Electronic Supplementary Material (ESI) for Chemical Communications

A Highly Chemoselective and Enantioselective Aza-Henry Reaction of Cyclic α-Carbonyl Ketimines under Bifunctional Catalysis

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Supporting Information

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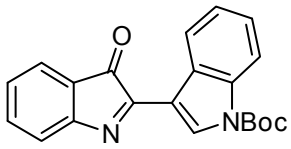
General Methods

NMR spectra were acquired on a Bruker 300 spectrometer, running at 300 and 75 MHz for ^{1}H and ^{13}C, 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 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 column).

Materials. Commercially available nitroalkanes **2**, catalysts **6**, and **7** and solvents were used without further purification. 2-Aryl-3*H*-indol-3-ones **1a-j,**[1] catalysts **4a-e**[2] and **5**[3] were synthesized according to the literature.

tert-Butyl 3-oxo-1'H,3H-2,3'-biindole-1'-carboxylate (1j):



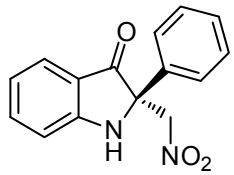
The product was obtained following the reported procedure[1] as red solid (45% yield) after FC (eluent 1/1; hexane/AcOEt).; ^{1}H-NMR ($CDCl_3$): δ = 8.68 (s, 1H), 8.50-8.47 (m, 1H), 8.11-8.08 (m, 3H), 6.98 (d, *J* = 8.2 Hz, 1H), 6.84 (t, *J* = 7.7 Hz, 1H), 5.88 (s, 1H), 7.40 (t, *J* = 7.3 Hz, 3H), 7.32-7.28 (m, 3H), 7.08 (t, *J* = 7.5 Hz, 1H), 1.63 (s, 9H). ^{13}C-NMR ($CDCl_3$): δ = 194.1, 162.1, 158.1, 149.0, 136.9, 135.1, 132.3, 128.1, 127.4, 125.7, 125.6, 124.1, 123.3, 122.7, 121.8, 115.2, 111.3, 85.0, 28.1. HRMS: calculated for $C_{21}H_{18}N_2O_3$ $[M]^+$ 346.1317; found 346.1319.

Experimental Procedures and Characterizations

*General Procedure for the synthesis of compounds **3***. To an ordinary vial charged with corresponding 2-aryl-3*H*-indol-3-ones **1a-i** (0.2 mmol) was added the catalyst **4e** (10 mol%), and the corresponding nitroalkane **3** (2.0 mmol) in *p*-xilene (0.72 mL). The reaction mixture was stirring at room temperature for 48 h. Once the reaction was finished (followed by TLC), the crude was directly charged and purified by FC, affording pure products.

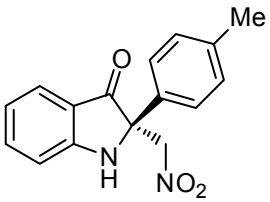
[1] Y. Liu, W. W. McWhorter Jr. *J. Am. Chem. Soc.* 2003, **125**, 4240.
[2] B. Vakulya, V. Szilárd, C. Antal, T. Soós *Org. Lett.* 2005, **7**, 1967
[3] J. P. Malerich, K. Hagihara, V. H. Rawal *J. Am. Chem. Soc.* 2008, **130**, 14416.

(*S*)-2-(Nitromethyl)-2-phenylindolin-3-one (3a):



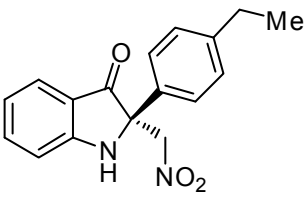
The product was obtained following the standard procedure using catalyst **4e** as yellow oil (90% yield) after FC (eluent 5/1; hexane/AcOEt). The *ee* was determined by HPLC using a Chiralpak IC column [hexane/*i*PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor} = 18.2 min, τ_{major} = 20.1 min (*e.r.* = 95:5). $[\alpha]^{20}_D$ = -322.0 (*c* = 0.4 in $CHCl_3$); ^{1}H-NMR ($CDCl_3$): δ = 7.56-7.47 (m, 4H), 7.32-7.29 (m, 3H), 6.98 (d, *J* = 8.2 Hz, 1H), 6.84 (t, *J* = 7.7 Hz, 1H), 5.88 (s, 1H), 5.19 (d, *J* = 13.7 Hz, 1H), 4.75 (d, *J* = 13.7 Hz, 1H). ^{13}C-NMR ($CDCl_3$): δ = 196.2, 160.1, 138.3, 134.4, 129.2, 128.8, 125.8, 125.1, 120.1, 118.3, 112.2, 80.3, 69.2. HRMS: calculated for $C_{15}H_{12}N_2O_3$ $[M]^+$ 268.0848; found 268.0837.

(*S*)-2-(Nitromethyl)-2-(p-tolyl)indolin-3-one (3b):



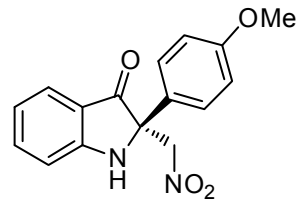
The product was obtained following the standard procedure using catalyst **4e** as yellow oil (93% yield) after F-C (eluent 5/1; hexane/AcOEt). The *ee* was determined by HPLC using a Chiralpak IC column [hexane/*i*PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor} = 22.9 min, τ_{major} = 19.1 min (*e.r.* = 91:9). $[\alpha]^{20}_D$ = -331.1 (*c* = 0.35 in $CHCl_3$); ^{1}H-NMR ($CDCl_3$): δ = 7.50 (d, *J* = 7.7 Hz, 1H), 7.44 (td, *J* = 7.0, 1.3 Hz, 1H), 7.32 (d, *J* = 9.0 Hz, 2H), 7.08 (d, *J* = 9.0 Hz, 2H), 6,93 (d, *J* = 8.3 Hz, 1H), 6.79 (t, *J* = 7.0 Hz, 1H), 5.80 (s, 1H), 5.12 (d, *J* = 15.0 Hz, 1H), 4.70 (d, *J* = 15.0 Hz, 1H), 2.22 (s, 3H). ^{13}C-NMR ($CDCl_3$): δ = 196.5, 160.1, 138.7, 138.2, 131.4, 130.0, 125.9, 125.4, 120.4, 118.5, 112.2, 80.2, 69.2, 21.0. HRMS: calculated for $C_{16}H_{14}N_2O_3$ $[M]^+$ 282.1004; found 282.0996.

(*S*)-2-(4-Ethylphenyl)-2-(nitromethyl)indolin-3-one (3c):



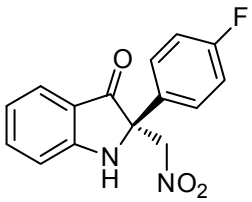
The product was obtained following the standard procedure using catalyst **4e** as yellow oil (93% yield) after F-C (eluent 6/1; hexane/AcOEt). The *ee* was determined by HPLC using a Chiralpak IC column [hexane/*i*PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor} = 18.6 min, τ_{major} = 22.4 min (*e.r.* = 92:8). $[\alpha]^{20}_D$ = -390.1 (*c* = 0.15 in $CHCl_3$); ^{1}H-NMR ($CDCl_3$): δ = 7.51 (d, *J* = 7.7 Hz, 1H), 7.48 (td, J_1 = 7.0, 1.3 Hz, 1H), 7.36 (d, *J* = 9.0 Hz, 2H), 7.13 (d, *J* = 9.0 Hz, 2H), 6,94 (d, *J* = 8.3 Hz, 1H), 6.81 (t, *J* = 7.0 Hz, 1H), 5.77 (s, 1H), 5.40 (d, *J* = 12.0 Hz, 1H), 4.72 (d, *J* = 12.0 Hz, 1H), 2.53 (q, *J* = 6.0 Hz, 2H), 1.12 (t, *J* = 6.0 Hz, 3H). ^{13}C-NMR ($CDCl_3$): δ = 195.9, 159.6, 144.5, 137.7, 131.1, 128.3, 125.3, 124.6, 119.6, 118.0, 111.7, 79.8, 68.7, 27.9, 14.8. HRMS: calculated for $C_{17}H_{16}N_2O_3$ $[M]^+$ 296.1161; found 296.1153.

(*S*)-2-(4-Methoxyphenyl)-2-(nitromethyl)indolin-3-one (3d):



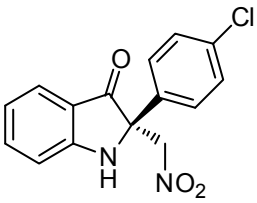
The product was obtained following the standard procedure using catalyst **4e** as yellow oil (95% yield) after FC (eluent 5/1; hexane/AcOEt). The *ee* was determined by HPLC using a Chiralpak ID column [hexane/*i*PrOH (80:20)]; flow rate 1.0 mL/min; τ_{minor} = 18.6 min, τ_{major} = 23.4 min (*e.r.* = 85:15). $[\alpha]^{20}_{D}$ = -158.4 (*c* = 0.19 in $CHCl_3$); ^{1}H-NMR ($CDCl_3$): δ = 7.51 (d, *J* = 7.7 Hz, 1H), 7.45 (td, J_1 = 7.4, J_2 = 0.9 Hz, 1H), 7.37 (d, *J* = 9.0 Hz, 2H), 6.80 (d, *J* = 9.0 Hz, 2H), 6,93 (d, *J* = 8.2 Hz, 1H), 6.807 (t, *J* = 6.9 Hz, 1H), 5.79 (s, 1H), 5.10 (d, *J* = 12.0 Hz, 1H), 4.68 (d, *J* = 12.0 Hz, 1H), 3.69 (s, 3H). ^{13}C-NMR ($CDCl_3$): δ = 196.5, 160.0, 138.2, 126.5, 126.2, 125.8, 102.1, 118.5, 114.6 (2C), 112.2, 80.46, 68.7, 55.3. HRMS: calculated for $C_{16}H_{14}N_2O_4$ $[M]^+$ 298.0954; found 298.0954.

(*S*)-2-(4-Fluorophenyl)-2-(nitromethyl)indolin-3-one (3e):



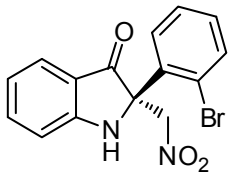
The product was obtained following the standard procedure using catalyst **4e** as yellow oil (93% yield) after FC (eluent 5/1; hexane/AcOEt). The *ee* was determined by HPLC using a Chiralpak IC column [hexane/*i*PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor} = 15.0 min, τ_{major} = 13.2 min (*e.r.* = 91:9). $[\alpha]^{20}_{D}$ = -415.6 (*c* = 0.14 in CH_2Cl_2); ^{1}H-NMR ($CDCl_3$): δ = 7.53-7.46 (m, 4H), 6.98 (t, *J* = 8.51 Hz, 3H), 6.83 (t, *J* = 7.55 Hz, 1H), 5.88 (s, 1H), 5.12 (d, *J* = 15.0 Hz, 1H), 4.63 (d, *J* = 15.0 Hz, 1H). ^{13}C-NMR ($CDCl_3$): δ = 196.0, 164.7, 160.9 (d, $J_{C\text{-}F}$= 426 Hz), 138.6, 130.1 (d, $J_{C\text{-}F}$= 12.0 Hz), 127.2 (d, $J_{C\text{-}F}$= 36.0 Hz), 125.9, 120.4, 118.2, 116.1 (d, $J_{C\text{-}F}$= 87 Hz), 112.3, 80.5, 68.7. HRMS: calculated for $C_{15}H_{11}FN_2O_3$ $[M]^+$ 286.0754; found 286.0765.

(*S*)-2-(4-Chlorophenyl)-2-(nitromethyl)indolin-3-one (3f):



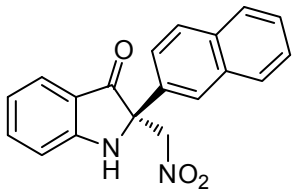
The product was obtained following the standard procedure using catalyst **4e** as yellow oil (81% yield) after FC (eluent 5/1; hexane/AcOEt). The *ee* was determined by HPLC using a Chiralpak IC column [hexane/*i*PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor} = 14.2 min, τ_{major} = 12.3 min (*e.r.* = 93:7). $[\alpha]^{20}_{D}$ = -305.1 (*c* = 0.4 in $CHCl_3$); ^{1}H-NMR ($CDCl_3$): δ = 7.52-7.41 (m, 2H), 7.44 (d, *J* = 9.0 Hz, 2H), 7.26 (d, *J* = 9.0 Hz, 2H), 6.97 (d, *J* = 8.2 Hz, 1H), 6.83 (t, *J* = 7.5 Hz, 1H), 5.89 (s, 1H), 5.12 (d, J = 15.0 Hz, 1H), 4.63 (d, *J* = 15.0 Hz, 1H). ^{13}C-NMR ($CDCl_3$): δ = 195.7, 160.1, 138.6, 135.1, 133.0, 129.3, 126.7, 125.9, 120.4, 118.0, 112.4, 80.3, 68.8. HRMS: calculated for $C_{15}H_{11}N_2O_3Cl$ $[M]^+$ 302.0458; found 302.0468.

(*S*)-2-(2-Bromophenyl)-2-(nitromethyl)indolin-3-one (3g):



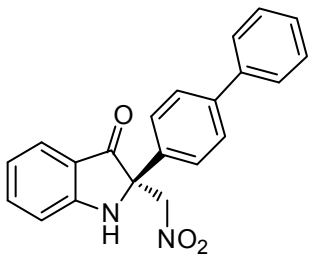
The product was obtained following the standard procedure using catalyst **4e** as yellow solid (81% yield) after FC (eluent 7/1; hexane/AcOEt). The *ee* was determined by HPLC using a Chiralpak IC column [hexane/*i*PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor} = 21.7 min, τ_{major} = 24.1 min (*e.r.* = 2:98). $[\alpha]^{20}_{D}$ = -346.7 (*c* = 0.15 in $CHCl_3$). Mp: 198-200 ºC. ^{1}H-NMR ($CDCl_3$): δ = 7.69 (d, *J* = 9.0 Hz, 1H), 7.64- 7.61 (m, 1H), 7,48 (m, 2H), 7.25 (m, 2H), 6.87-6.81 (m, 2H), 6.24 (s, 1H), 5.45 (d, *J* = 12.0 Hz, 1H), 4.96 (d, *J* = 12.0 Hz, 1H). ^{13}C-NMR ($CDCl_3$): δ = 195.9, 158.9, 137.0, 134.8, 131.5, 129.7, 128.9, 127.9, 124.1, 121.7, 119.4, 119.2, 111.9, 76.9, 68.8. HRMS: calculated for $C_{15}H_{11}BrN_2O_3$ $[M]^+$ 345.9953; found 345.9939.

(*S*)-2-(Naphthalen-2-yl)-2-(nitromethyl)indolin-3-one (3h):



The product was obtained following the standard procedure using catalyst **4e** as yellow oil (>99% yield) after FC (eluent 5/1; hexane/AcOEt). The *ee* was determined by HPLC using a Chiralpak IC column [hexane/*i*PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor} = 20.6 min, τ_{major} = 23.8 min (*e.r.* = 92:8). $[\alpha]^{20}_{D}$ = -341.0 (*c* = 1.0 in CH_2Cl_2); ^{1}H-NMR ($CDCl_3$): δ = 7.99 (d, *J* = 1.8 Hz, 1H), 7.84 (d, *J* = 8.8 Hz, 1H), 7.81-7.79 (m, 2H), 7.64 (dd, *J* = 8.7, 2.0 Hz, 1H), 7.60 (d, *J* = 7.9 Hz, 1H), 7.59-7.53 (m, 1H), 7.51-7.45 (m, 2H), 7.07 (d, *J* = 8.2 Hz, 1H), 6.70 (t, *J* = 7.7 Hz, 1H), 6.05 (s, 1H), 5.35 (d, *J* = 15.0 Hz, 1H), 4.87 (d, *J* = 15.0 Hz, 1H). ^{13}C-NMR ($CDCl_3$): δ = 196.2, 160.2, 138.4, 133.2, 133.2, 131.8, 129.3, 128.3, 127.6, 126.8, 126.7, 125.9, 124.7, 122.5, 120.2, 118.5, 112.4, 80.4, 69.4. HRMS: calculated for $C_{19}H_{14}N_2O_3$ $[M]^+$ 318.1004; found 318.1007.

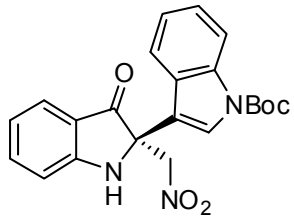
(*S*)-2-([1,1'-Biphenyl]-4-yl)-2-(nitromethyl)indolin-3-one (3i):



The product was obtained following the standard procedure using catalyst **4e** as yellow oil (37% yield) after FC (eluent 5/1; hexane/AcOEt). The *ee* was determined by HPLC using a Chiralpak IA column [hexane/*i*PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor} = 34.9 min, τ_{major} = 52.3 min (*e.r.* = 92:8). $[\alpha]^{20}_{D}$ = -415.6 (*c* = 0.14 in CH_2Cl_2); ^{1}H-NMR ($CDCl_3$): δ = 7.62-7.52 (m, 9H), 7.42 (t, *J* = 7.0 Hz, 1H), 7.35 (d, *J* = 7.1 Hz, 1H), 7.06 (d, *J* = 8.2 Hz, 1H), 6.90 (t, *J* = 7.6 Hz, 1H), 5.94 (s, 1H), 5.29 (d, *J* = 12.0 Hz, 1H), 4.81 (d, *J* = 12.0 Hz, 1H). ^{13}C-NMR ($CDCl_3$): δ = 196.1, 160.1, 141.8, 140.1, 138.4, 133.3,

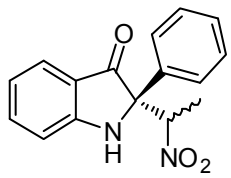
128.8, 127.9, 127.7, 127.1, 125.9, 125.6, 120.3, 118.4, 112.3, 80.3, 69.2. HRMS: calculated for $C_{21}H_{16}N_2O_3$ $[M]^+$ 344.1161; found 344.1154.

(*S*)-*tert*-Butyl 2-(nitromethyl)-3-oxo-2,3'-biindoline-1'-carboxylate (3j):



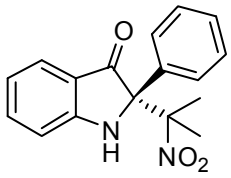
The product was obtained following the standard procedure using catalyst **4e** as yellow oil (52% yield) after FC (eluent 5/1; hexane/AcOEt). The *ee* was determined by HPLC using a Chiralpak IC column [hexane/*i*PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 19.5 min, τ_{minor} = 21.5 min (*e.r.* = 80:20). $[\alpha]^{20}_D$ = -49.3 (*c* = 0.75 in CH_2Cl_2); ^{1}H-NMR ($CDCl_3$): δ = 8.09 (d, *J* = 8.3 Hz, 1H), 7.64-7.58 (m, 3H), 7.50 (t, *J* = 8.3 Hz, 1H), 7.26 (t, *J* = 8.3 Hz, 1H), 7.15 (d, *J* = 7.2 Hz, 1H), 6.94 (d, *J* = 8.2 Hz, 1H), 6.88 (t, *J* = 7.8 Hz, 1H), 5.62 (sb, 1H), 5.26 (d, *J* = 13.2 Hz, 1H), 4.86 (d, *J* = 13.2 Hz, 1H), 1.58 (s, 9H). ^{13}C-NMR ($CDCl_3$): δ = 194.6, 160.1, 138.3, 135.9, 126.9, 125.7, 125.1, 124.4, 123.2, 120.6, 119.9, 119.6, 115.9, 114.4, 112.9, 84.6, 79.2, 77.2, 66.6, 28.1. HRMS: calculated for $C_{22}H_{21}N_3O_5$ $[M]^+$ 407.1481; found 407.1481.

(*S*)-2-[(*S*/*R*)-1-Nitroethyl]-2-phenylindolin-3-one (3k/3k'):



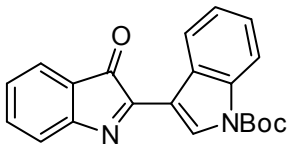
These products were obtained as a mixture of diastereoisomers (dr=3:1) following the standard procedure using catalyst **4e**. *Major diasterisomer:* it was isolated as a yellow oil in 73% yield after FC (eluent 6/1; hexane/AcOEt). the *ee* was determined by HPLC using a Chiralpak IA column [hexane/*i*PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor} = 8.3 min, τ_{major} = 7.3 min (*e.r.* = 91:9). $[\alpha]^{20}_D$ = -276,5 (*c* = 0.78 in CH_2Cl_2); ^{1}H-NMR ($CDCl_3$): δ = 7.54-7.21 (m, 7H), 7.02 (d, *J* = 8.3 Hz, 1H), 6.78-6,73 (m, 1H), 6.00 (sb, 1H), 5.46 (q, *J* = 6.5 Hz, 1H), 1.64 (d, *J* =4.0 Hz, 3H). ^{13}C-NMR ($CDCl_3$): δ =195.7, 160.4, 137.6, 134.6, 128.2, 127.9, 124.6, 124.4, 118.7, 117.5, 111.1, 87.4, 71.3, 14.1. *Minor diasterisomer:* it was isolated as yellow oil in 24% yield after FC (eluent 6/1; hexane/AcOEt). The *ee* was determined by HPLC using a Chiralpak IA column [hexane/*i*PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor} = 42.0 min, τ_{major} = 31.0 min (*e.r.* = 89:11). $[\alpha]^{20}_D$ = -168.8 (*c* = 0.40 in CH_2Cl_2); ^{1}H-NMR ($CDCl_3$): δ = 7.49-1.17 (m, 7H), 7.0 (d, *J* = 8.1 Hz , 1H), 6.95-6.78 (m, 1H), 5.43(q, *J* = 6.1 Hz, 1H), 5.26 (sb, 1H), 1.24 (d, *J* = 3.2 Hz, 1H). ^{13}C-NMR ($CDCl_3$): 180.1, 144.2, 121.2, 118.3, 112.3, 111.8, 109.8, 109.1, 104.1, 103.3, 95.7, 69.6, 55.6, 12.3. HRMS: calculated for $C_{16}H_{14}N_2O_3$ $[M]^+$ 282.1000; found 282.1011

(*S*)-2-(2-Nitropropan-2-yl)-2-phenylindolin-3-one (3l):

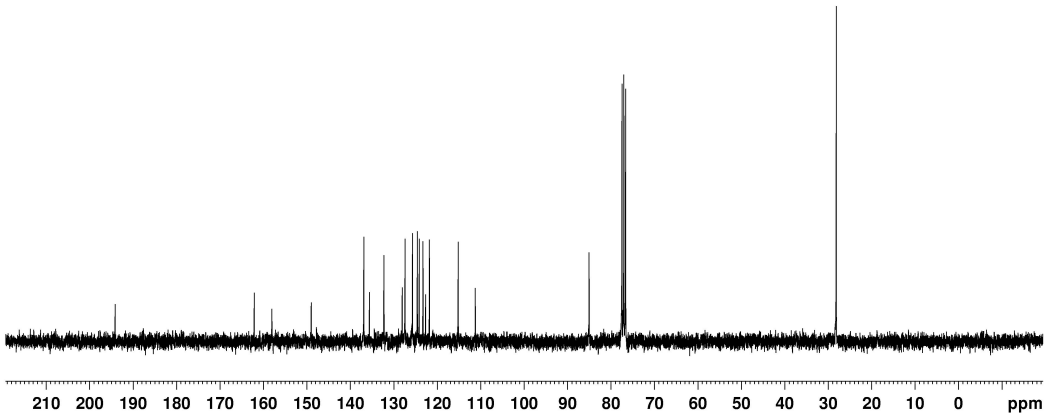


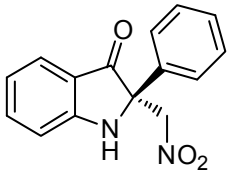
The product was obtained following the standard procedure using catalyst **4e** as yellow oil (87% yield) after FC (eluent 6/1; hexane/AcOEt). The *ee* was determined by HPLC using a Chiralpak IA column [hexane/*i*PrOH (90:10)]; flow rate 1.0 mL/min; τ_{minor} = 11.8 min, τ_{major} = 9.8 min (*e.r.* = 56:44). ^{1}H-NMR ($CDCl_3$): δ = 7.62-7.18 (m, 7H), 6.88 (d, *J* = 8.7 Hz , 1H), 6,76-6.71 (m, 1H), 2,01 (s, 6H). ^{13}C-NMR ($CDCl_3$): δ = 196.8, 159.5, 137.8, 133.6, 128.7, 128.1, 127.4, 125.1, 120.6, 119.4, 111.8, 94.2, 71.8, 22.8, 21.0. HRMS: calculated for $C_{17}H_{16}N_2O_3$ $[M]^+$ 296.1161; found 296.1246.

Spectra of compounds 1j and 3a-l

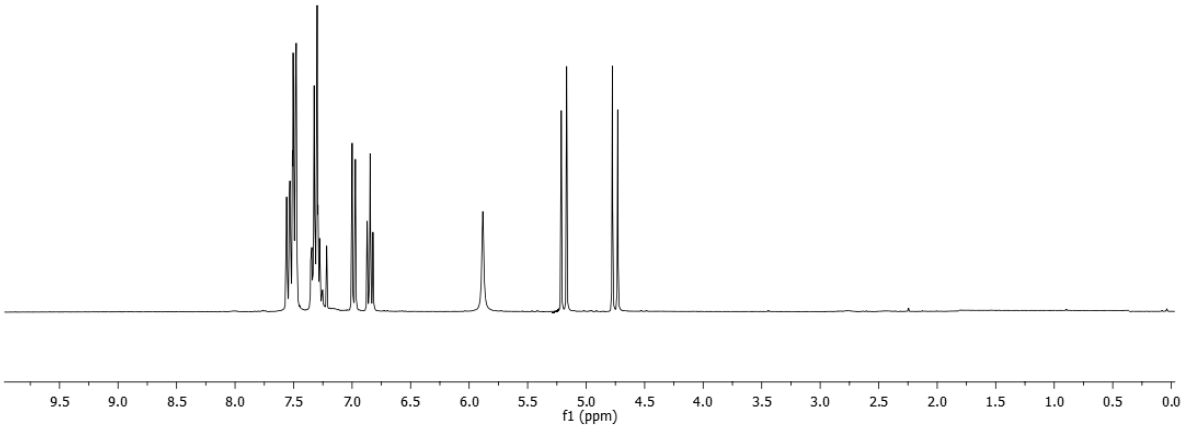


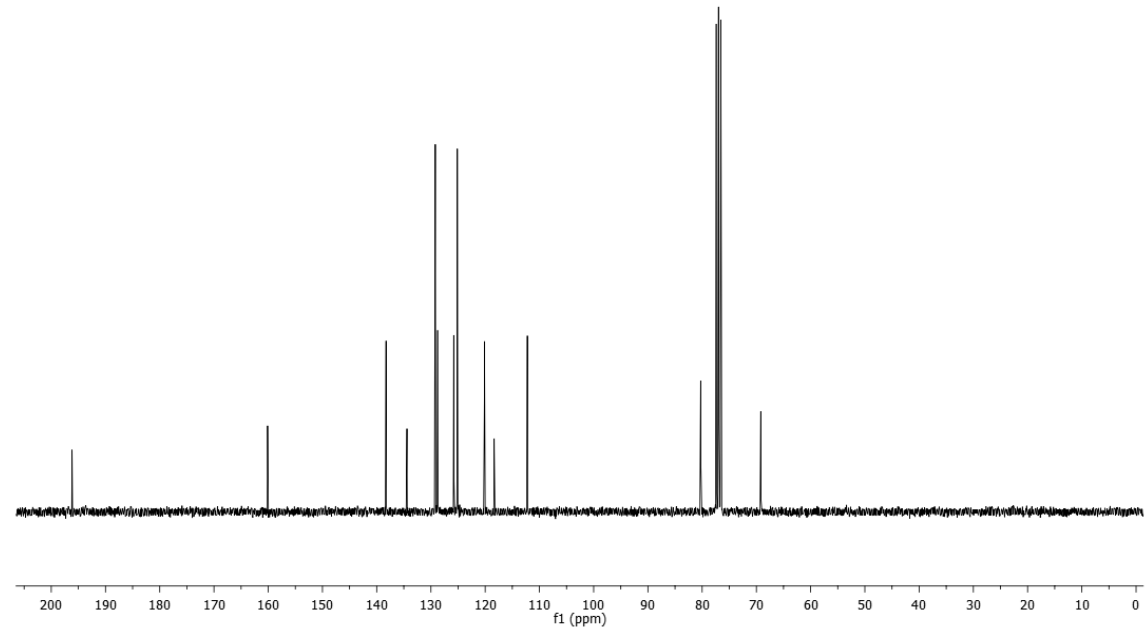
1j

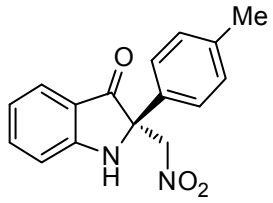



O
N
H
NO2

3a

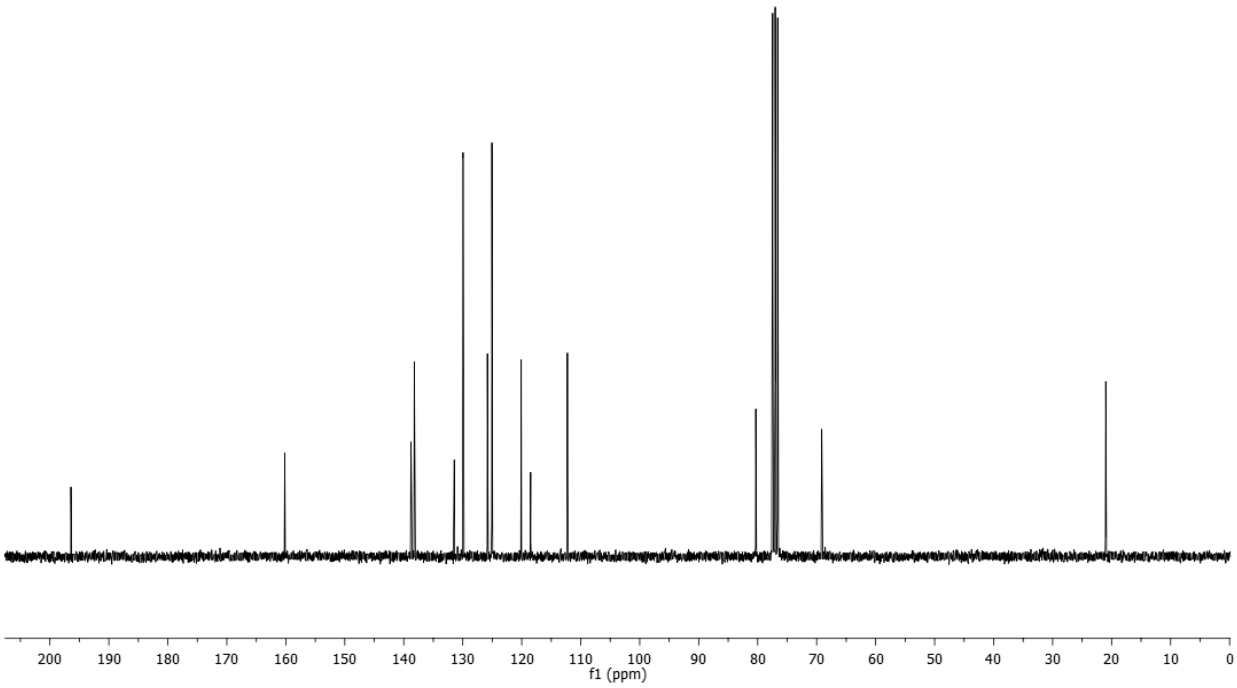

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

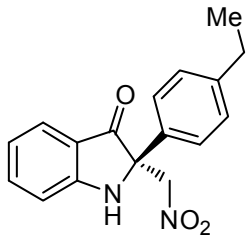

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Me
O
N
H
NO2

3b

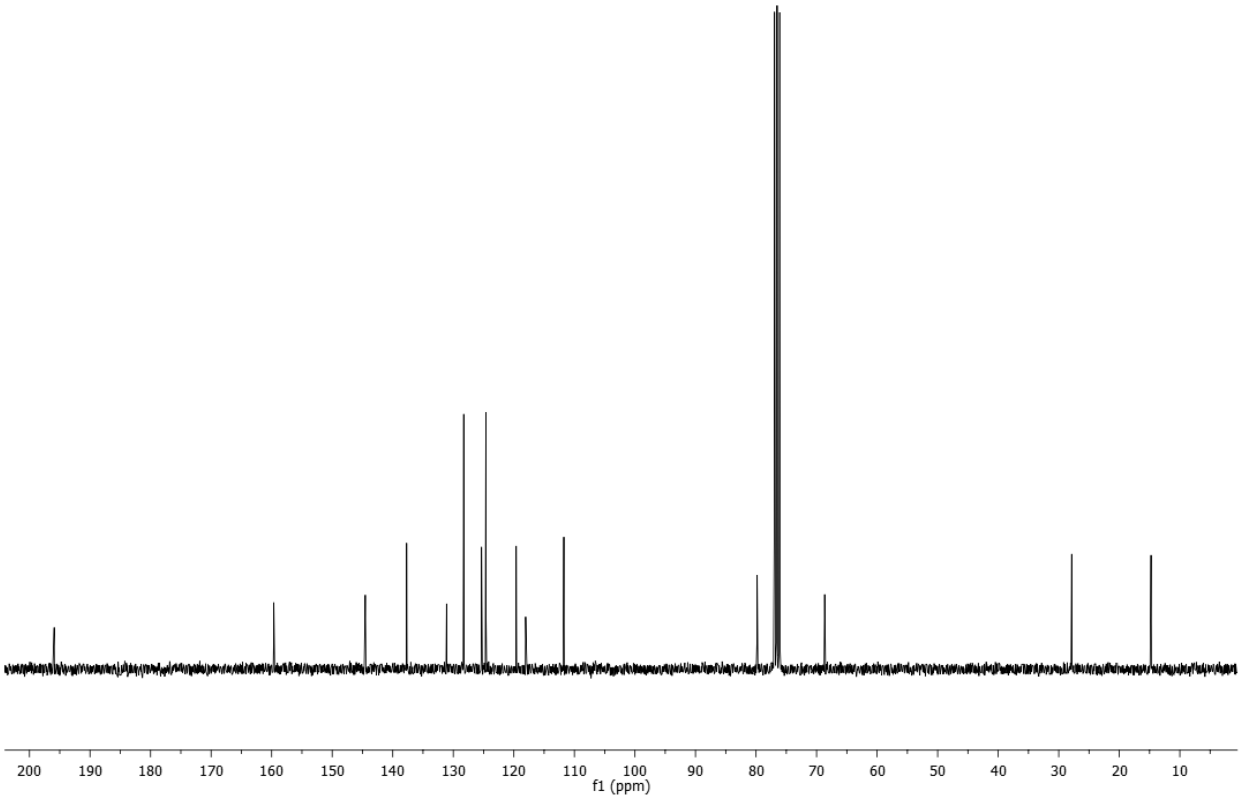
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

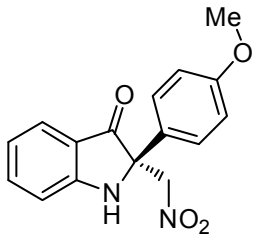

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Me
O
N
H
NO2

3c

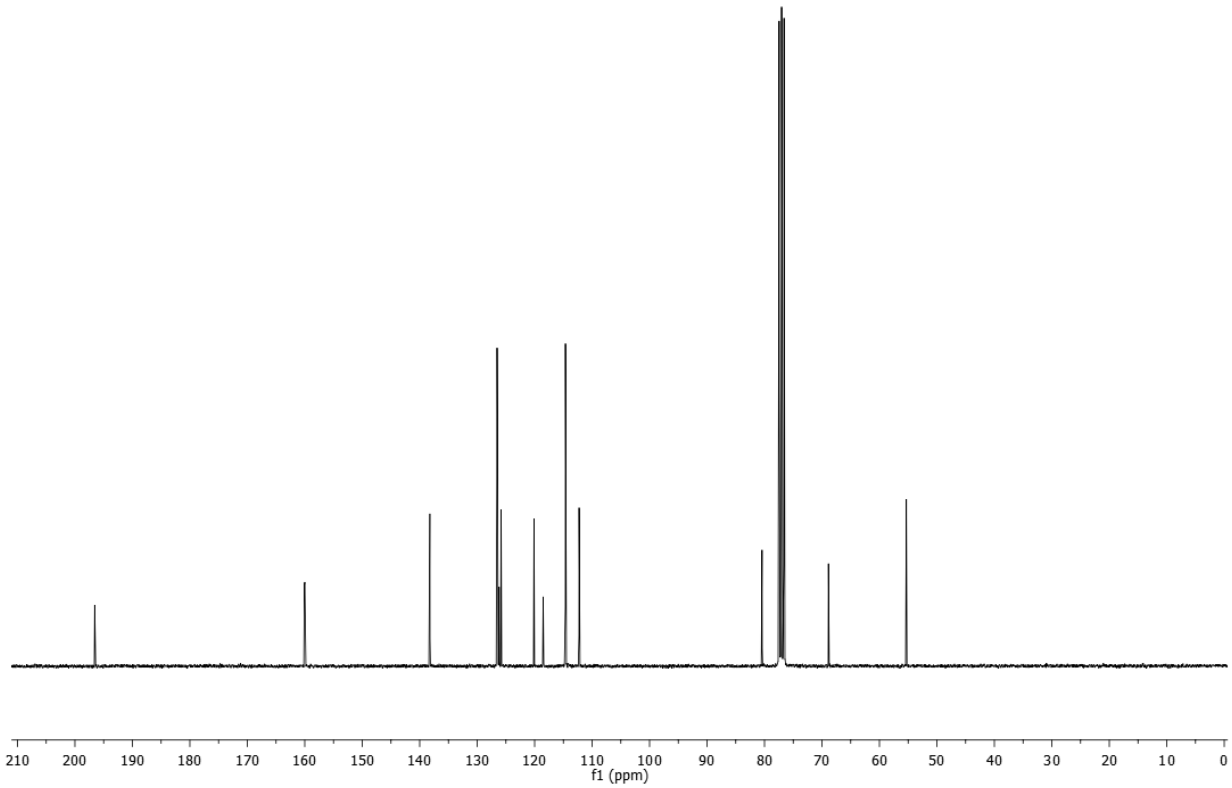
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

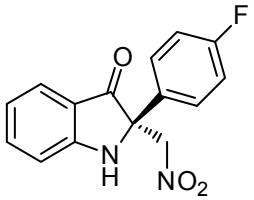

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


Me
O
O
N
H
NO2

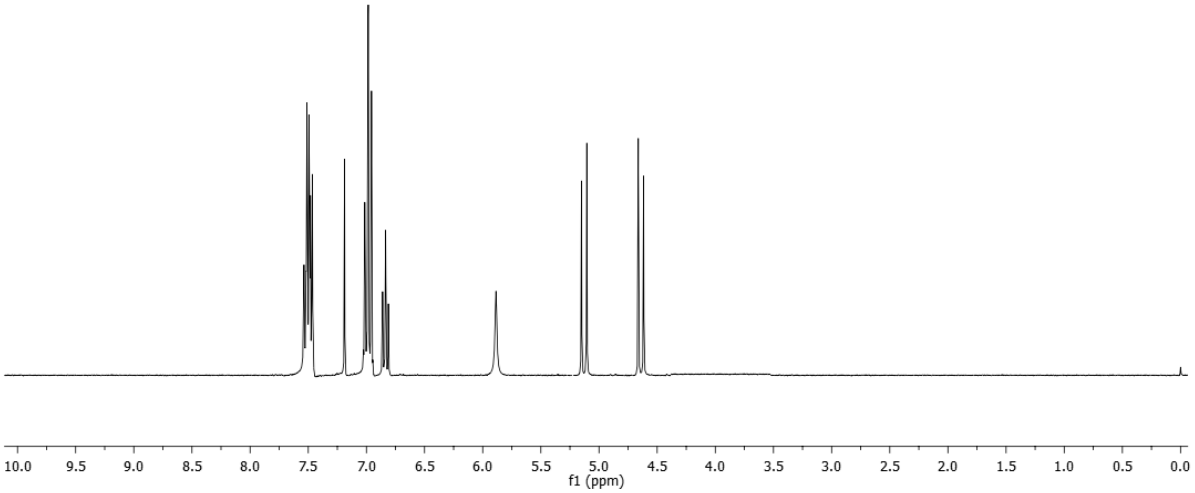
3d

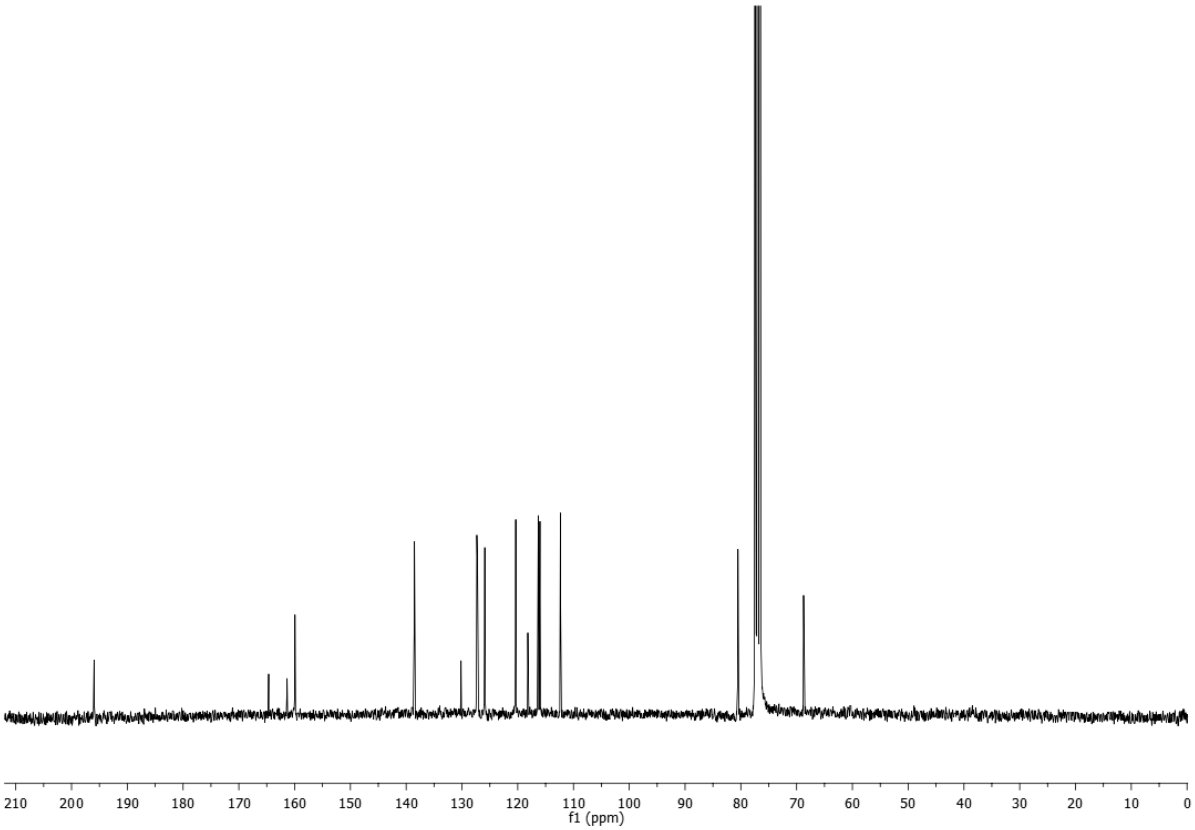
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

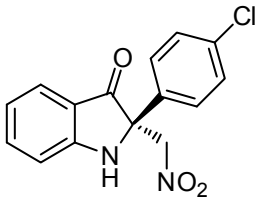

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


F
O
N
H
NO2

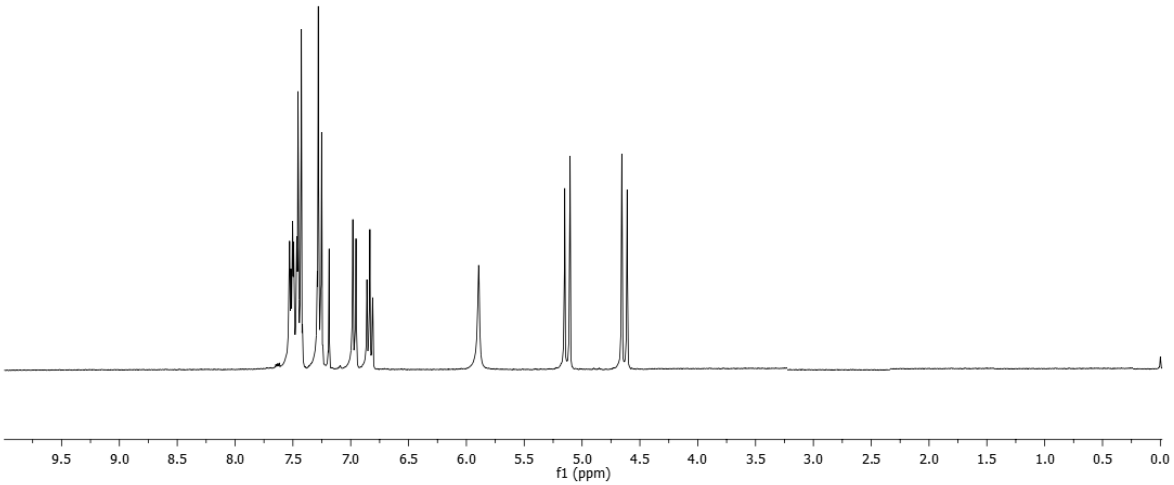
3e

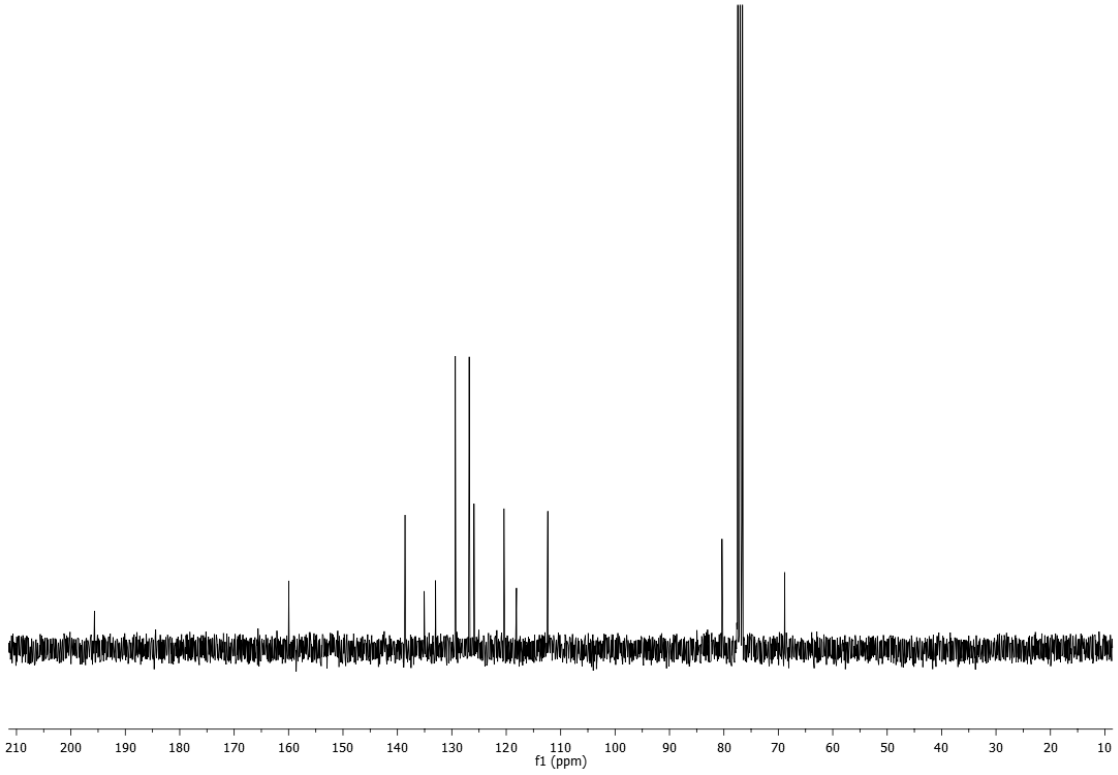

10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

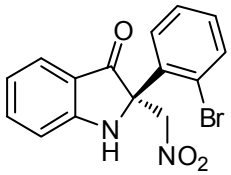

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



3f

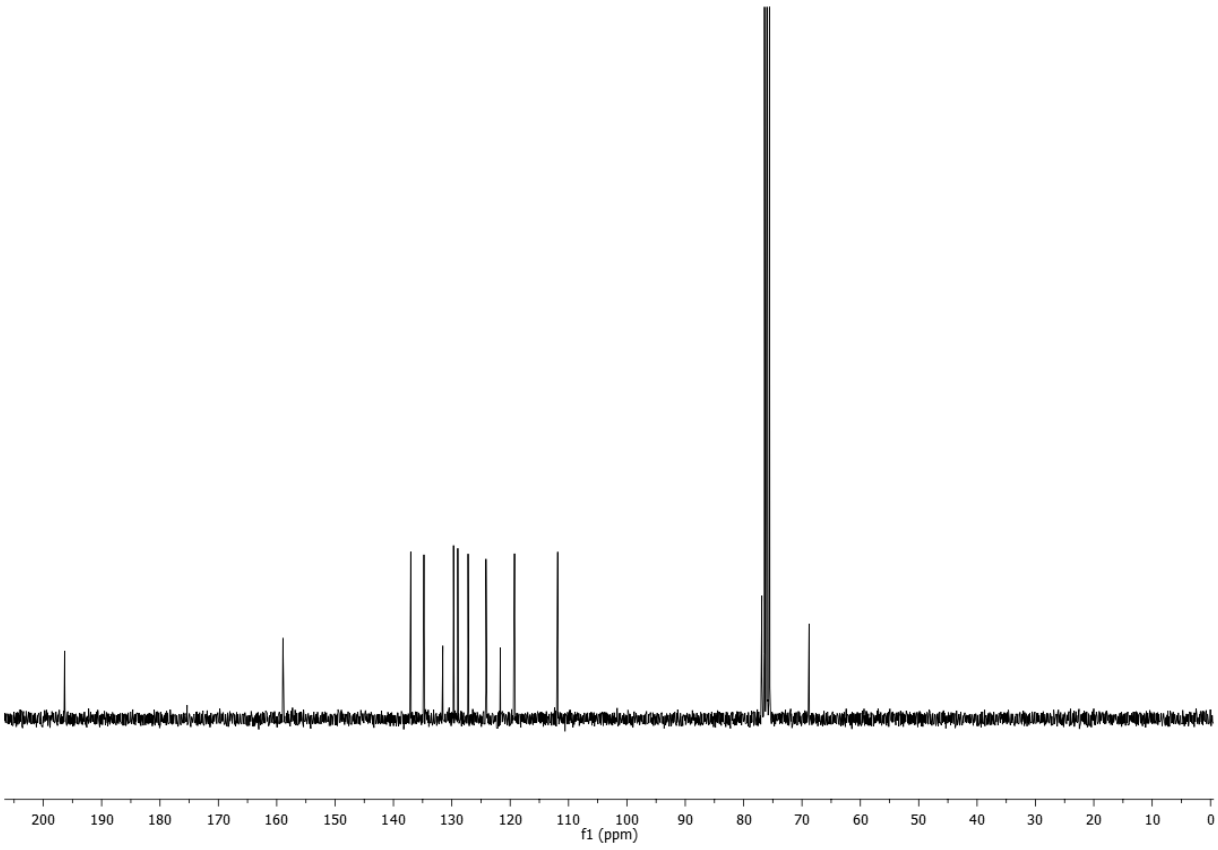


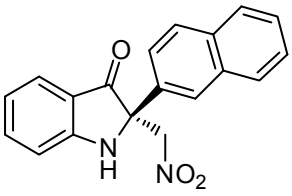



O
Br
N
H
NO2

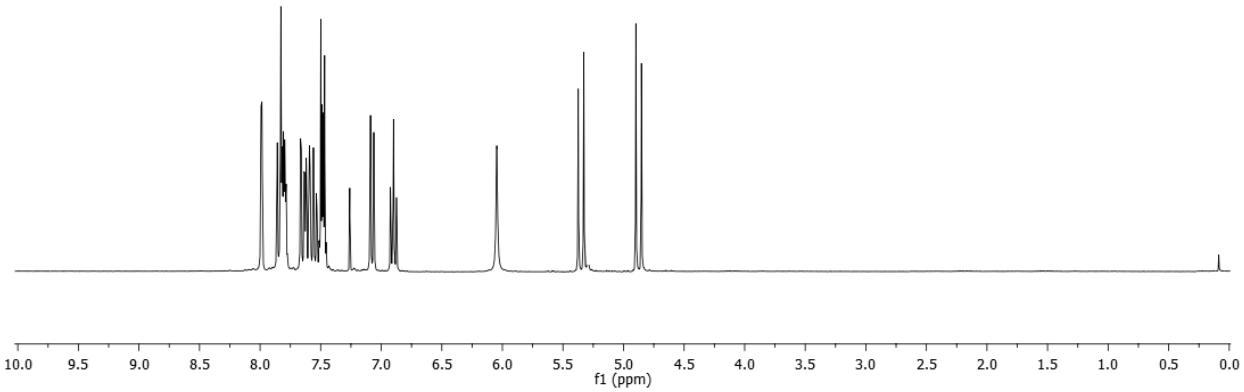
3g

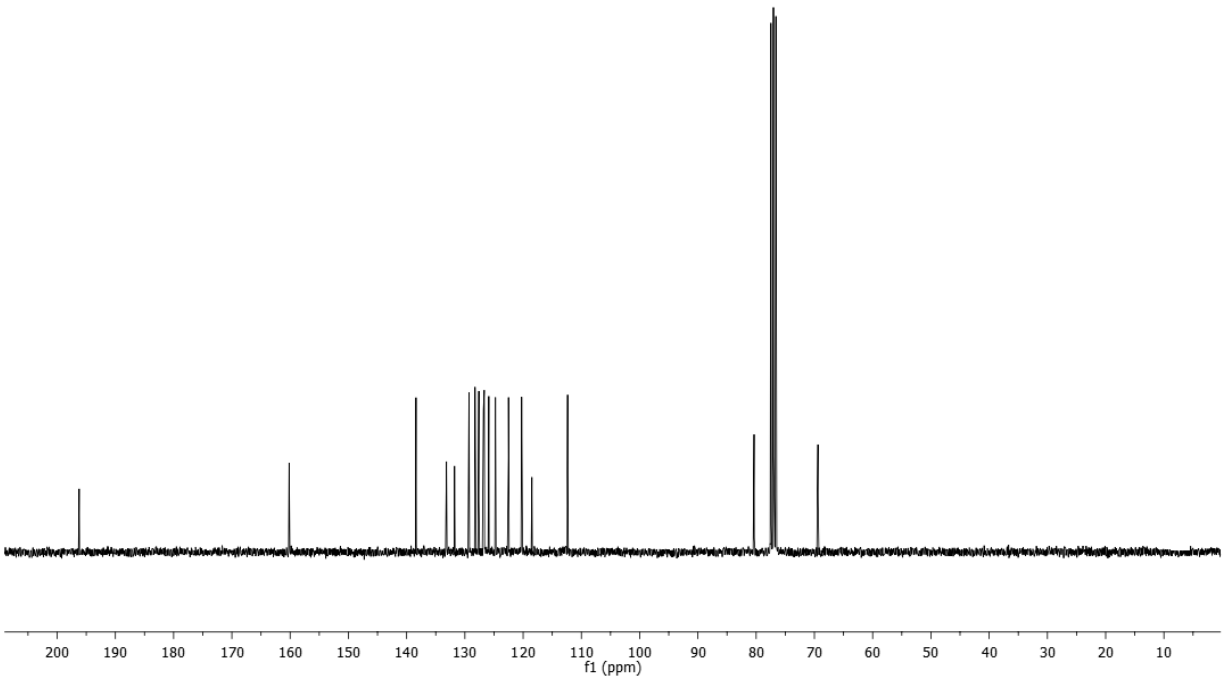
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

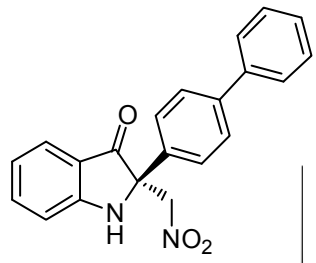

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O
N
H
NO2

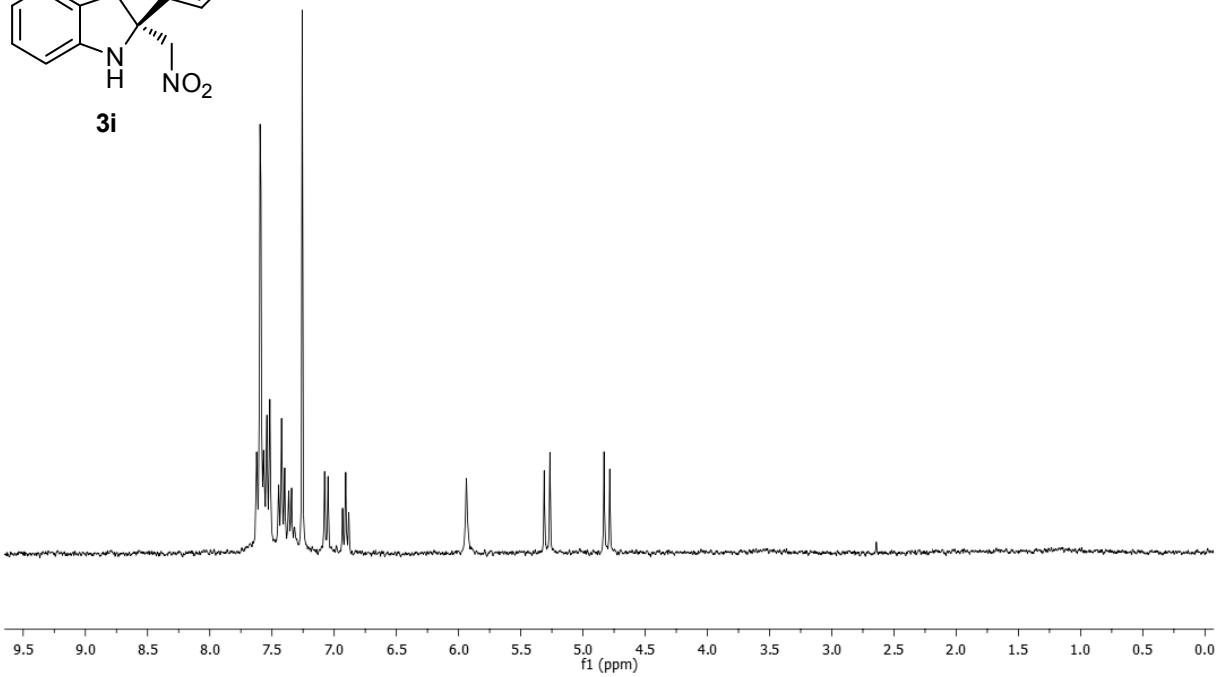
3h

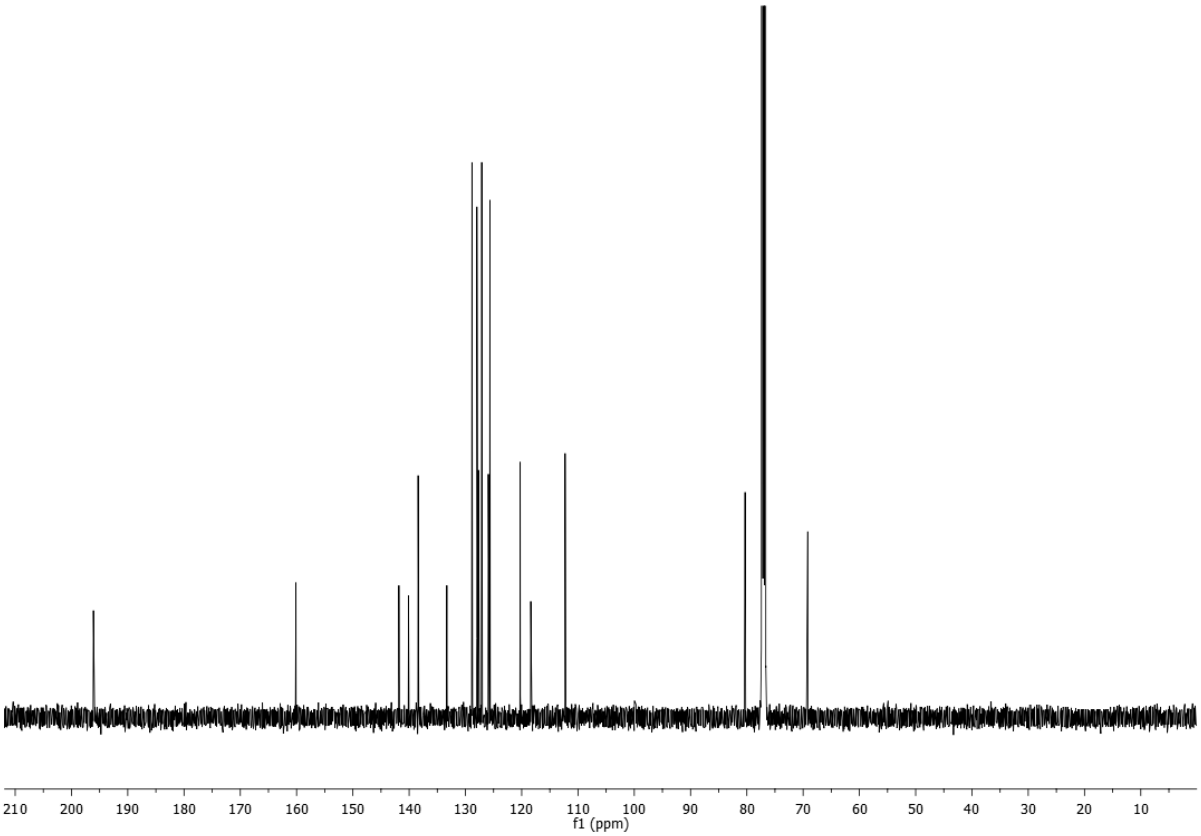

10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

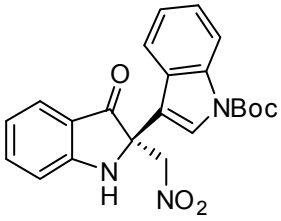

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


O
N
H
NO2

3i

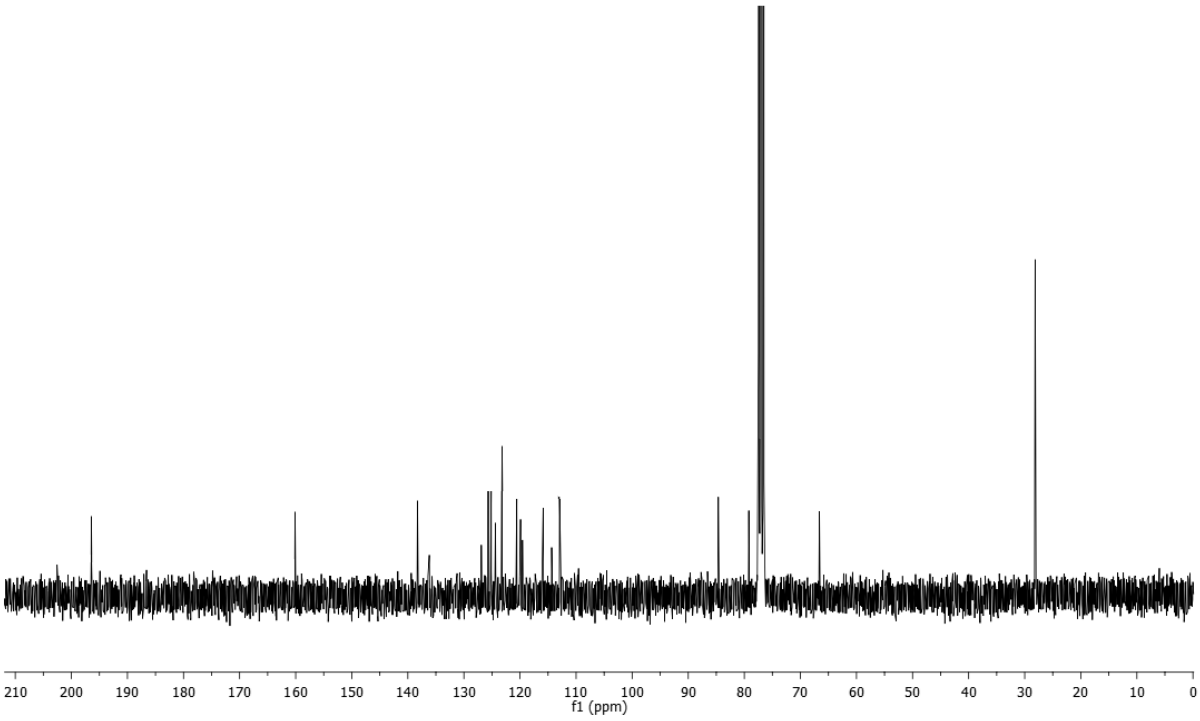

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

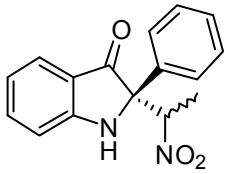

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


O
NBoc
N
H
NO2

3j

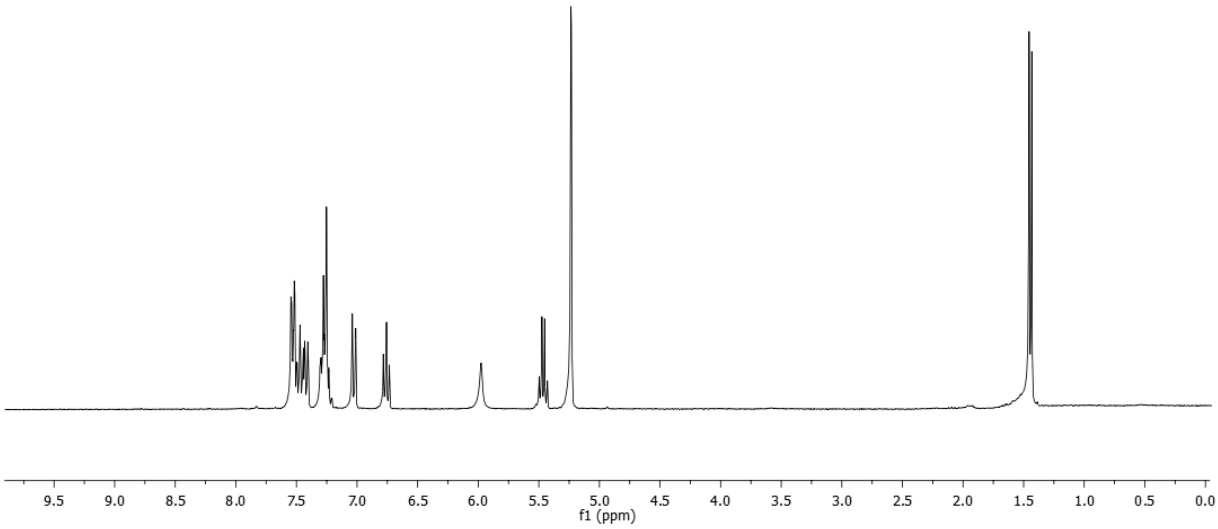
10
9
8
7
6
5
4
3
2
1
0
ppm

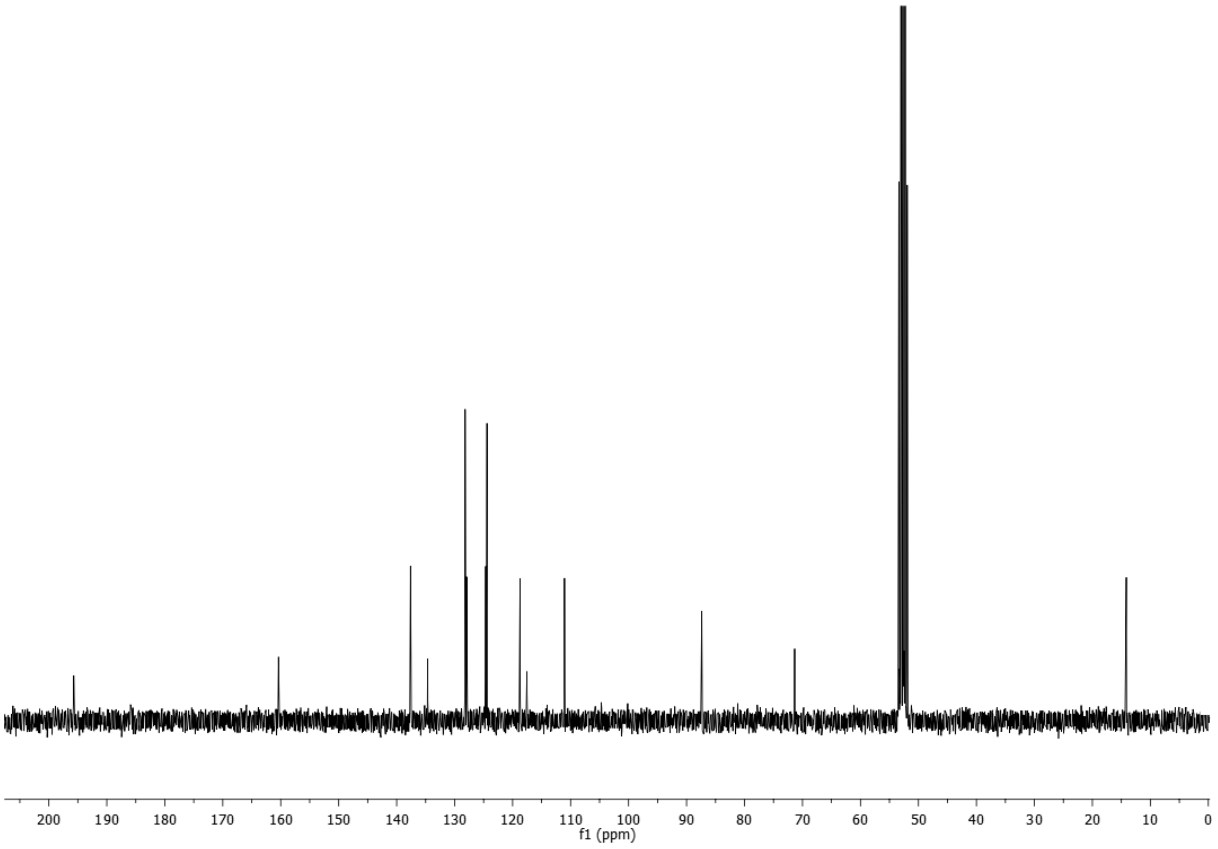

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

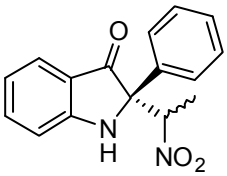


3k

Major diastereoisomer

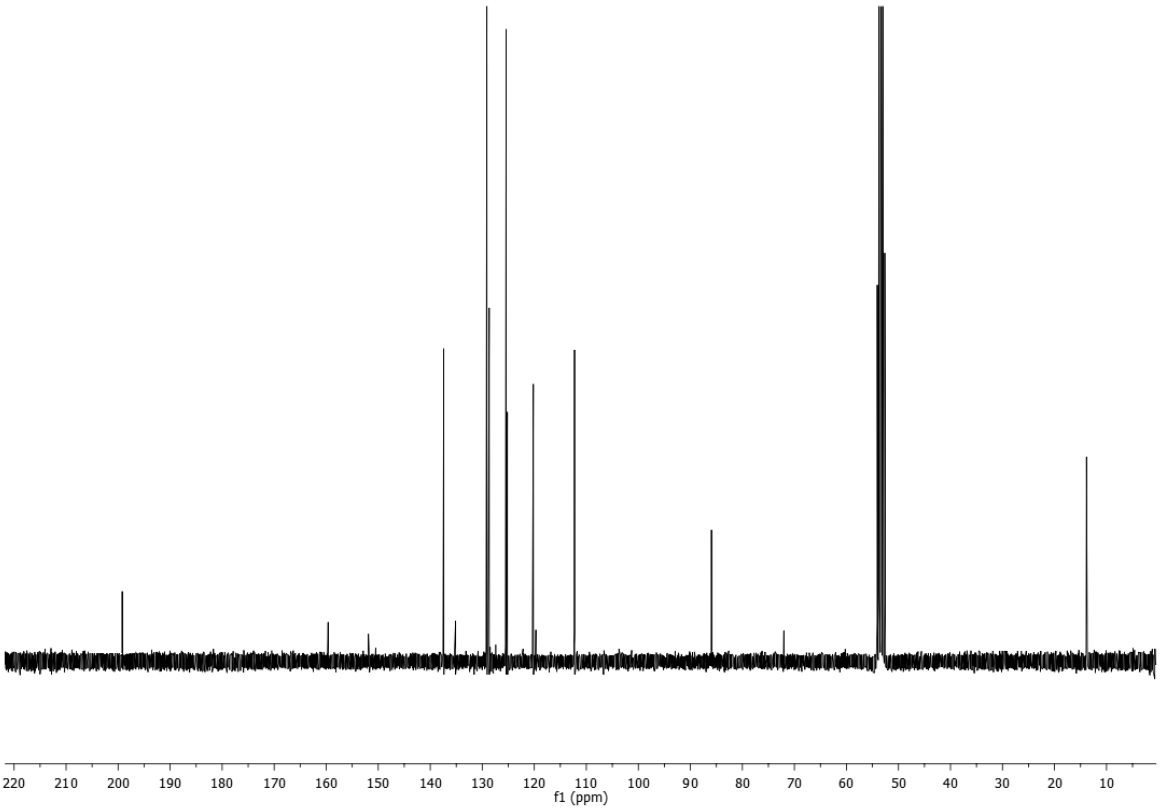


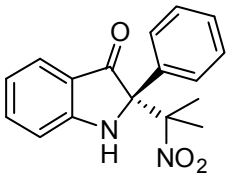




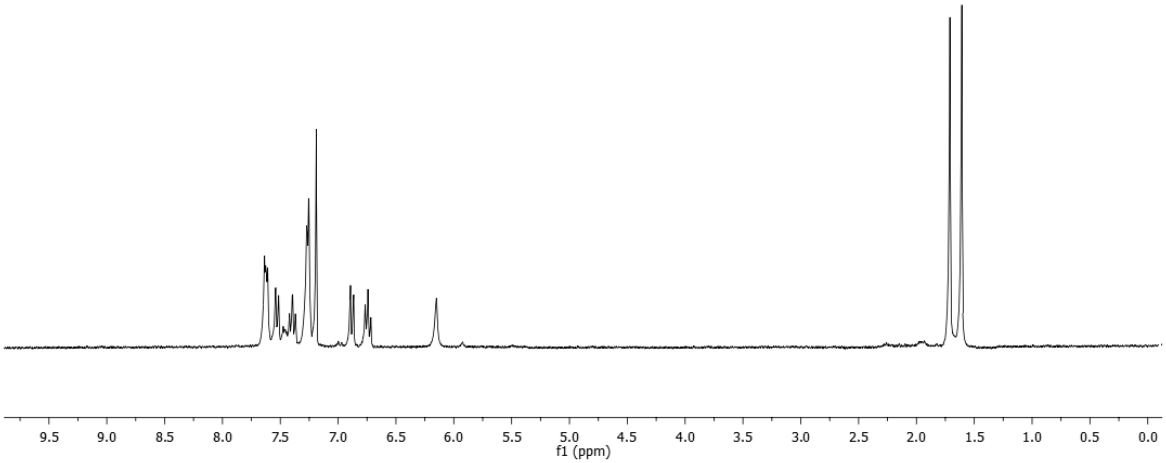
3k'

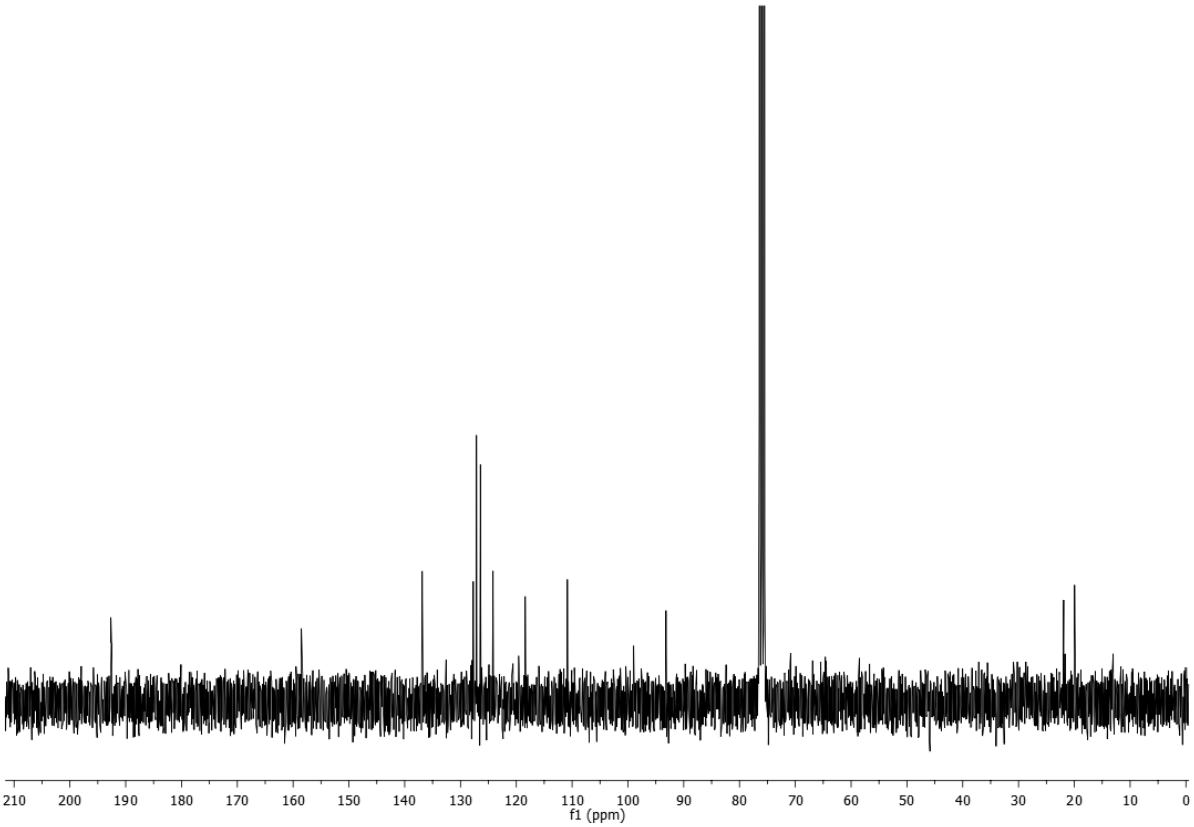
Minor diastereoisomer



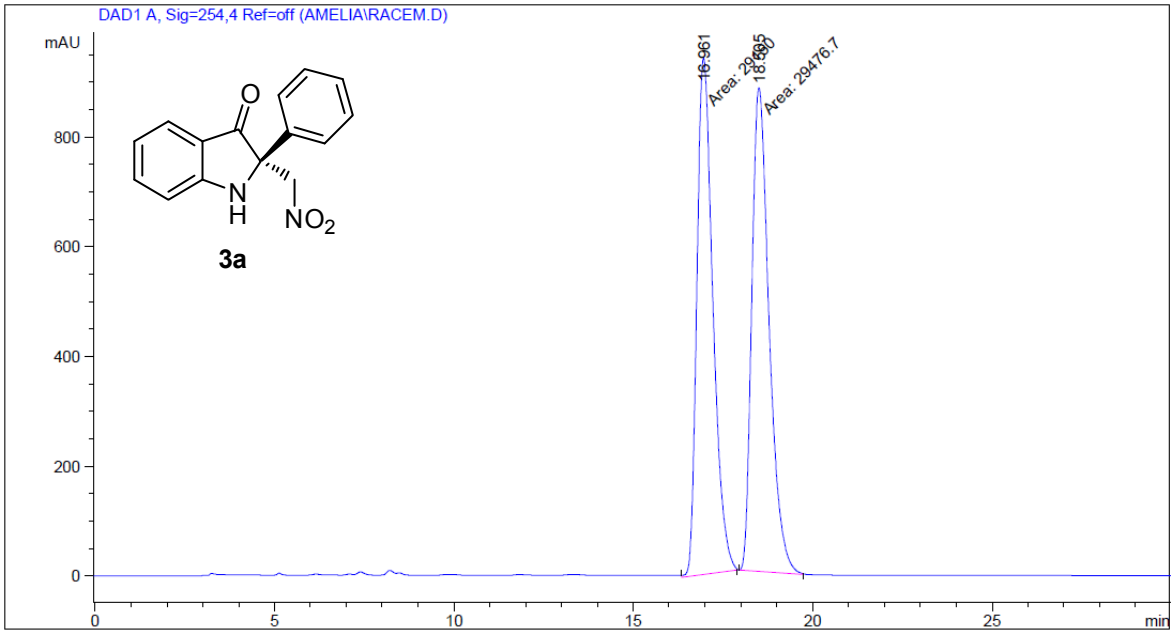

O
N
H
NO2

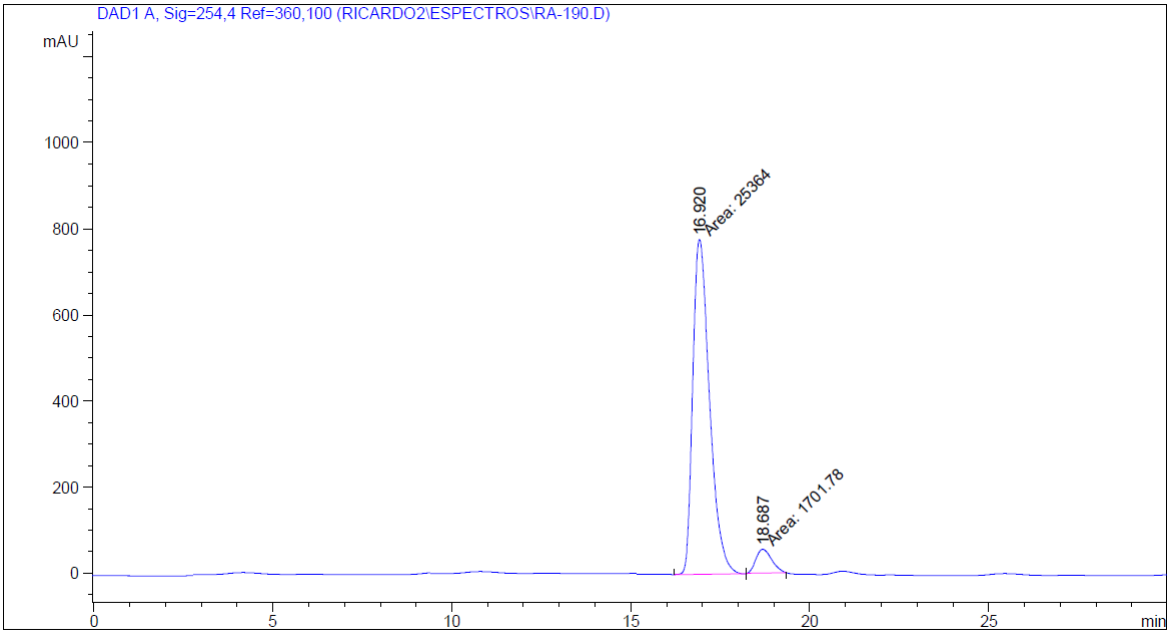
3l

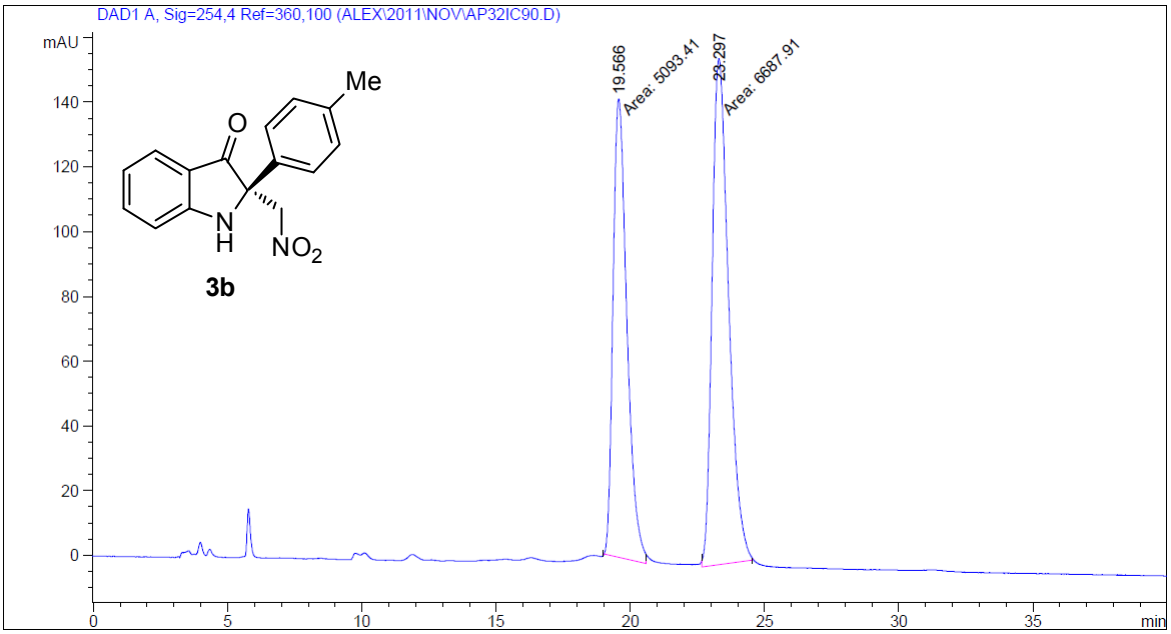

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

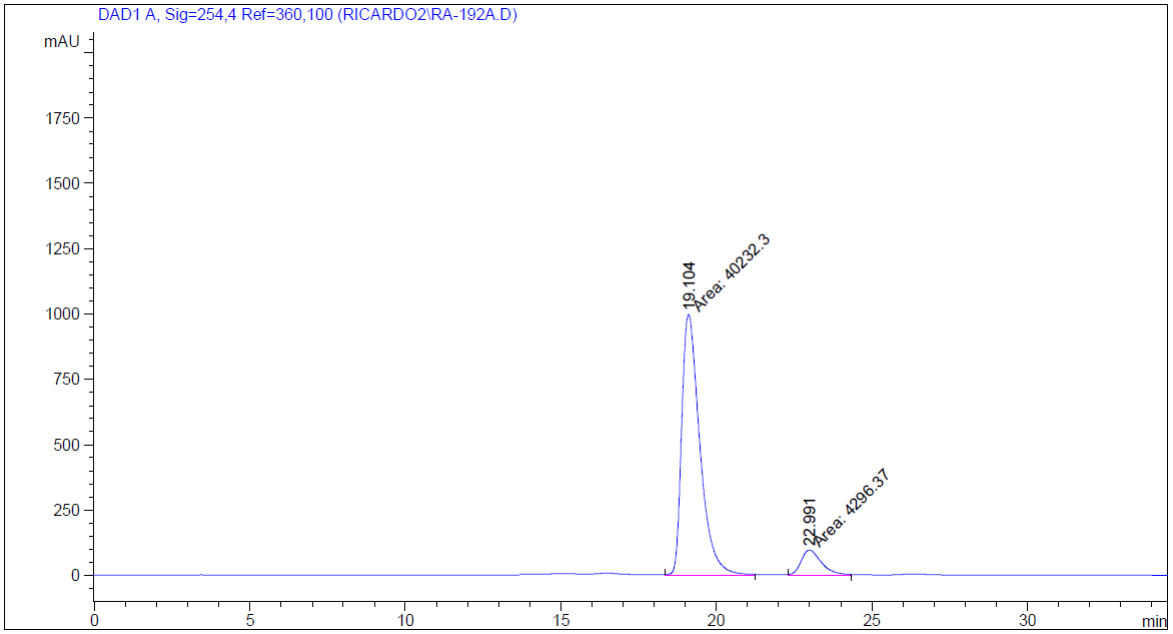

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

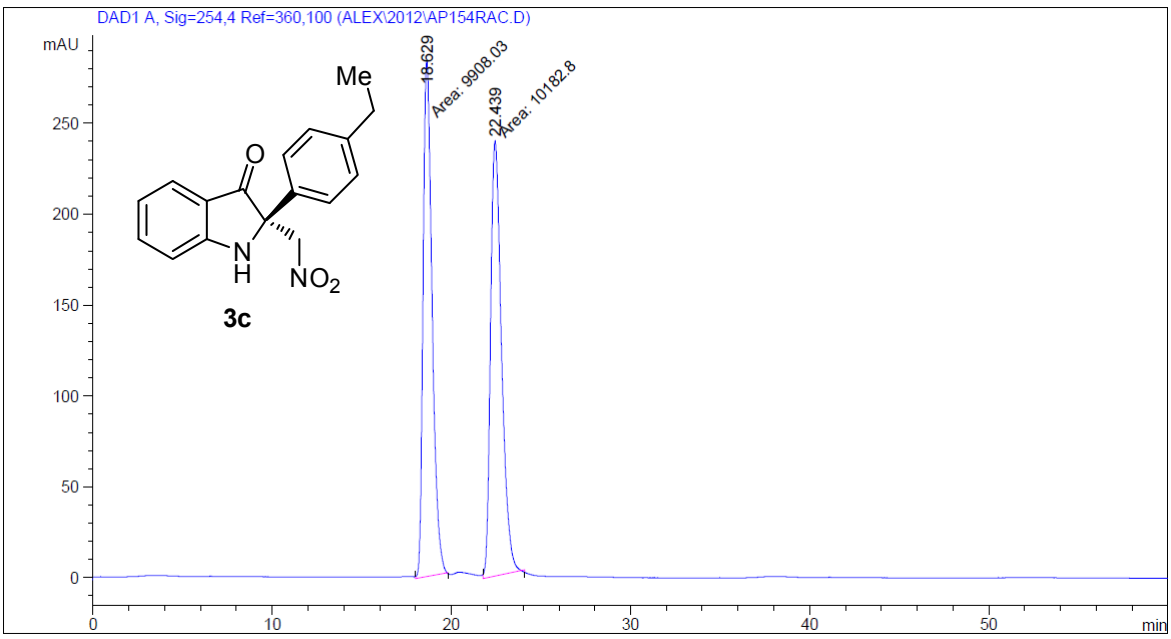
HPLC chromatograms of compound 3a-k

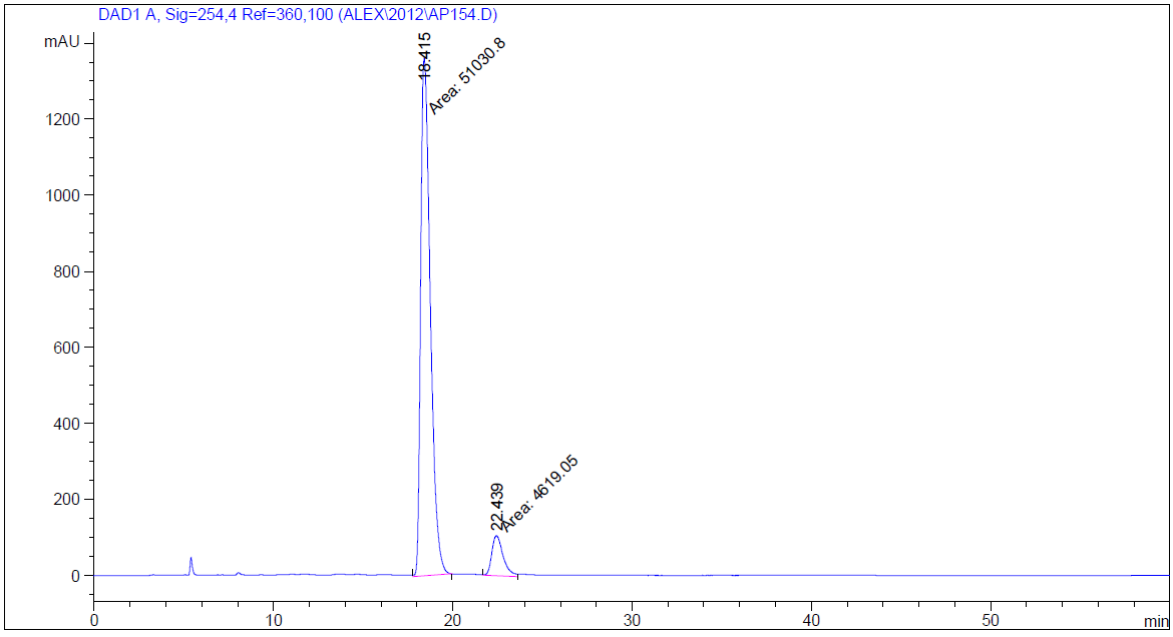


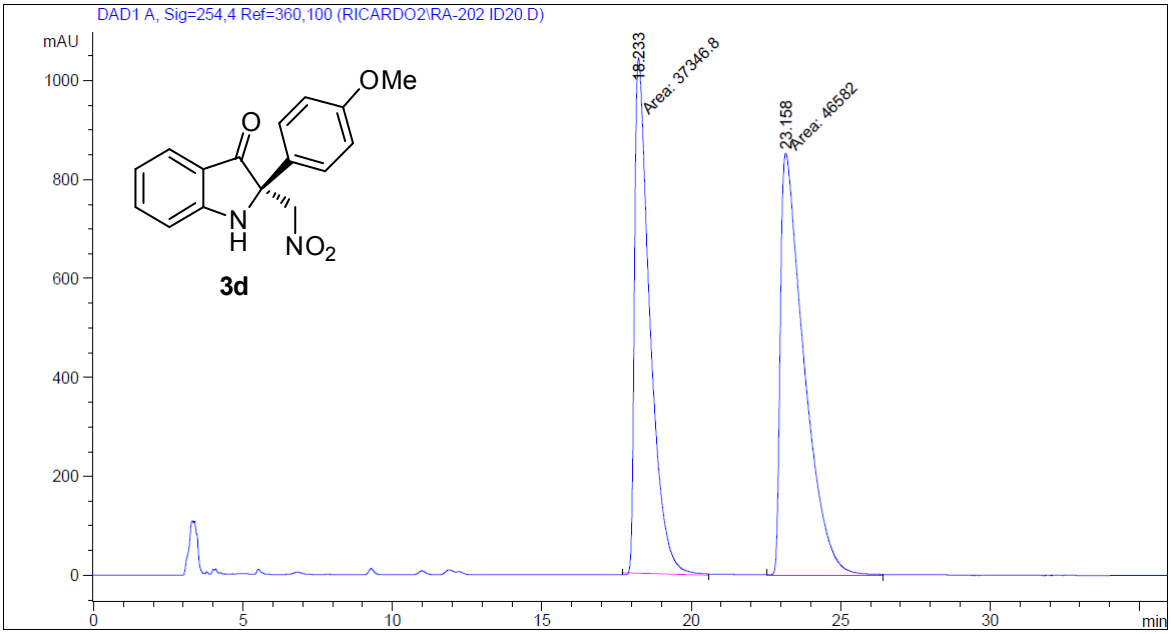


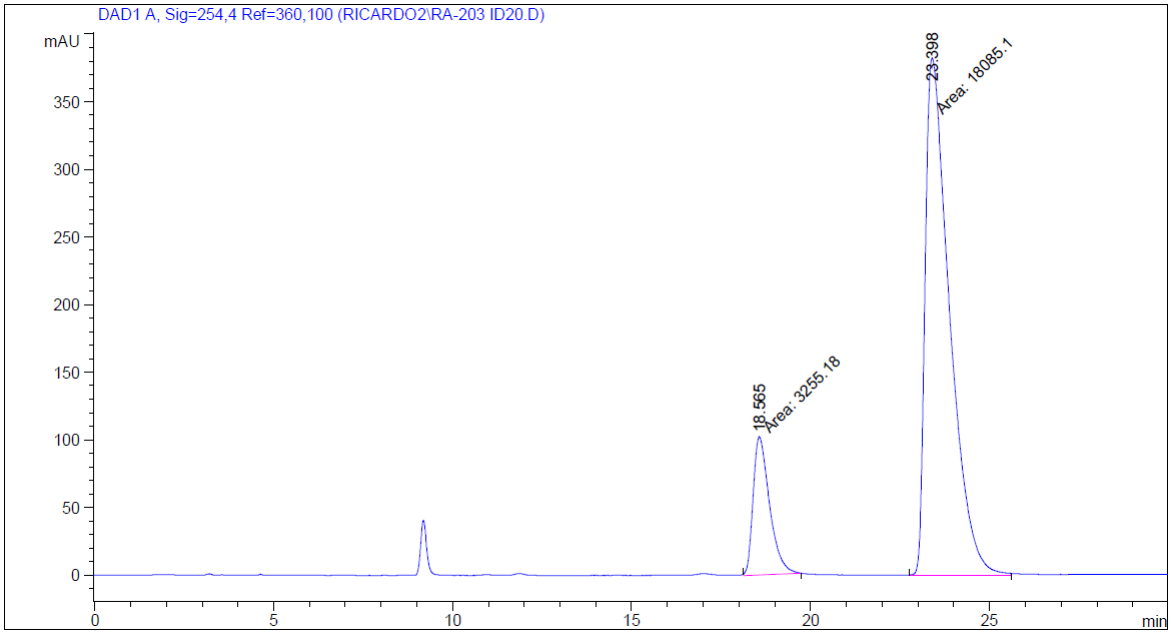

DAD1 A, Sig=254,4 Ref=360,100 (ALEX\2011\NOV\AP32IC90.D)
mAU
Me
O
N
H
NO2
3b
19.566
Area: 5093.41
23.297
Area: 6687.91
min

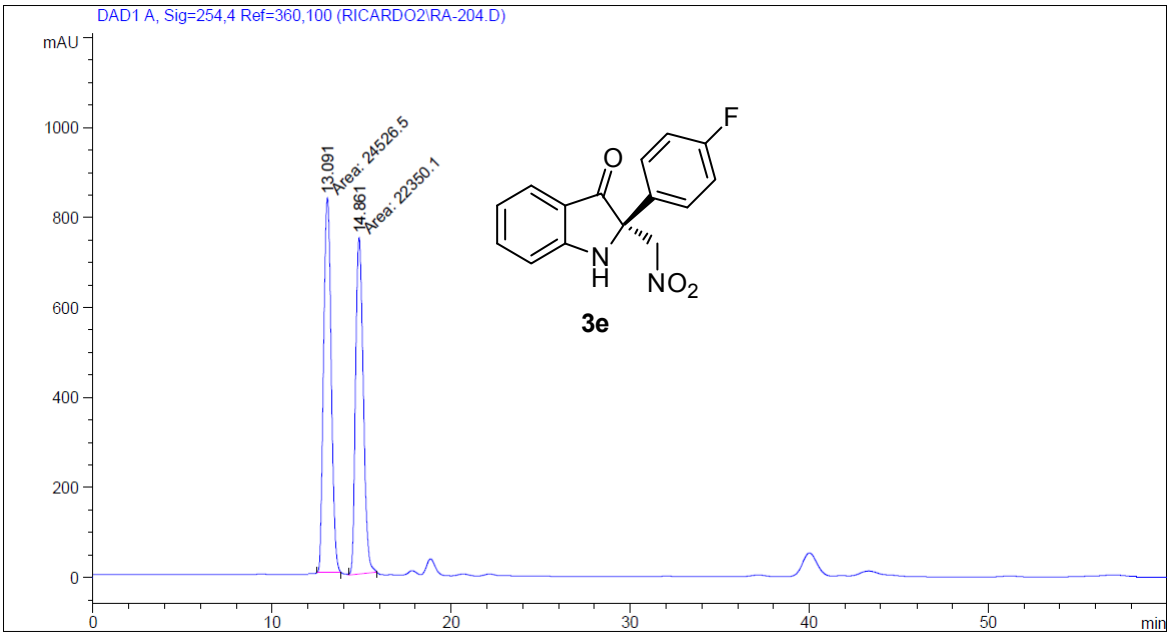

DAD1 A, Sig=254,4 Ref=360,100 (RICARDO2\RA-192A.D)
mAU
19.104
Area: 40232.3
22.991
Area: 4296.37
min


DAD1 A, Sig=254,4 Ref=360,100 (ALEX\2012\AP154RAC.D)
mAU
Me
O
N
H
NO2
3c
18.629
Area: 9908.03
22.439
Area: 10182.8
min

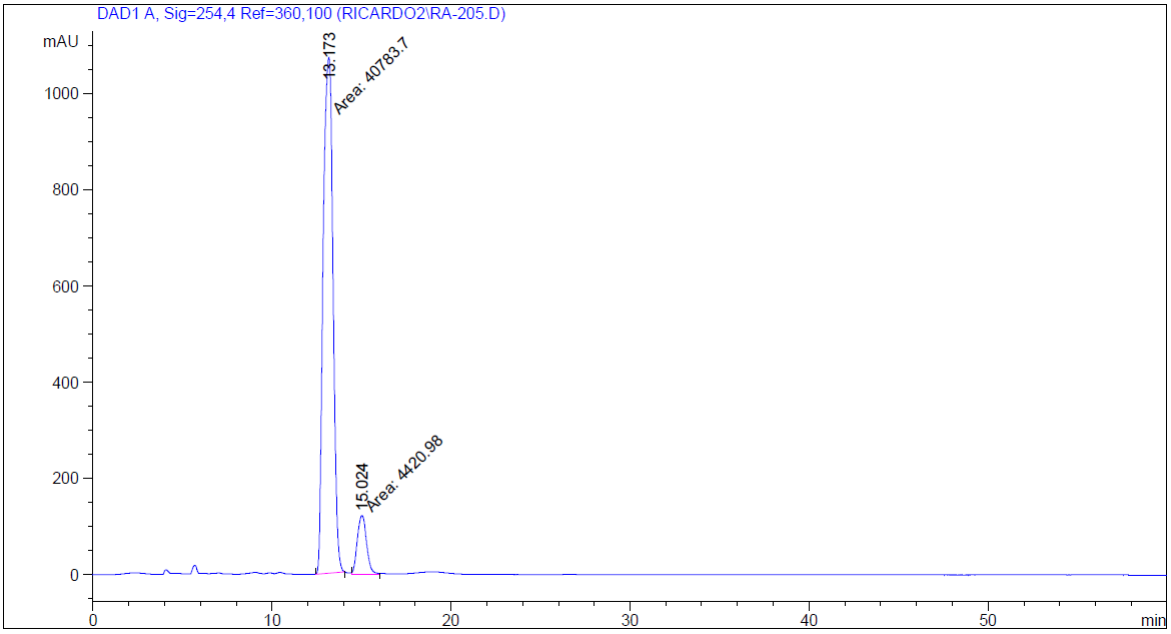

DAD1 A, Sig=254,4 Ref=360,100 (ALEX\2012\AP154.D)
mAU
18.415
Area: 51030.8
22.439
Area: 4619.05
min

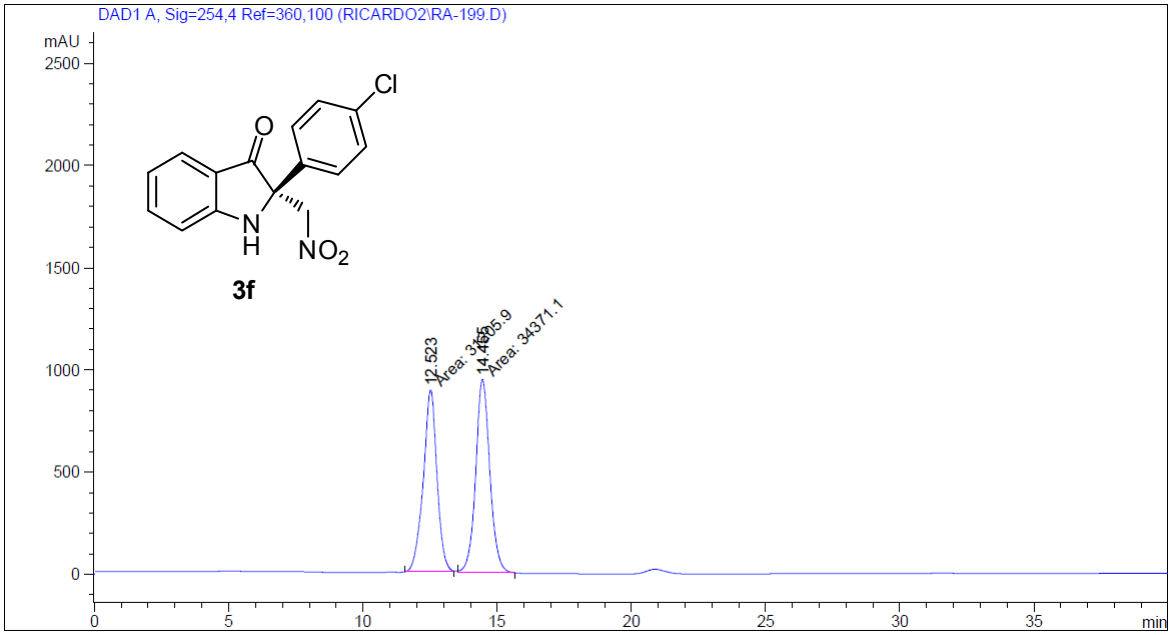

DAD1 A, Sig=254,4 Ref=360,100 (RICARDO2\RA-202 ID20.D)
mAU
1000
800
600
400
200
0
OMe
O
N
H
NO2
3d
18.233
Area: 37346.8
23.158
Area: 46582
0
5
10
15
20
25
30
min

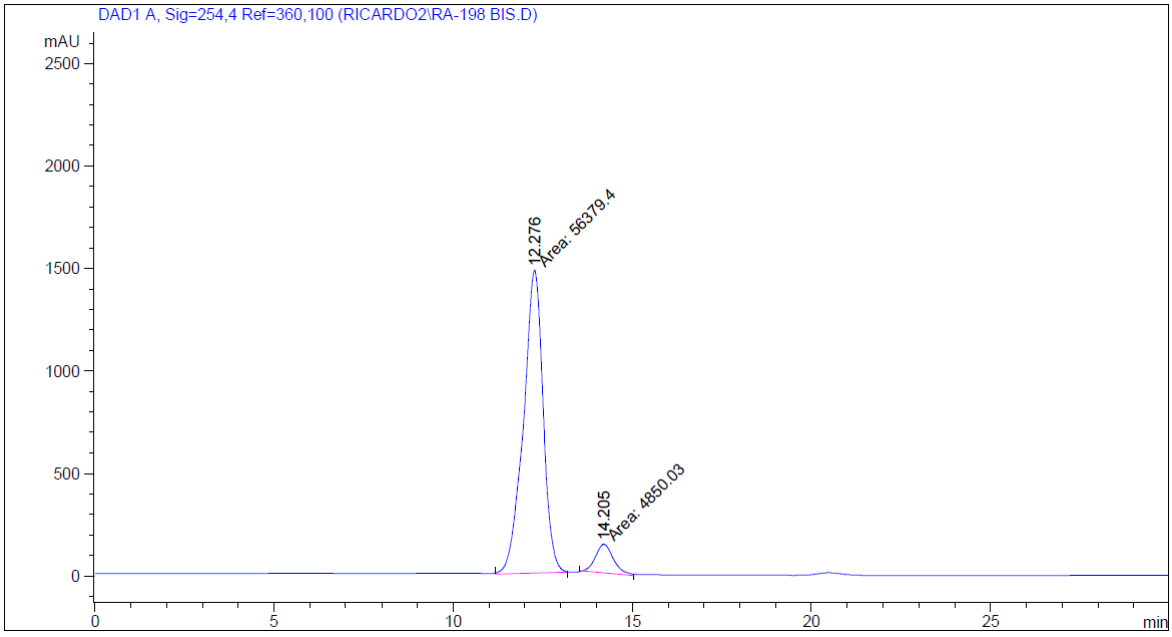

DAD1 A, Sig=254,4 Ref=360,100 (RICARDO2\RA-203 ID20.D)
mAU
350
300
250
200
150
100
50
0
18.565
Area: 3255.18
23.398
Area: 18085.1
0
5
10
15
20
25
min

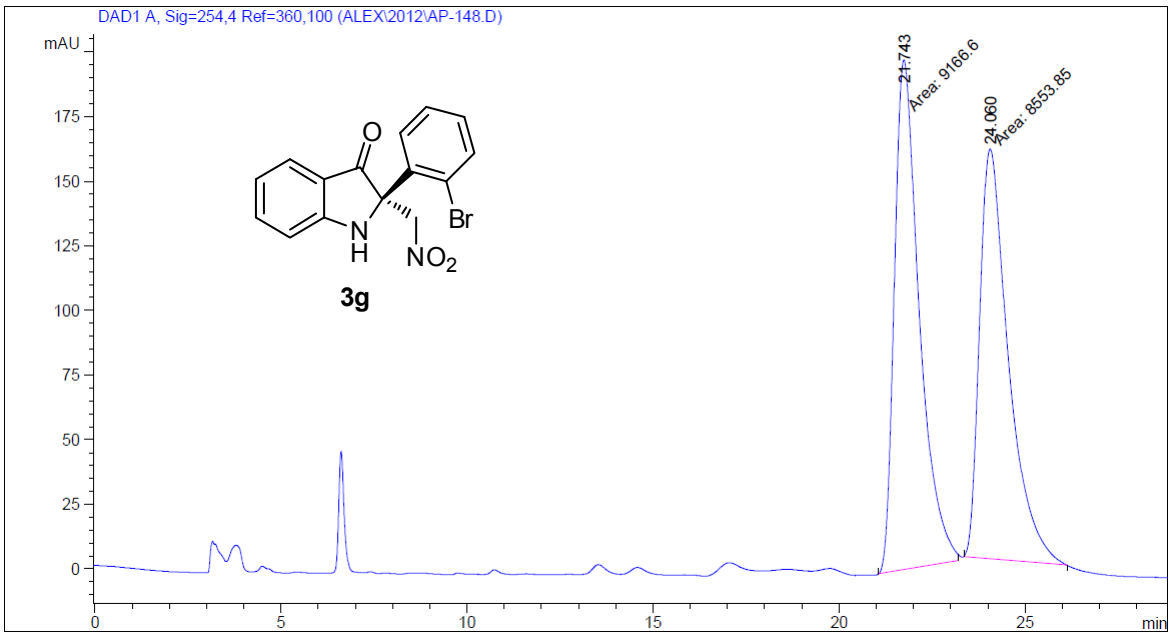

DAD1 A, Sig=254,4 Ref=360,100 (RICARDO2\RA-204.D)
mAU
1000
800
600
400
200
0
13.091
Area: 24526.5
14.861
Area: 22350.1
0
10
20
30
40
50
min
F
O
N
H
NO2

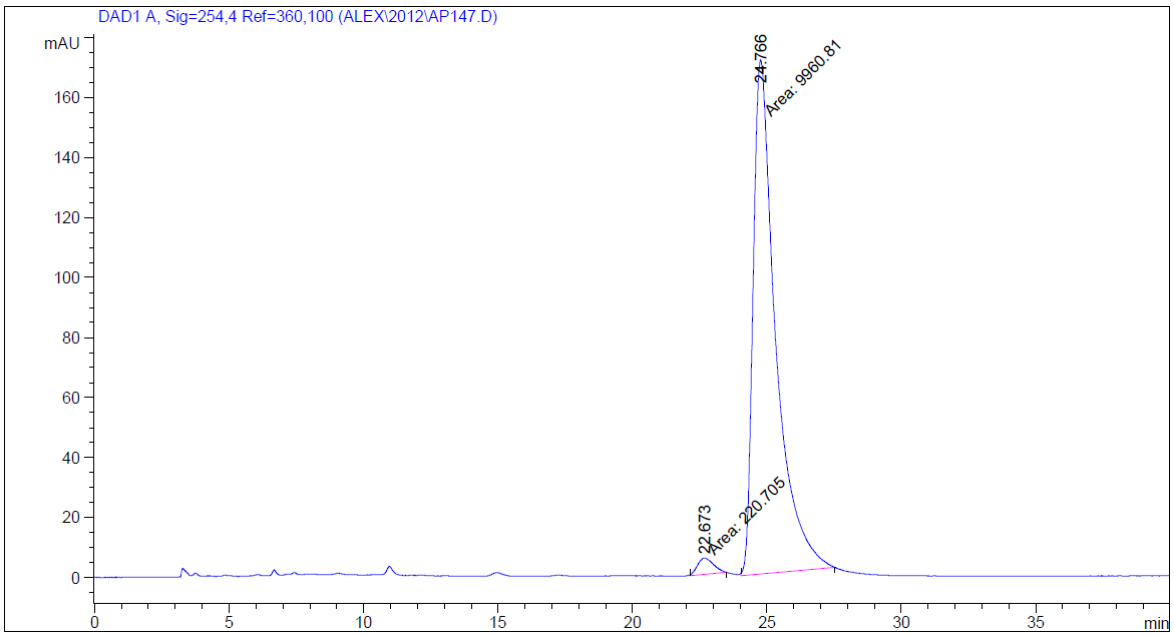
3e

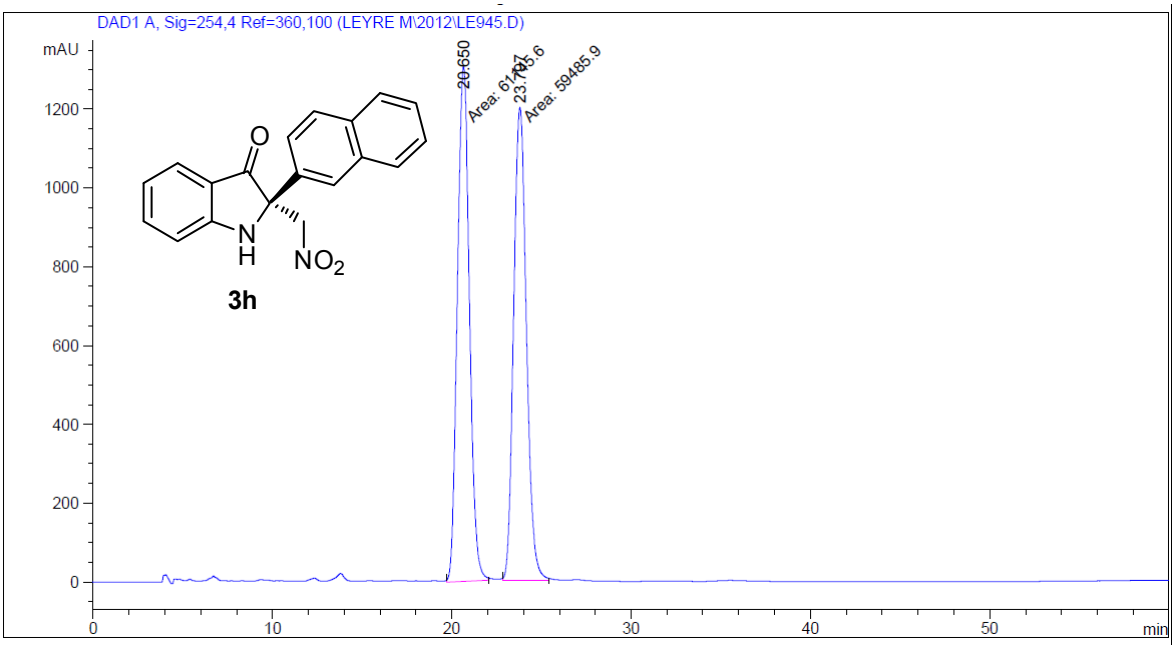

DAD1 A, Sig=254,4 Ref=360,100 (RICARDO2\RA-205.D)
mAU
1000
800
600
400
200
0
13.173
Area: 40783.7
15.024
Area: 4420.98
0
10
20
30
40
50
min

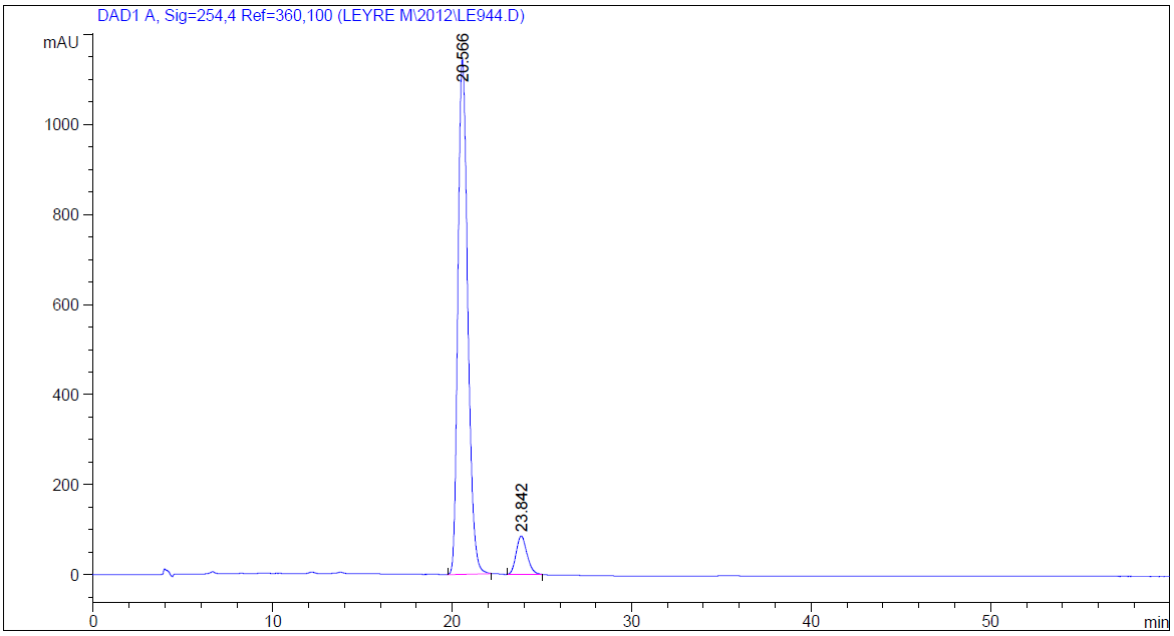

DAD1 A, Sig=254,4 Ref=360,100 (RICARDO2\RA-199.D)
mAU
2500
2000
1500
1000
500
0
Cl
O
N
H
NO2
3f
12.523
Area: 3165.9
14.465
Area: 34371.1
0
5
10
15
20
25
30
35
min

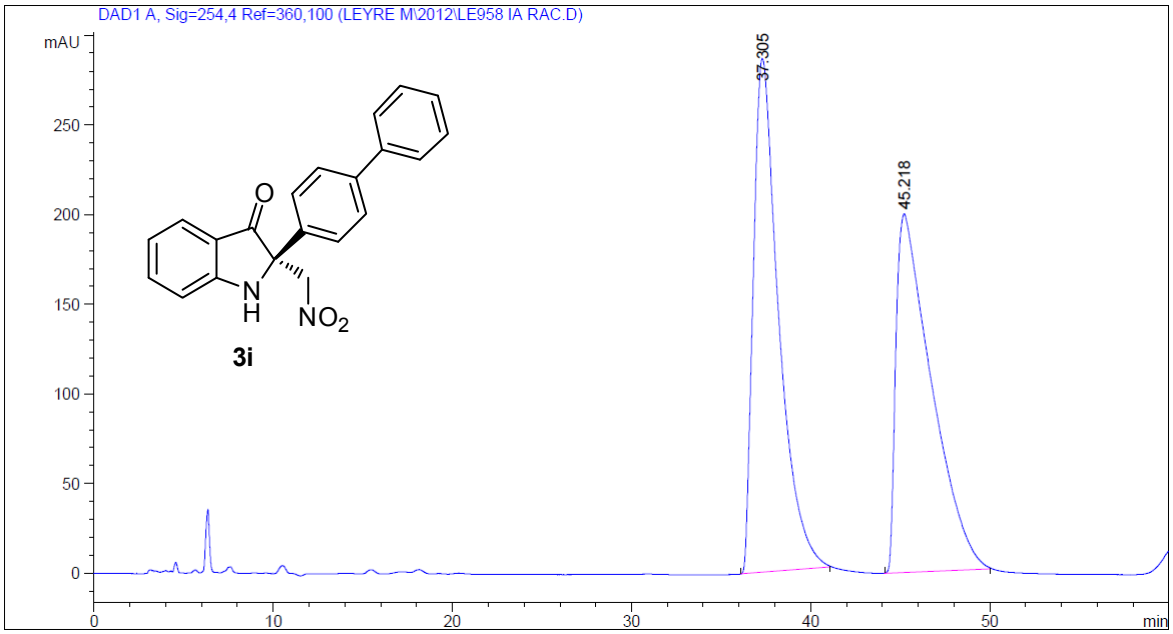

DAD1 A, Sig=254,4 Ref=360,100 (RICARDO2\RA-198 BIS.D)
mAU
2500
2000
1500
1000
500
0
12.276
Area: 56379.4
14.205
Area: 4850.03
0
5
10
15
20
25
min


DAD1 A, Sig=254,4 Ref=360,100 (ALEX\2012\AP-148.D)
mAU
21.743
Area: 9166.6
24.060
Area: 8553.85
O
N
H
Br
NO2
3g
min

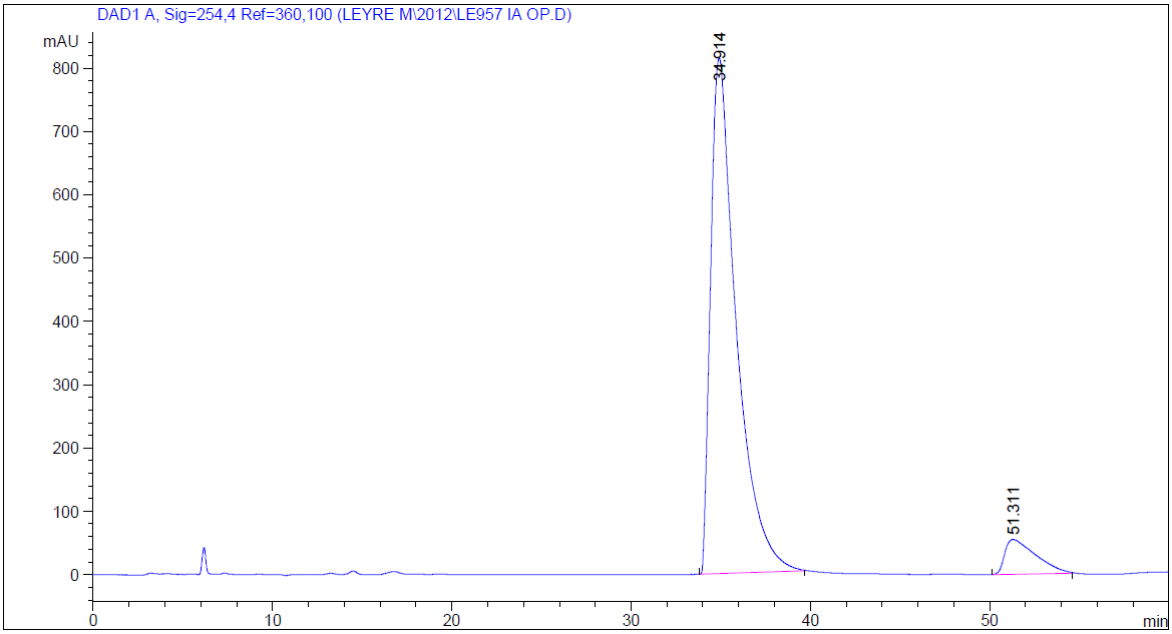

DAD1 A, Sig=254,4 Ref=360,100 (ALEX\2012\AP147.D)
mAU
24.766
Area: 9960.81
22.673
Area: 220.705
min

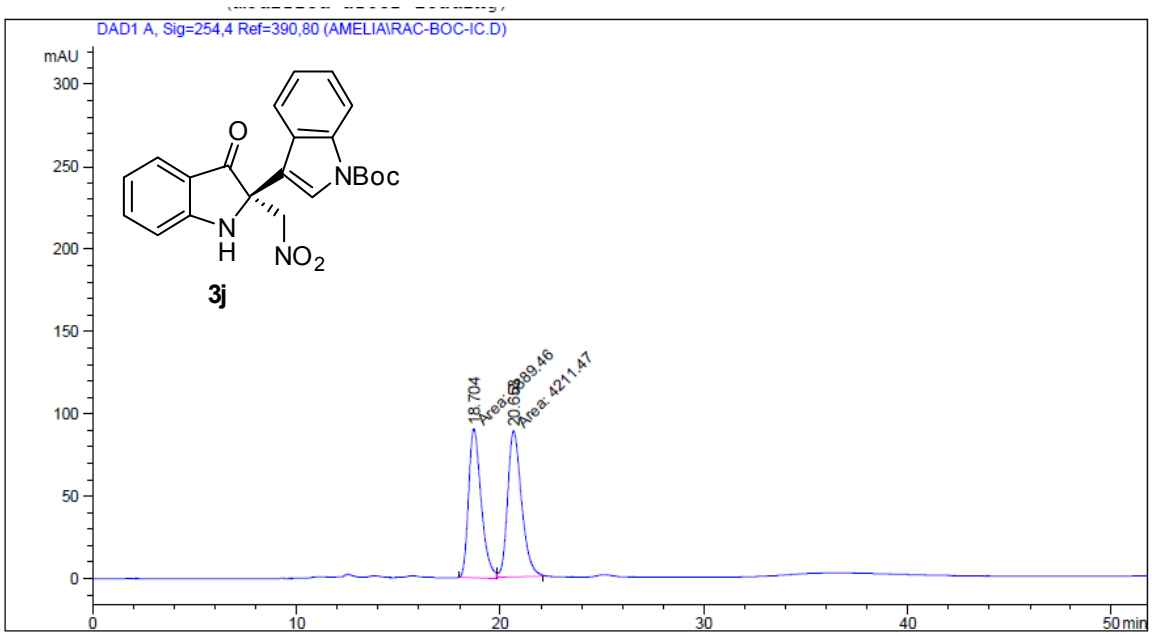

DAD1 A, Sig=254,4 Ref=360,100 (LEYRE M\2012\LE945.D)
mAU
1200
1000
800
600
400
200
0
20.650
Area: 61781
23.765
Area: 59485.9
O
N
H
NO2
3h
0
10
20
30
40
50
min

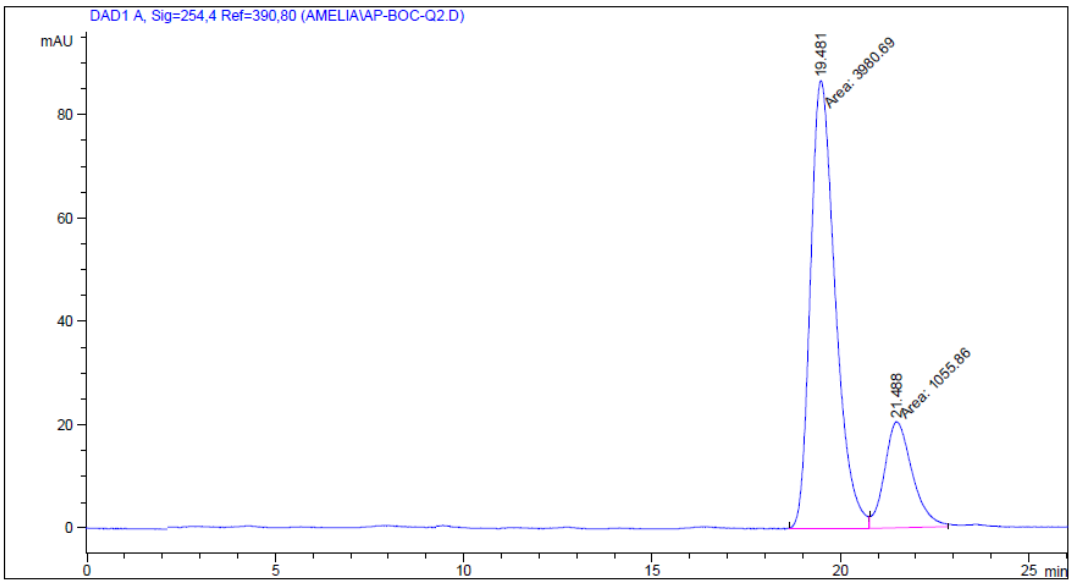

DAD1 A, Sig=254,4 Ref=360,100 (LEYRE M\2012\LE944.D)
mAU
1000
800
600
400
200
0
20.566
23.842
0
10
20
30
40
50
min

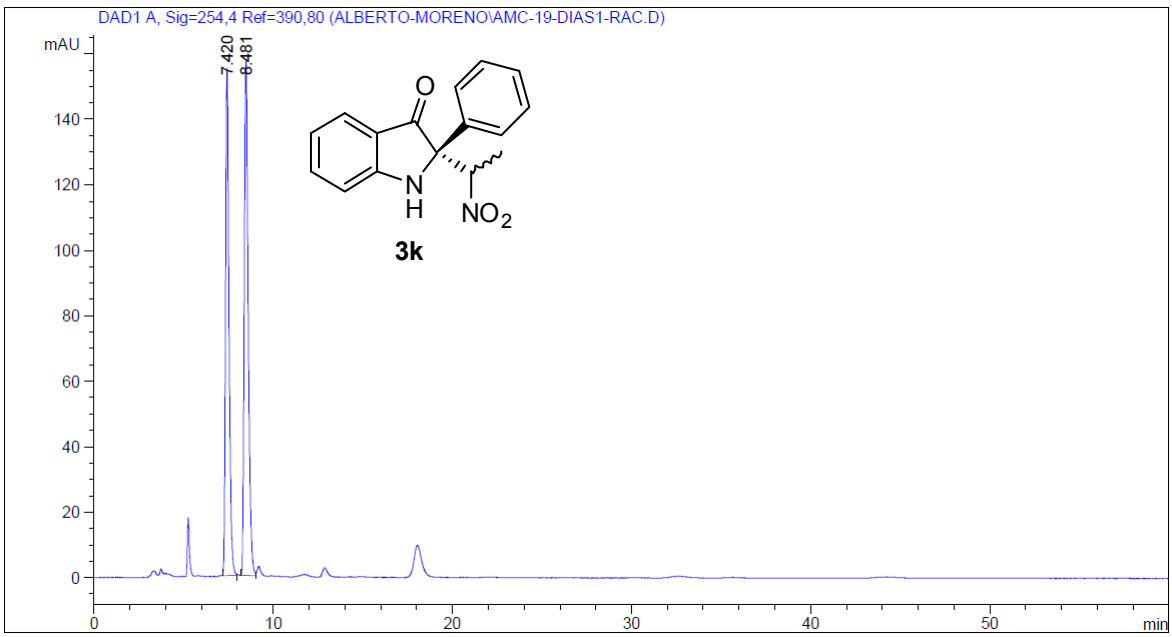

DAD1 A, Sig=254,4 Ref=360,100 (LEYRE M\2012\LE958 IA RAC.D)
mAU
250
200
150
100
50
0
37.305
45.218
0
10
20
30
40
50
min
O
N
H
NO2

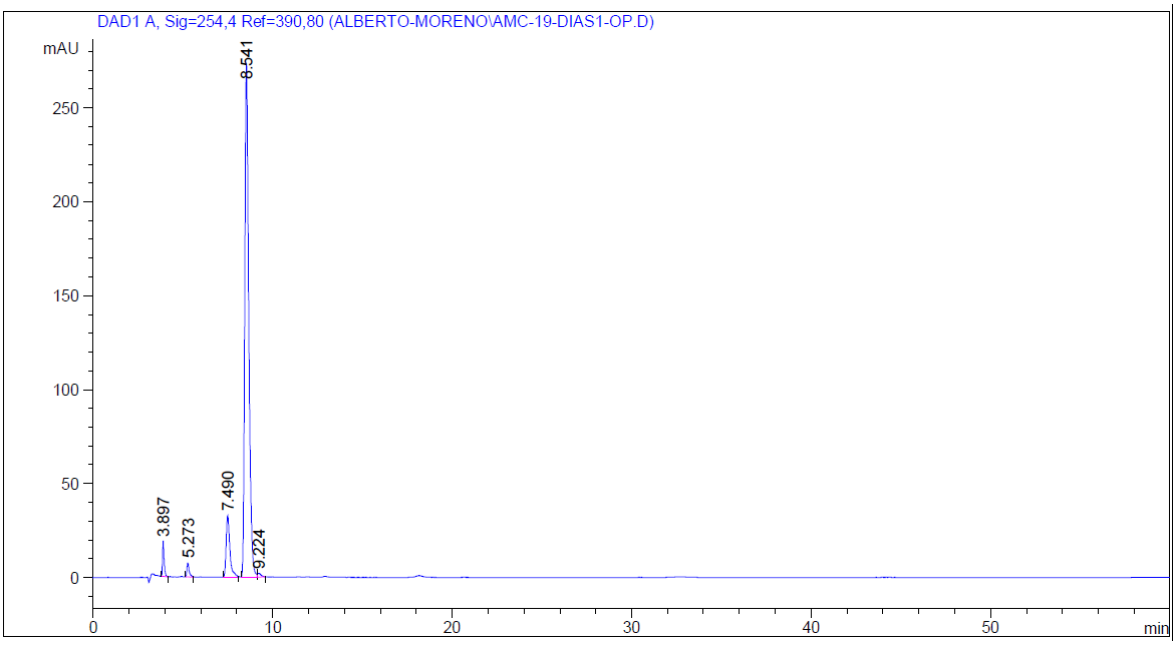
3i

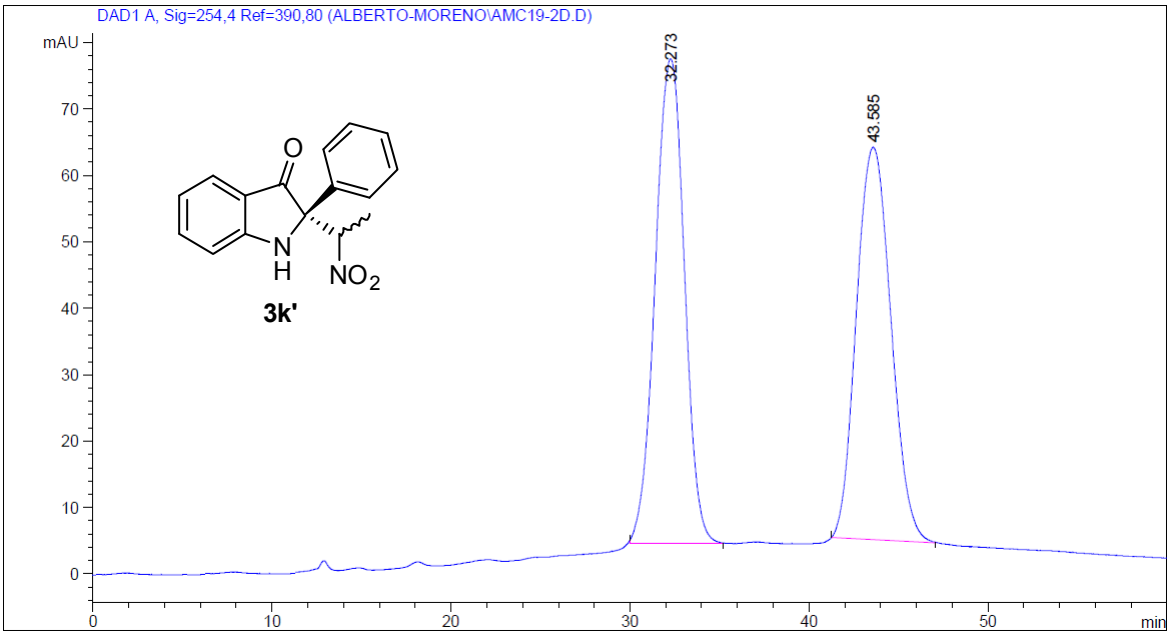

DAD1 A, Sig=254,4 Ref=360,100 (LEYRE M\2012\LE957 IA OP.D)
mAU
800
700
600
500
400
300
200
100
0
34.914
51.311
0
10
20
30
40
50
min

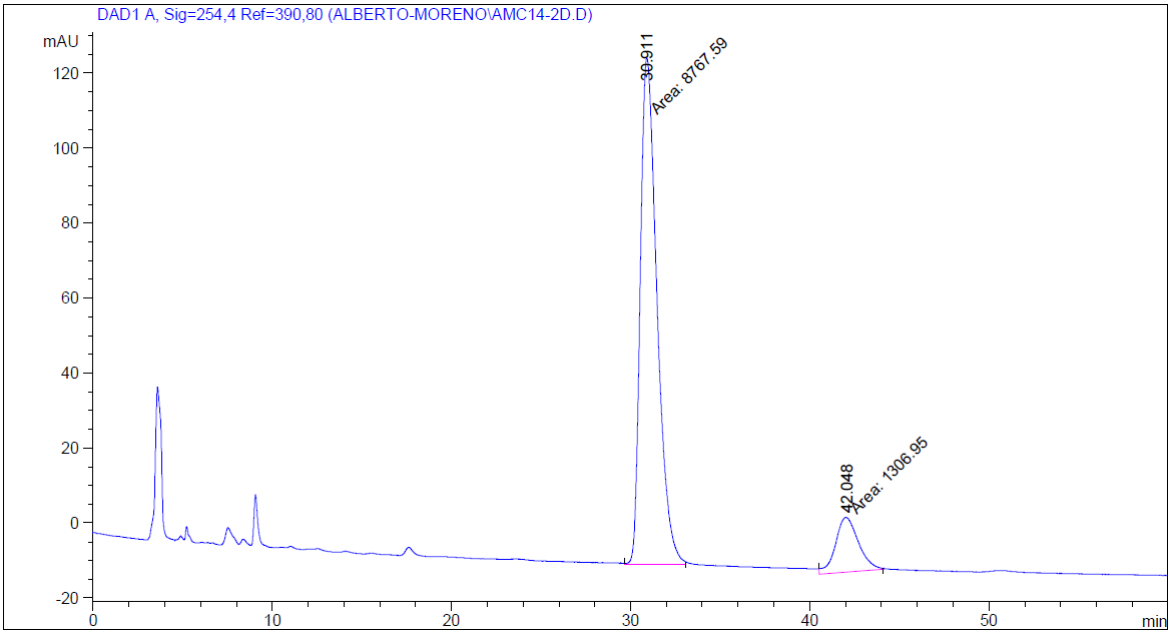

DAD1 A, Sig=254,4 Ref=390,80 (AMELIA\RAC-BOC-IC.D)
mAU
300
250
200
150
100
50
0
O
NBoc
N
H
NO2
3j
18.704
Area: 3889.46
20.658
Area: 4211.47
0
10
20
30
40
50 min

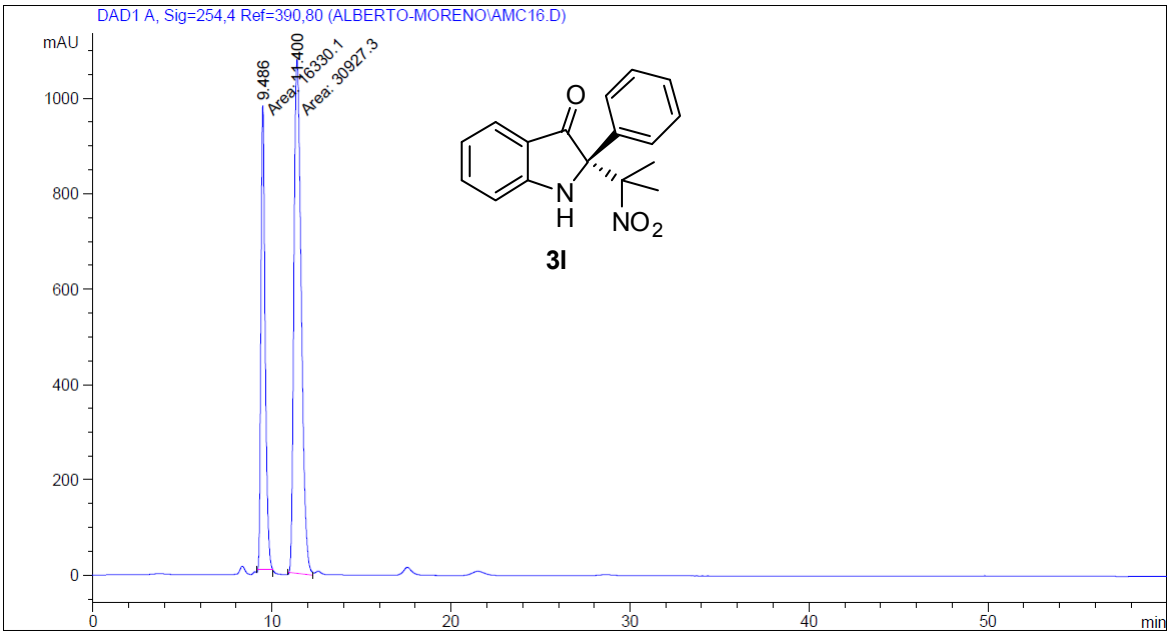

DAD1 A, Sig=254,4 Ref=390,80 (AMELIA\AP-BOC-Q2.D)
mAU
80
60
40
20
0
19.481
Area: 3980.69
21.488
Area: 1055.86
0
5
10
15
20
25 min

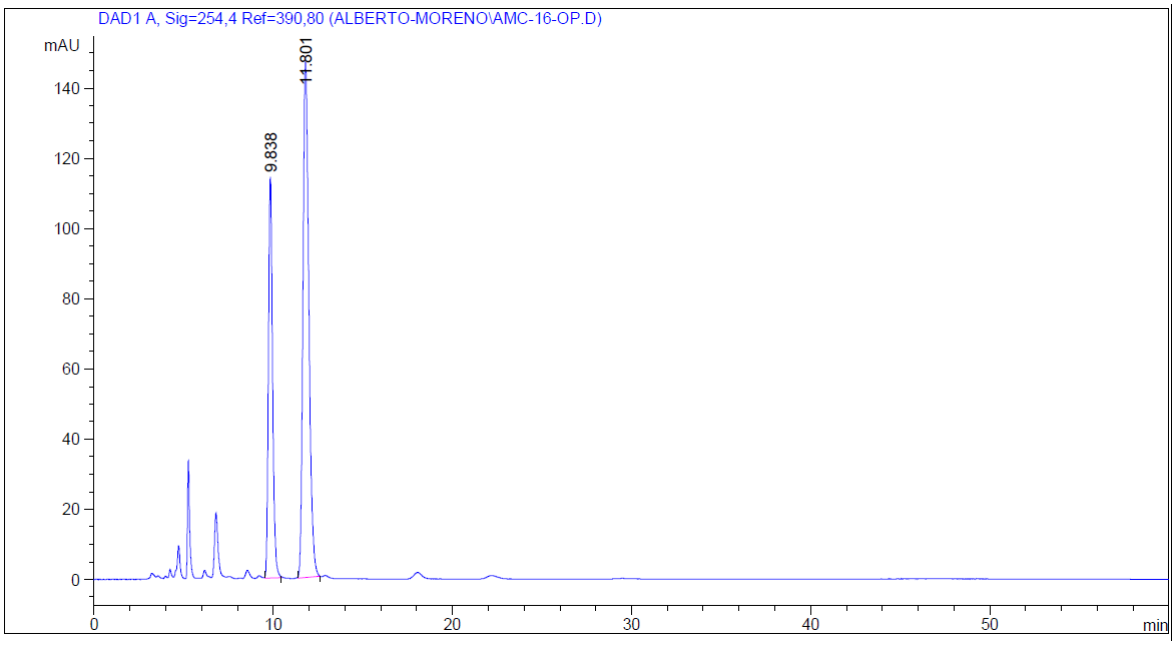

DAD1 A, Sig=254,4 Ref=390,80 (ALBERTO-MORENO\AMC-19-DIAS1-RAC.D)
mAU
7.420
8.481
O
N
H
NO2
3k
0
20
40
60
80
100
120
140
0
10
20
30
40
50
min


DAD1 A, Sig=254,4 Ref=390,80 (ALBERTO-MORENO\AMC-19-DIAS1-OP.D)
mAU
8.541
3.897
5.273
7.490
9.224
0
50
100
150
200
250
0
10
20
30
40
50
min


DAD1 A, Sig=254,4 Ref=390,80 (ALBERTO-MORENO\AMC19-2D.D)
mAU
32.273
43.585
O
N
H
NO2
3k'
min


DAD1 A, Sig=254,4 Ref=390,80 (ALBERTO-MORENO\AMC14-2D.D)
mAU
39.911
Area: 8767.59
42.048
Area: 1306.95
min


DAD1 A, Sig=254,4 Ref=390,80 (ALBERTO-MORENO\AMC16.D)
mAU
9.486
Area: 11400
16330.1
Area: 30927.3
O
N
H
NO2
3l
min


DAD1 A, Sig=254,4 Ref=390,80 (ALBERTO-MORENO\AMC-16-OP.D)
mAU
9.838
11.801
min

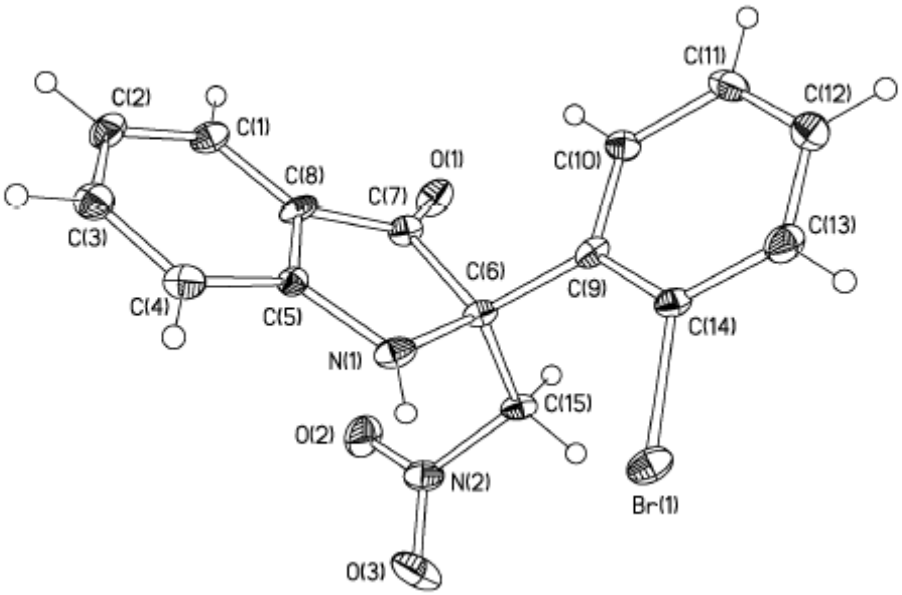


Figure 1. ORTEP of the compound **3g.**[4]

[4] The structure of a compound derived **3g** was determined by X-ray crystal analysis. Complete structural data have been deposited at the CCDC (CCDC 884937).