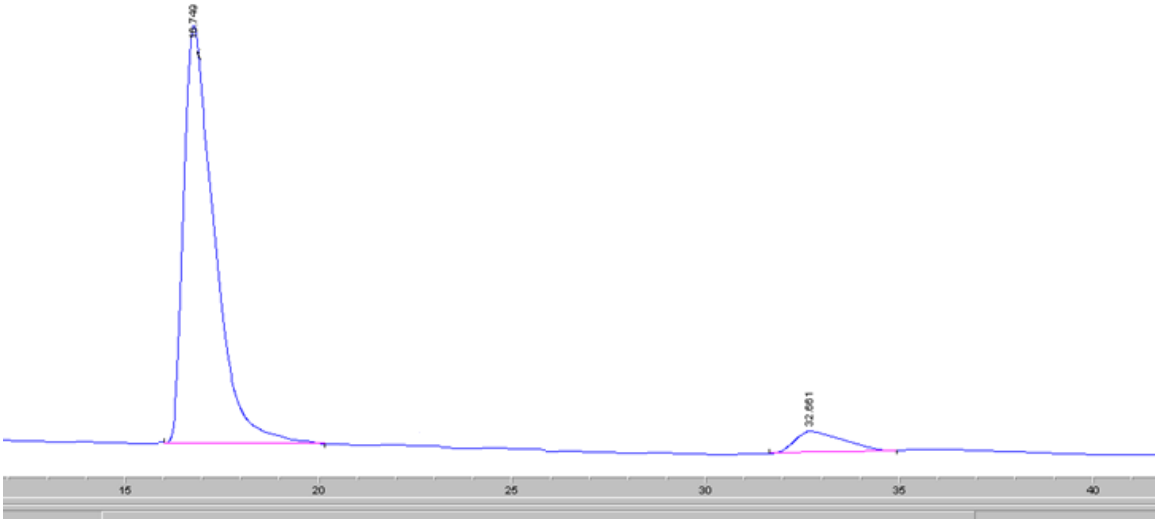


#	Time	Area	Height	Width	Area%	Symmetry
1	27.628	30209.7	348.7	1.444	95.408	0.637
2	33.821	1453.9	13.3	1.8243	4.592	0.673

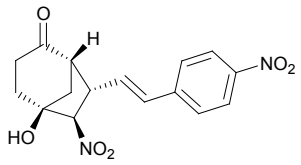


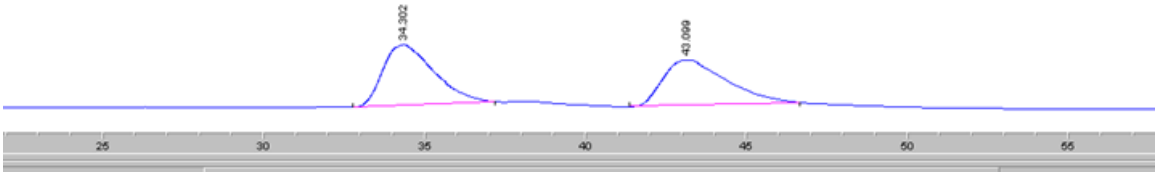


#	Time	Area	Height	Width	Area%	Symmetry
1	16.687	12218.5	212	0.9105	51.772	0.519
2	33.867	11382.1	71.8	1.9908	48.228	0.414

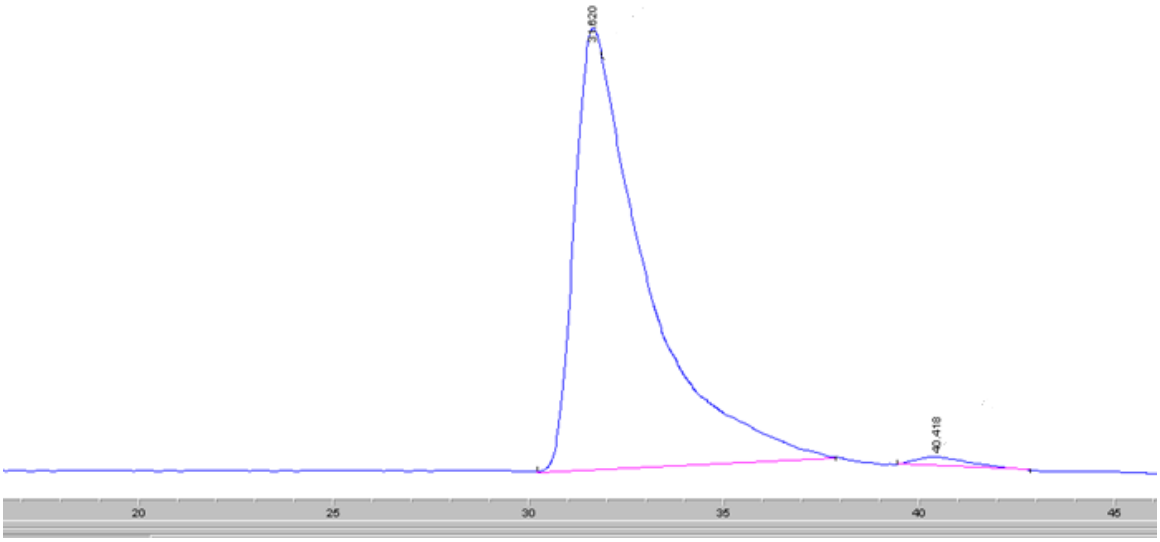


#	Time	Area	Height	Width	Area%	Symmetry
1	16.749	31088.8	563.1	0.9202	92.721	0.468
2	32.661	2440.5	28.7	1.165	7.279	0.452

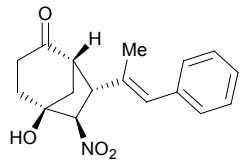


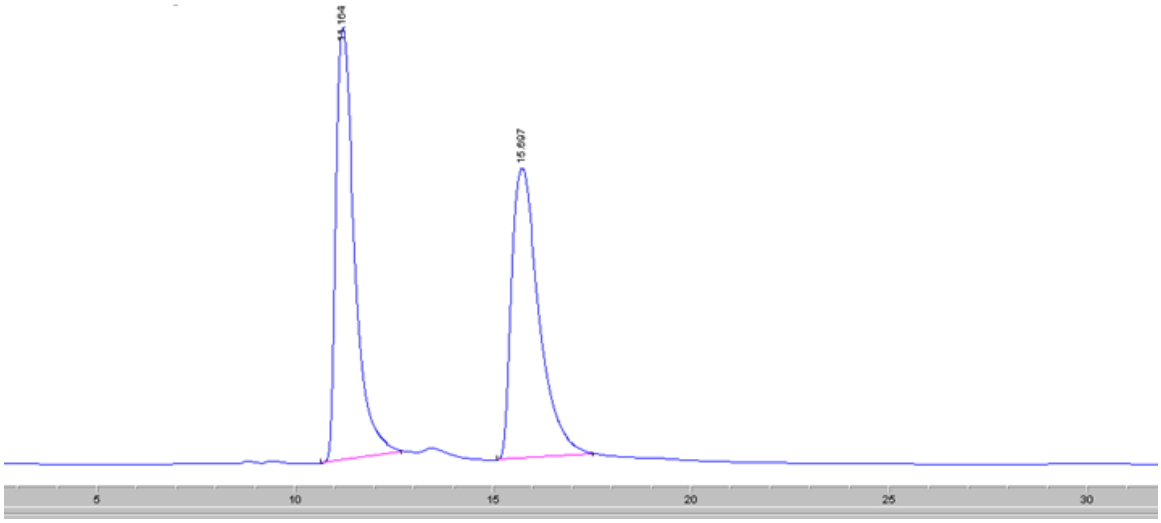


#	Time	Area	Height	Width	Area%	Symmetry
1	34.302	8201	74.9	1.5335	51.746	0.619
2	43.099	7647.4	56.1	1.7726	48.254	0.536

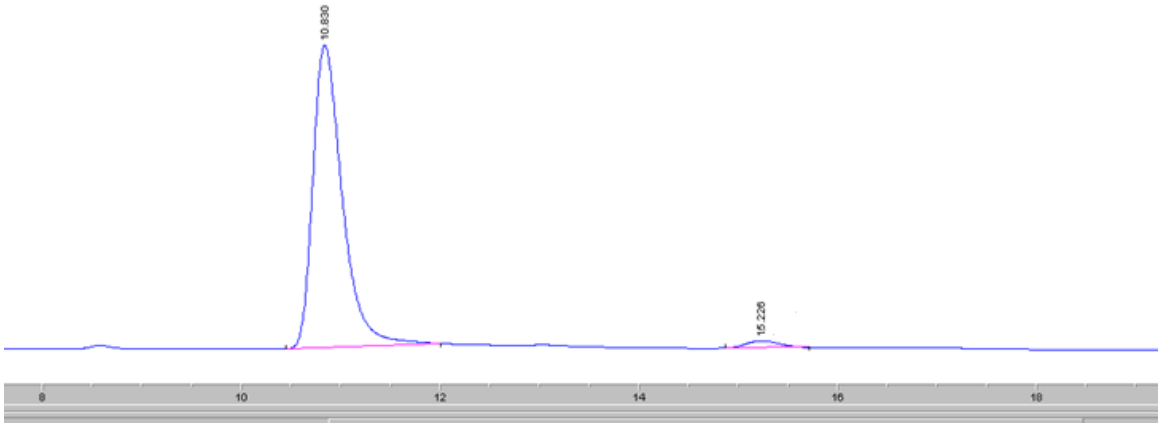


#	Time	Area	Height	Width	Area%	Symmetry
1	31.62	12766.5	100.8	2.1113	98.472	0.35
2	40.418	198.1	2	1.6183	1.528	0.488

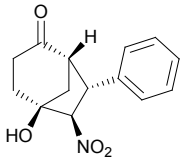


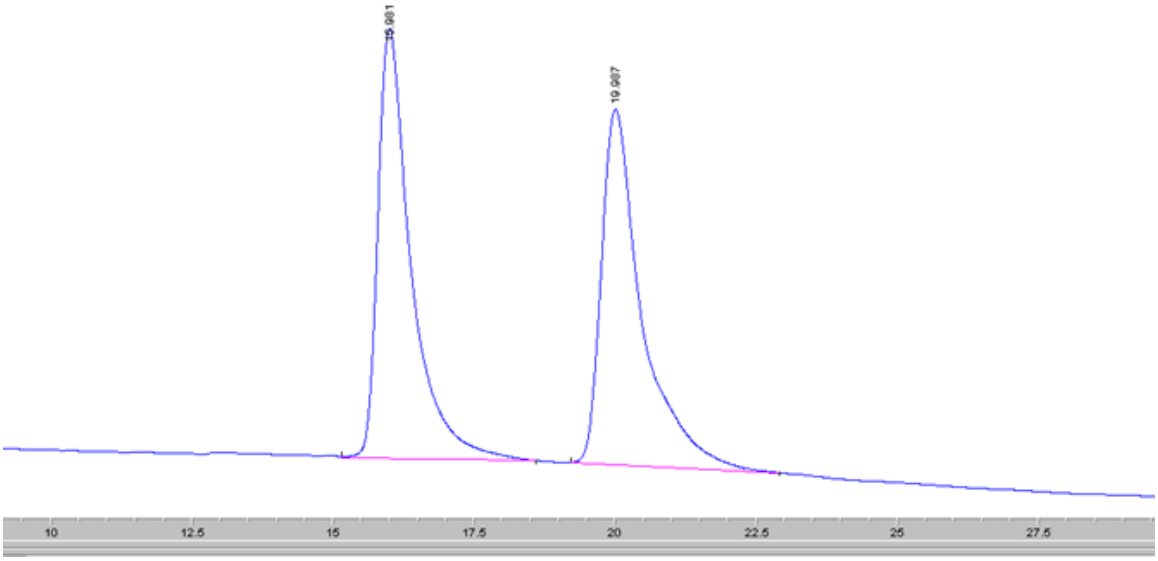


#	Time	Area	Height	Width	Area%	Symmetry
1	11.164	7743.9	234.1	0.5079	50.674	0.5
2	15.697	7537.8	157.2	0.7393	49.326	0.55

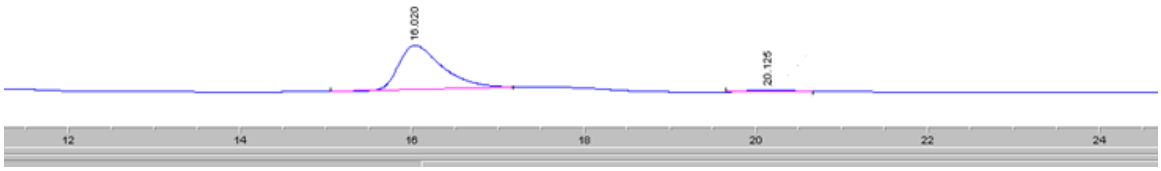


#	Time	Area	Height	Width	Area%	Symmetry
1	10.83	5978.8	288.4	0.3139	97.380	0.609
2	15.226	160.9	6.7	0.4024	2.620	0.842

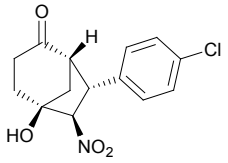


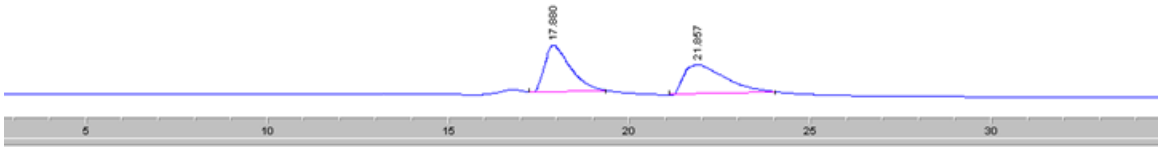


#	Time	Area	Height	Width	Area%	Symmetry
1	15.981	17596.7	426.5	0.6054	49.978	0.48
2	19.987	17611.9	353	0.7241	50.022	0.485

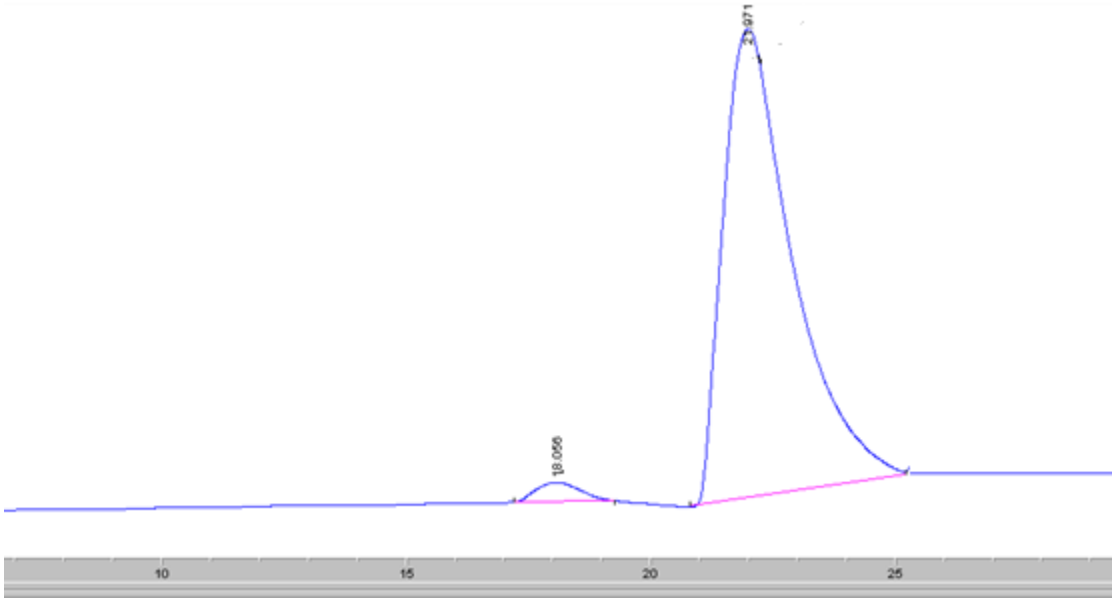


#	Time	Area	Height	Width	Area%	Symmetry
1	16.02	3960.6	111.2	0.5334	96.330	0.556
2	20.125	150.9	4.8	0.5269	3.670	0.919

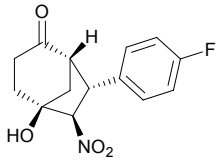


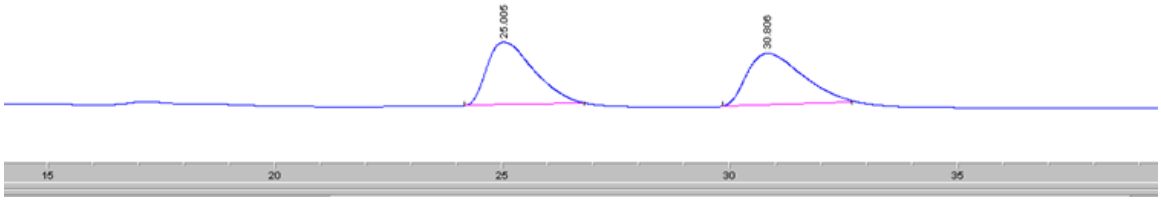


#	Time	Area	Height	Width	Area%	Symmetry
1	17.88	1507.3	30.3	0.7236	49.528	0.497
2	21.857	1536	19.3	1.1184	50.472	0.461

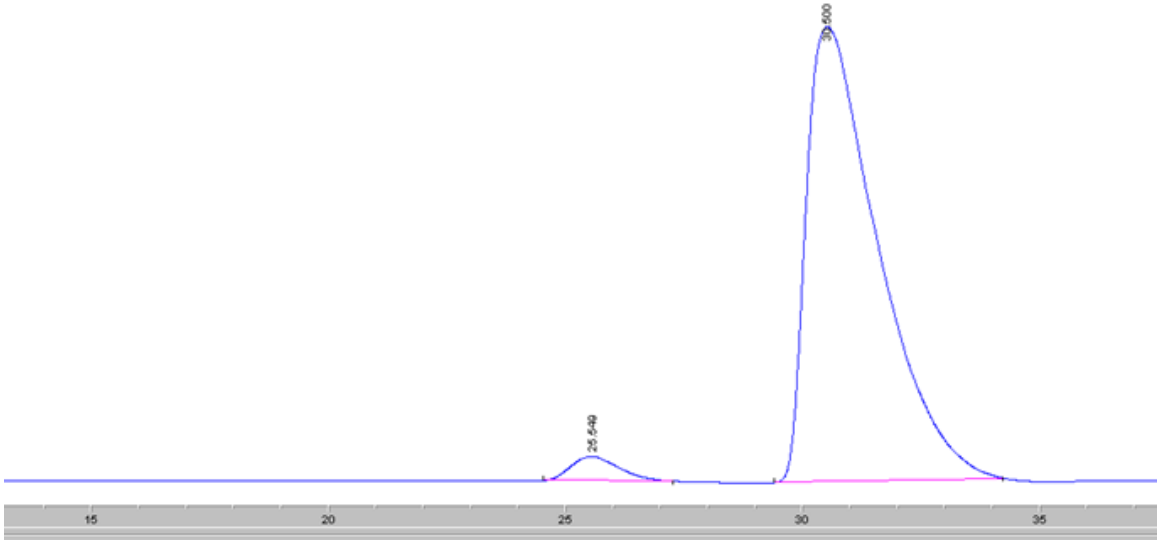


#	Time	Area	Height	Width	Area%	Symmetry
1	18.056	1400.1	22.1	1.0575	2.593	0.885
2	21.971	52598.4	533.2	1.644	97.407	0.546

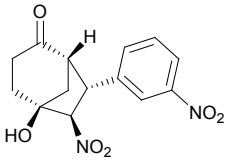


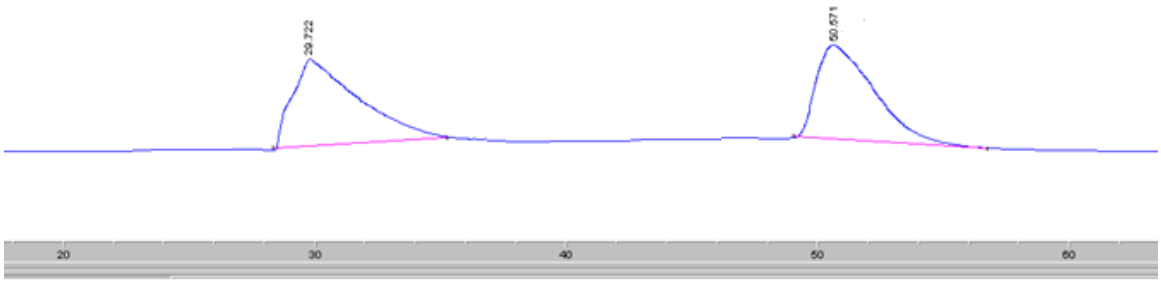


#	Time	Area	Height	Width	Area%	Symmetry
1	25.005	932.1	12.8	0.9715	51.065	0.51
2	30.806	893.2	10.6	1.0394	48.935	0.553

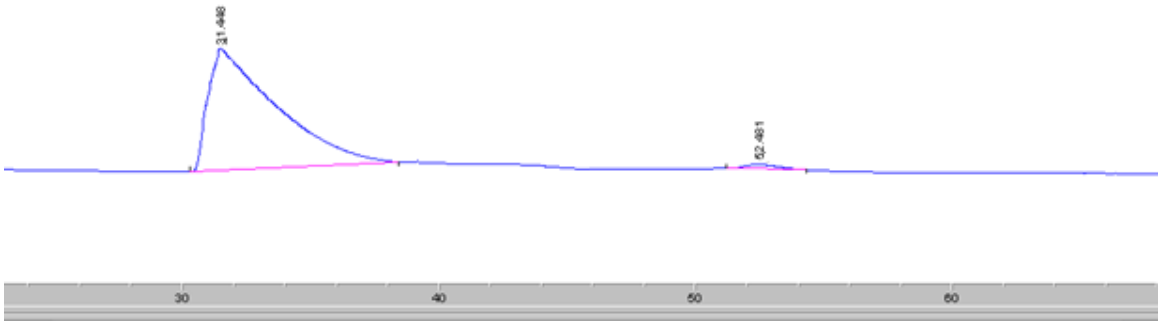


#	Time	Area	Height	Width	Area%	Symmetry
1	25.549	883	12.5	0.9178	3.485	0.778
2	30.5	24454.9	232.3	1.4961	96.515	0.385

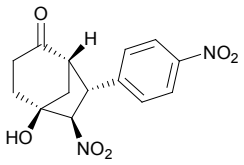


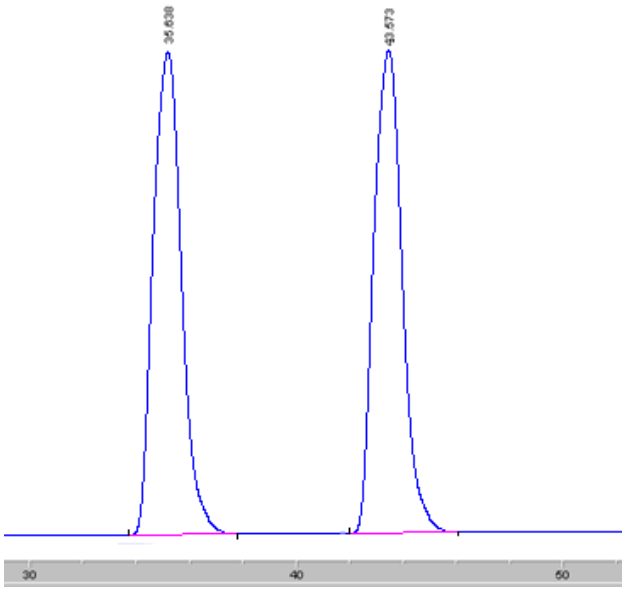


#	Time	Area	Height	Width	Area%	Symmetry
1	29.722	12077.7	66.2	3.0398	51.142	0.346
2	50.571	11538.5	71.5	2.6883	48.858	0.4

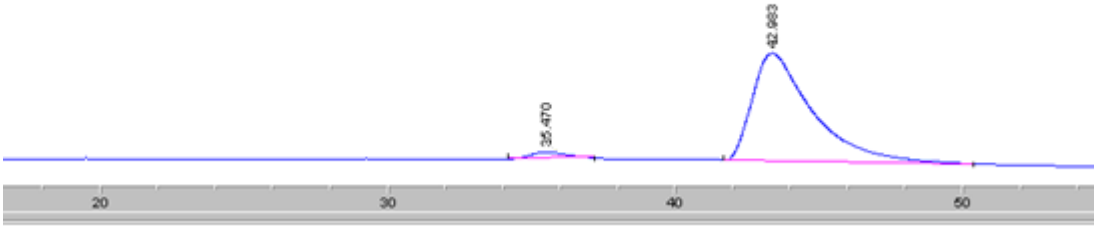


#	Time	Area	Height	Width	Area%	Symmetry
1	31.448	10216.9	55.3	3.08	98.066	0.227
2	52.481	201.5	2.1	1.5651	1.934	0.812

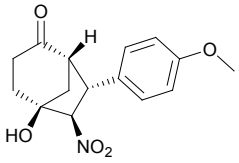


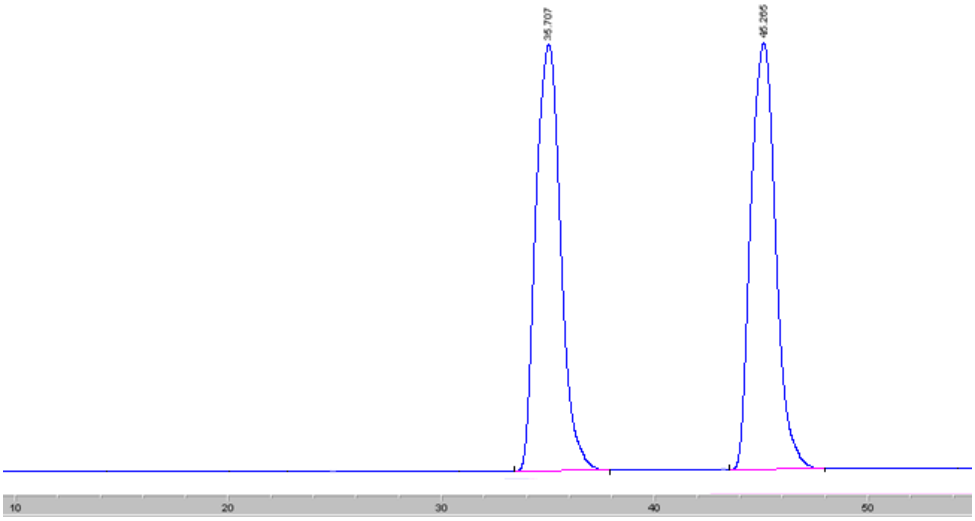


#	Time	Area	Height	Width	Area%	Symmetry
1	35.638	37969.7	323.3	1.6702	51.425	0.591
2	43.573	35865.8	162.6	3.6755	48.575	0.384

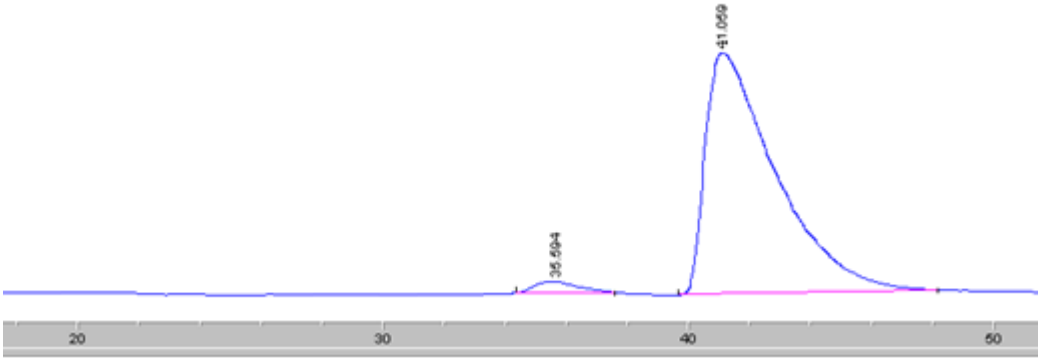


#	Time	Area	Height	Width	Area%	Symmetry
1	35.47	416.4	4.6	1.5008	3.527	0.892
2	42.983	11389	78.8	2.4102	96.473	0.475

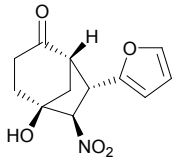


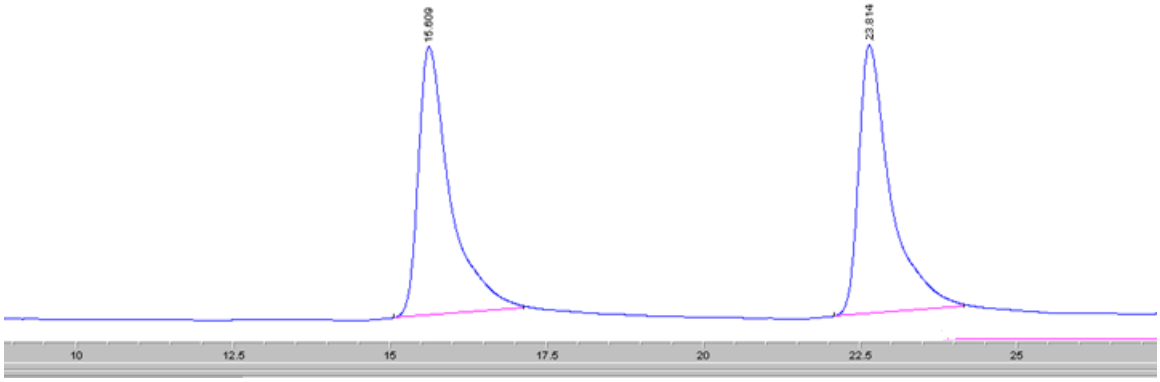


#	Time	Area	Height	Width	Area%	Symmetry
1	35.707	7583.9	51.2	2.4663	52.602	0.313
2	45.265	6833.5	20.2	5.6348	47.398	0.343

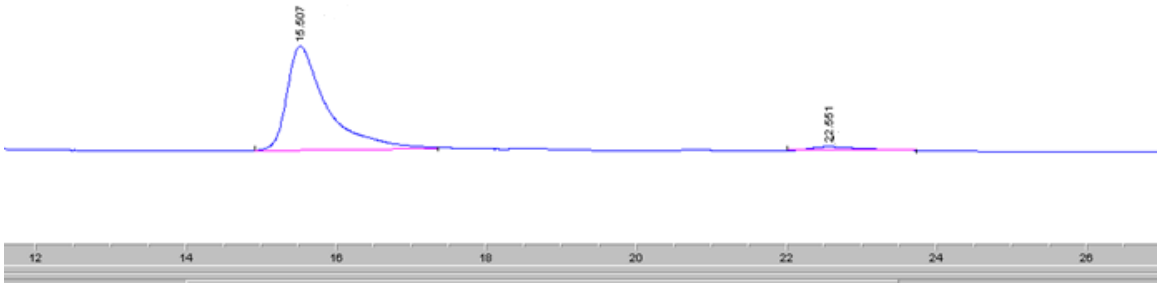


#	Time	Area	Height	Width	Area%	Symmetry
1	35.594	643	6.2	1.2162	2.811	0.864
2	41.059	22233.7	138.5	2.6757	97.189	0.311

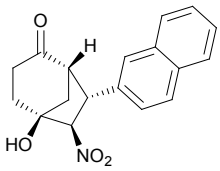


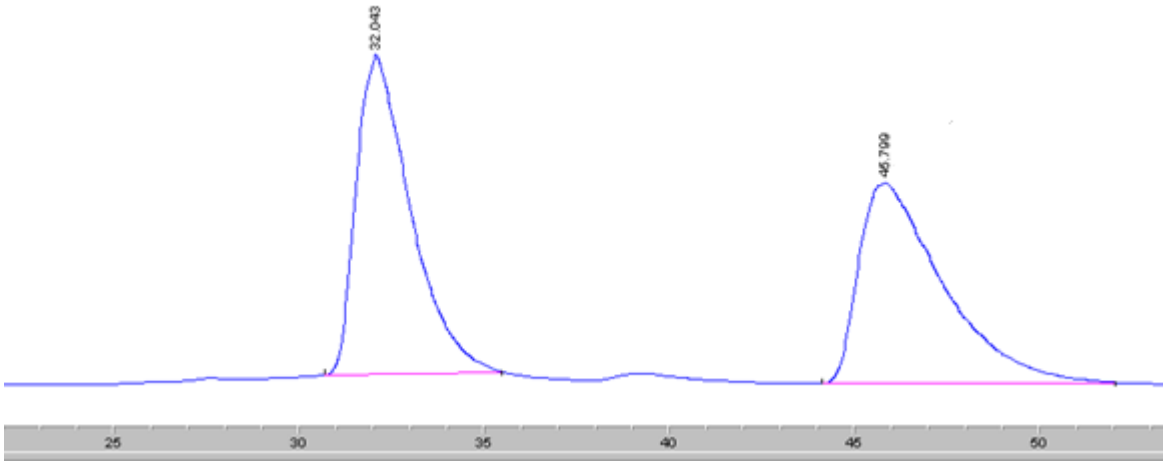


#	Time	Area	Height	Width	Area%	Symmetry
1	15.609	2989.6	84.3	0.5195	51.611	0.46
2	23.814	2803	21.8	1.5189	48.389	0

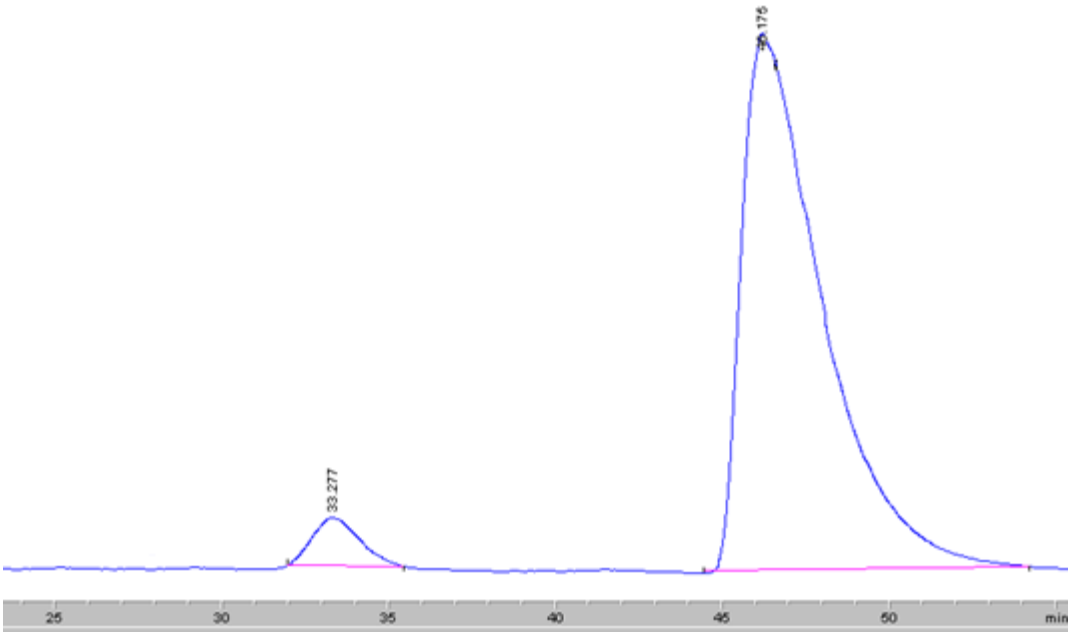


#	Time	Area	Height	Width	Area%	Symmetry
1	15.507	586.8	15.6	0.6259	95.357	0.481
2	22.551	28.6	6E-1	0.8002	4.643	0.554





#	Time	Area	Height	Width	Area%	Symmetry
1	32.043	15864.1	155.3	1.2619	50.885	0.543
2	45.799	15312.3	97.2	2.6249	49.115	0.447



#	Time	Area	Height	Width	Area%	Symmetry
1	33.277	935.3	9.5	1.16	5.041	0.736
2	46.175	17616.9	104.9	2.7985	94.959	0.342

Crystal data

$C_{16}H_{17}NO_4$	D_x = 1.311 Mg m^{-3}
M_r = 287.30	Mo $K\alpha$ radiation, λ = 0.71073 Å
Orthorhombic, $P2_12_12$	Cell parameters from 4795 reflections
a = 10.3329 (10) Å	θ = 2.2–27.6°
b = 19.6202 (19) Å	μ = 0.10 mm^{-1}
c = 7.1804 (7) Å	T = 150 K
V = 1455.7 (2) Å^3	Block, colourless
Z = 4	0.70 × 0.21 × 0.17 mm
F(000) = 608	

Data collection

Bruker APEX 2 CCD diffractometer	4410 independent reflections
Radiation source: fine-focus sealed X-ray tube	3804 reflections with $I > 2\sigma(I)$
graphite	R_{int} = 0.033
ω rotation with narrow frames scans	θ_{max} = 30.5°, θ_{min} = 2.1°
Absorption correction: multi-scan *SADABS* v2009/1, Sheldrick, G.M., (2009)	h = -14→14
T_{min} = 0.937, T_{max} = 0.984	k = -27→27
17114 measured reflections	l = -10→10

Refinement

Refinement on F^2	Secondary atom site location: all non-H atoms found by direct methods
Least-squares matrix: full	Hydrogen site location: difference Fourier map
$R[F^2 > 2\sigma(F^2)]$ = 0.041	Only H-atom coordinates refined
$wR(F^2)$ = 0.107	$w = 1/[\sigma^2(F_o^2) + (0.0675P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
S = 1.04	$(\Delta/\sigma)_{max} < 0.001$
4410 reflections	$\Delta\rangle_{max}$ = 0.30 e Å^{-3}
238 parameters	$\Delta\rangle_{min}$ = -0.15 e Å^{-3}
0 restraints	Absolute structure: Flack x determined using 1476 quotients [(I+)-(I-)]/[(I+)+(I-)] (Parsons and Flack (2004), Acta Cryst. A60, s61).
Primary atom site location: structure-invariant direct methods	Flack parameter: -0.6 (4)

Fractional atomic coordinates and isotropic or equivalent isotropic displacement

parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.68101 (16)	0.69495 (8)	0.3963 (2)	0.0245 (3)
H1	0.591 (2)	0.6966 (11)	0.437 (3)	0.029*
C2	0.70054 (16)	0.66993 (8)	0.1957 (2)	0.0231 (3)
H2A	0.7675 (19)	0.6372 (11)	0.191 (3)	0.028*
C3	0.75866 (15)	0.73238 (9)	0.0906 (2)	0.0243 (3)
H3	0.805 (2)	0.7188 (10)	-0.018 (3)	0.029*
C4	0.65653 (15)	0.78368 (8)	0.0352 (2)	0.0253 (3)
O1	0.64093 (13)	0.80169 (7)	-0.12638 (17)	0.0331 (3)
C5	0.57270 (18)	0.81037 (10)	0.1909 (3)	0.0294 (4)
H5A	0.534 (2)	0.8523 (12)	0.151 (3)	0.035*
H5B	0.503 (2)	0.7765 (11)	0.209 (3)	0.035*
C6	0.64812 (17)	0.82148 (9)	0.3739 (2)	0.0270 (3)
H6A	0.689 (2)	0.8670 (11)	0.369 (3)	0.032*
H6B	0.591 (2)	0.8227 (11)	0.483 (3)	0.032*
C7	0.74992 (15)	0.76609 (8)	0.4082 (2)	0.0234 (3)
O2	0.81770 (13)	0.77705 (7)	0.57636 (17)	0.0308 (3)
H2	0.763 (2)	0.7844 (13)	0.661 (4)	0.046*
C8	0.84433 (16)	0.76412 (9)	0.2437 (2)	0.0262 (3)
H8A	0.922 (2)	0.7340 (11)	0.270 (3)	0.031*
H8B	0.876 (2)	0.8118 (12)	0.211 (3)	0.031*
N1	0.74299 (18)	0.64776 (8)	0.5359 (2)	0.0374 (4)
O3	0.6862 (3)	0.64078 (9)	0.6833 (2)	0.0676 (6)
O4	0.84749 (16)	0.62182 (8)	0.5007 (2)	0.0484 (4)
C9	0.58685 (17)	0.63541 (8)	0.1059 (3)	0.0263 (3)
H9	0.593 (2)	0.6295 (10)	-0.018 (3)	0.032*
C10	0.48719 (17)	0.60781 (9)	0.1943 (3)	0.0283 (4)
H10	0.482 (2)	0.6118 (11)	0.321 (4)	0.034*
C11	0.38010 (16)	0.56865 (8)	0.1112 (3)	0.0321 (4)
C12	0.3751 (2)	0.55292 (9)	-0.0796 (3)	0.0380 (5)
H12	0.448 (3)	0.5686 (13)	-0.161 (4)	0.046*
C13	0.2727 (2)	0.51428 (10)	-0.1501 (4)	0.0533 (7)
H13A	0.2697	0.5039	-0.2793	0.064*
C14	0.1760 (2)	0.49101 (11)	-0.0342 (5)	0.0622 (8)
H14	0.106 (3)	0.4647 (16)	-0.089 (5)	0.075*

C15	0.1798 (2)	0.50631 (11)	0.1536 (5)	0.0598 (8)
H15	0.120 (3)	0.493 (2)	0.236 (5)	0.072*
C16	0.2814 (2)	0.54497 (10)	0.2264 (4)	0.0448 (6)
H16	0.281 (3)	0.5595 (14)	0.361 (4)	0.054*

Geometric parameters (Å, º)

C1—N1	1.507 (2)	O2—H2	0.84 (3)
C1—C2	1.535 (2)	C8—H8A	1.01 (2)
C1—C7	1.569 (2)	C8—H8B	1.02 (2)
C1—H1	0.98 (2)	N1—O3	1.218 (2)
C2—C9	1.501 (2)	N1—O4	1.220 (2)
C2—C3	1.559 (2)	C9—C10	1.325 (3)
C2—H2A	0.95 (2)	C9—H9	0.90 (2)
C3—C4	1.512 (2)	C10—C11	1.473 (2)
C3—C8	1.543 (2)	C10—H10	0.92 (2)
C3—H3	0.95 (2)	C11—C16	1.392 (3)
C4—O1	1.223 (2)	C11—C12	1.405 (3)
C4—C5	1.508 (3)	C12—C13	1.396 (3)
C5—C6	1.543 (2)	C12—H12	1.00 (3)
C5—H5A	0.96 (2)	C13—C14	1.379 (4)
C5—H5B	0.99 (2)	C13—H13A	0.9500
C6—C7	1.532 (2)	C14—C15	1.382 (5)
C6—H6A	0.99 (2)	C14—H14	0.97 (3)
C6—H6B	0.98 (2)	C15—C16	1.397 (3)
C7—O2	1.4126 (19)	C15—H15	0.89 (4)
C7—C8	1.532 (2)	C16—H16	1.01 (3)
N1—C1—C2	111.82 (14)	C8—C7—C1	102.98 (13)
N1—C1—C7	108.51 (13)	C6—C7—C1	108.10 (13)
C2—C1—C7	106.01 (13)	C7—O2—H2	108.2 (18)
N1—C1—H1	103.0 (13)	C7—C8—C3	101.18 (12)
C2—C1—H1	114.7 (13)	C7—C8—H8A	112.1 (12)
C7—C1—H1	112.7 (12)	C3—C8—H8A	110.5 (12)
C9—C2—C1	116.37 (14)	C7—C8—H8B	111.0 (12)
C9—C2—C3	116.64 (14)	C3—C8—H8B	113.2 (13)
C1—C2—C3	104.66 (13)	H8A—C8—H8B	108.7 (17)

C9—C2—H2A	104.4 (12)	O3—N1—O4	124.01 (19)
C1—C2—H2A	110.5 (13)	O3—N1—C1	116.25 (18)
C3—C2—H2A	103.5 (13)	O4—N1—C1	119.64 (16)
C4—C3—C8	108.64 (14)	C10—C9—C2	125.94 (17)
C4—C3—C2	112.44 (13)	C10—C9—H9	118.2 (14)
C8—C3—C2	101.17 (12)	C2—C9—H9	115.6 (14)
C4—C3—H3	108.7 (12)	C9—C10—C11	127.08 (18)
C8—C3—H3	114.1 (13)	C9—C10—H10	119.1 (14)
C2—C3—H3	111.7 (12)	C11—C10—H10	113.8 (14)
O1—C4—C5	121.81 (16)	C16—C11—C12	118.6 (2)
O1—C4—C3	122.28 (15)	C16—C11—C10	118.9 (2)
C5—C4—C3	115.91 (14)	C12—C11—C10	122.47 (18)
C4—C5—C6	112.96 (14)	C13—C12—C11	120.1 (2)
C4—C5—H5A	108.3 (14)	C13—C12—H12	121.5 (15)
C6—C5—H5A	110.2 (14)	C11—C12—H12	118.4 (15)
C4—C5—H5B	106.4 (13)	C14—C13—C12	120.6 (3)
C6—C5—H5B	110.4 (13)	C14—C13—H13A	119.7
H5A—C5—H5B	108.5 (19)	C12—C13—H13A	119.7
C7—C6—C5	112.55 (14)	C13—C14—C15	119.8 (2)
C7—C6—H6A	110.4 (13)	C13—C14—H14	118 (2)
C5—C6—H6A	108.2 (13)	C15—C14—H14	122 (2)
C7—C6—H6B	107.5 (13)	C14—C15—C16	120.3 (3)
C5—C6—H6B	112.4 (12)	C14—C15—H15	124 (2)
H6A—C6—H6B	105.6 (18)	C16—C15—H15	115 (2)
O2—C7—C8	110.31 (13)	C11—C16—C15	120.6 (3)
O2—C7—C6	111.71 (13)	C11—C16—H16	118.7 (17)
C8—C7—C6	109.34 (13)	C15—C16—H16	120.5 (17)
O2—C7—C1	114.00 (13)		
N1—C1—C2—C9	102.20 (17)	C2—C1—C7—C6	95.05 (15)
C7—C1—C2—C9	-139.73 (15)	O2—C7—C8—C3	164.81 (14)
N1—C1—C2—C3	-127.49 (14)	C6—C7—C8—C3	-71.97 (15)
C7—C1—C2—C3	-9.42 (16)	C1—C7—C8—C3	42.78 (15)
C9—C2—C3—C4	50.08 (19)	C4—C3—C8—C7	69.84 (15)
C1—C2—C3—C4	-80.07 (16)	C2—C3—C8—C7	-48.67 (15)
C9—C2—C3—C8	165.80 (14)	C2—C1—N1—O3	-144.57 (18)
C1—C2—C3—C8	35.64 (16)	C7—C1—N1—O3	98.9 (2)

C8—C3—C4—O1	125.41 (16)	C2—C1—N1—O4	38.9 (2)
C2—C3—C4—O1	-123.46 (17)	C7—C1—N1—O4	-77.66 (19)
C8—C3—C4—C5	-55.86 (18)	C1—C2—C9—C10	-20.1 (2)
C2—C3—C4—C5	55.27 (18)	C3—C2—C9—C10	-144.45 (18)
O1—C4—C5—C6	-143.33 (16)	C2—C9—C10—C11	-174.41 (16)
C3—C4—C5—C6	37.9 (2)	C9—C10—C11—C16	-178.31 (18)
C4—C5—C6—C7	-37.9 (2)	C9—C10—C11—C12	3.1 (3)
C5—C6—C7—O2	-179.87 (14)	C16—C11—C12—C13	0.0 (3)
C5—C6—C7—C8	57.74 (17)	C10—C11—C12—C13	178.52 (17)
C5—C6—C7—C1	-53.67 (17)	C11—C12—C13—C14	-0.2 (3)
N1—C1—C7—O2	-19.84 (19)	C12—C13—C14—C15	0.3 (3)
C2—C1—C7—O2	-140.09 (14)	C13—C14—C15—C16	-0.3 (3)
N1—C1—C7—C8	99.66 (15)	C12—C11—C16—C15	0.1 (3)
C2—C1—C7—C8	-20.59 (16)	C10—C11—C16—C15	-178.50 (18)
N1—C1—C7—C6	-144.69 (14)	C14—C15—C16—C11	0.0 (3)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O2—H2···O1^{i}	0.84 (3)	2.01 (3)	2.8506 (19)	177 (2)

Symmetry code: (i) *x*, *y*, *z*+1.

Computing details

Data collection: Bruker *APEX* 2; cell refinement: Bruker *SAINT*; data reduction: Bruker *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL2012* (Sheldrick, 2012); molecular graphics: Bruker *SHELXTL*; software used to prepare material for publication: Bruker *SHELXTL*.

Special details

Geometry. All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s.

planes.

Additional figures of **3a** showing H-bonding between pairs of molecules and hence chains of H-bonded molecules parallel to *c*.