Asymmetric Synthesis of *trans*-Dihydroarylfurans in a Friedel-Crafts/Substitution Domino Reaction under Squaramide Catalysis

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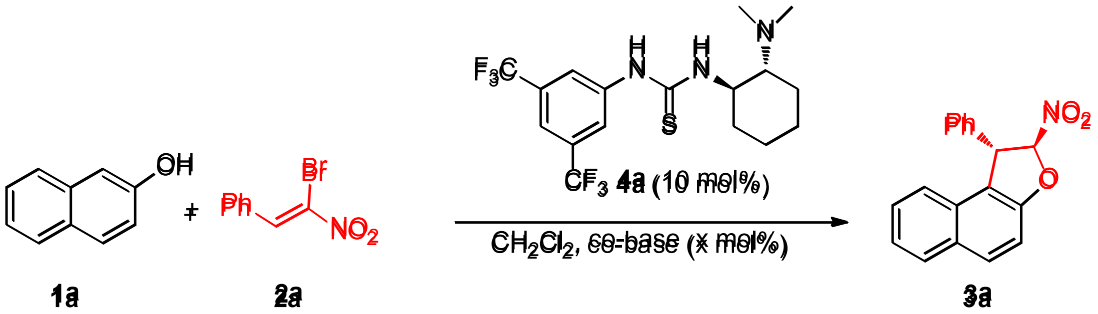
Supporting Information

Contents

Table ESI-1. Other co-bases that were evaluated on screening.



Entry	Base	Co-base (mol%)	Conversion (%) (ee%)	Reaction time
1	N/A	0	10(50)	24h
2	DIPEA	20	31	24h
3	Et_3N	10	30	24h
4	NaOAc	10	26	24h
5	K_2CO_3	10	12	24h
6	Pyridine	10	8	24h
7	$NaHCO_3$	10	0	24h
8	DMAP	10	37	4d
9	DBU	10	32	4d
10	Dimethylaniline	10	22	4d
11	Pyridine	10	41	4d
12	Et_3N	100	100 (28)	3d
13	**NaOAc**	**100**	**81 (50)**	**3d**
14	DMAP	50	67 (45)	3d
15	DBU	50	77 (43)	3d
16	Methylimidazole	10	27	24h
17	DABCO	10	56	24h
18	Diethylamine	10	29	24h
19	TMEDA	10	27	24h
20	DABCO	20	53	18h

General Methods

NMR spectra were acquired on a Bruker 300 spectrometer, running at 300, 75 and 282 MHz for ^{1}H,^{13}C and ^{19}F respectively. Chemical shifts (δ) are reported in ppm relative to residual solvent signals ($CHCl_3$, 7.26 ppm for ^{1}H NMR, $CDCl_3$, 77.0 ppm). ^{13}C-NMR spectra were acquired on a broad band decoupled mode. Analytical thin layer chromatography (TLC) was performed using pre-coated aluminium-backed plates (Merck Kieselgel 60 F254) and visualized by ultraviolet irradiation, phosphomolybdic acid or $KMnO_4$ dip. Purification of reaction products was carried out by flash chromatography (FC) using silica gel Merck-60. Optical rotation was measured on a Perkin-Elmer 241 polarimeter. The enantiomeric excesses (*ee*) of products were determined by chiral stationary phase HPLC (Daicel Chiralcel IC and IB columns) or SFC (Supercritical fluid chromatography) system.

Materials

Commercially available naphtols **1a-g**, phenols, catalysts **4a**, **4e**, and solvents were used without further purification. Bromonitroalkenes,[1] catalysts **4b-c**[2] and **4d**[3] were synthesized according to the literature.

Experimental Procedures and Characterizations

*General Procedure for the synthesis of compounds **3***. In To an ordinary vial charged with corresponding naphtol **1** (0.18 mmol) was added the catalyst **4e** (10 mol%) and the corresponding bromonitroalkene **2** (0.1 mmol) in $CHCl_3$ (0.2 mL) at 0 ºC. Once the reaction was finished (as monitored by ^{1}H NMR spectroscopy, usually 16-40h), the solvent of the reaction was eliminated under reduce pressure and the crude was directly charged and purified by FC (eluent indicated in each case), affording pure products.

(1*S*,2*S*)-2-Nitro-1-phenyl-1,2-dihydronaphtho[2,1-b]furan (3a)

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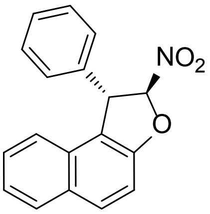
[1] (a) R. R. Dauzonne *Synthesis*, 1987, 1021; b) D. Dauzonne, H, Josien, P. Demerseman *Tetrahedron* **1990**, *21*, 7359; c) D. Dauzonne, P. Demerseman *Synthesis*, 1990, 67.

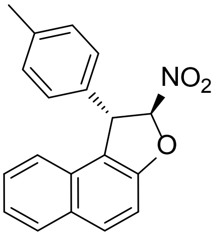
[2] B. Vakulya, V. Szilárd, C. Antal, T. Soós *Org. Lett.* 2005, **7***,* 1967

[3] J. P. Malerich, K. Hagihara, V. H. Rawal *J. Am. Chem. Soc.* 2008, **130**, 14416.



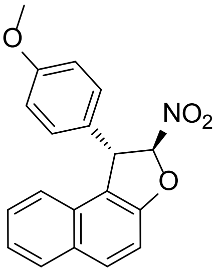
The product was obtained following the standard procedure, and the crude was charged in FC (25/1 Hexane: AcOEt), affording the pure product as white solid (71% yield). M.p.= 135.5 ˚C. $[\alpha]^{20}_D$ = +67.5 (*c* = 0.2, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96-7.85 (m, 2H), 7.45 (d, *J* = 8.9, Hz, 1H), 7.40-7-30 (m, 6H), 7.24-7.16 (m, 2H), 6.11 (d, *J* = 1.8 Hz, 1H), 5.32 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.5 (C), 138.3 (C), 131.8 (CH), 131.2 (C), 129.9 (C), 129.7 (CH, 2C), 129.4 (CH), 128.8 (CH), 128.0 (CH), 127.9 (CH, 2C), 124.8 (CH), 123.3 (CH), 118.6 (C), 112.9 (CH), 112.2 (CH), 55.7 (CH). MS (FB+): calcd. for $C_{18}H_{13}NO_3$: $[M]^+$, 291.0895, found 291.0897. Enantiomeric excess was determinated by HPLC using a IC Chiralcell column [hexane/iPrOH (90:10)]; flow rate 1 ml/min; τ_{major} = 6.5 min, τ_{minor} = 5.5 min (ee= 98%).

(1*S*,2*S*)-2-Nitro-1-*p*-tolyl-1,2-dihydronaphtho[2,1-b]furan (3b)



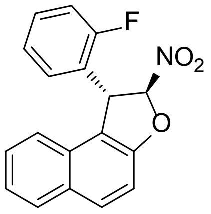
The product was obtained following the standard procedure, and the crude was charged in FC (50/1 Hexane: AcOEt), affording the pure product as yellow oil (85% yield). $[\alpha]^{20}_D$ = +78.2 (*c* = 0.9, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82-7.73 (m, 2H), 7.32 (d, *J* = 8.9 Hz, 1H), 7.28-7.22 (m, 2H), 7.14 (s, 1H), 7.03 (d, *J* = 8.1 Hz, 2H), 6.96 (d, *J* = 8.1 Hz, 2H), 5.97 (d, *J*= 0.9, 1H), 5.17 (s, 1H), 2.21 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.2 (C), 138.3 (C), 135.0 (C), 131.3 (CH), 130.9 (C), 130.0 (CH) (2 C), 129.6 (CH), 129.0 (CH), 127.6 (CH), 127.4 (CH, 2C), 124.5 (CH), 123.0 (CH),118.4 (C), 112.7 (CH), 111.8 (CH), 55.1 (CH), 21.1 (CH_3). MS (ESI^+): calcd. for $C_{19}H_{15}O$: $[M-NO_2]^+$: 259.1117, found 259.1146. Enantiomeric excess was determinated by HPLC using a IC Chiralcell column [hexane/iPrOH (90:10)]; flow rate 1 ml/min; τ_{major} = 6.4 min, τ_{minor} = 5.4 min (ee= 94%).

(1*S*,2*S*)-1-(4-Methoxyphenyl)-2-nitro-1,2-dihydronaphtho[2,1-b]furan (3c)



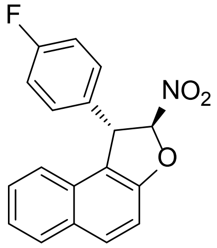
The product was obtained following the standard procedure, and the crude was charged in FC (50/1 Hexane: AcOEt), affording the pure product as yellow oil (45% yield). $[\alpha]^{20}_D$ = +58.4 (*c* = 0.4, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94-7.83 (m, 2H), 7.43 (d, *J* = 8.9 Hz, 1H), 7.39-7.33 (m, 3H), 7.10 (d, *J* = 8.6, 2H), 6.85 (d, *J* = 8.7, 1H), 6.07 (d, *J* = 1.7 Hz, 1H), 5.27 (s, 1H), 3.77 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.6 (C), 156.1 (C), 136.7 (CH), 131.2 (C), 130.3 (C), 129.9 (C), 129.3 (CH), 129.0 (CH, 2C), 127.9 (CH), 124.8 (CH), 123.3 (CH), 118.8 (C), 115.0 (CH, 2C), 113.0 (CH), 112.2 (CH), 55.6 (CH), 55.1 (CH_3). MS (ESI$^+$): calcd. for $C_{19}H_{15}O_2$:[M-NO_2]$^+$, 275.1072, found 275.1096. Enantiomeric excess was determinated by HPLC using a IC Chiralcell column [hexane/iPrOH (90:10)]; flow rate 1 ml/min; τ_{major} = 10.1 min, τ_{minor} = 7.1 min (ee= 94%).

(1*S*,2*S*)-1-(2-Fluorophenyl)-1,2-dihydro-2-nitronaphtho[2,1-b]furan (3d)



The product was obtained following the standard procedure, and the crude was charged in FC (15/1 Hexane: AcOEt), affording the pure product as red solid (94% yield). M.p. = 86 ˚C. [α]$^{20}_D$ = +103.2 (*c* = 1.5, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96-7.82 (m, 2H), 7.48-7,14 (m, 6H), 6.99 (t, *J* = 7.5 Hz , 1H), 6.75 (t, *J* = 7.6 Hz, 1H), 6.16 (s, 1H), 5,56 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.2 (d, J_{CF} = 246.5 Hz, C), 156.6 (C), 131.9 (CH), 131.2 (C), 130.6 (d, J_{CF} = 8.1 Hz, C), 129.8 (C), 129.4 (CH), 129.3 (d, *J* = 3.1 Hz, CH), 128.1 (CH), 125.3 (d, J_{CF} = 3.5 Hz, CH), 125.1 (C), 124.9 (CH), 123.0 (CH), 117.8 (CH), 116.5 (CH), 116.3 (CH), 112.1 (d, J_{CF} = 10.1 Hz, CH), 48.3 (d, J_{CF} = 3.7 Hz, CH). ^{19}F NMR (282 MHz, $CDCl_3$) δ -116.8. MS (ESI+): calcd. for $C_{18}H_{12}OF$: [M-NO_2]$^+$, 263.0866, found 263.0859. Enantiomeric excess was determinated by HPLC using a IC Chiralcell column [hexane/iPrOH (90:10)]; flow rate 1 ml/min; τ_{major} = 6.4 min, τ_{minor} = 5.8 min (ee= 88%).

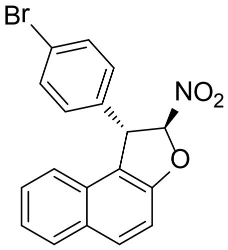
(1*S*,2*S*)-1-(4-Fluorophenyl)-2-nitro-1,2-dihydronaphtho[2,1-b]furan (3e)



The product was obtained following the standard procedure, and the crude was charged in FC (50/1 Hexane: AcOEt), affording the pure product as red solid (59% yield). M.p. = 127 ˚C. [α]$^{20}_D$ = +6.2 (*c* = 0.8, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97-7.86 (m, 2H), 7.45 (d, *J* = 8.9 Hz, 1H) 7.41-7.30 (m, 3H), 7.17 (dd, *J* = 8.5, 5.4 Hz, 1H), 7.03 (t, *J* = 8.5 Hz, 2H), 6.07 (d, *J* = 1.4 Hz, 1H), 5.32 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.6 (d, J_{CF} = 150 Hz, C), 162.7 (C), 156.2 (C), 133.7 (C), 133.6 (C), 131.7 (CH), 130.2 (d, J_{CF} = 108.75 Hz, CH), 129.3 (CH), 129.2 (CH) 129.1 (CH), 127.8 (CH), 124.6 (CH), 122.9 (CH) , 118.0 (C), 116.4 (d, J_{CF} = 12.7 Hz, CH),

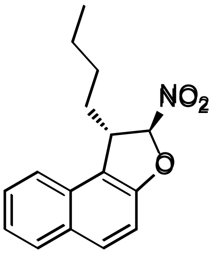
112.3 (CH), 111.9 (CH), 54.6 (CH). {^{1}H} ^{19}F NMR (282 MHz, $CDCl_3$) δ -113.2. MS (EI^+): calcd. for $C_{18}H_{13}OF$: [$M-NO_2^+$], 264.0950, found 263.0881. Enantiomeric excess was determined by HPLC using a IC Chiralcell column [hexane/iPrOH (90:10)]; flow rate 1 ml/min; τ_{major} = 7.6 min, τ_{minor} = 5.8 min (ee= 97%).

(1*S*,2*S*)-1-(4-Bromophenyl)-1,2-dihydro-2-nitronaphtho[2,1-b]furan (3f)



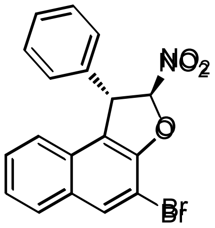
The product was obtained following the standard procedure, and the crude was charged in FC (60/1 Hexane: AcOEt), affording the pure product as red solid (78% yield). M.p. = 91 ˚C. $[\alpha]^{20}_D$ = +6.3 (*c* = 1, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98-7.84 (m, 2H), 7.47 (t, *J* = 7.9 Hz, 3H), 7.42-7.28 (m, 3H), 7.07 (d, *J* = 8.2 Hz, 2H), 6.05 (s, 1H), 5.28 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.6 (C), 137.2 (C), 132.9 (CH, 2C), 132.1 (CH), 131.2 (C), 129.8 (C), 129.6 (CH, 2C), 129.5 (CH), 125.0 (CH), 128.2 (CH), 123.1 (CH), 122.9 (C), 118.0 (C), 112.4 (CH), 112.2 (CH), 55.1 (CH). MS (EI^+): calcd for $C_{18}H_{13}BrO$: $[M-NO_2]^+$, 323.9997, found 323,9970. Enantiomeric excess was determined by HPLC using a IC Chiralcell column [hexane/iPrOH (90:10)]; flow rate 1 ml/min; τ_{major} = 11.5 min, τ_{minor} = 7.6 min (ee= 92%)

(1*S*,2*S*)-1-Butyl-1,2-dihydro-2-nitronaphtho[2,1-b]furan (3g)



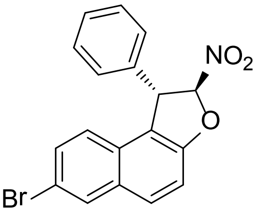
The product was obtained following the standard procedure, and the crude was charged in FC (55/1 Hexane: AcOEt), affording the pure product as orange oil (55% yield). $[\alpha]^{20}_D$ = +6.9 (*c* = 1.1, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (d , *J* = 8.3 Hz , 1H), 7.83 (d , *J* = 8.8 Hz , 1H), 7.65 (d , *J* = 8.3 Hz , 1H), 7.52 (t, *J* = 8.2 Hz , 1H), 7.40 (t, *J* = 7.6 Hz , 1H), 7.26 (d , *J* = 8.9 Hz , 1H), 6.04 (d, *J* = 1.4 Hz, 1H), 5.30 (s, 1H), 4.07 (dd, *J* = 9.2, 3.4 Hz , 1H), 2.21-2.03 (m , 1H), 1.88-1.67 (m, 2H), 1.64-1.18 (m, 2H), 0.95 (t, *J* = 7.2 Hz , 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.1 (C), 130.8 (C), 130.6 (C), 129.4 (C), 129.2 (C), 127.4 (C), 124.2 (C), 122.4 (C), 119.4 (C), 111.8 (C), 110.4 (CH), 50.2 (CH), 32.7 (CH_2), 28.6 (CH_2), 22.4 (CH_2), 13.9 (CH_3). MS (EI^+): calcd. for $C_{16}H_{16}O$: $[M-NO_2]^+$, 224.1201, found 224.1198. Enantiomeric excess was determined by HPLC using a IC Chiralcell column [hexane/iPrOH (90:10)]; flow rate 1 ml/min; τ_{major} = 6.2 min, τ_{minor} = 5.3 min (ee= 91%).

(1*S*,2*S*)-4-Bromo-1,2-dihydro-2-nitro-1-phenylnaphtho[2,1-b]furan (3h).



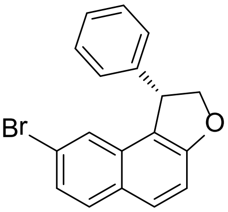
The product was obtained following the standard procedure, and the crude was charged in FC (12/1 Hexane: AcOEt), affording the pure product as yellow solid (72% yield). M.p. = 130 ˚C. $[\alpha]^{20}_D$ = +57.6 (*c* = 0.2, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.12 (s, 1H), 8.03 (s, 2H), 7.68 (d, *J* = 8.6 Hz, 1H), 7.40-7.35 (m, 4H), 7.22-7.16 (m, 2H), 6.15 (s, 1H), 5.39 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.3 (C), 137.3 (C), 133.3 (CH), 131.9 (C), 129.5 (CH, 2C), 128.7 (CH), 128.5 (C), 128.2 (CH), 127.9 (CH), 127.5 (CH, 2C), 125.5 (CH), 123.1 (CH), 119.8 (C), 111.7 (CH), 104.2 (C), 56.3 (CH). MS (EI$^+$): calcd. for $C_{18}H_{13}BrO$: $[M-NO_2]^+$, 323.9997, found 323.9975. Enantiomeric excess was determined by HPLC using a IC Chiralcell column [hexane/iPrOH (90:10)]; flow rate 1 ml/min; τ_{major} = 13.2 min, τ_{minor} = 7.1 min (ee= 87%).

(1*S*,2*S*)-7-Bromo-2-nitro-1-phenyl-1,2-dihydronaphtho[2,1-b]furan (3i).



The product was obtained following the standard procedure, and the crude was charged in FC (8/1 Hexane: AcOEt), affording the pure product as red solid (68% yield). M.p = 128 ˚C. $[\alpha]^{20}_D$ = +39.3, (*c* = 0.1, CH_2Cl_2). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.9 Hz, 1H), 7.74 (d, *J* = 8.8 Hz, 1H), 7.51 (d, *J* = 1.6 Hz, 1H), 7.49-7.42 (m, 3H), 7.41-7.32 (m, 3H), 7.18 (dd, *J* = 7.3, 2.2 Hz, 1H), 6.09 (d, *J* = 1.7 Hz, 1H), 5.22 (s, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 156.5 (C), 137.6 (C), 132.0 (C), 131.1 (CH), 131.0 (CH), 130.6 (CH), 129.5 (CH, 2C), 128.6 (CH), 128.1 (C), 127.5 (CH, 2C), 124.6 (CH), 118.7 (C), 118.3 (C), 113.0 (CH), 112.4 (CH), 55.2 (CH). MS (EI$^+$): calcd for $C_{18}H_{12}OBr$: $[M-NO_2]^+$, 325.0150, found 325.0072. Enantiomeric excess was determined by HPLC using a Chiralcell IC column [hexane/iPrOH (90:10)]; flow rate 0.5 ml/min; τ_{major} = 14.3 min, τ_{minor} = 12.0 min (ee = 91 %).

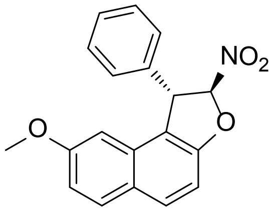
(1*S*,2*S*)-8-Bromo-1,2-dihydro-2-nitro-1-phenylnaphtho[2,1-b]furan (3j)



The product was obtained following the standard procedure, and the crude was charged in FC (8/1 Hexane: AcOEt), affording the pure product as red solid (83% yield). M.p = 132 ˚C. $[\alpha]^{20}_D$ = +3.5 (*c* = 1.8, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.9 Hz, 1H), 7.74 (d, *J* = 8.9 Hz, 1H), 7.71 (d, *J* = 1.6 Hz, 1H), 7.49-7.51

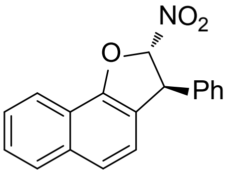
(m, 2H), 7.41-7.32 (m, 3H), 7.23-7.14 (m, 2H), 6.09 (d, *J* = 1.7 Hz, 1H), 5.27 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.3 (C), 137.7 (C), 131.8 (CH), 131.1 (C), 131.0 (CH), 129.9 (CH, 2C), 129.6 (C), 129.0 (CH), 128.4 (CH), 127.7 (CH, 2C), 125.5 (CH), 122.6 (C), 118.0 (C), 112.7 (CH), 112.6 (CH), 55.4 (CH). MS (EI$^+$): calcd for $C_{18}H_{13}BrO$: $[M-NO_2]^+$, 324.0150, found 323.9949. Enantiomeric excess was determinate by HPLC using a IC Chiralcell column [hexane/iPrOH (90:10)]; flow rate 1 ml/min; τ_{major} = 11.4 min, τ_{minor} = 6.5 min (ee= 93%).

(1*S*,2*S*)-1,2-Dihydro-8-methoxy-2-nitro-1-phenylnaphtho[2,1-b]furan (3k).



The product was obtained following the standard procedure, and the crude was charged in FC (Hexane), affording the pure product as yellow solid (68% yield). M.p. = 123 ˚C. $[\alpha]^{20}_D$ = 13.7 (*c* = 1.9 CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 18.8, 8.9 Hz, 2H), 7.31-7.14 (m, 5H), 6.94 (dd, *J* = 9.0, 2.4 Hz, 1H), 6.52 (d, *J* = 2.2 Hz, 1H), 6.04 (d, *J* = 1.7 Hz, 1H), 5.19 (s, 1H), 3.69 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.9 (C), 155.7 (C), 136.8 (C), 130.0 (CH), 129.9 (C), 129.5 (CH), 128.3 (CH, 2C), 127.4 (CH), 126.5 (CH, 2C), 125.2 (C), 116.3 (C), 115.9 (CH), 111.5 (CH), 108.1 (CH), 100.5 (CH), 54.3 (CH), 54.1 (CH_3). MS (FB$^+$): calcd for $C_{19}H_{15}O_2$:$[M-HNO_2]^+$, 275.1072, found 275.1077. Enantiomeric excess was determinated by HPLC using a IC Chiralcell column [hexane/iPrOH (90:10)]; flow rate 1 ml/min; τ_{major} = 9.7 min, τ_{minor} = 6.4 min (ee= 93%).

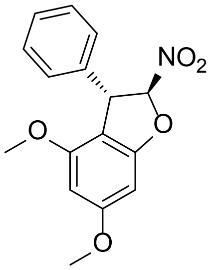
(2*S*,3*S*)-2-Nitro-3-phenyl-2,3-dihydronaphtho[1,2-b]furan (3l)



The product was obtained following the standard procedure, and the crude was charged in FC (12/1 Hexane: AcOEt), affording the pure product as white oil (50% yield). $[\alpha]^{20}_D$ = +3.0 (*c* = 0.5, CH_2Cl_2). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.8 Hz, 1H), 7.82 (d, *J* = 7.6 Hz, 1H), 7.5 5-7.48 (m, 4H), 7.30-7.25 (m, 2H), 7.16 (d, *J* = 8.3 Hz, 1H), 7.11-7.05 (m, 2H), 6.12 (d, *J* = 1.8 Hz, 1H), 5.04 (s, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 153.8 (C), 138.7 (C), 134.7 (C), 129.3 (CH, 2C), 128.4 (CH), 128.1 (CH), 127.5 (CH, 2C), 127.0 (CH), 126.7 (CH), 123.9 (CH), 121.7 (CH), 121.4 (CH), 120.4 (C), 119.9 (C), 112.3 (CH), 56.5 (CH). MS (EI+): calcd for $C_{18}H_{14}O$: $[M-NO_2]^+$, 246.1045, found 245.0852.

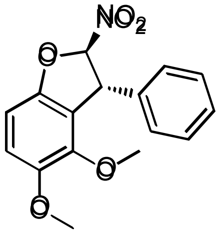
Enantiomeric excess was determined by HPLC using a Chiralcell IA column [hexane/iPrOH (90:10)]; flow rate 1 ml/min; τ_{major} = 5.7 min, τ_{minor} = 7.4 min (ee = 98 %).

(2*S*,3*S*)-4,6-Dimethoxy-2-nitro-3-phenyl-2,3-dihydrobenzofuran (3m)



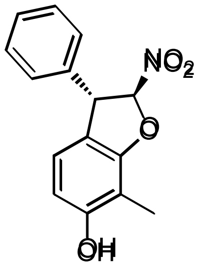
The product was obtained following the standard procedure and the crude was charged in FC (55/1 Hexane: AcOEt, after tube 40, 20/1 Hexane: AcOEt), affording the pure product as white solid (57% yield). M.p. = 105 °C. $[\alpha]^{20}_{D}$ = +26.0 (*c* = 0.2, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$) δ 7.32-7.21 (m, 3H), 7.15-7.05 (m, 2H), 6.33 (d, *J* = 1.5 Hz, 1H), 6.09 (d, *J* = 1.8 Hz, 1H), 5.88 (d, *J* = 1.2 Hz, 1H), 4.83 (s, 1H), 3.77 (s, 3H), 3.59 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.1 (C), 160.2 (C), 156.9 (C), 138.3 (C), 129.0 (2C), 128.0 (C), 127.2 (2C), 112.6 (CH), 105.2 (C), 94.1 (C), 89.0 (C), 55.8 (CH3), 55.5 (CH3), 53.5 (CH). MS (ESI$^+$): calcd for $C_{16}H_{16}NO_5$: $[M]^+$, 302,1022, found 302,1047. Enantiomeric excess was determined by HPLC using a IC Chiralcell column [hexane/iPrOH (90:10)]; flow rate 1 ml/min; τ_{major} = 6.1 min, τ_{minor} = 6.6 min (ee= 66%).

(2*R*, 3*R*)-5,6-dimethoxy-2-nitro-3-phenyl-2,3-dihydrobenzofuran (3n)



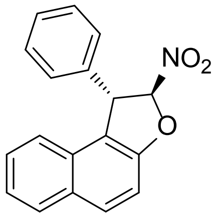
The product was obtained following the standard procedure and the crude was charged in FC (3/1 Hexane: AcOEt), affording the pure product as white solid (50% yield). M.p. = 90-95 °C. $[\alpha]^{20}_{D}$ = +40.7 (*c* = 1.2, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ 7.41-7.31 (m, 3H), 7.19–7.12 (m, 2H), 6.80 (s, 1H), 6.67 (s, 1H), 5.95 (s, 1H), 4.89 (s, 1H), 3.93 (s, 3H), 3.78 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.7 (C), 151.1 (C), 146.3 (C), 139.3 (C), 129.6 (CH, 2C), 128.7 (CH), 127.7 (CH, 2C), 116.2 (C), 112.9 (CH), 108.4 (CH), 96.0 (CH), 57.0 (CH), 56.6 (CH_3) 56.3 (CH_3). Enantiomeric excess was determinate by SFC-HPLC using an IB Chiralcell column [CO_2/MeOH (95:5)]; flow rate 3 ml/min; τ_{major} = 3.8 min, τ_{minor} = 3.5 min (ee= 97%).

(2*S*,3*S*)-7-methyl-2-nitro-3-phenyl-2,3-dihydrobenzofuran-6-ol (3o)

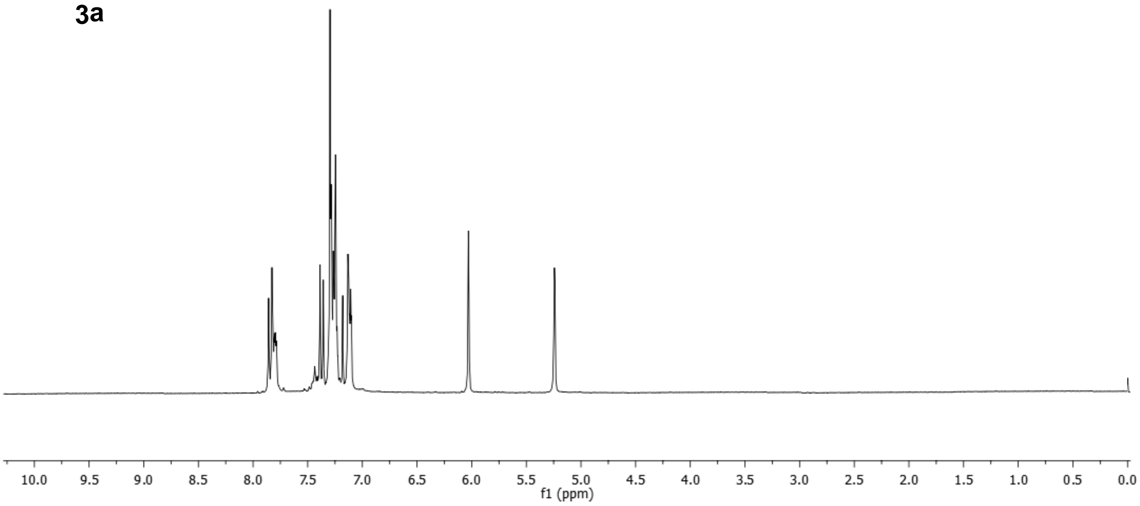


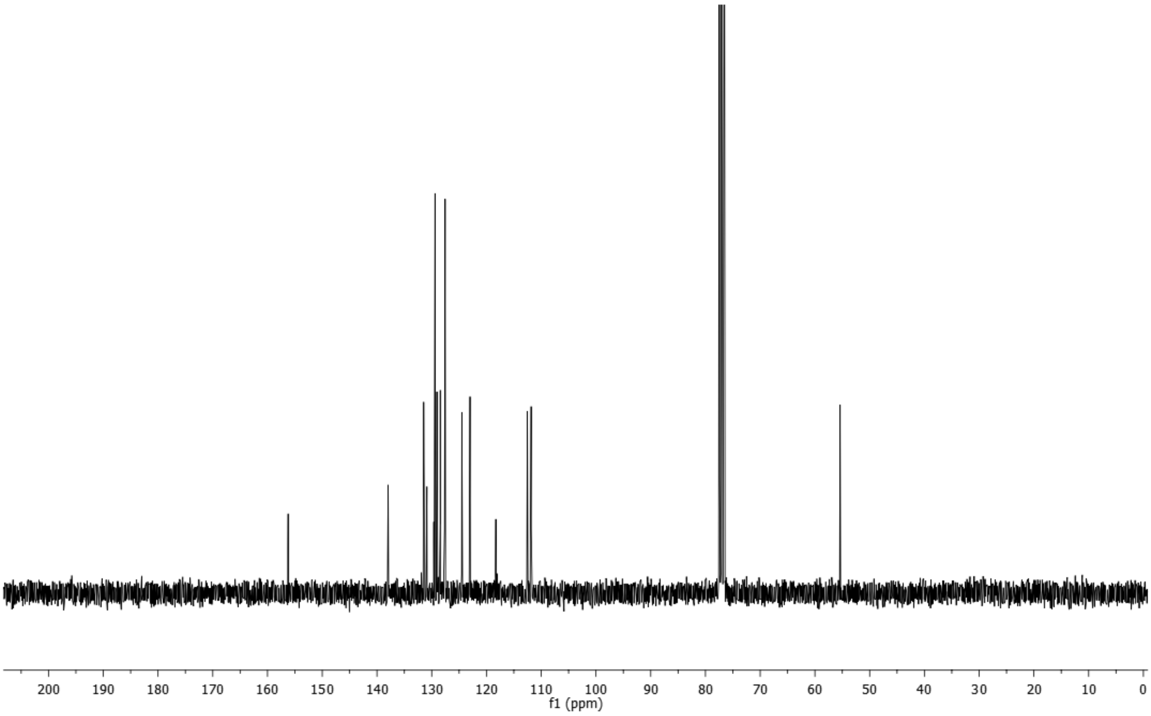
The product was obtained following the standard procedure and the crude was charged in FC (5/1 Hexane: AcOEt), affording the pure product as yellow oil (29% yield). $[\alpha]^{20}_{D}$ = +7.5 (*c* = 1.4, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ 7.39-7.30 (m, 3H), 7.18–7.13 (m, 2H), 6.83 (d, *J* = 8.1 Hz, 1H), 6.51 (d, *J* = 8.1 Hz, 1H), 6.01 (d, *J* = 1.6 Hz, 1H), 4.87 (s, 1H), 2.31 (d, *J* = 9.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.5 (C), 155.6 (C), 139.7 (C), 129.6 (CH, 2C), 128.5 (CH), 127.7 (CH, 2C), 122.7 (CH), 117.9 (C) 112.8 (CH), 110.7 (CH), 108.5 (C), 55.9 (CH), 8.82 (CH_3). Enantiomeric excess was determinate by SFC-HPLC using an IB Chiralcell column [CO_2/MeOH (95:5)]; flow rate 3 ml/min; τ_{major} = 13.5 min, τ_{minor} = 9.2 min (ee= 95%).

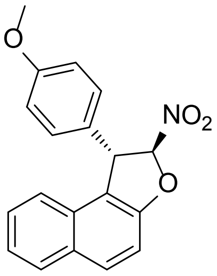
Spectra of compounds 3a-o



3a



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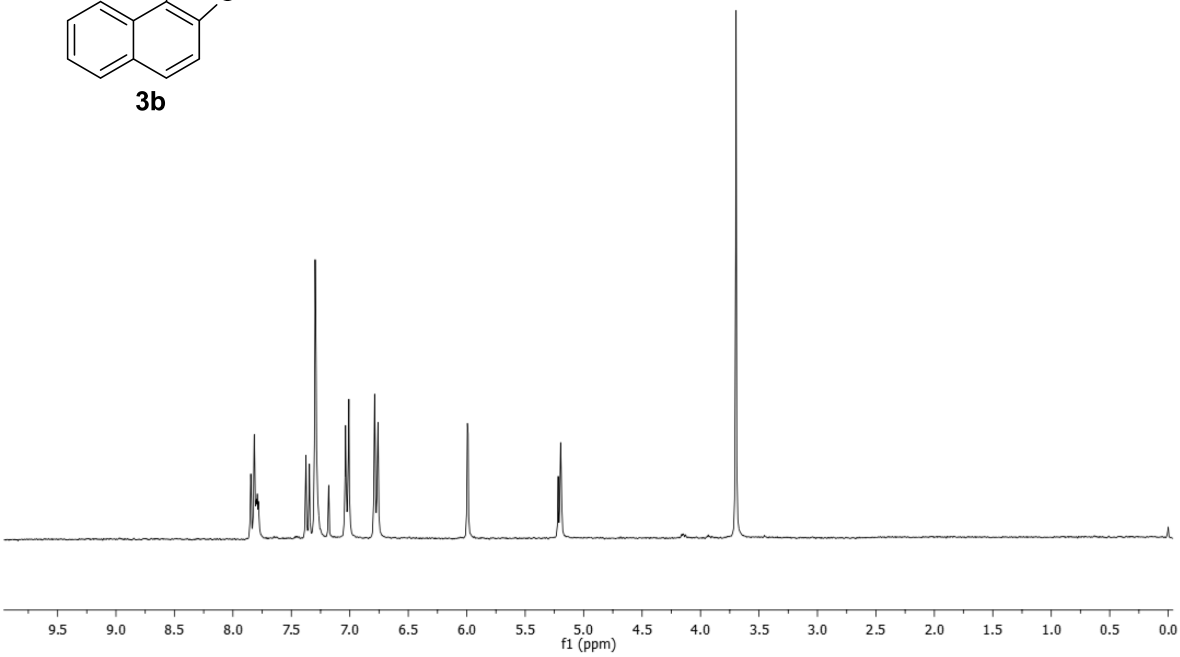
3b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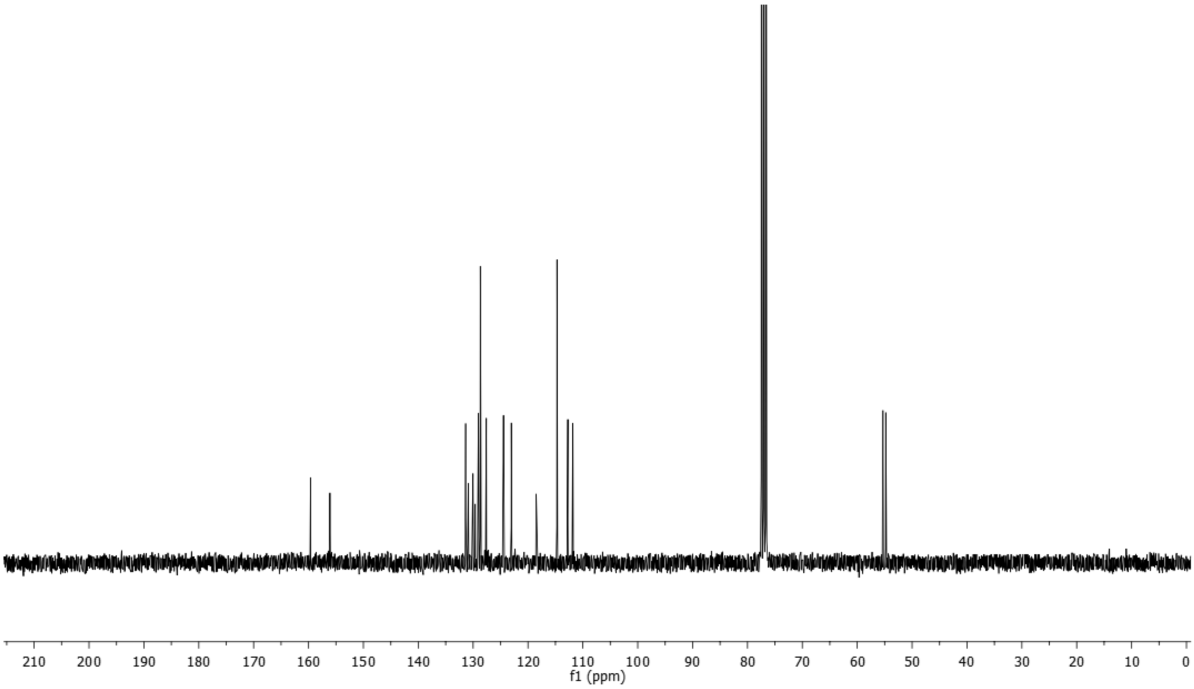
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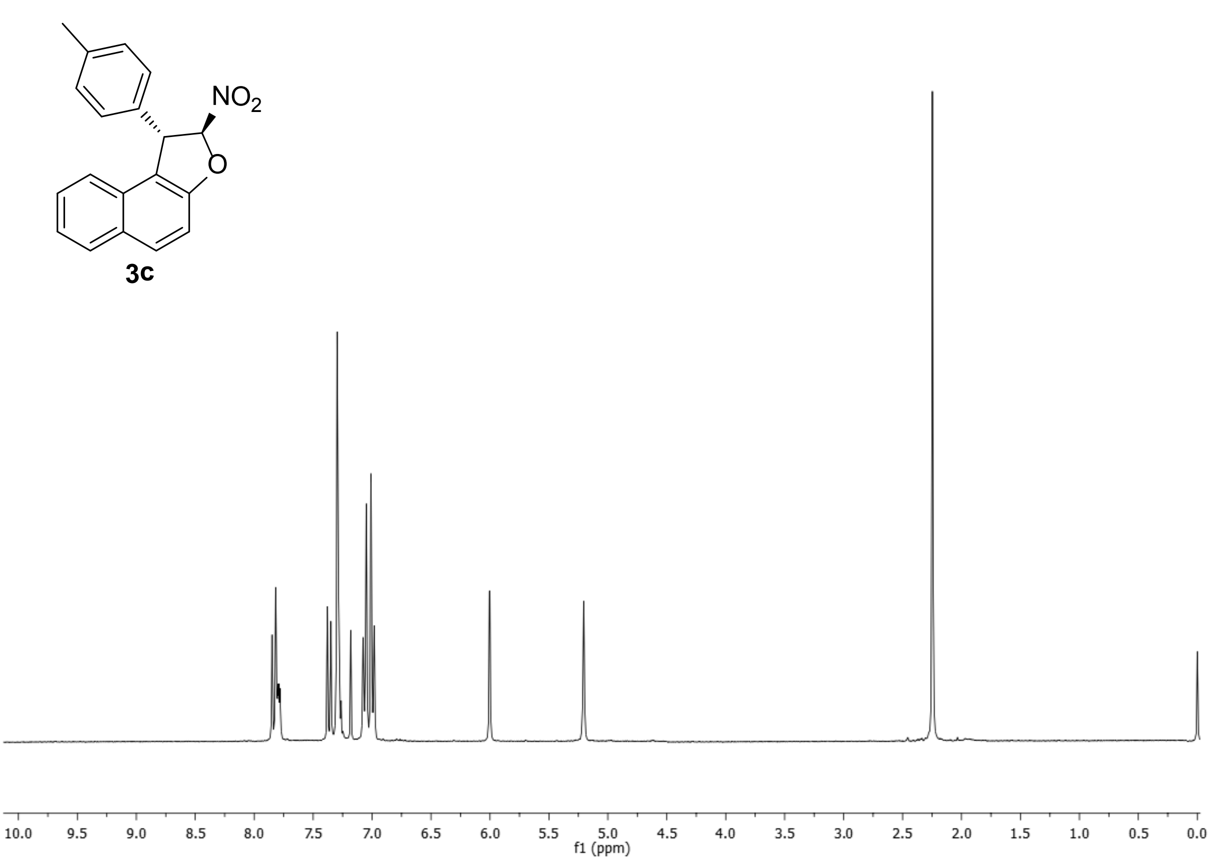
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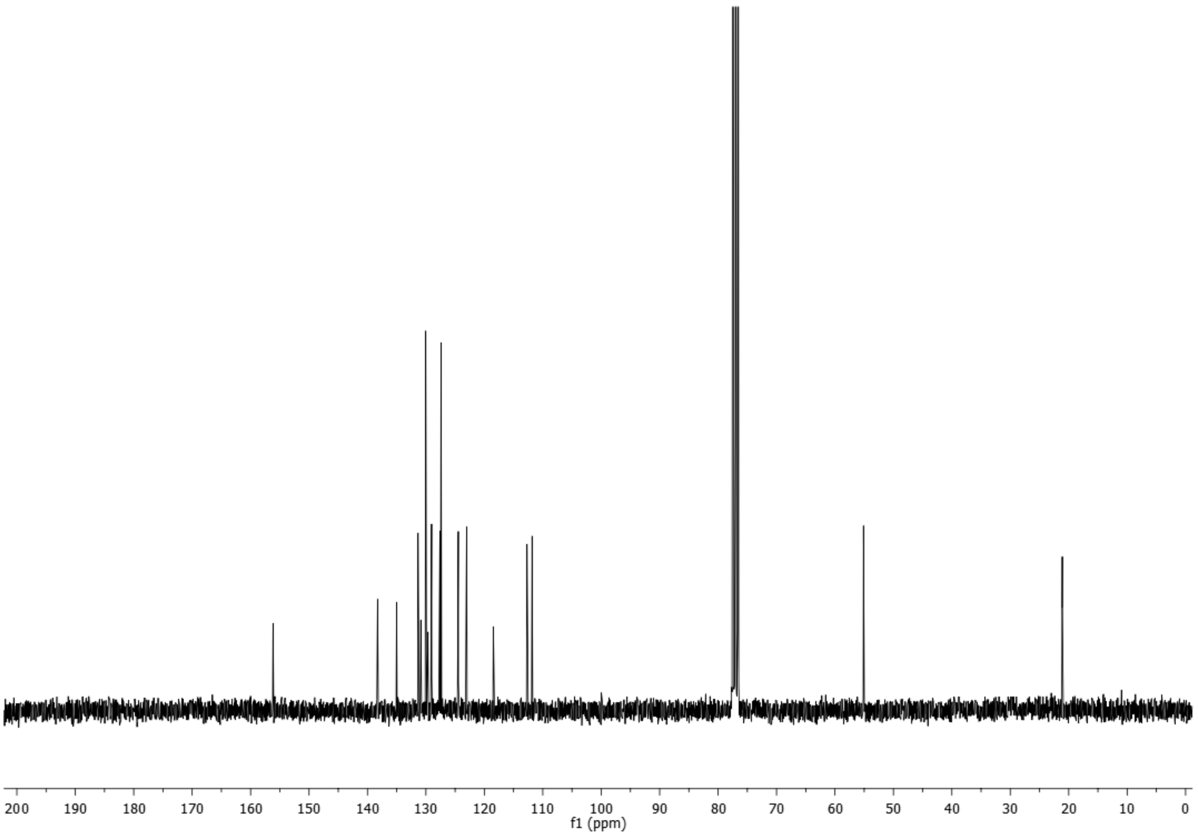
f1 (ppm)

3c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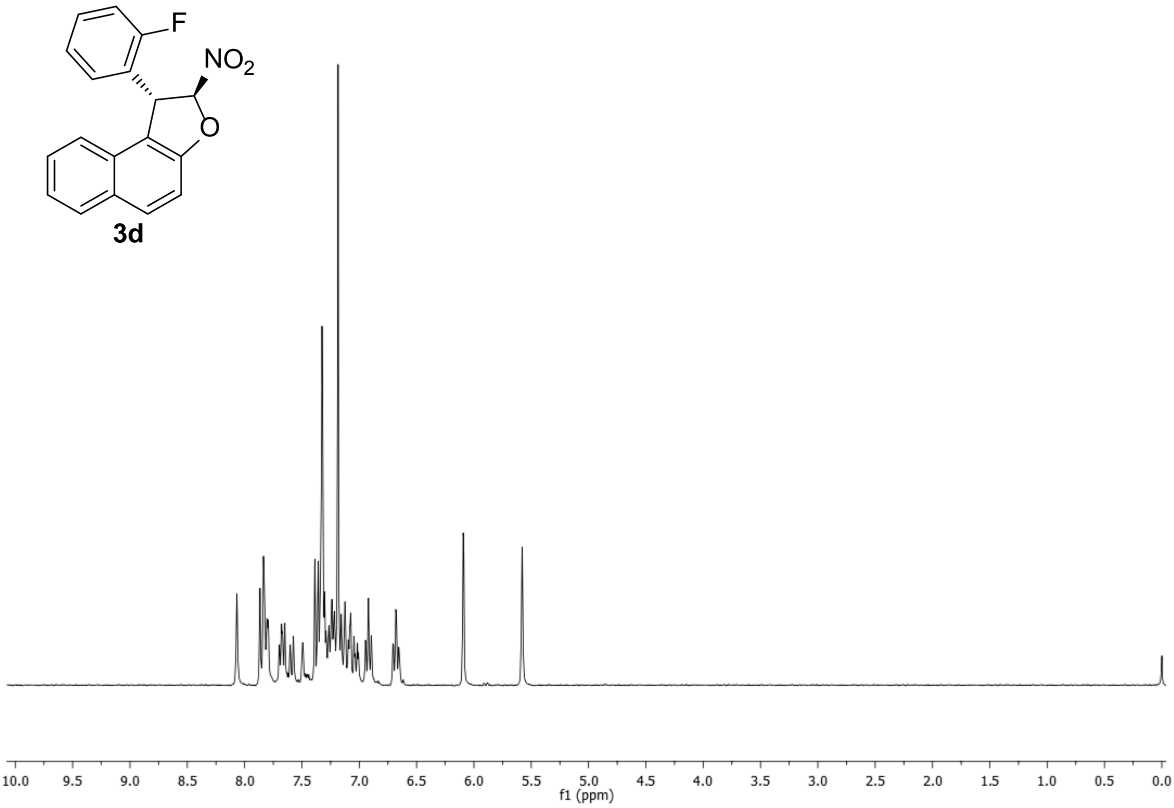
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O
3d
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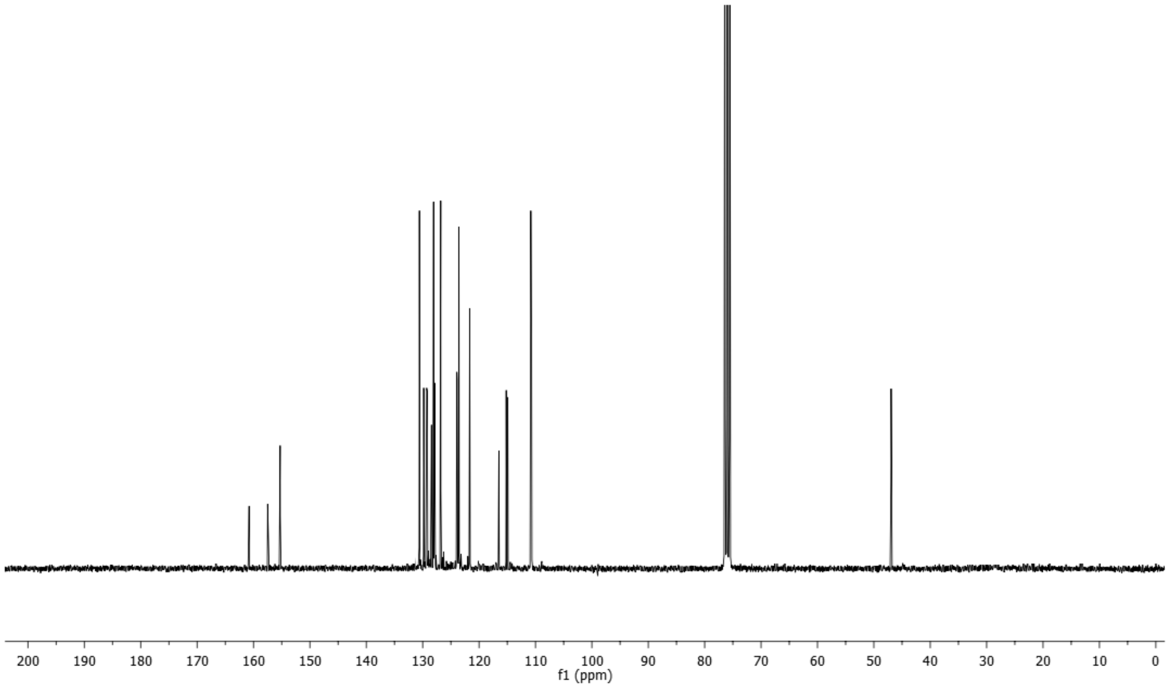
f1 (ppm)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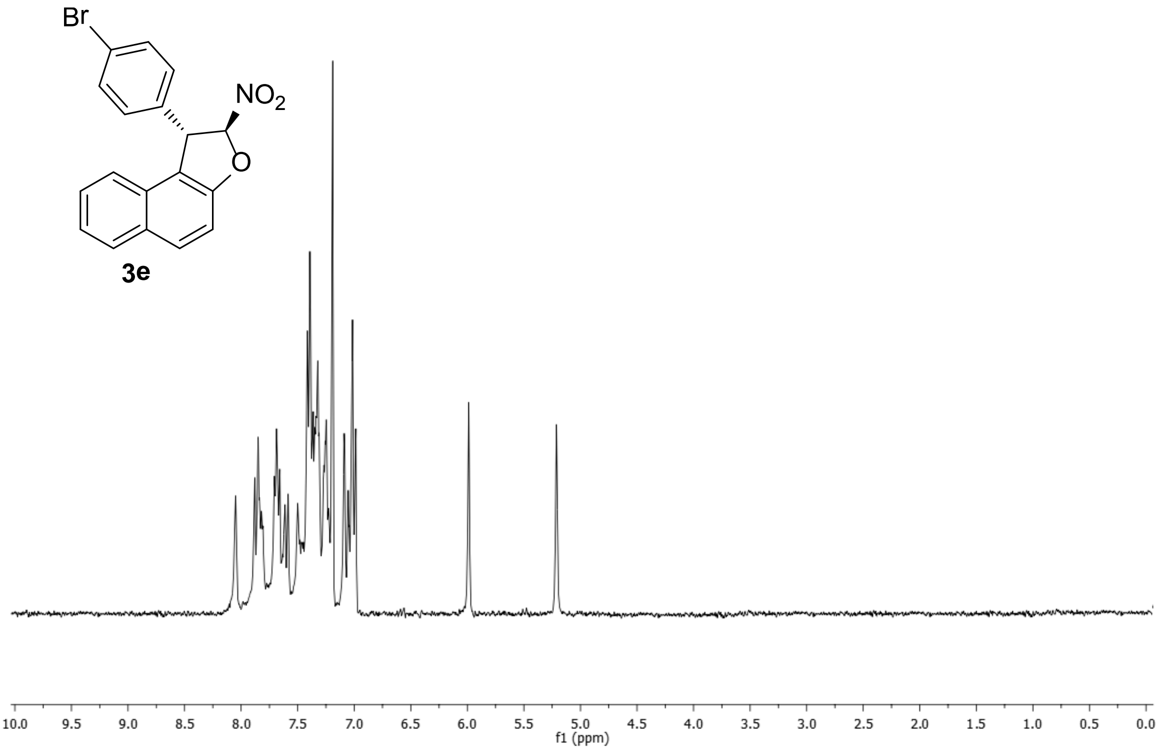
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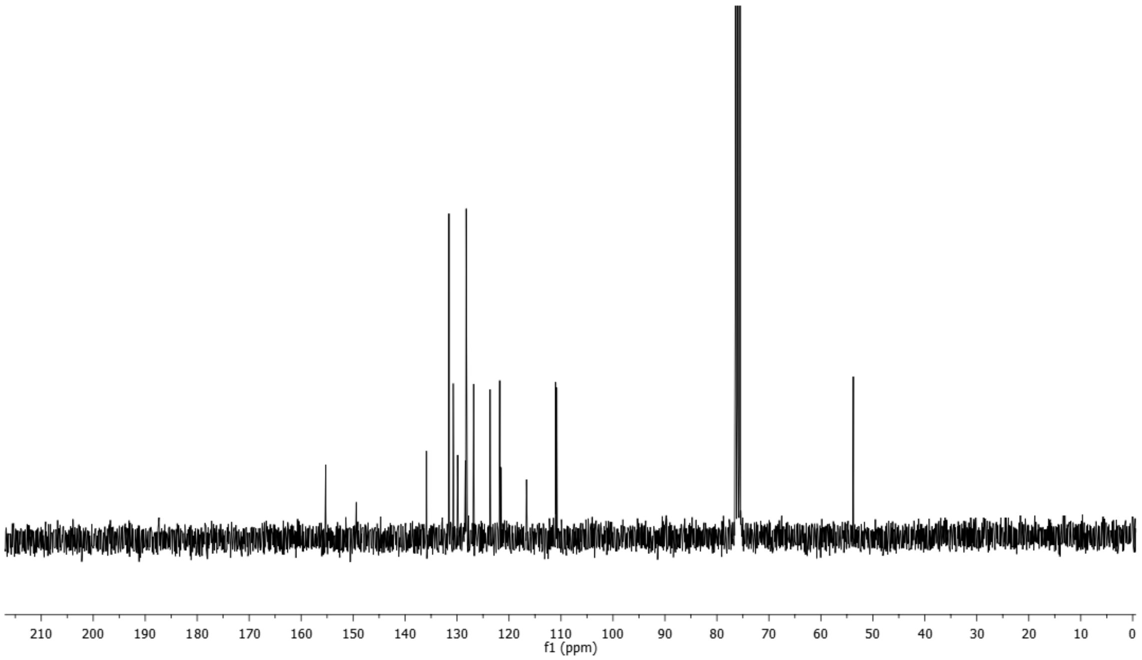
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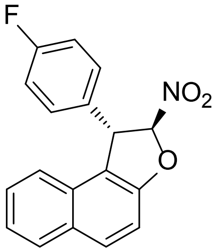
F
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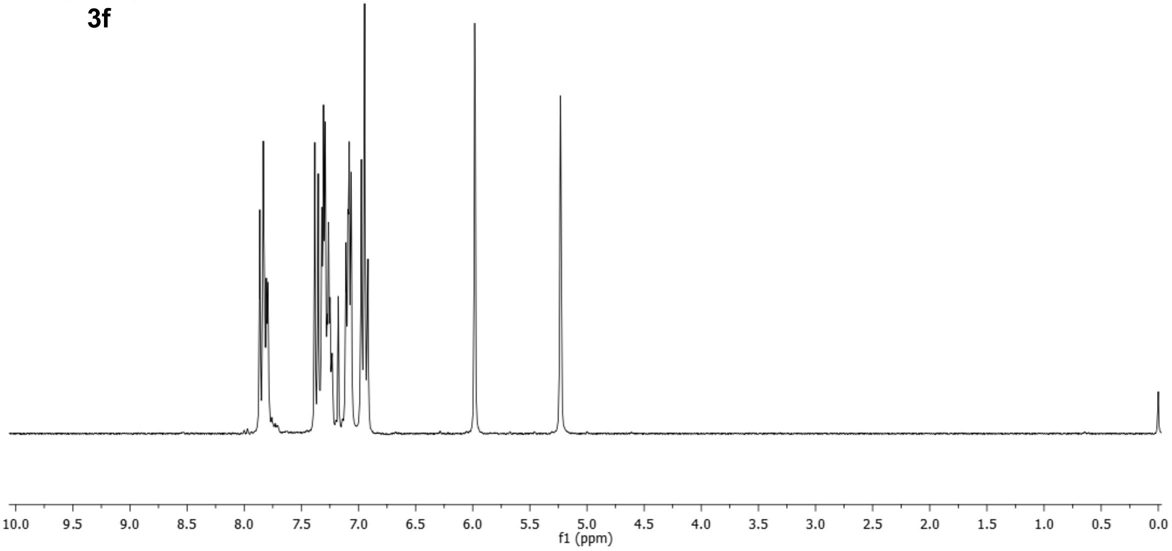
O

3f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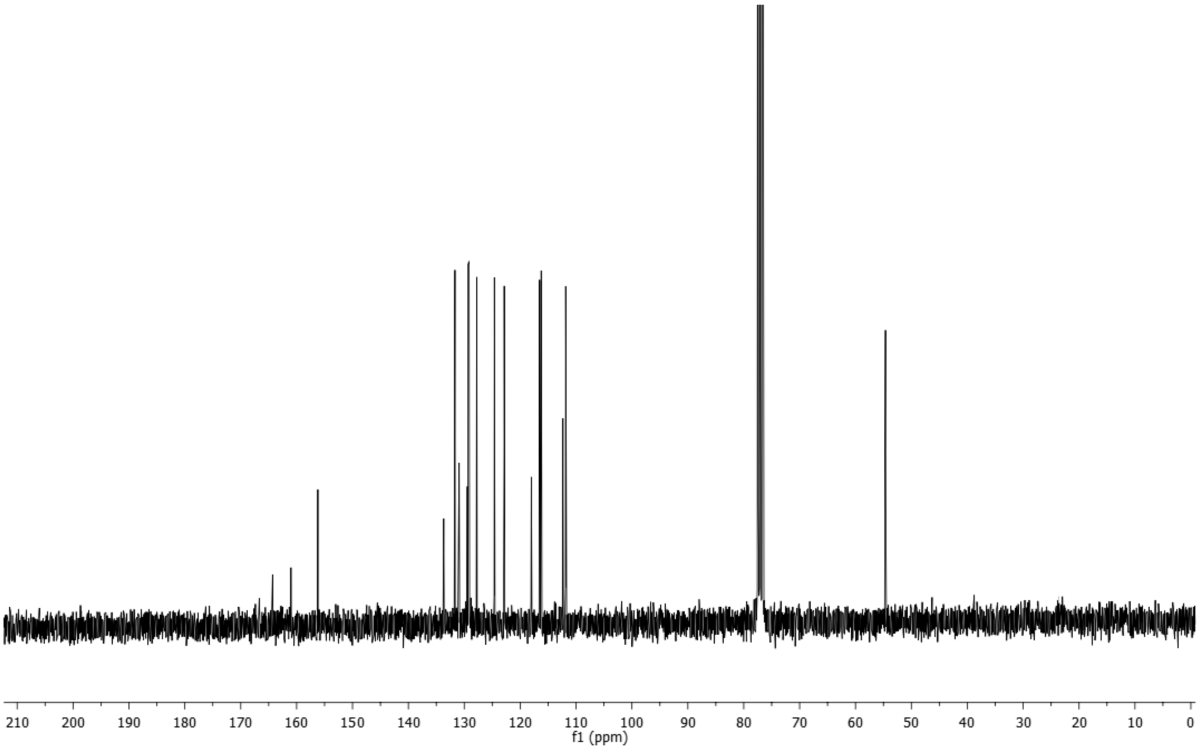
f1 (ppm)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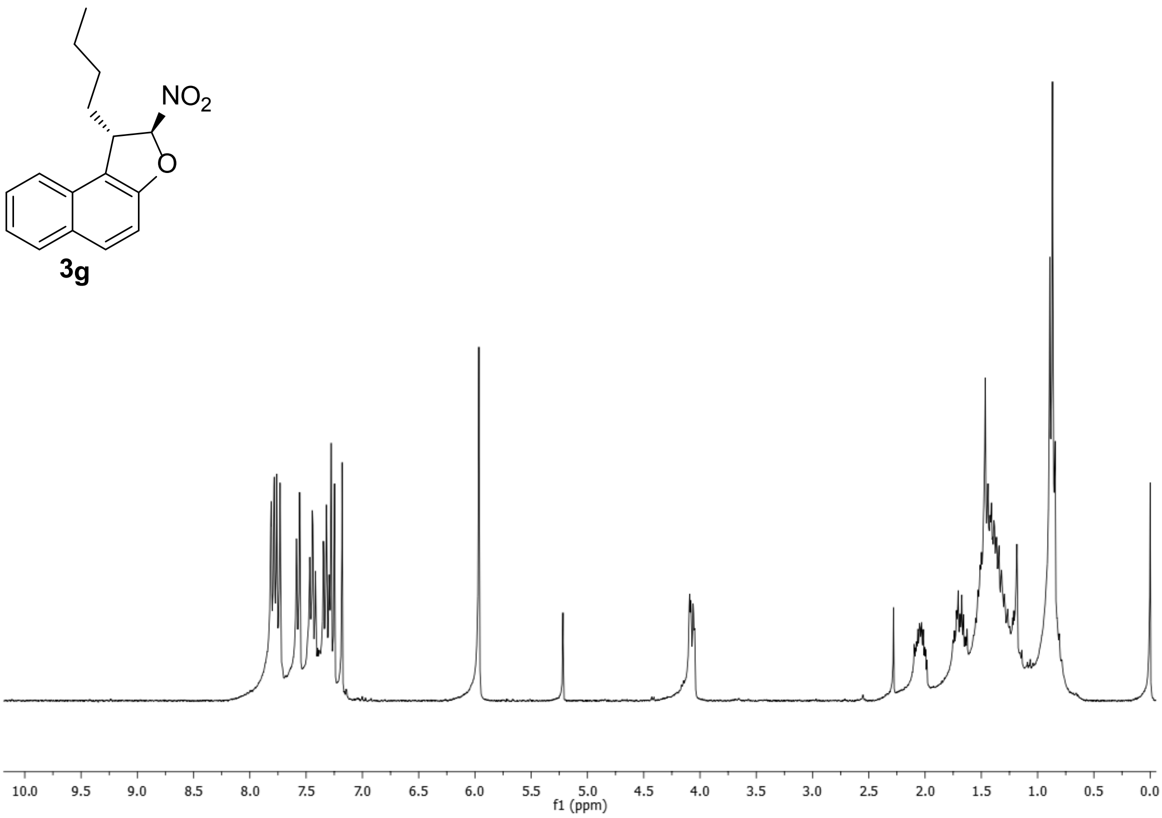
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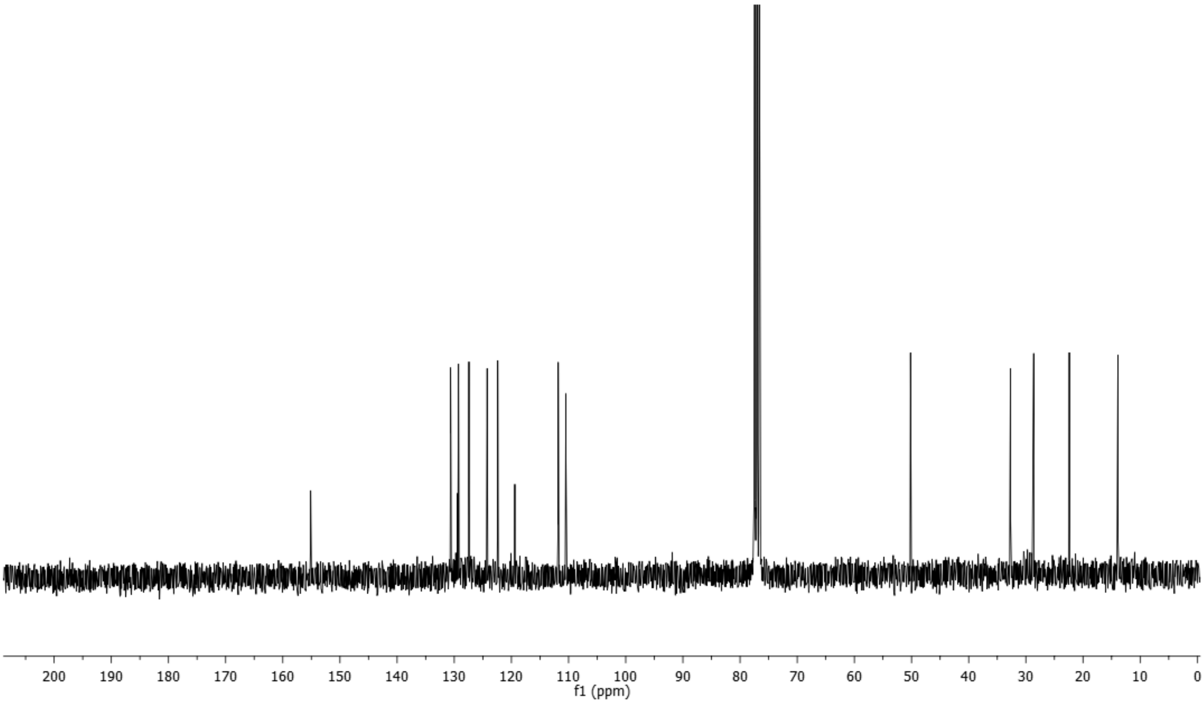
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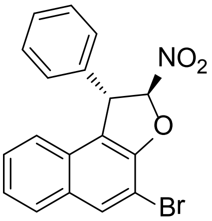
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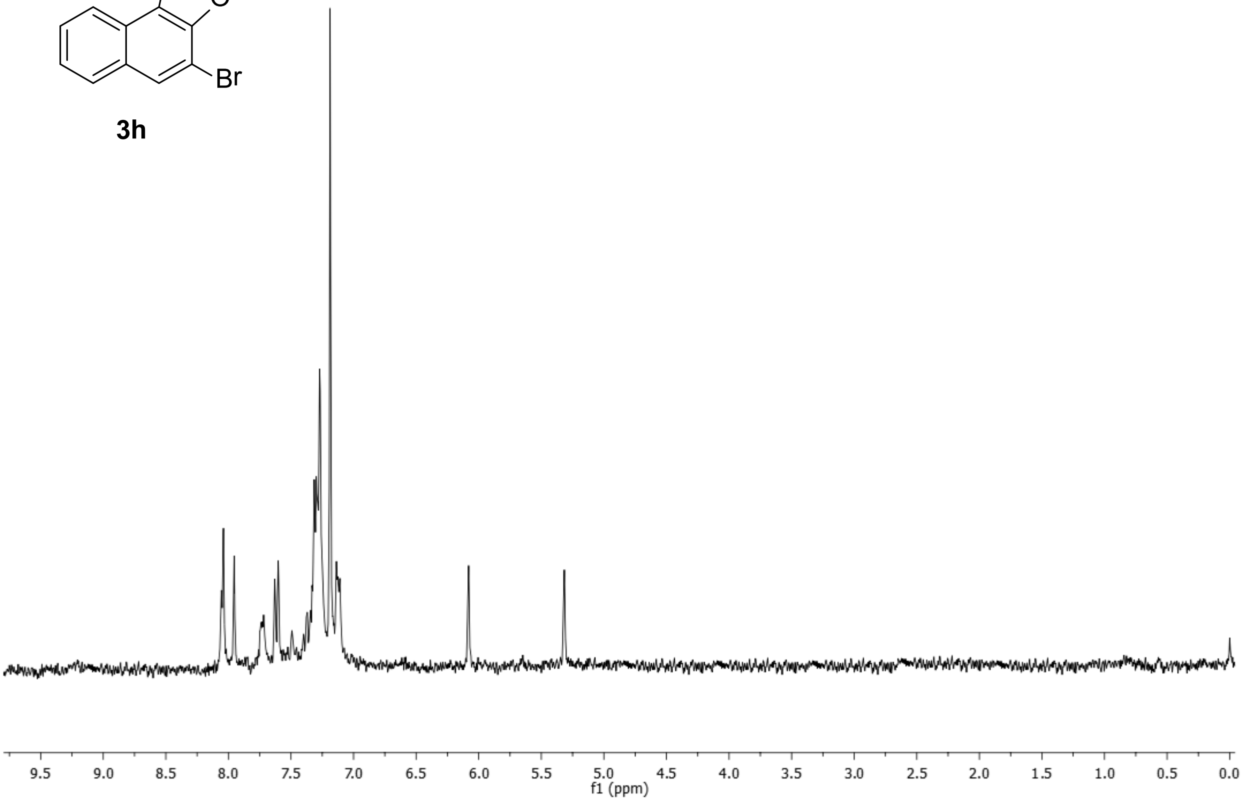
Br

3h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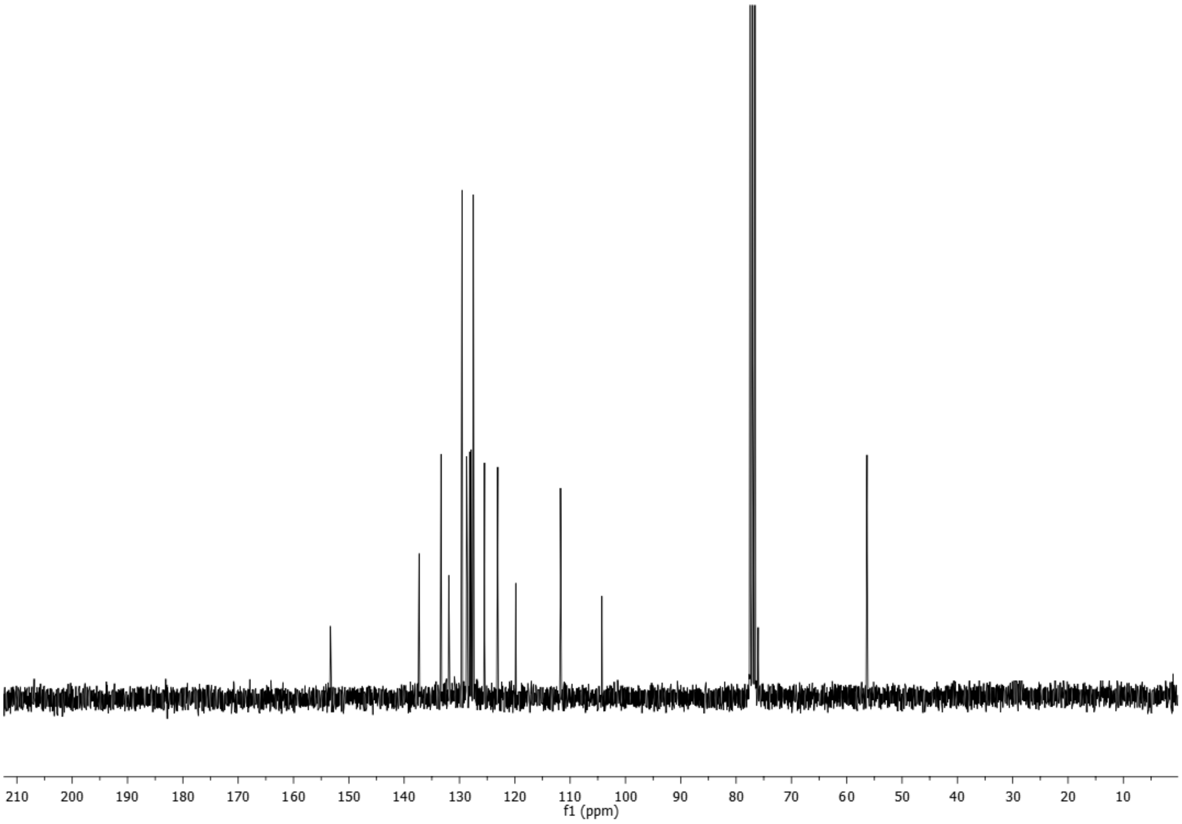
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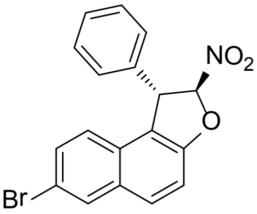
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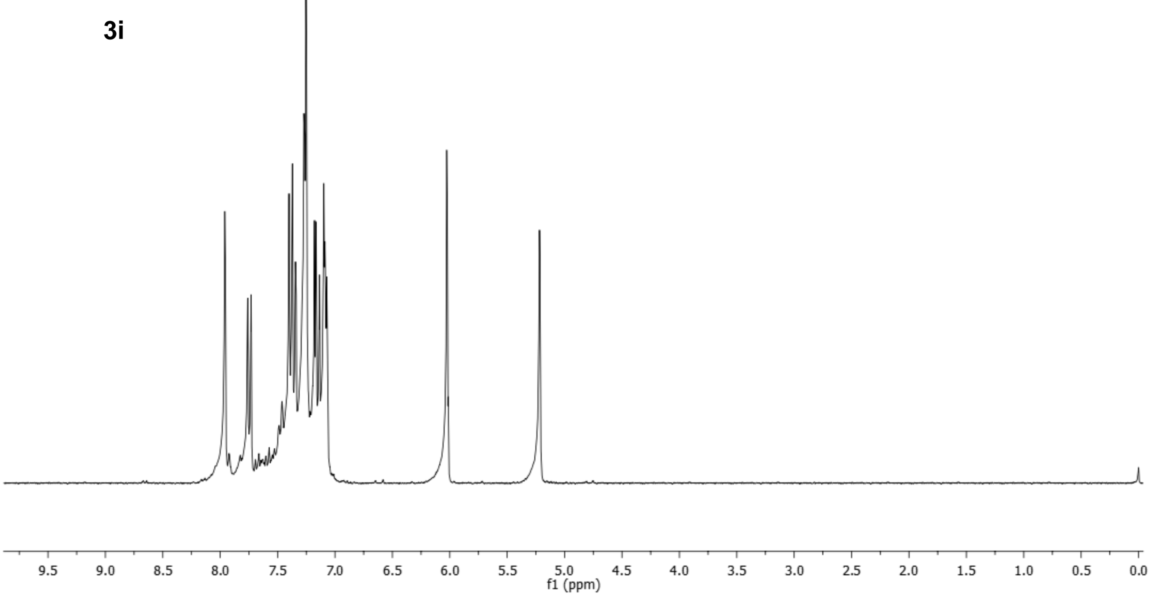
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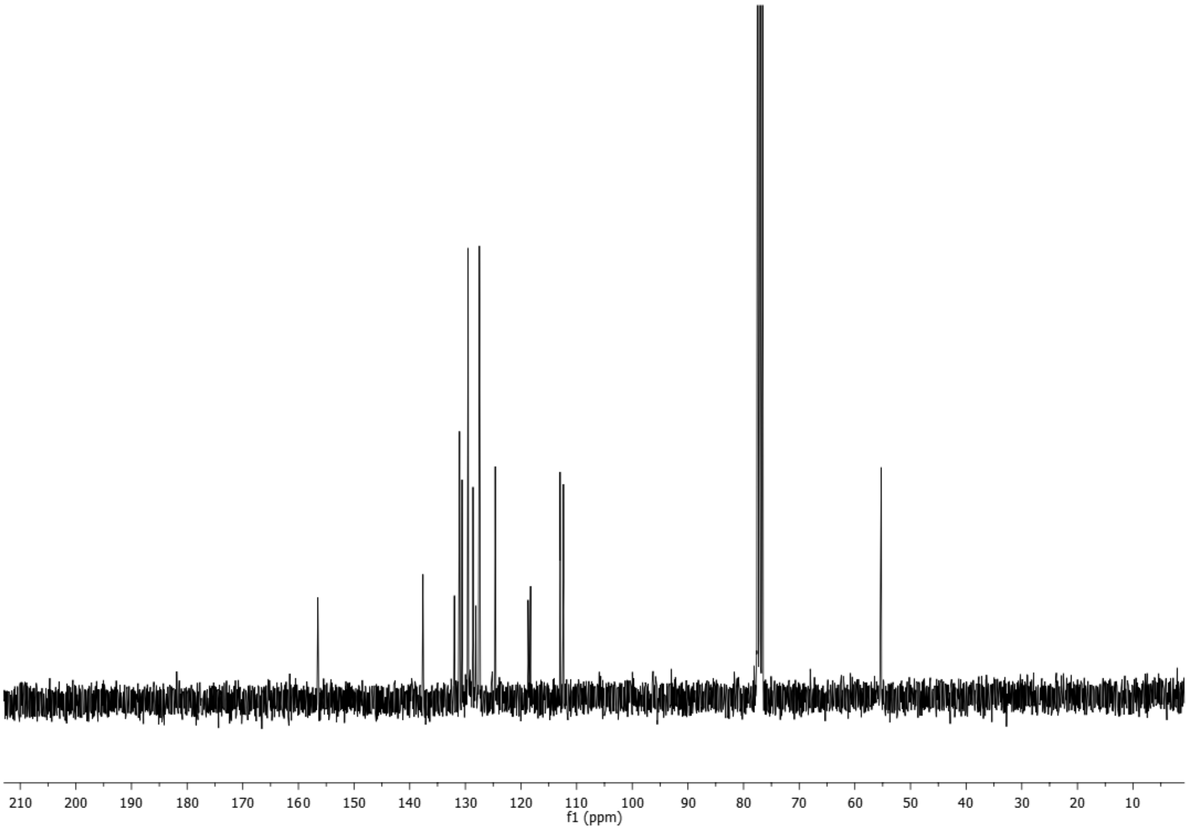
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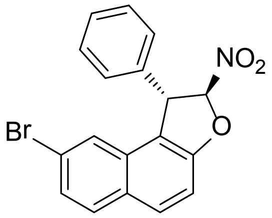
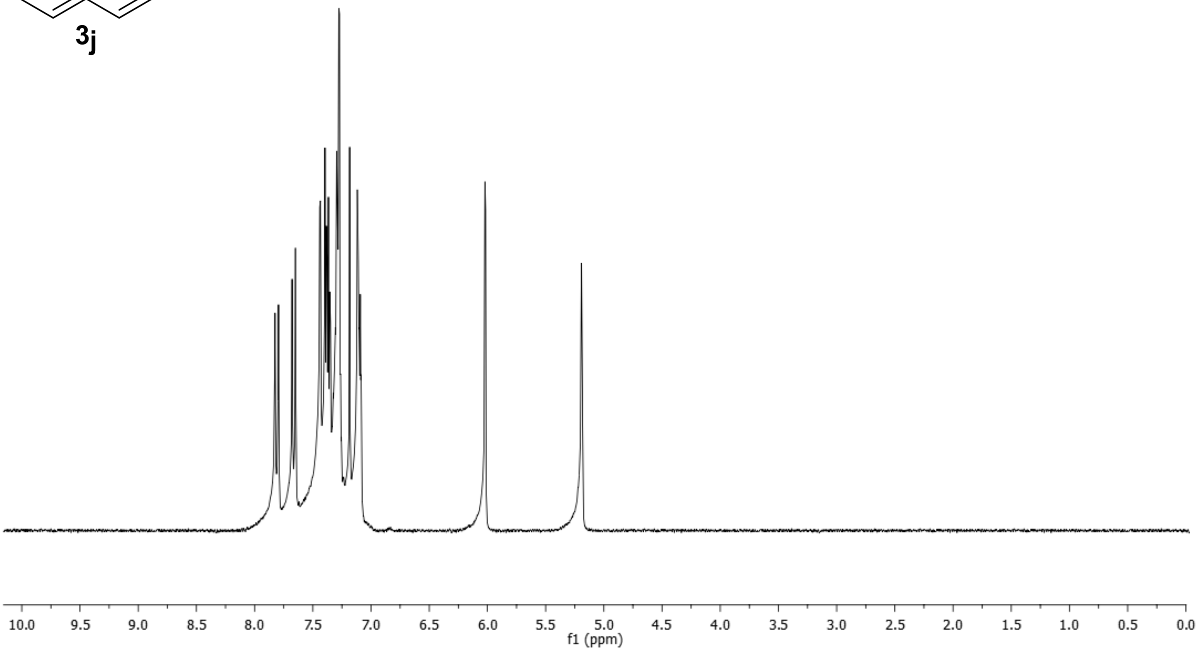

NO$_2$
Br
O

3j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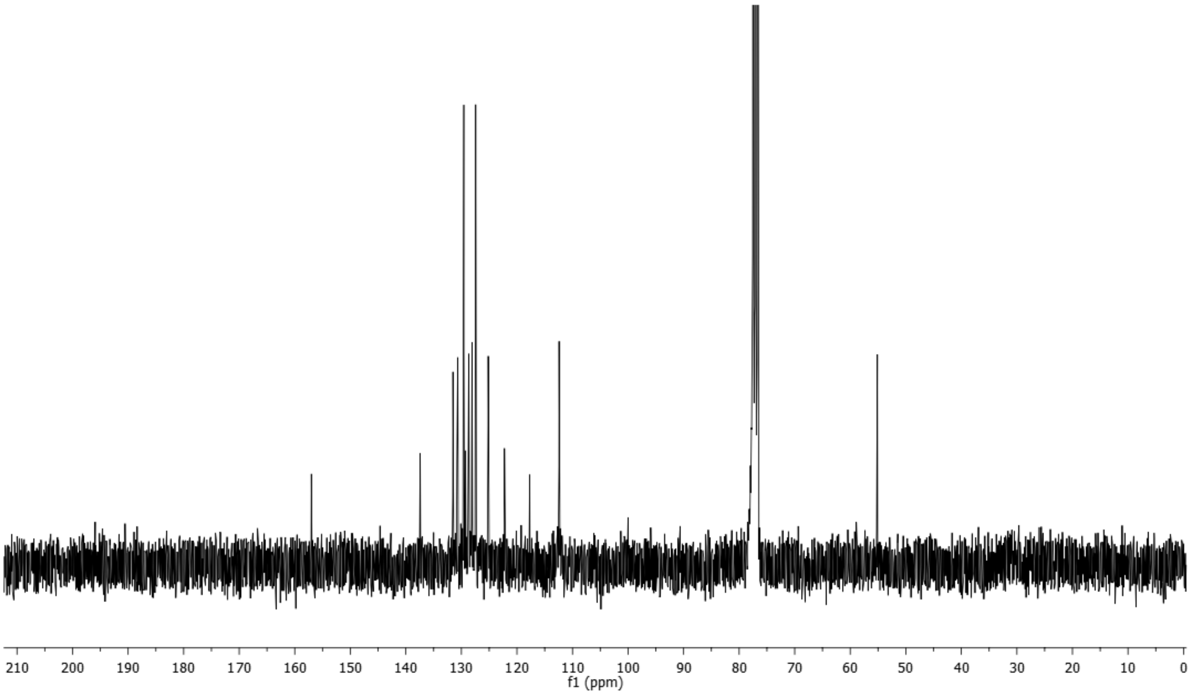
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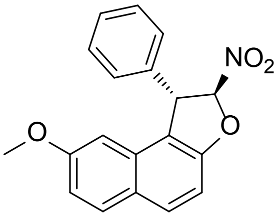
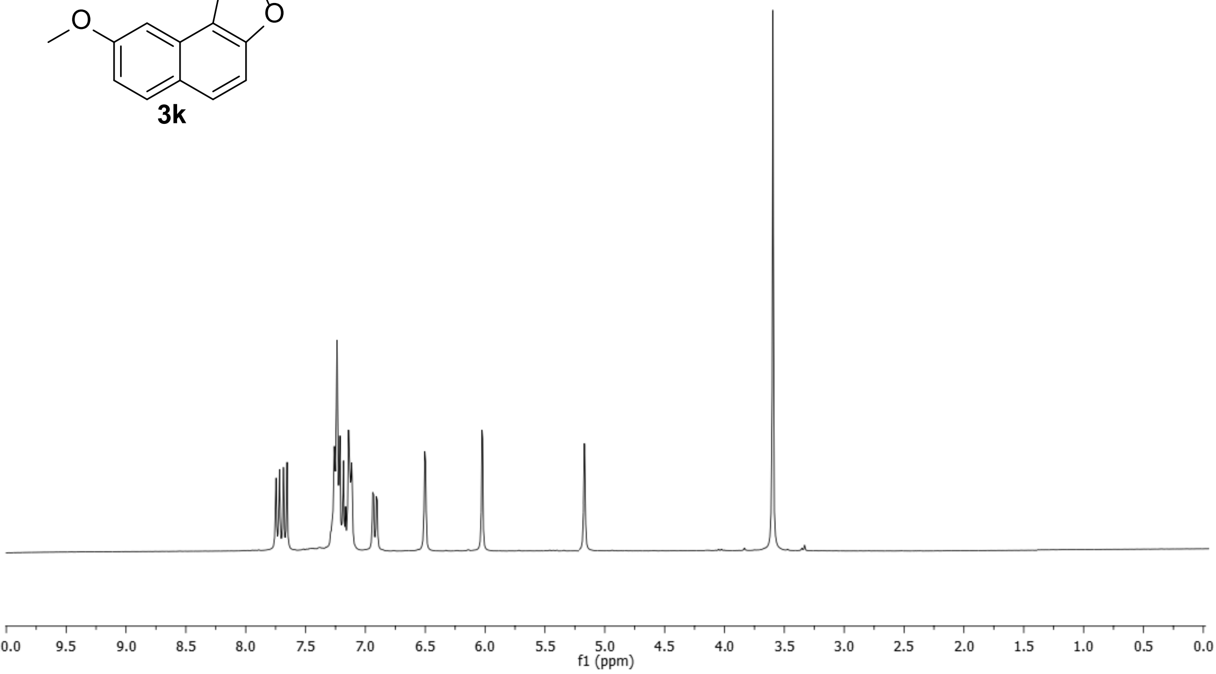

NO$_2$
O
O

3k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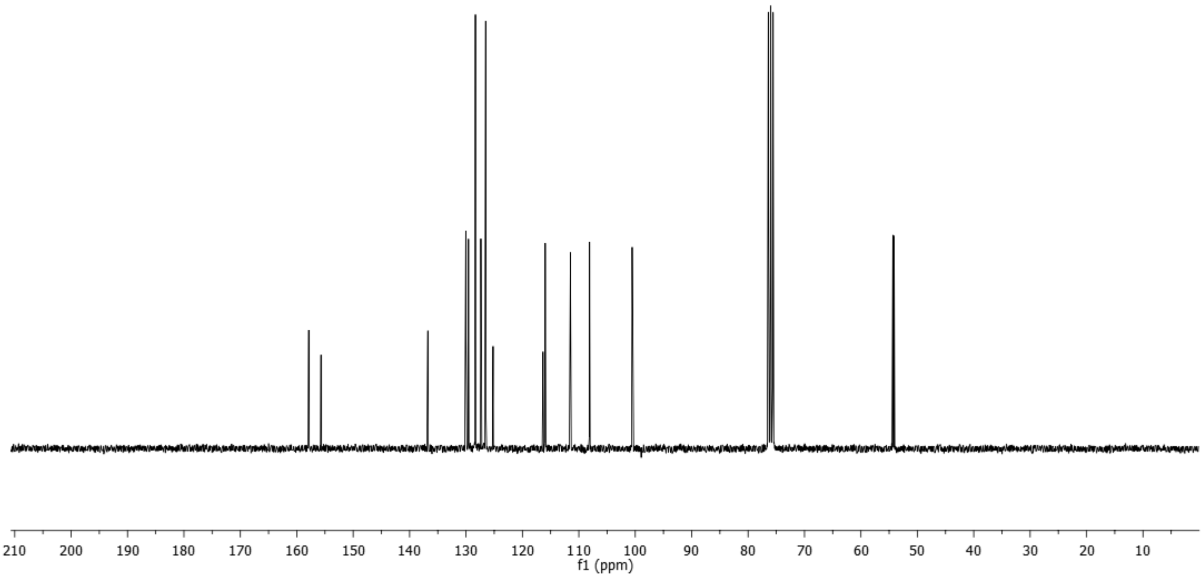
f1 (ppm)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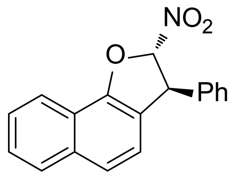
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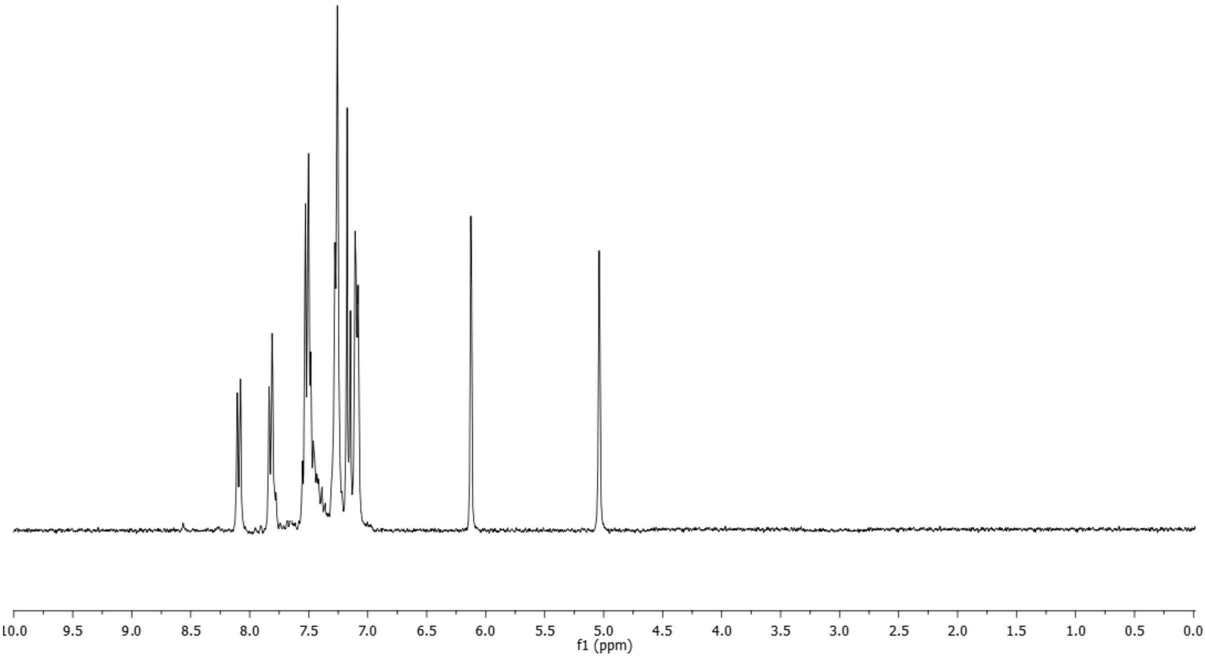
Ph

3l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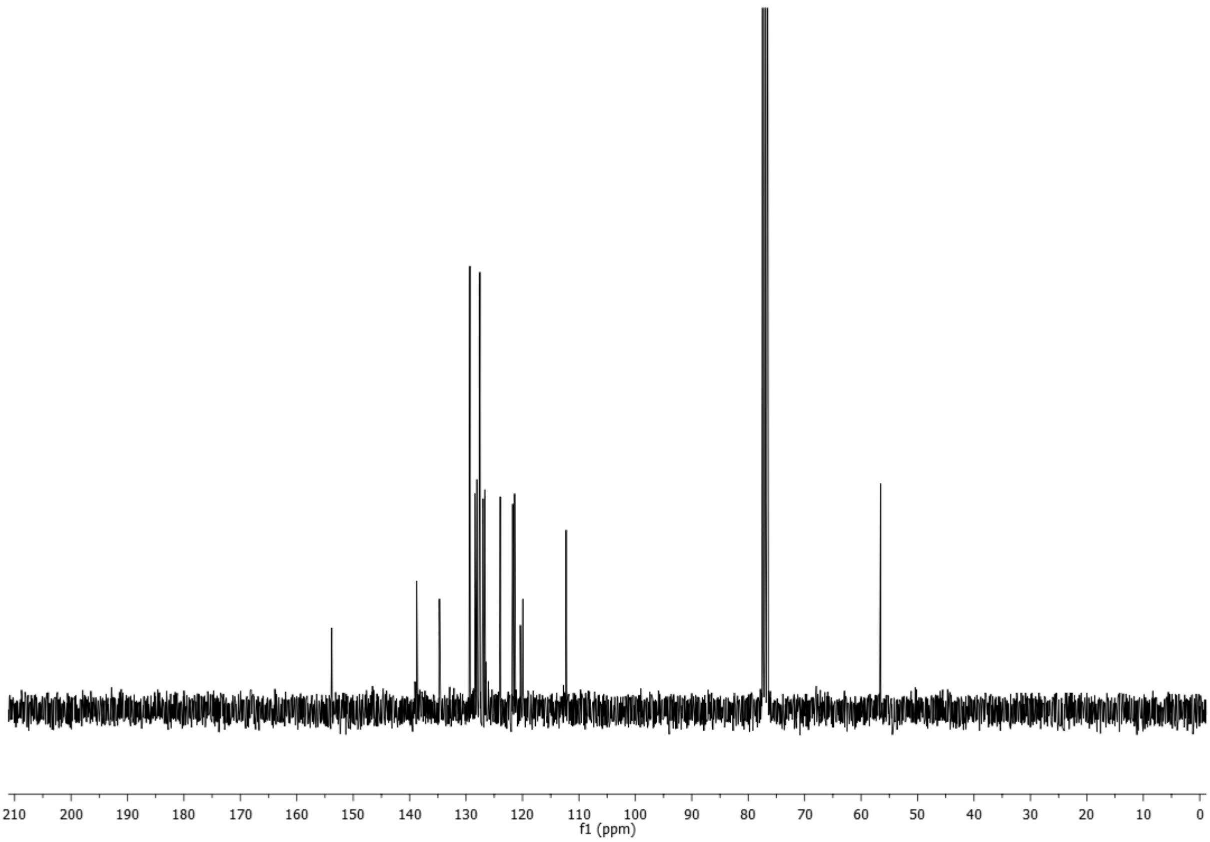
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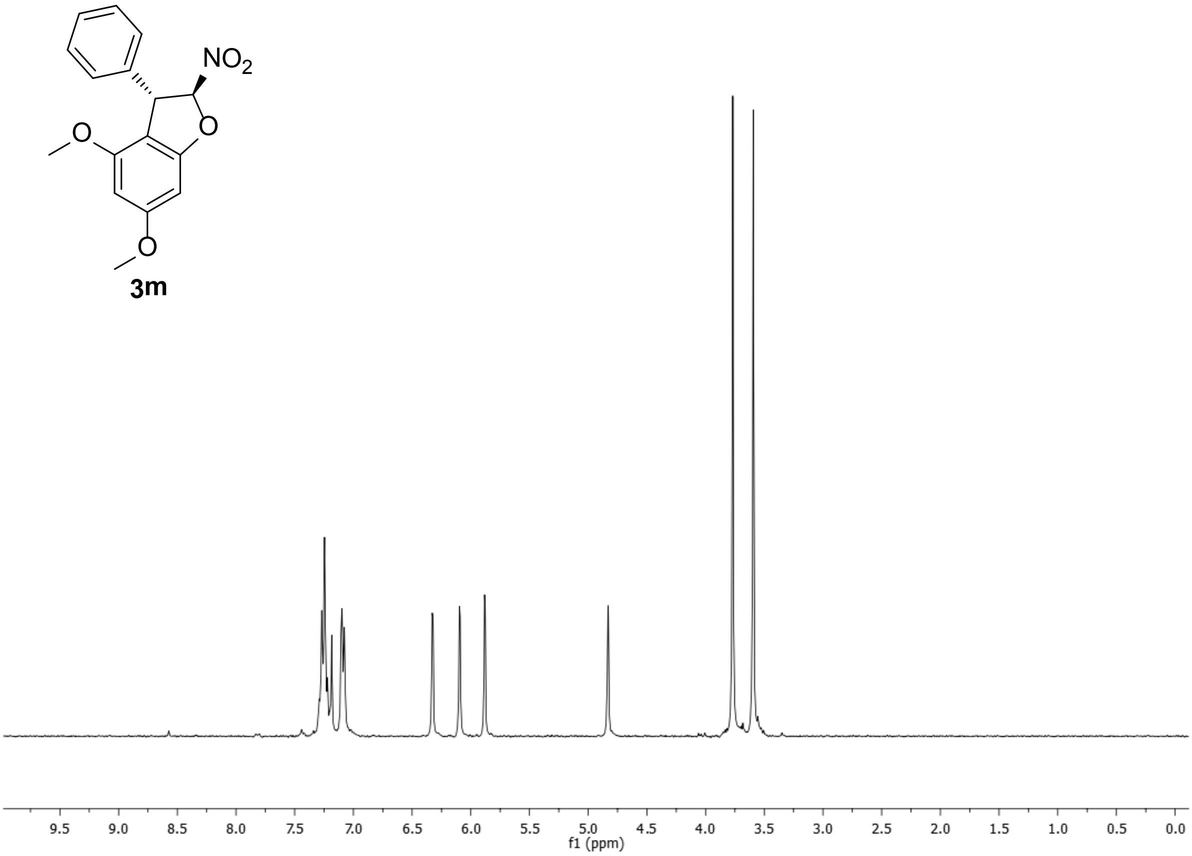
NO2
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O
O

3m

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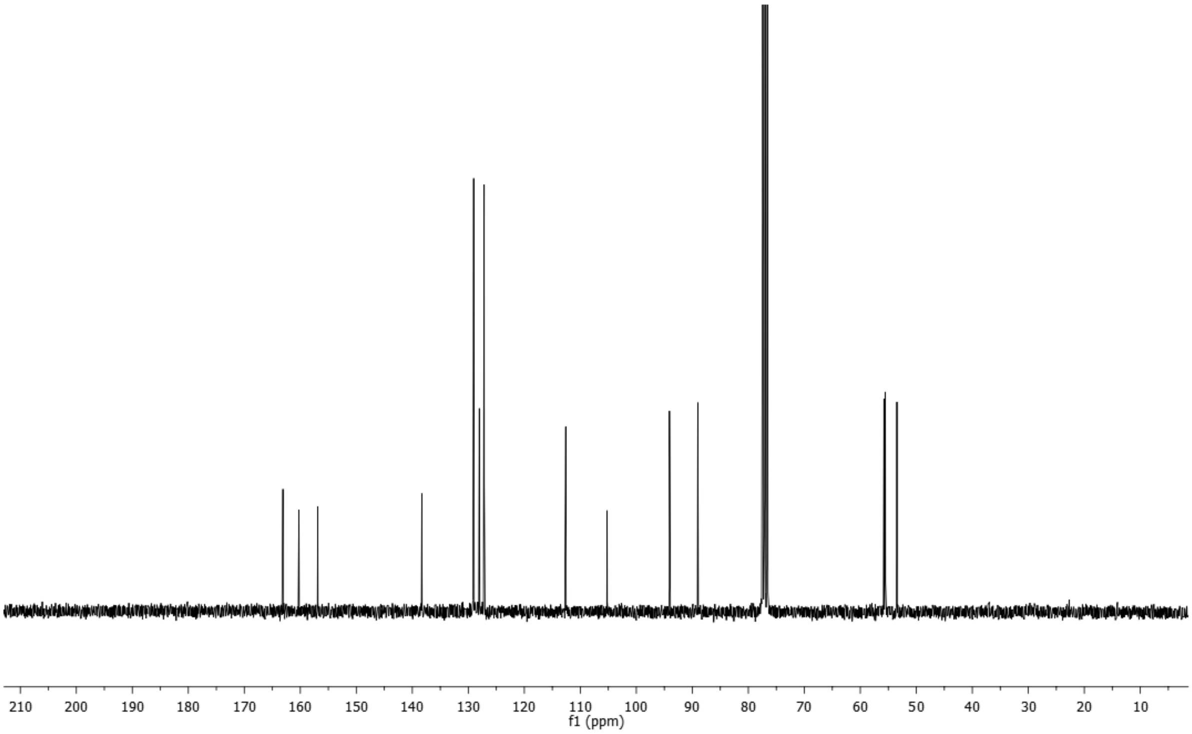
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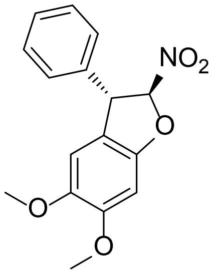
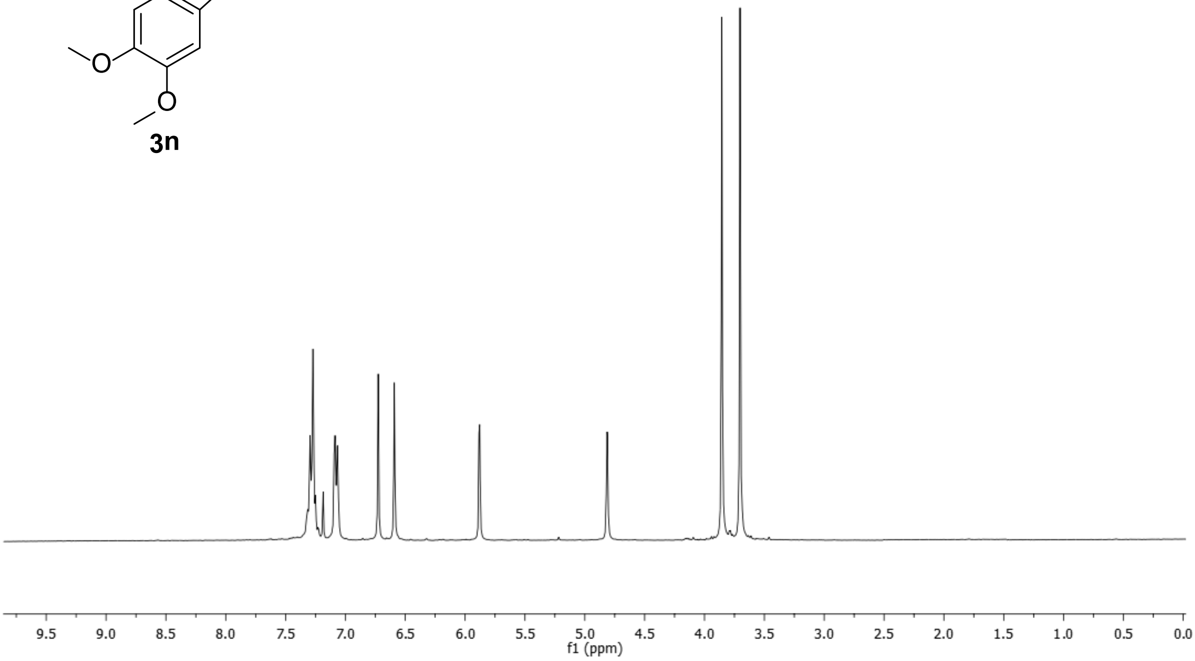
f1 (ppm)


NO2
O
O
O

3n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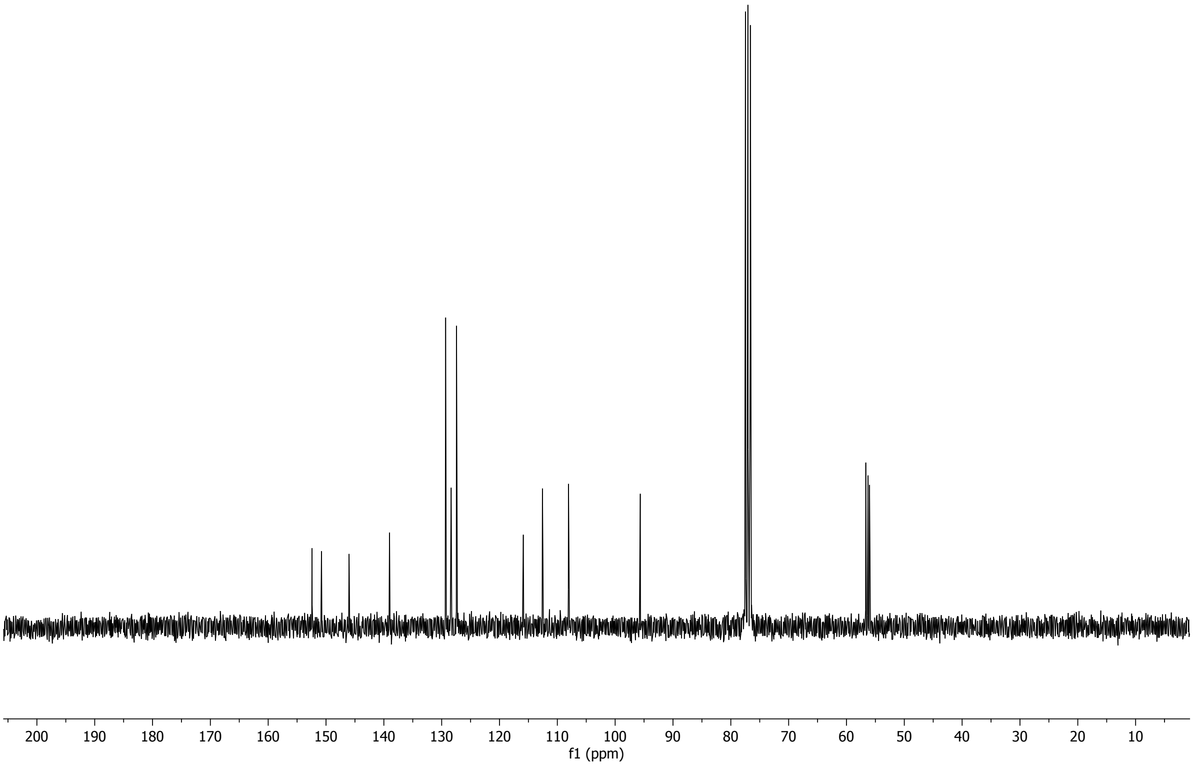
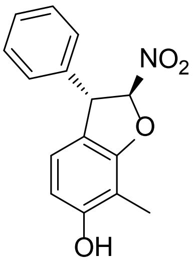
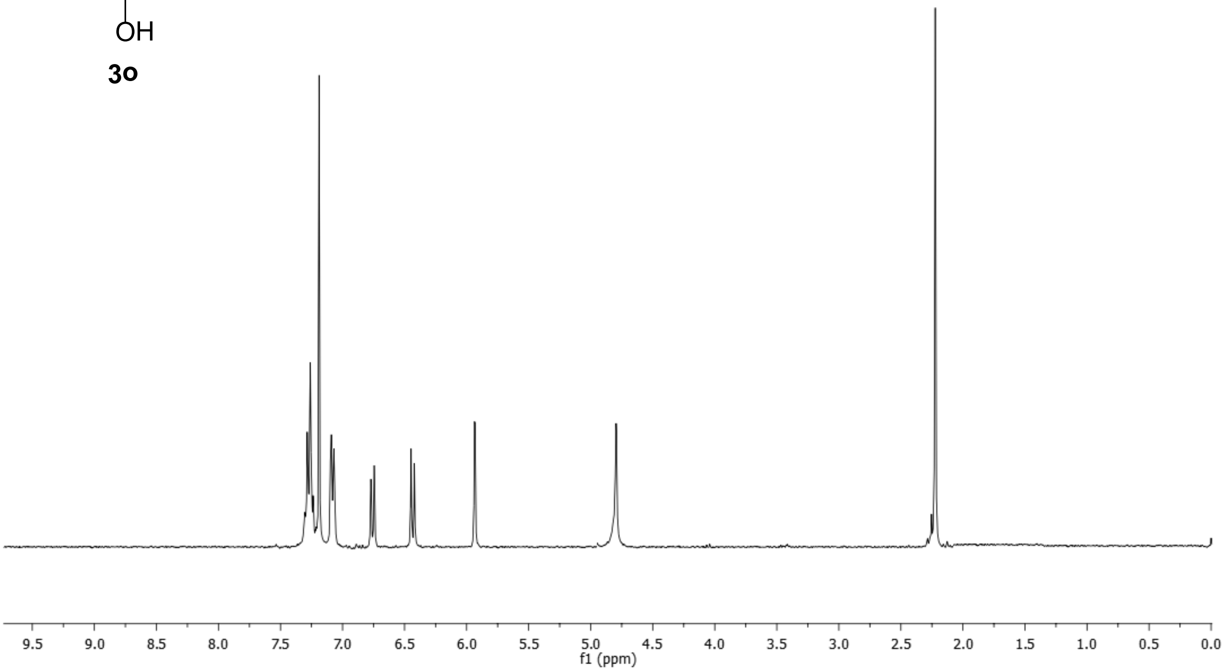
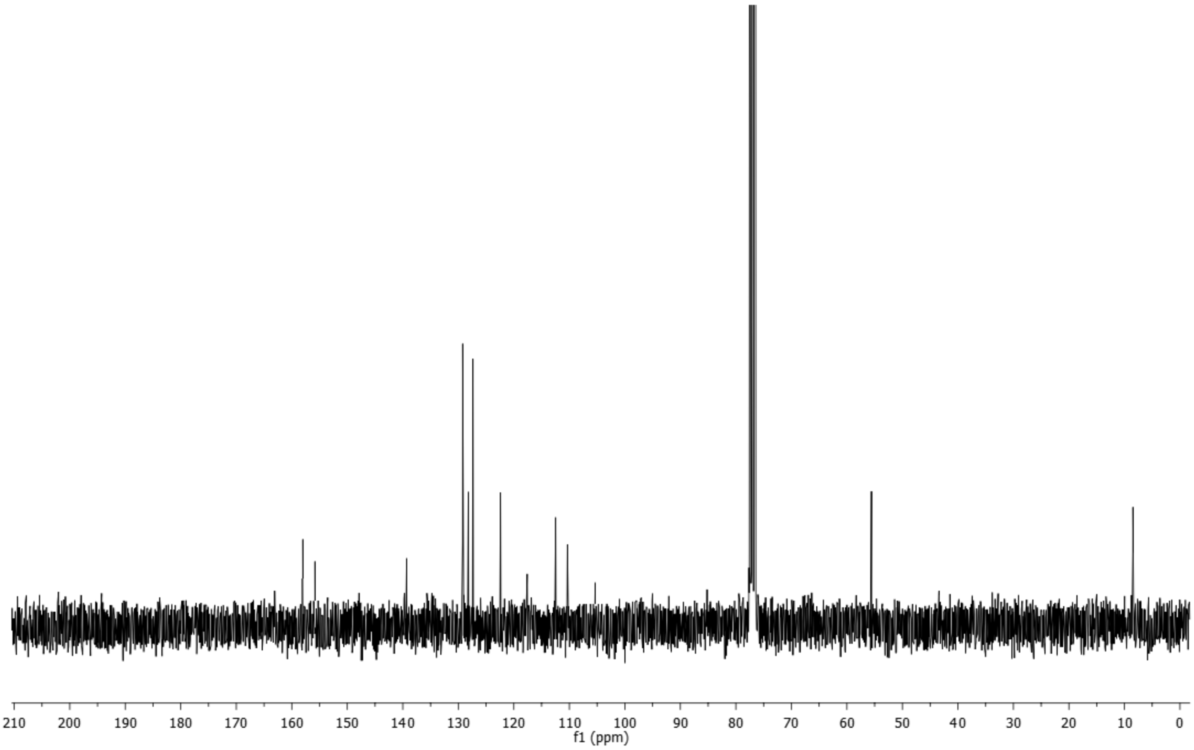
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

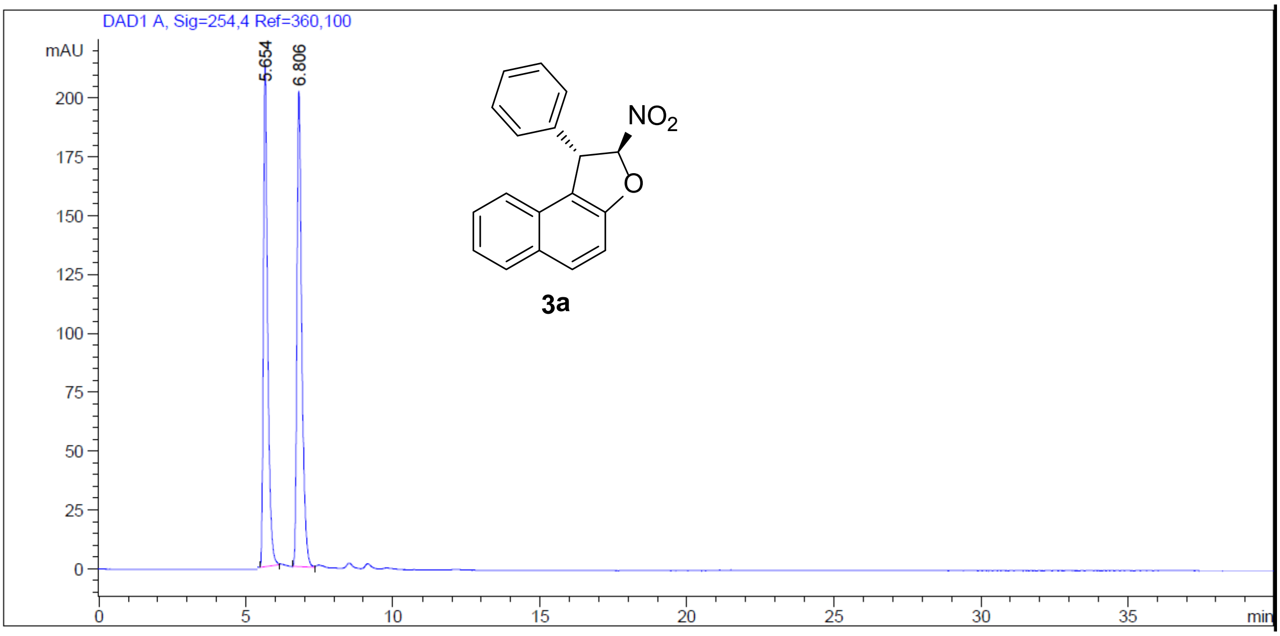

NO2
O
OH

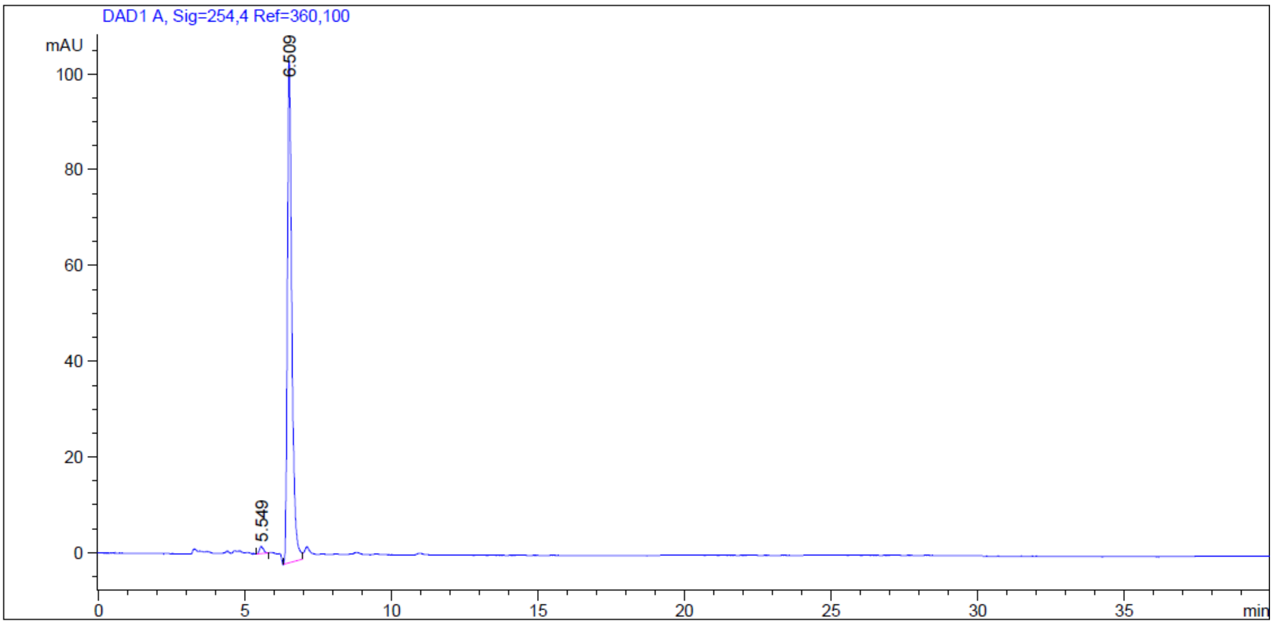
3o

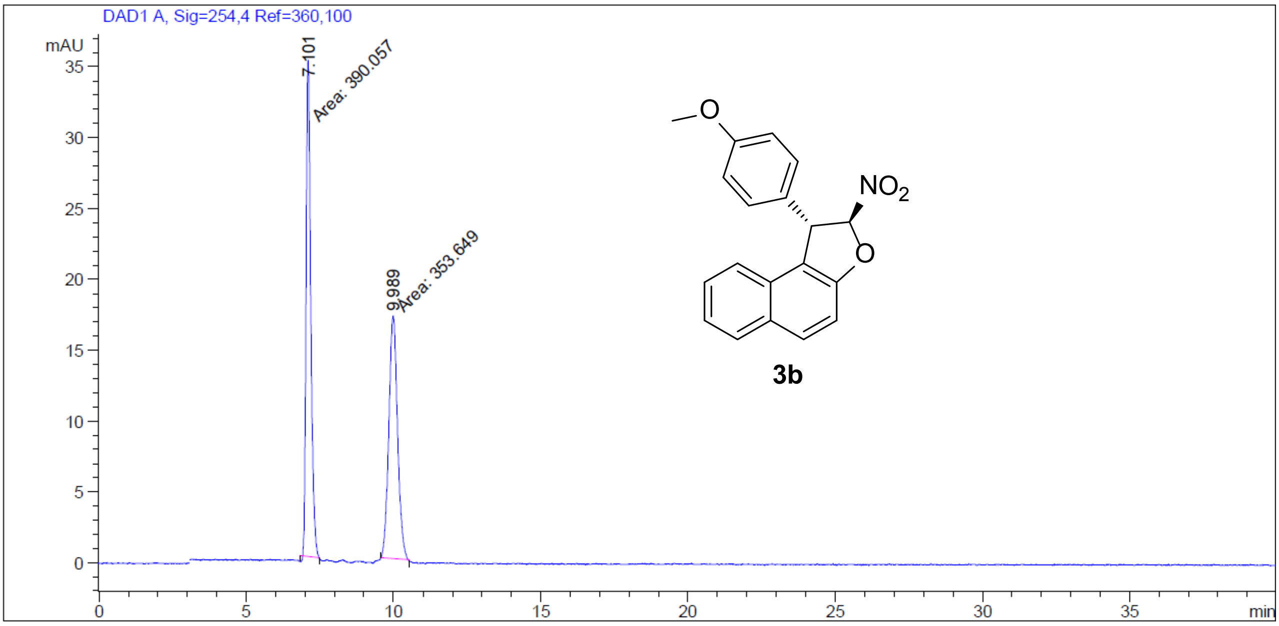

9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

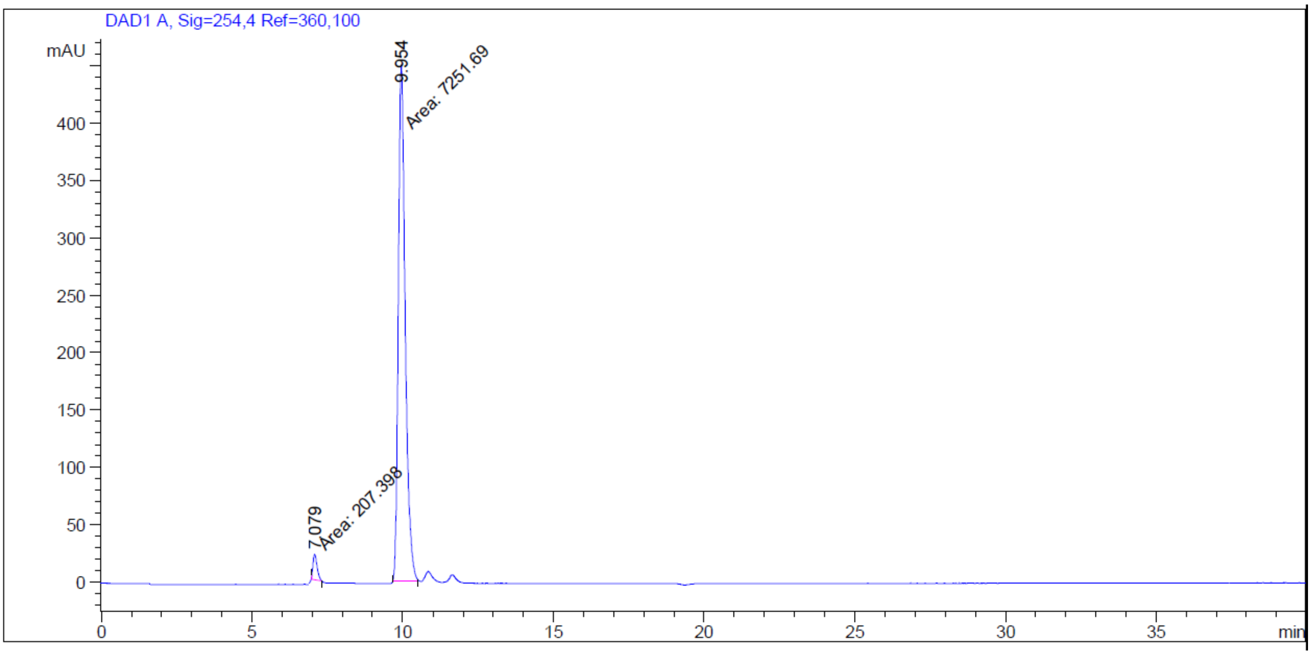
HPLC chromatograms of compound 3a-o

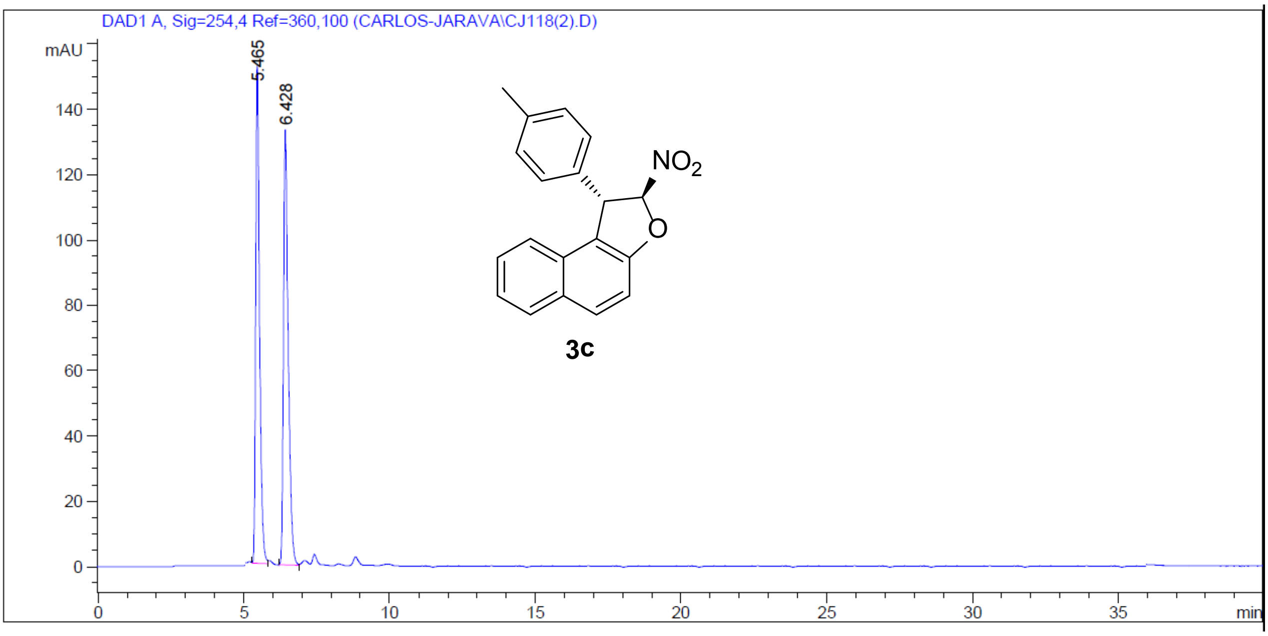


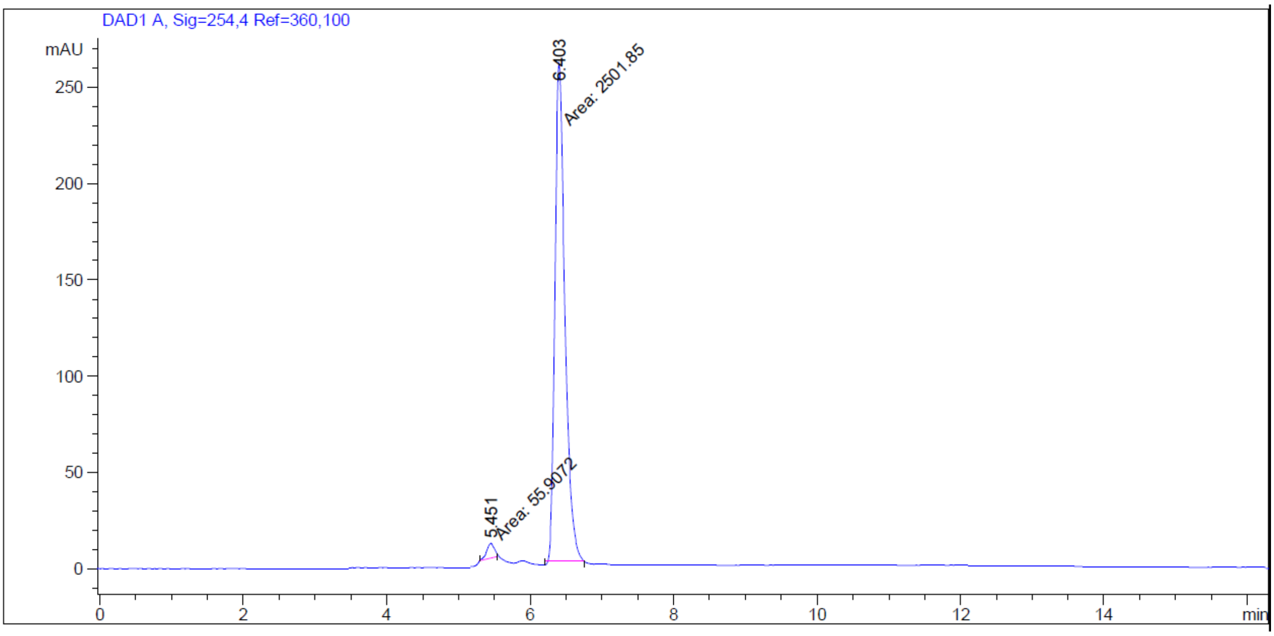


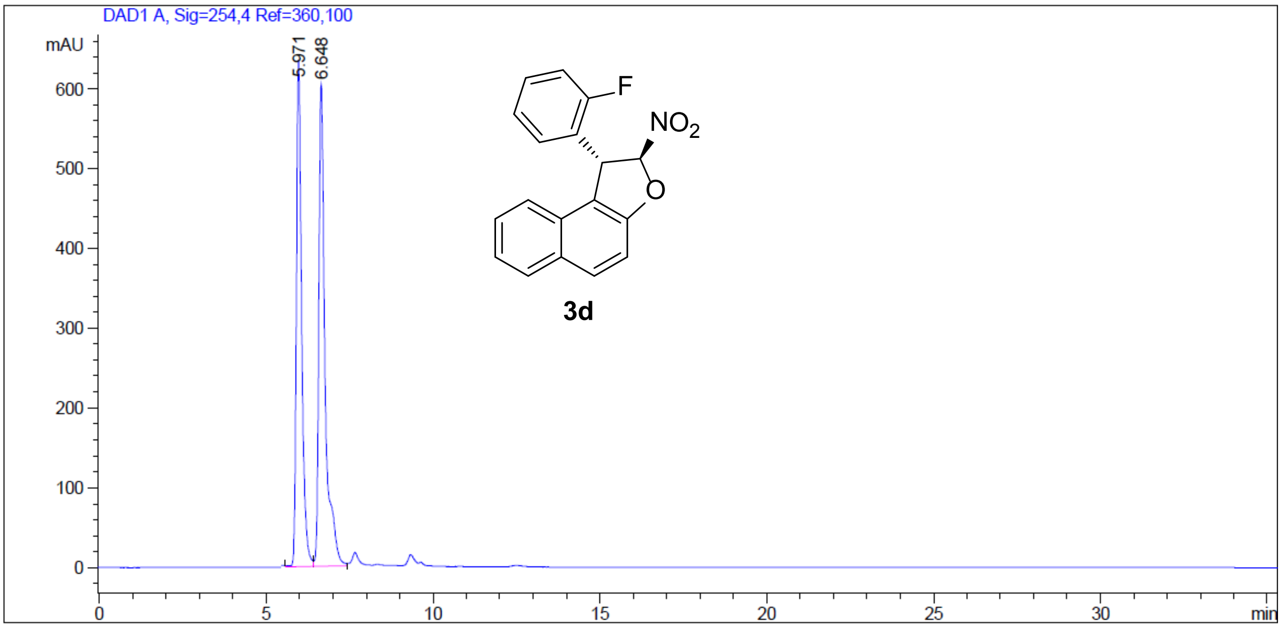

DAD1 A, Sig=254,4 Ref=360,100
mAU
35
30
25
20
15
10
5
0
7.101
Area: 390.057
9.989
Area: 353.649
0
5
10
15
20
25
30
35
min
O
NO2
O

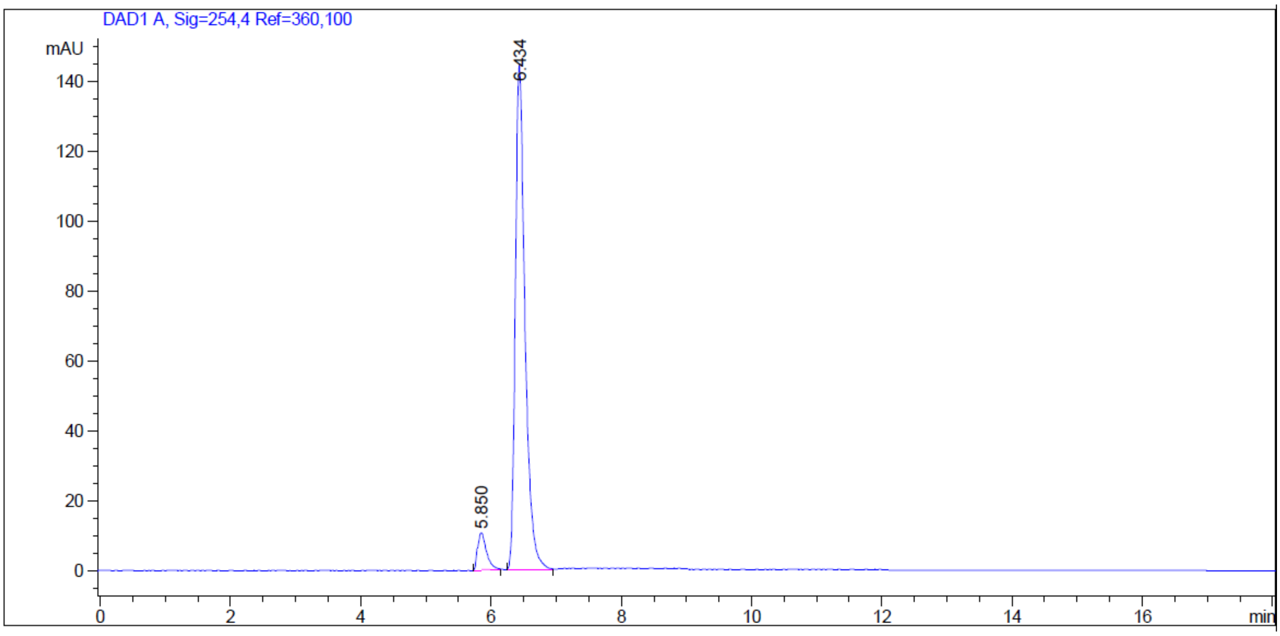
3b

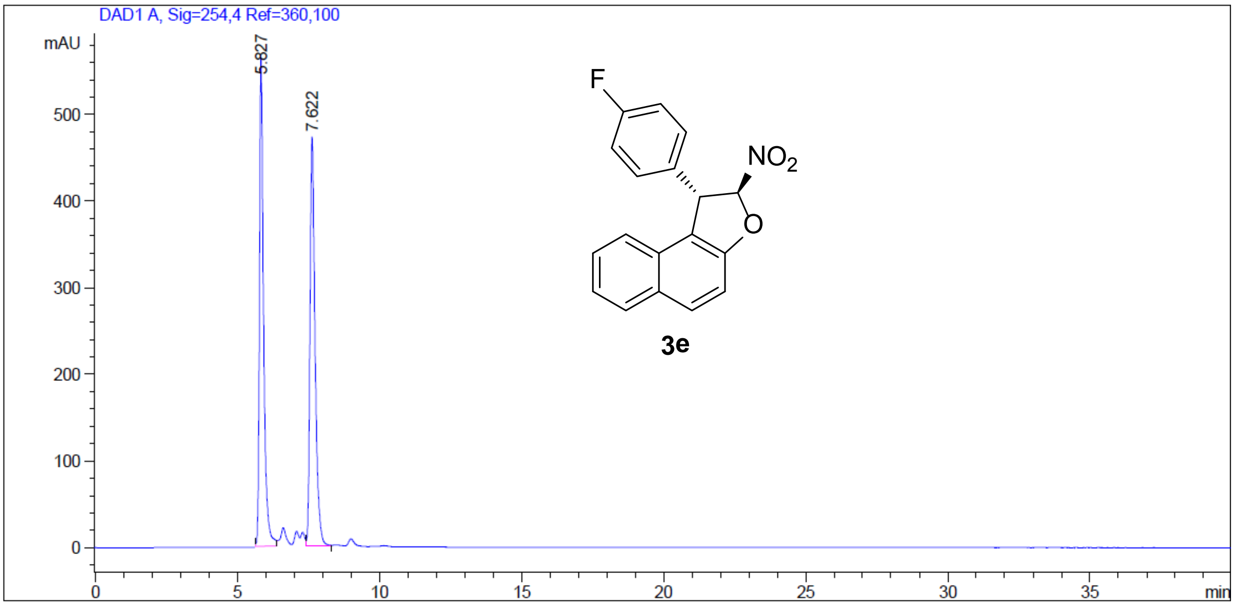

DAD1 A, Sig=254,4 Ref=360,100
mAU
400
350
300
250
200
150
100
50
0
9.954
Area: 7251.69
7.079
Area: 207.398
0
5
10
15
20
25
30
35
min

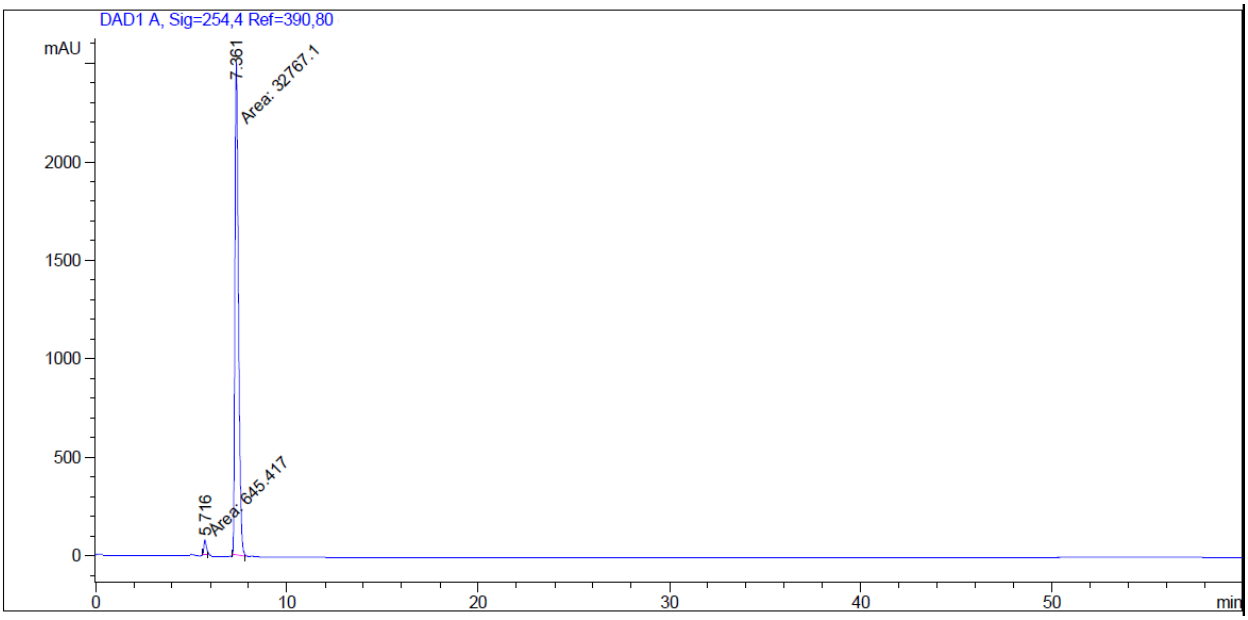

DAD1 A, Sig=254,4 Ref=360,100 (CARLOS-JARAVA\CJ118(2).D)
mAU
140
120
100
80
60
40
20
0
5.465
6.428
NO_2
O
3c
0
5
10
15
20
25
30
35
min

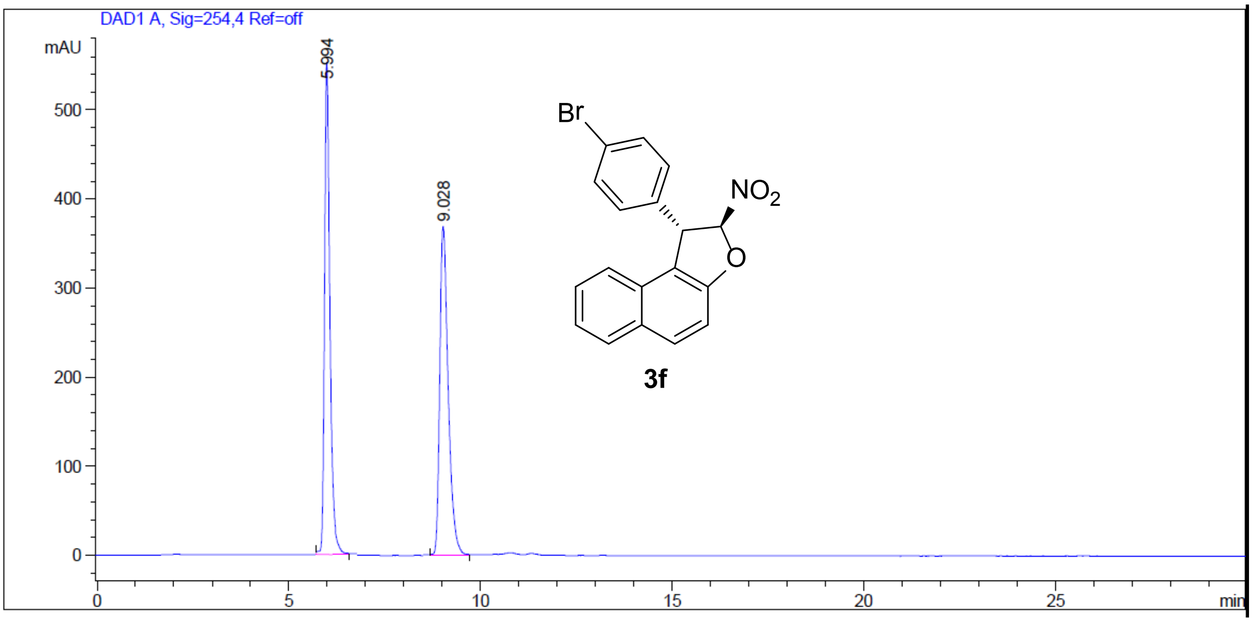

DAD1 A, Sig=254,4 Ref=360,100
mAU
250
200
150
100
50
0
6.403
Area: 2501.85
5.451
Area: 55.9072
0
2
4
6
8
10
12
14
min


DAD1 A, Sig=254,4 Ref=360,100
mAU
600
500
400
300
200
100
0
5.971
6.648
F
NO$_2$
O
3d
0
5
10
15
20
25
30
min

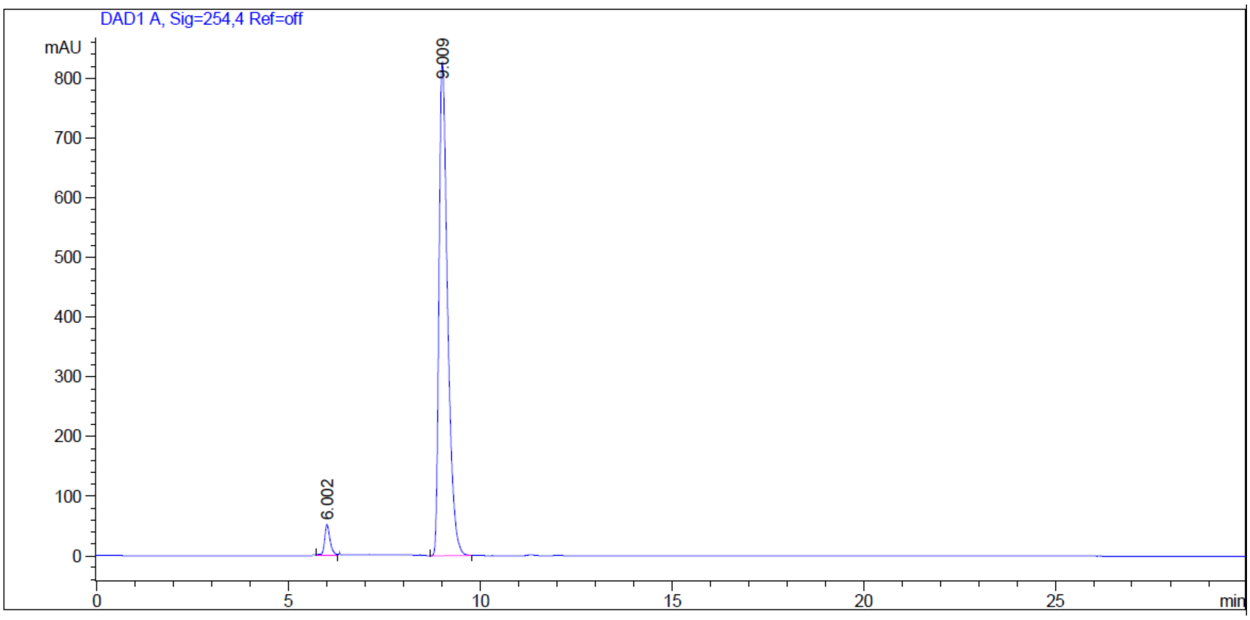

DAD1 A, Sig=254,4 Ref=360,100
mAU
140
120
100
80
60
40
20
0
5.850
6.434
0
2
4
6
8
10
12
14
16
min

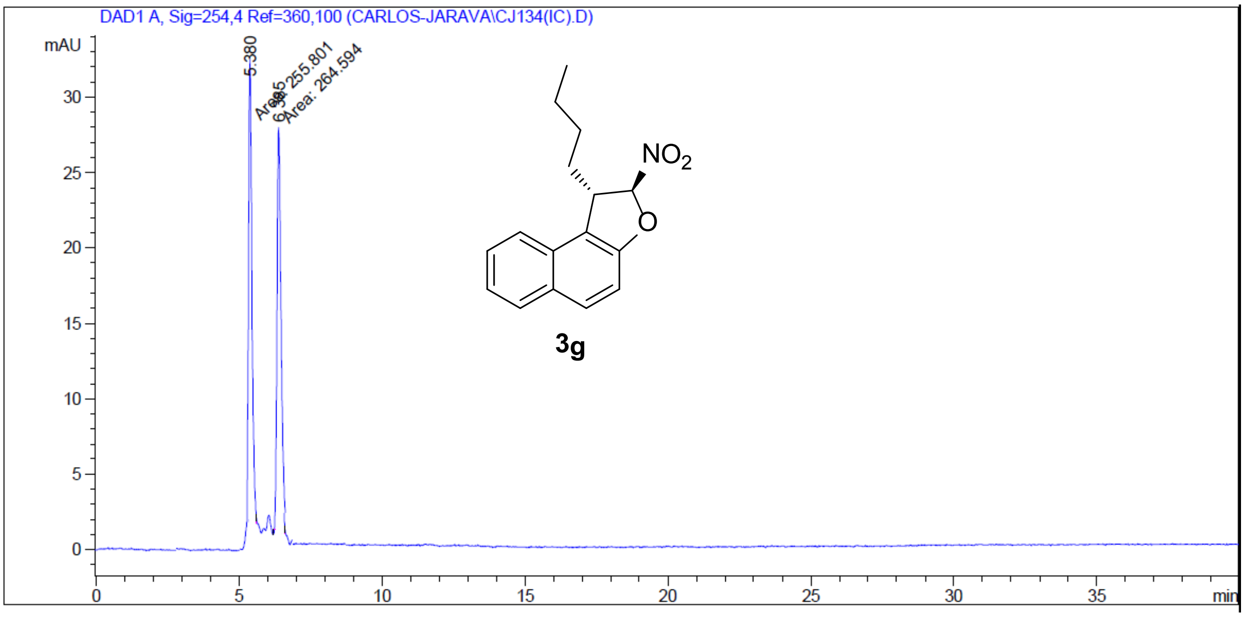

DAD1 A, Sig=254,4 Ref=360,100
mAU
500
400
300
200
100
0
5.827
7.622
F
NO_2
O
3e
0
5
10
15
20
25
30
35
min

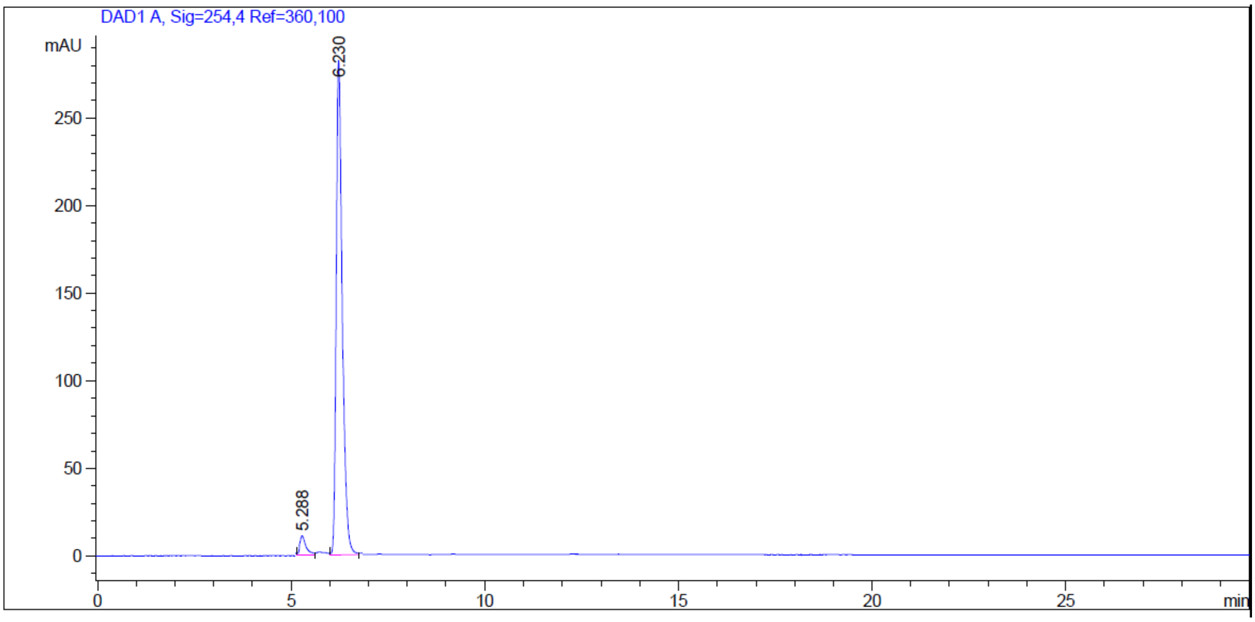

DAD1 A, Sig=254,4 Ref=390,80
mAU
2000
1500
1000
500
0
7.361
Area: 32767.1
5.716
Area: 645.417
0
10
20
30
40
50
min

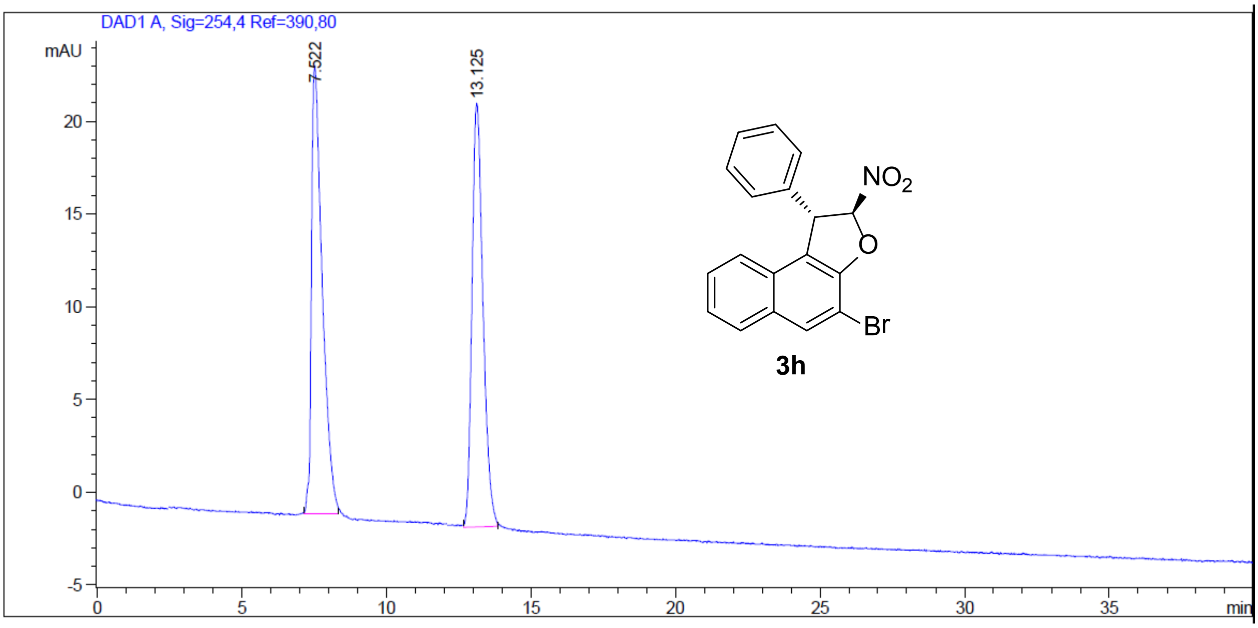

DAD1 A, Sig=254,4 Ref=off
mAU
500
400
300
200
100
0
5.994
9.028
Br
NO2
O
0
5
10
15
20
25
min

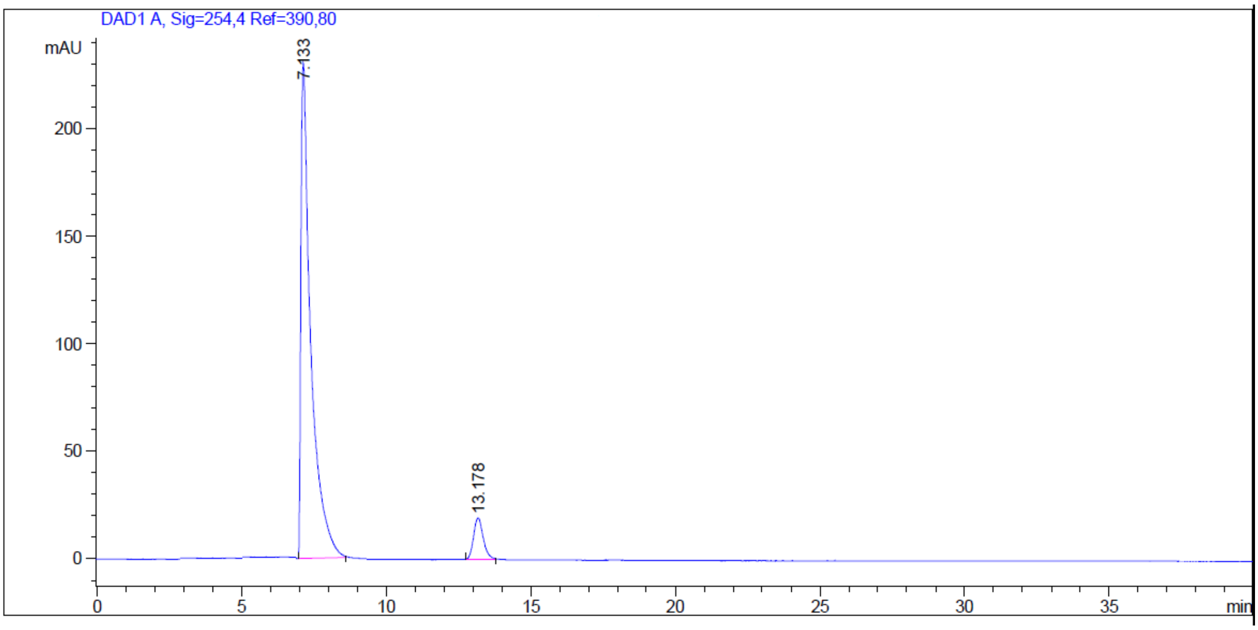
3f

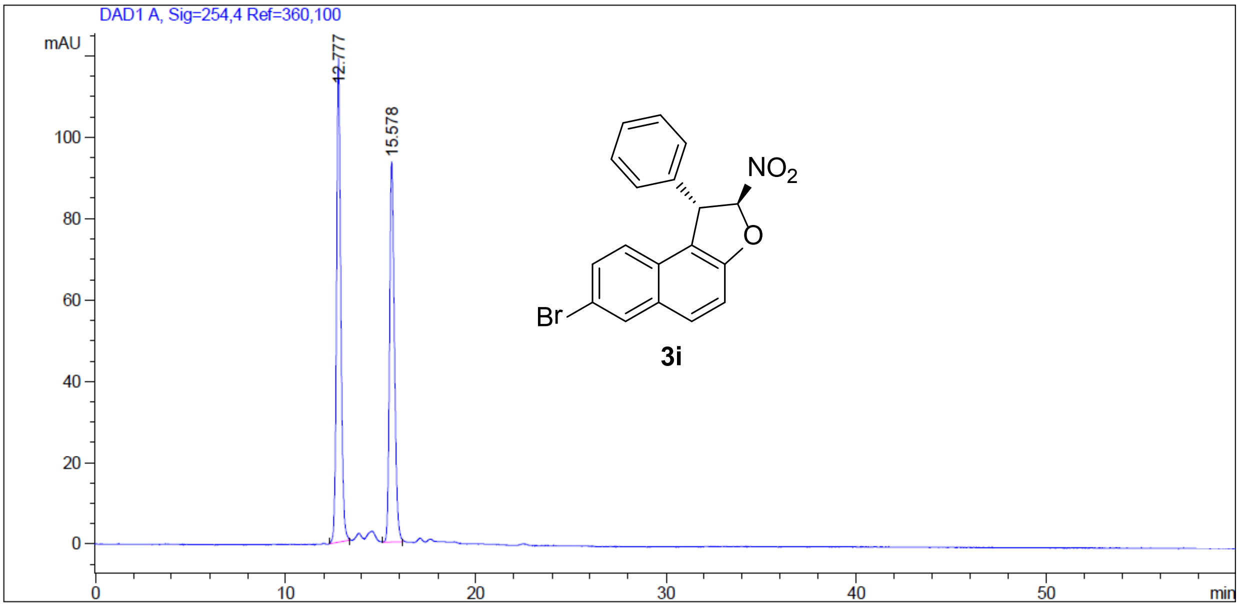

DAD1 A, Sig=254,4 Ref=off
mAU
800
700
600
500
400
300
200
100
0
9.009
6.002
0
5
10
15
20
25
min

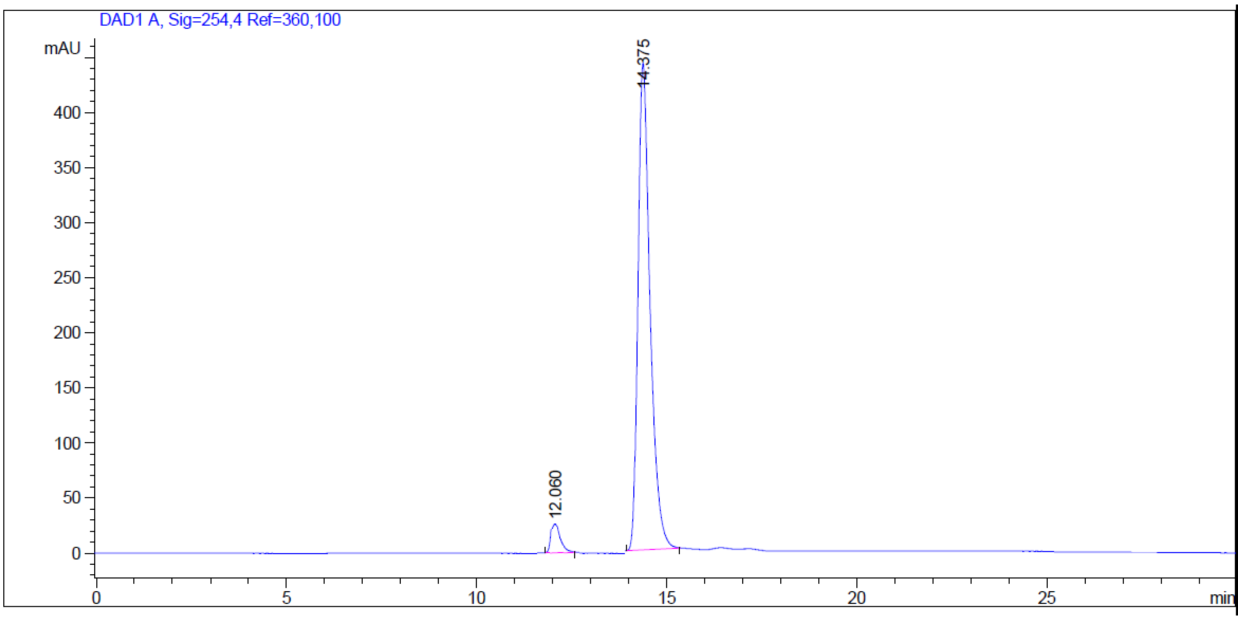

DAD1 A, Sig=254,4 Ref=360,100 (CARLOS-JARAVA\CJ134(IC).D)
mAU
30
25
20
15
10
5
0
5.380
Area: 255.801
6.385
Area: 264.594
NO2
O
3g
0
5
10
15
20
25
30
35
min

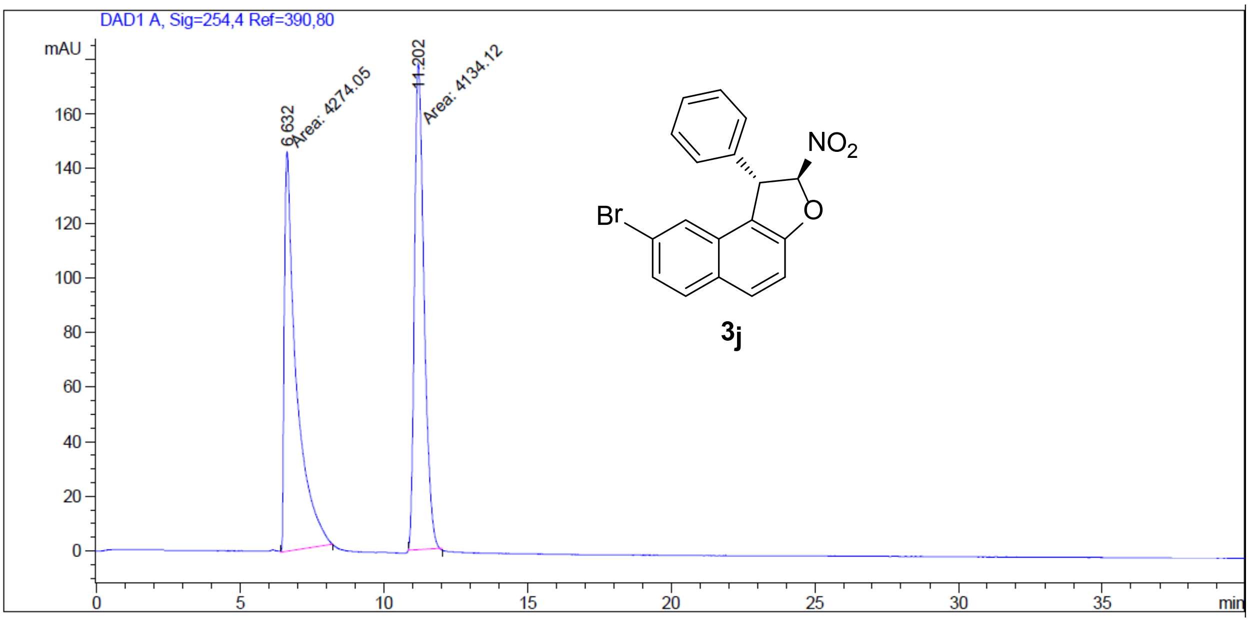

DAD1 A, Sig=254,4 Ref=360,100
mAU
250
200
150
100
50
0
6.230
5.288
0
5
10
15
20
25
min


DAD1 A, Sig=254,4 Ref=390,80
mAU
20
15
10
5
0
-5
7.522
13.125
NO2
O
Br
3h
0
5
10
15
20
25
30
35
min

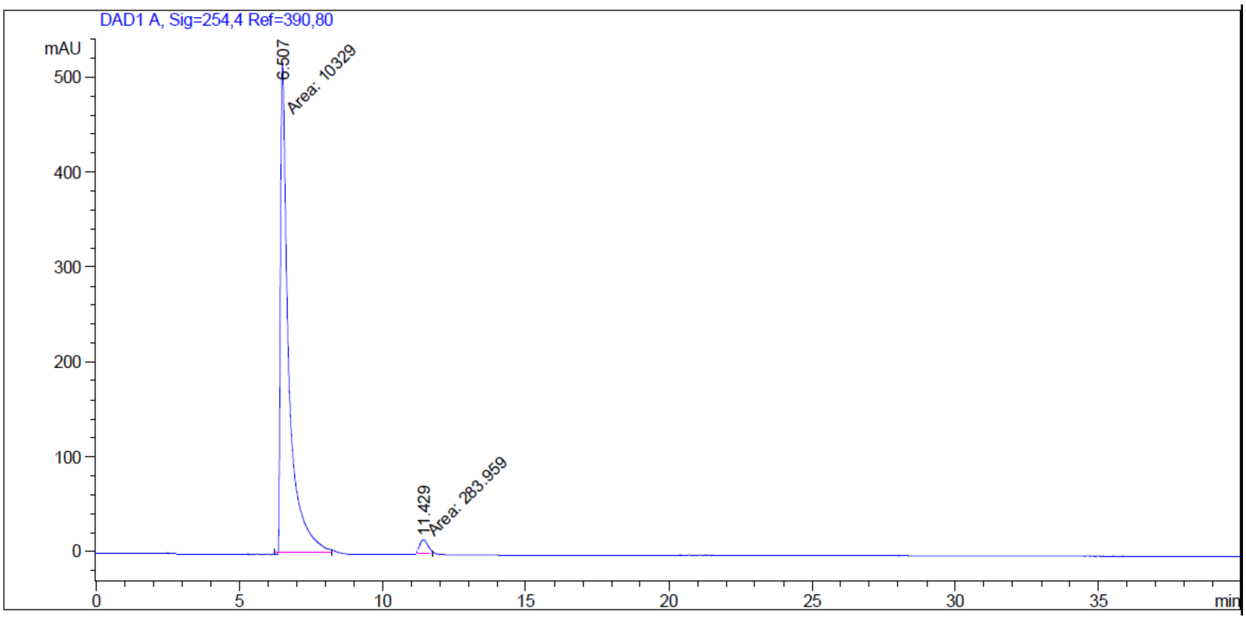

DAD1 A, Sig=254,4 Ref=390,80
mAU
200
150
100
50
0
7.133
13.178
0
5
10
15
20
25
30
35
min

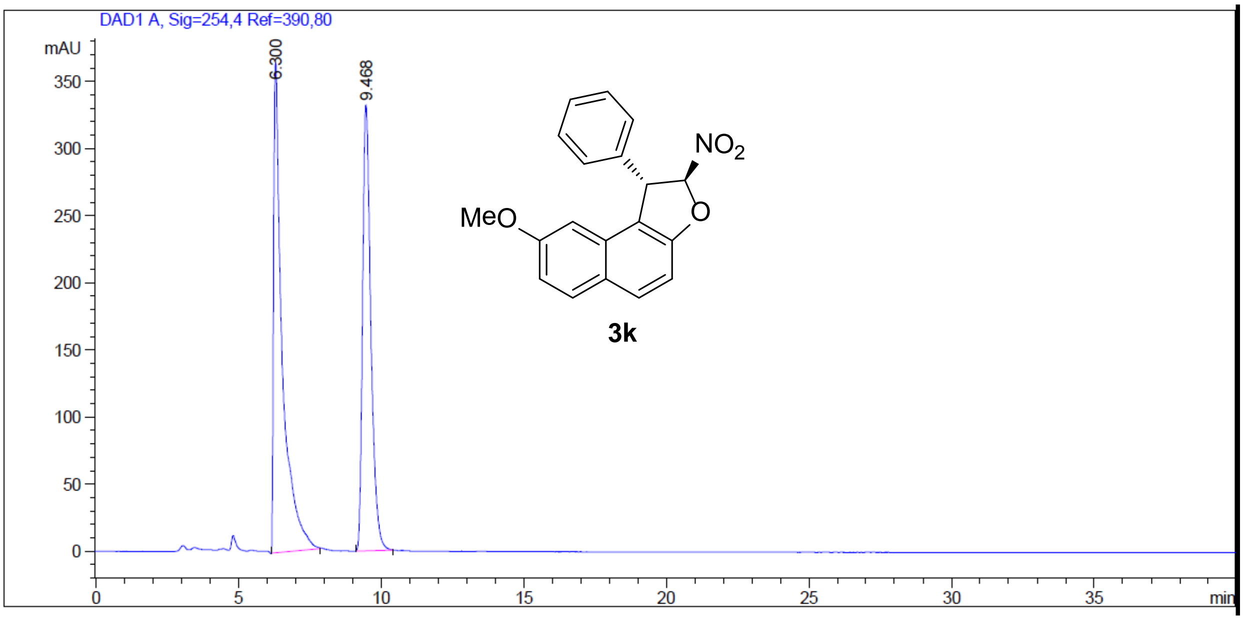

DAD1 A, Sig=254,4 Ref=360,100
mAU
100
80
60
40
20
0
12.777
15.578
0
10
20
30
40
50
min
NO2
O
Br
3i

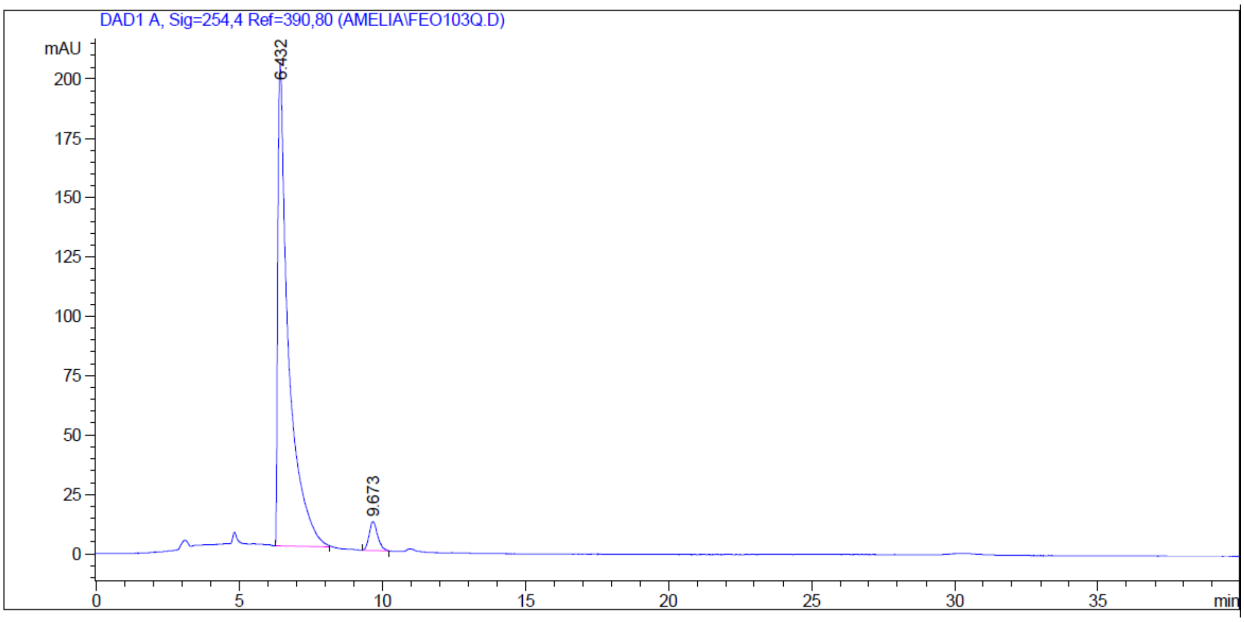

DAD1 A, Sig=254,4 Ref=360,100
mAU
400
350
300
250
200
150
100
50
0
14.375
12.060
0
5
10
15
20
25
min

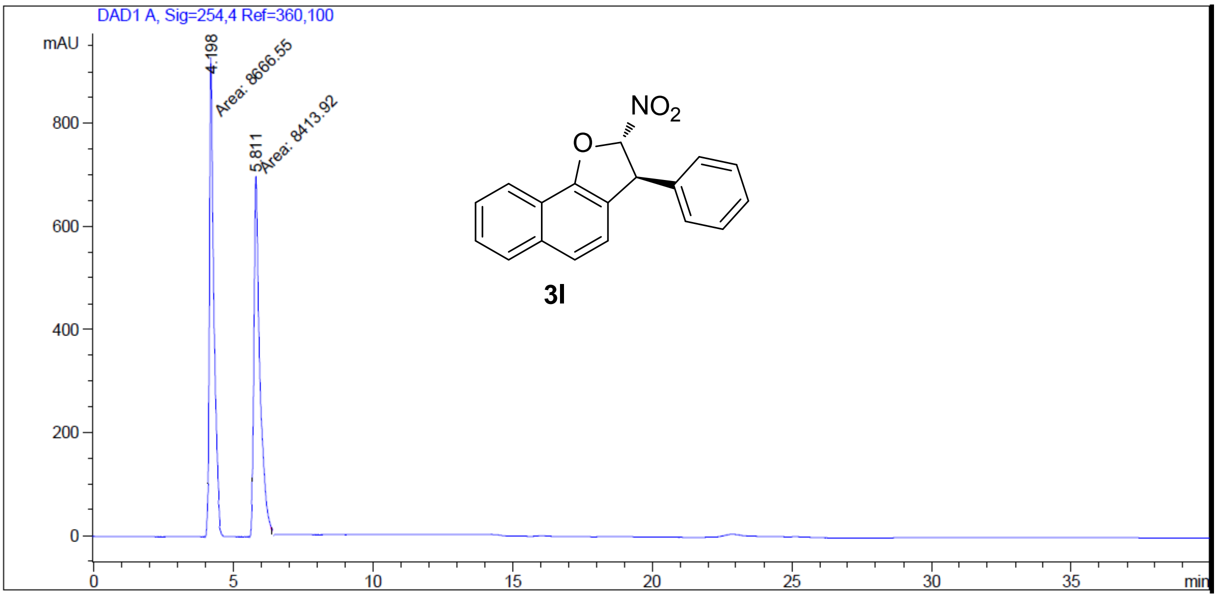

DAD1 A, Sig=254,4 Ref=390,80
mAU
160
140
120
100
80
60
40
20
0
6.632
Area: 4274.05
11.202
Area: 4134.12
0
5
10
15
20
25
30
35
min
Br
NO2
O

3_j

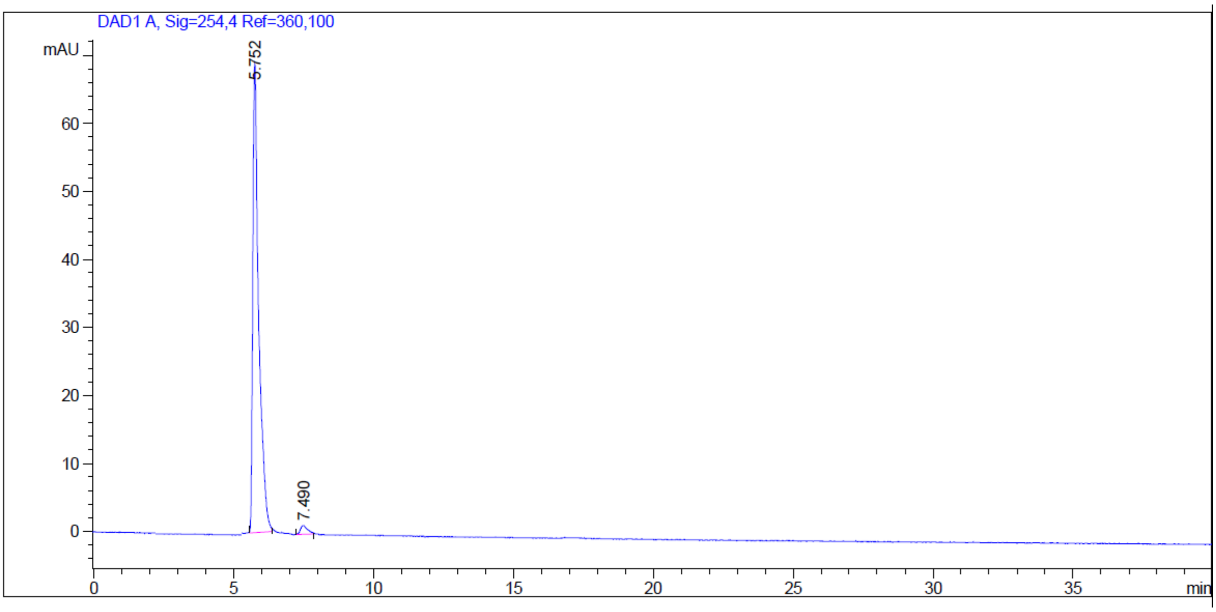

DAD1 A, Sig=254,4 Ref=390,80
mAU
500
400
300
200
100
0
6.507
Area: 10329
11.429
Area: 283.959
0
5
10
15
20
25
30
35
min


DAD1 A, Sig=254,4 Ref=390,80
mAU
350
300
250
200
150
100
50
0
6.300
9.468
NO2
MeO
O
3k
0
5
10
15
20
25
30
35
min


DAD1 A, Sig=254,4 Ref=390,80 (AMELIA\FEO103Q.D)
mAU
200
175
150
125
100
75
50
25
0
6.432
9.673
0
5
10
15
20
25
30
35
min


DAD1 A, Sig=254,4 Ref=360,100
mAU
800
600
400
200
0
4.198
Area: 8666.55
5.811
Area: 8413.92
NO$_2$
O
0
5
10
15
20
25
30
35
min

3l


DAD1 A, Sig=254,4 Ref=360,100
mAU
60
50
40
30
20
10
0
5.752
7.490
0
5
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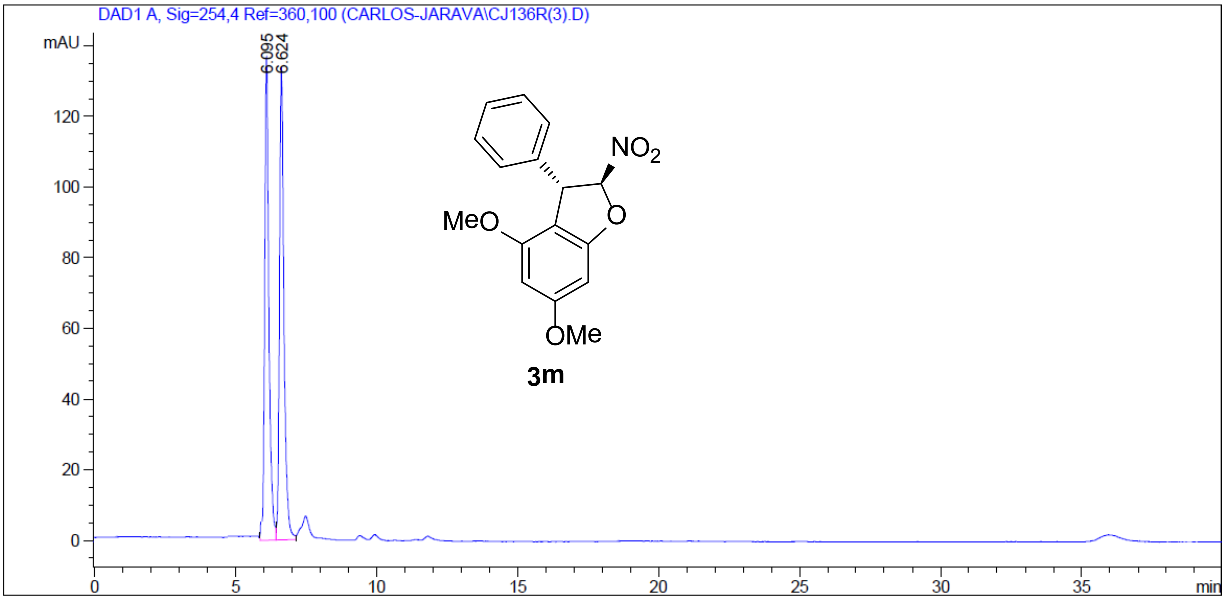
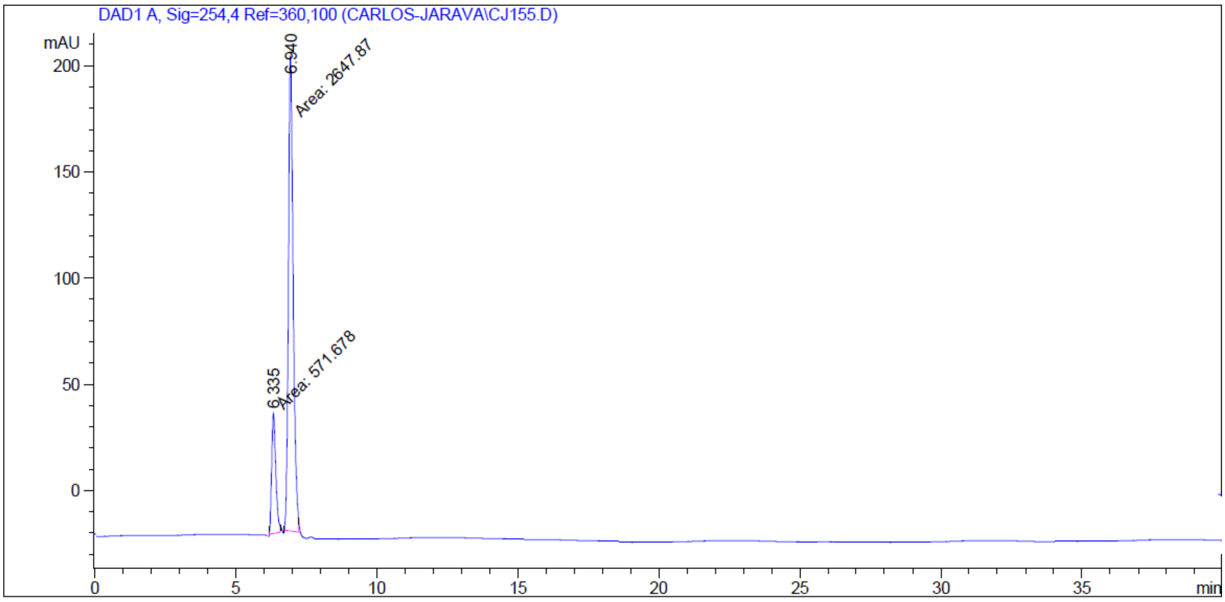
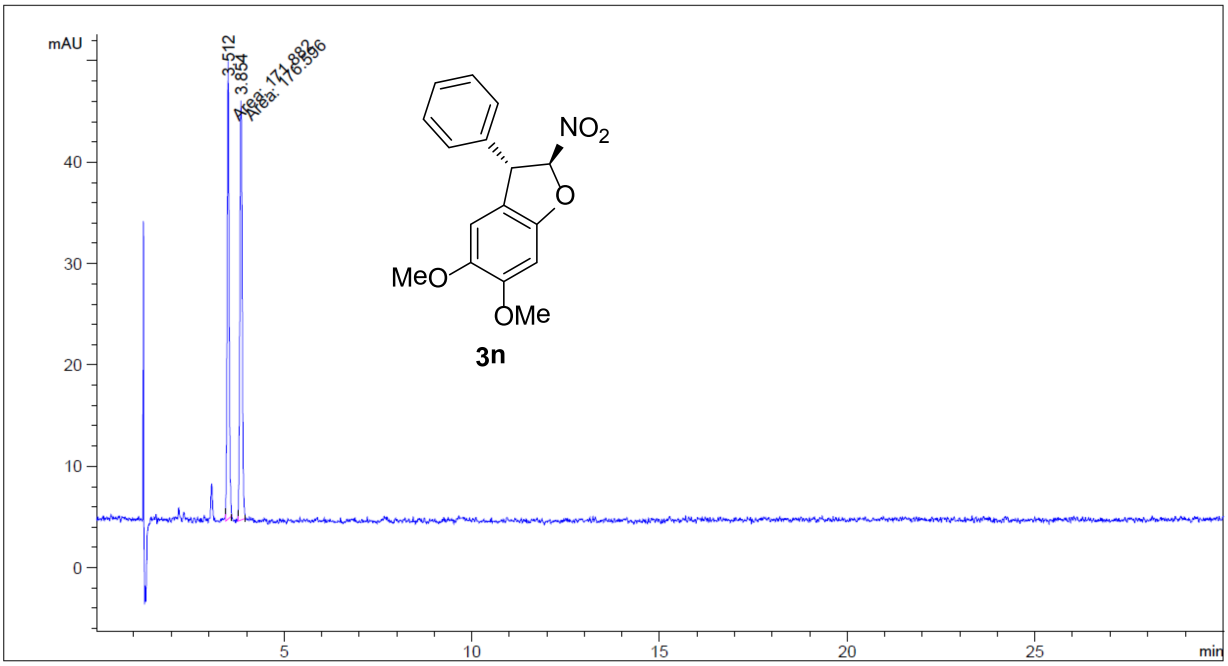
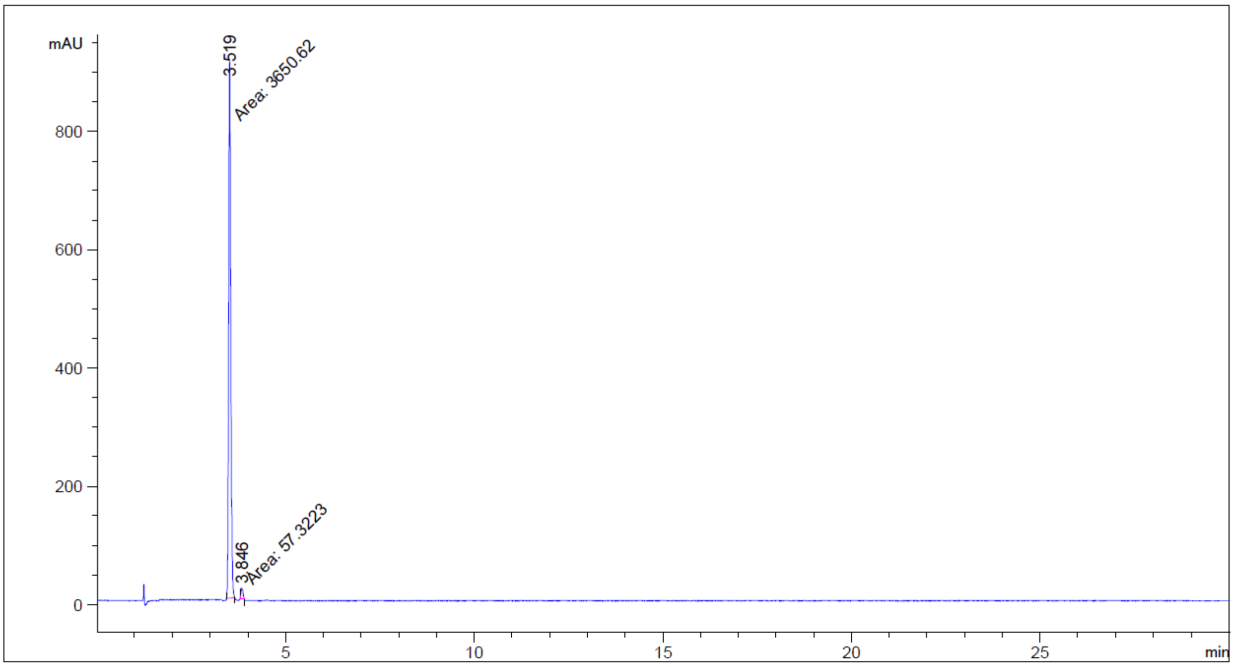
15
20
25
30
35
min

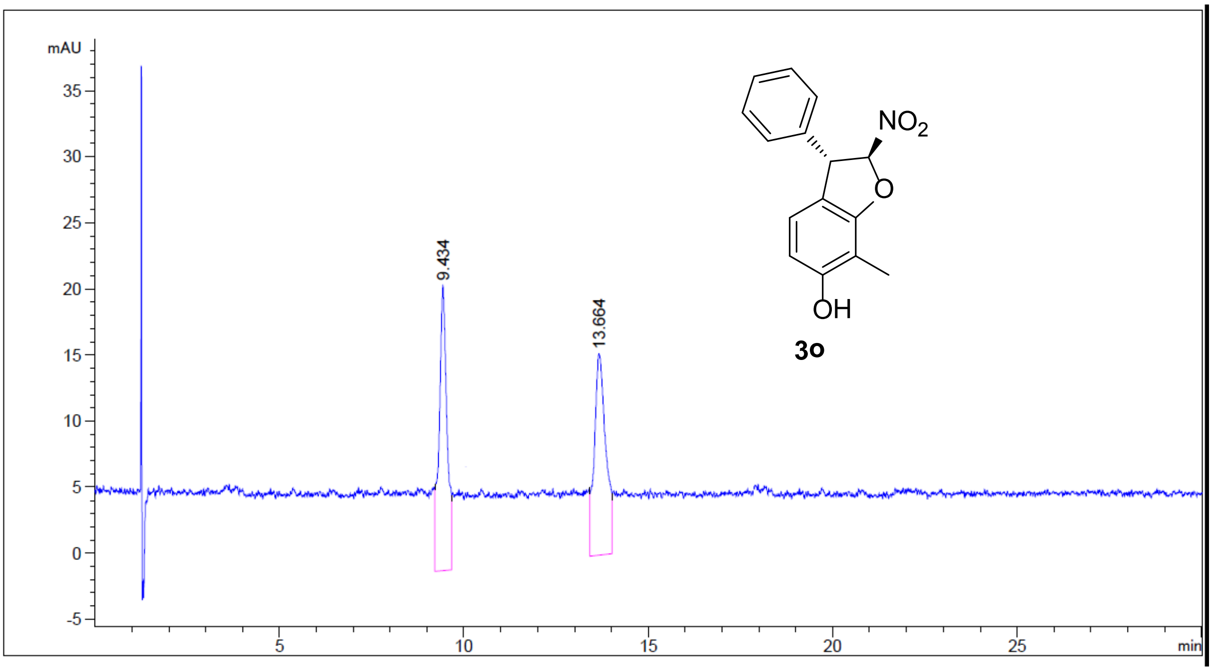

DAD1 A, Sig=254,4 Ref=360,100 (CARLOS-JARAVA\CJ136R(3).D)
mAU
120
100
80
60
40
20
0
6.095
6.624
NO2
MeO
O
OMe
3m
0
5
10
15
20
25
30
35
min

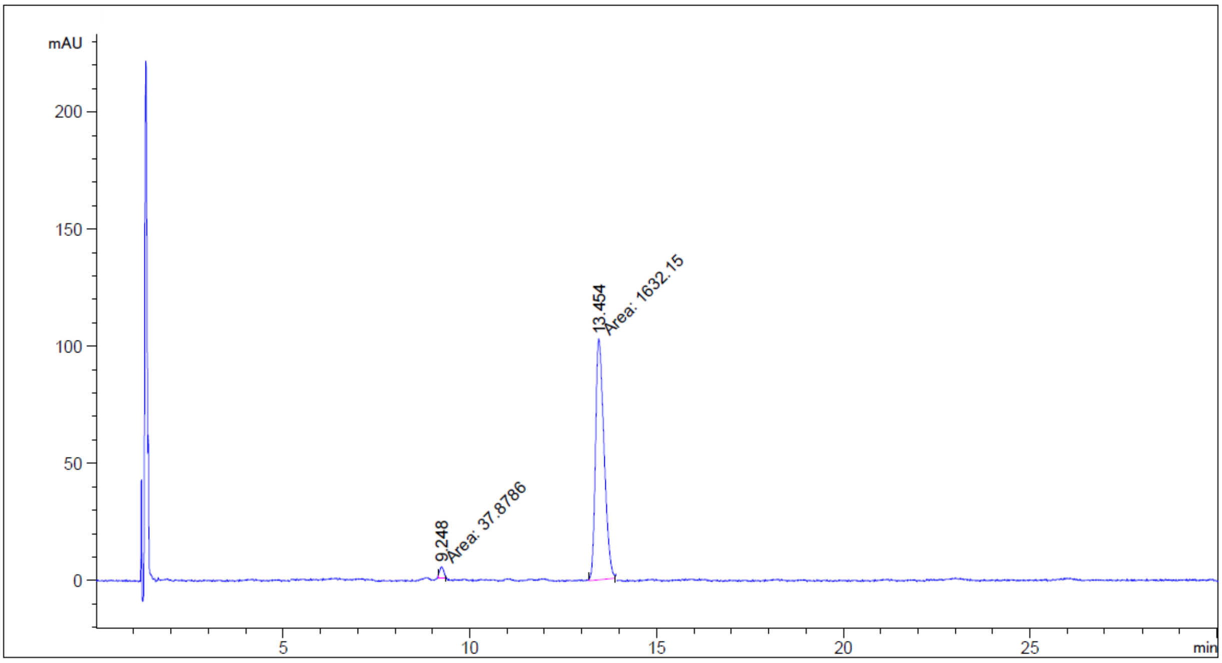

DAD1 A, Sig=254,4 Ref=360,100 (CARLOS-JARAVA\CJ155.D)
mAU
200
150
100
50
0
6.940
Area: 2647.87
6.335
Area: 571.678
0
5
10
15
20
25
30
35
min


mAU
40
30
20
10
0
3.512
3.854
Area: 171.882
Area: 176.596
NO2
O
MeO
OMe
5
10
15
20
25
min

3n


mAU
800
600
400
200
0
3.519
Area: 3650.62
3.846
Area: 57.3223
5
10
15
20
25
min


mAU
35
30
25
20
15
10
5
0
-5
9.434
13.664
5
10
15
20
25
min
NO2
O
OH
3o


mAU
200
150
100
50
0
9.248
Area: 37.8786
13.454
Area: 1632.15
5
10
15
20
25
min