Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.
This journal is © The Royal Society of Chemistry 2017

Bifunctional Catalysis in the Stereocontrolled Synthesis of Tetrahydro-1,2-oxazines

Marek Moczulski, Piotr Drelich and Łukasz Albrecht*

Institute of Organic Chemistry

Department of Chemistry, Lodz University of Technology

Zeromskiego 116, 90-924 Łódź, Poland

e-mail: lukasz.albrecht@p.lodz.pl

http://www.a-teamlab.p.lodz.pl

1. General methods

NMR spectra were acquired on a Bruker Ultra Shield 700 instrument, running at 700 MHz for ^{1}H and 176 MHz for ^{13}C, respectively. Chemical shifts (δ) are reported in ppm relative to residual solvent signals ($CDCl_3$: 7.26 ppm for ^{1}H NMR, 77.16 ppm for ^{13}C NMR). Mass spectra were recorded on a Bruker Maxis Impact spectrometer using electrospray (ES+) ionization (referenced to the mass of the charged species). Optical rotations were measured on a Perkin-Elmer 241 polarimeter and $[\alpha]_D$ values are given in deg•cm•g^{-1}•dm^{-1}; concentration *c* is listed in g•(100 mL)$^{-1}$. Analytical thin layer chromatography (TLC) was performed using pre-coated aluminum-backed plates (Merck Kieselgel 60 F254) and visualized by ultraviolet irradiation or $KMnO_4$ or phosphamolybdic acid stain. The enantiomeric ratio (er) of the products was determined by chiral stationary phase HPLC (Daicel Chiralpak IA). Unless otherwise noted, analytical grade solvents and commercially available reagents were used without further purification. For flash chromatography (FC) silica gel (Silica gel 60, 230-400 mesh, Fluka). Methyl (*E*)-4-(aminooxy)but-2-enoate, **1a** and **1b** were synthetized according to the literature procedure.[1] *N*-(Allyloxy)-2-nitrobenzenesulfonamide was synthetized according to the literature procedure.[2]

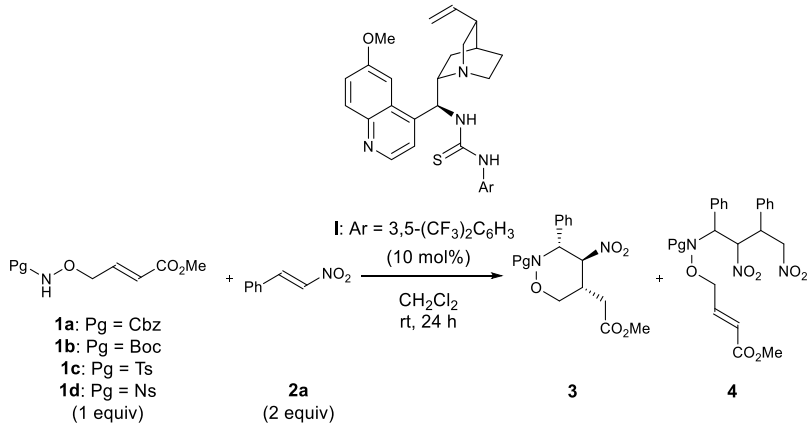
[1] P. Drelich, M. Moczulski and Ł. Albrecht, *Org. Lett.* 2017, **19**, 3143.
[2] P. A. Reddya, O. F. Schalla, J. R. Wheatleya, L. O. Rosika, J. P. McClurga, G. R. Marshalla and U. Slomczynska, *Synthesis* 2001, **7**, 1086.

2. Screening results

General procedure

In an ordinary 4 mL glass vial, equipped with a teflon-coated magnetic stirring bar and a screw cap, catalyst **5** (0.1 equiv, 0.01 mmol) and the corresponding aminooxylating reagent **1** (1. equiv, 0.2 mmol) were dissolved in a solvent (0.1 – 0.8 mL). After 5 min., nitroolefin **2a** (2 equiv, 0.4 mmol) was added and stirring was maintained for 24-48 h at given temperature. Reaction mixture was directly subjected to flash chromatography on silica gel (eluent: hexanes/ethyl acetate 70:30) to obtain pure product **3** which was subsequently analyzed by HPLC.

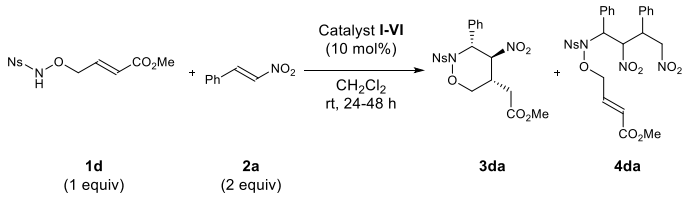
Aminooxylating reagent 1 screening

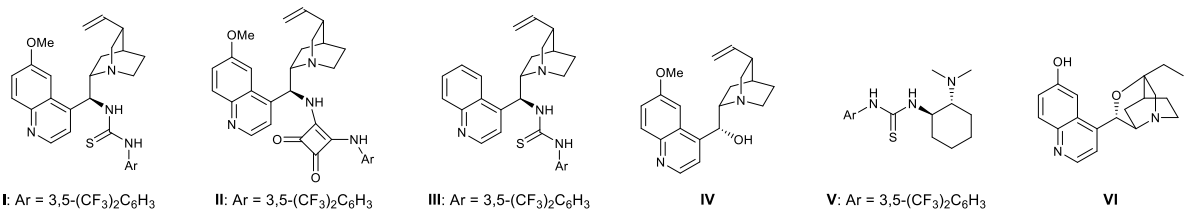


	Pg	Conv.[b] [%]	**3**:**4** ratio	dr[c]	er[d]
1	Cbz	>95	>99:1	3:1	>99.5:0.5
2	Boc	80	>99:1	2:1	>99.5:0.5
3	Ts	95	82:18	>20:1	>99.5:0.5
4	Ns	83	91:9	>20:1	>99.5:0.5

[a] Reactions performed on 0.1 mmol scale using **1a-d** (1 equiv) and **2a** (2 equiv) in 0.2 mL of the CH_2Cl_2. [b] As determined by ^{1}H NMR of a crude reaction mixture after 24 h. [c] Determined by ^{1}H NMR of a crude reaction mixture. [d] Determined by a chiral stationary phase HPLC.

Catalyst 5 screening

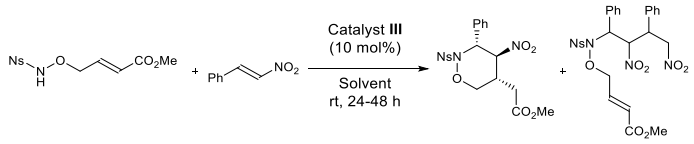




	Cat.	Conv.[b] [%]	**3da**:**4da** ratio	dr[c]	er[d]
1	**I**	83 (92)	91:9	>20:1	>99.5:0.5
2	**II**	66 (72)	67:33	>20:1	>99.5:0.5
3	**III**	86 (94)	93:7	>20:1	>99.5:0.5
4	**IV**	55 (65)	83:17	2:1	>99.5:0.5
5	**V**	91	86:14	>20:1	>99.5:0.5
6	**VI**	12 (17)	75:25	2:1	nd

[a] Reactions performed on 0.1 mmol scale using **1d** (1 equiv) and **2a** (2 equiv) in 0.2 mL of the CH_2Cl_2. [b] As determined by ^{1}H NMR of a crude reaction mixture after 24 h, in parenthesis after 48 h. [c] Determined by ^{1}H NMR of a crude reaction mixture after 48h. [d] Determined by a chiral stationary phase HPLC.

Solvent screening

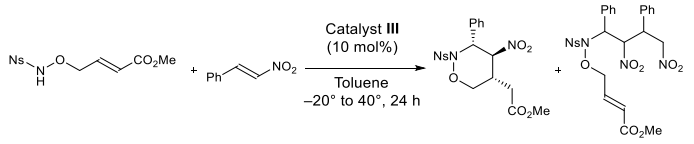


1d (1 equiv) **2a** (2 equiv) **3da** **4da**

	Solvent	Conv.[b] [%]	**3da**:**4da** ratio	dr[c]	er[d]
1	CH_2Cl_2	86 (94)	93:7	>20:1	>99.5:0.5
2	THF	21 (80)	91:9	>20:1	>99.5:0.5
3	$CHCl_3$	76 (79)	86:14	>20:1	>99.5:0.5
4	Et_2O	75 (76)	92:8	>20:1	>99.5:0.5
5	CH_3CN	49 (80)	75:25	17:1	>99.5:0.5
6	*i*PrOH	18 (20)	86:14	8:1	nd
7	CCl_4	89 (92)	90:10	>20:1	>99.5:0.5
8	1,4-Dioxane	45 (55)	90:10	>20:1	>99.5:0.5
9	Toluene	96 (97)	96:4	>20:1	>99.5:0.5

[a] Reactions performed on 0.1 mmol scale using **1d** (1 equiv) and **2a** (2 equiv) in 0.2 mL of the solvent. [b] As determined by ^{1}H NMR of a crude reaction mixture after 2 4h, in parenthesis after 48 h. [c] Determined by ^{1}H NMR of a crude reaction mixture after 48 h. [d] Determined by a chiral stationary phase HPLC.

Temperature experiments

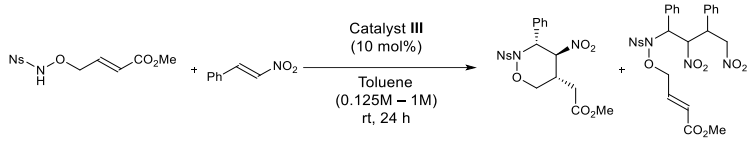


1d (1 equiv) **2a** (2 equiv) **3da** **4da**

	Temp. [˚C]	Conv.[b] [%]	**3da**:**4da** ratio	dr[c]	er[d]
1	rt	96 (97)	96:4	>20:1	>99.5:0.5
2	-20	85 (93)	80:20	>20:1	>99.5:0.5
3	0	94 (96)	92:8	>20:1	>99.5:0.5
4	40	85 (92)	93:7	>20:1	>99.5:0.5

[a] Reactions performed on 0.1 mmol scale using **1d** (1 equiv) and **2a** (2 equiv) in 0.2 mL of the solvent. [b] As determined by ^{1}H NMR of a crude reaction mixture after 24 h, in parenthesis after 48 h. [c] Determined by ^{1}H NMR of a crude reaction mixture after 48 h. [d] Determined by a chiral stationary phase HPLC.

Dilution experiments



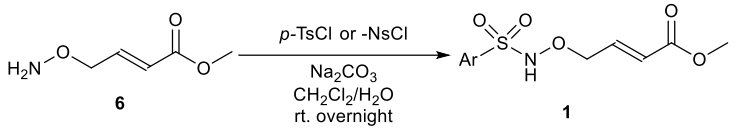
1d (1 equiv) **2a** (2 equiv) **3da** **4da**

	Conc. [M]	Conv.[f]	**3da**:**4da** ratio	dr[g]	er[h]
1	0.125[b]	86 (99)	98:2	>20:1	>99.5:0.5
2	0.25[c]	95 (98)	97:3	>20:1	>99.5:0.5
3	0.5[d]	94 (96)	96:4	>20:1	>99.5:0.5
4	1[e]	95 (>99)	94:6	>20:1	>99.5:0.5

[a] Reactions performed on 0.1 mmol scale using **1d** (1 equiv) and **2a** (2 equiv) [b] in 0.8 mL of the solvent [c] in 0.4 mL of the solvent [d] in 0.2 mL of the solvent [e] in 0.1 mL of the solvent. [f] As determined by ^{1}H NMR of a crude reaction mixture after 24 h, in parenthesis after 48 h. [g] Determined by ^{1}H NMR of a crude reaction mixture after 48 h. [h] Determined by a chiral stationary phase HPLC.

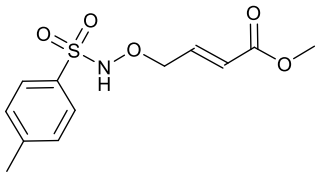
3. Synthesis of starting materials

Sulfonylation of Aminoxy Groups - General Procedure 1



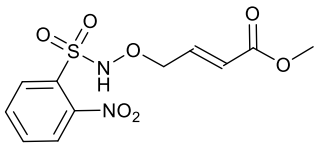
To a solution of methyl (*E*)-4-(aminooxy)but-2-enoate **6** (1 equiv, 5 mmol, 655 mg) in dichloromethane (0.5 M, 10 mL) in a (50 mL) round bottom flask equipped with a telfon-coated magnetic stirring bar and a glass stopper, water (10 mL) was added followed by anhydrous sodium carbonate (1.5 equiv, 7.5 mmol, 795 mg). After the dissolution of sodium carbonate arylsulfonyl chloride (1.5 equiv, 7.5 mmol) was added in one portion and the reaction was left stirring overnight. Afterwards, biphasic mixture was transferred to a separatory funnel and phases were separated. Aqueous layer was extracted with dichloromethane (2x 10 mL). Combined organic layers were dried over anhydrous magnesium sulfate, filtered and evaporated under reduced pressure. Pure product was obtained after FC (eluent: hexane/ethyl acetate 70:30).

Methyl (*E*)-4-(((4-methylphenyl)sulfonamido)oxy)but-2-enoate (1c)



Following the general procedure, using *p*-toluenesulfonyl chloride (1.5 equiv. 7.5 mmol, 1.43 g) product **1c** was isolated by FC (eluent: hexanes/ethyl acetate 70:30) as white amorphous solid in 52 % yield. ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.83 – 7.78 (m, 2H), 7.37 – 7.32 (m, 2H), 7.18 (bs, 1H), 6.87 (dt, *J* = 15.9, 5.2 Hz, 1H), 5.95 (dt, *J* = 15.9, 1.8 Hz, 1H), 4.64 (dd, *J* = 5.2, 1.8 Hz, 2H), 3.74 (s, 3H), 2.45 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 166.4, 145.3, 141.4, 133.5, 130.0 (2C), 128.7 (2C), 123.1, 75.6, 51.9, 21.8. HRMS: calculated for $[C_{12}H_{15}NO_5S+H]^+$: 286.0744; found: 286.0748.

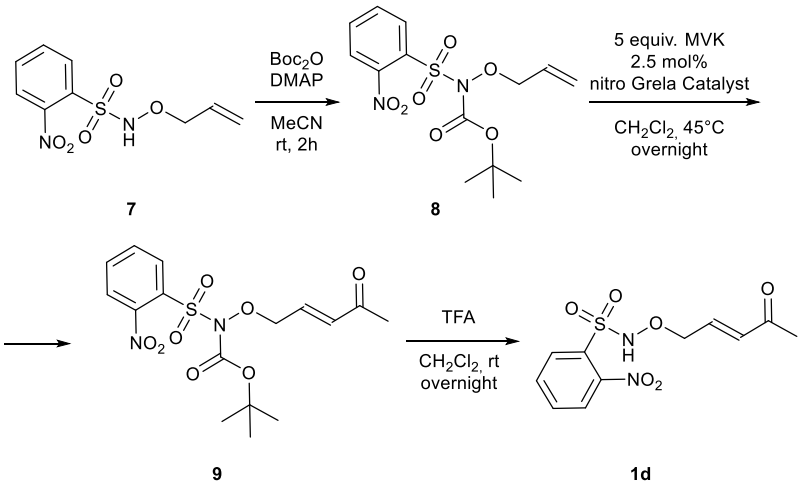
Methyl (*E*)-4-(((2-nitrophenyl)sulfonamido)oxy)but-2-enoate (1d)



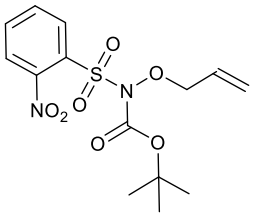
Following the general procedure, using *o*-nitrobenzenesulfonyl chloride (1.5 equiv. 7.5 mmol, 1.66 g) product **1d** was isolated by FC (eluent: hexanes/ethyl acetate 70:30) as white amorphous solid in 80 % yield. ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.24 (s, 1H), 8.21 (dd, *J* = 7.4, 1.8 Hz, 1H), 7.92 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.87 – 7.79 (m, 2H), 6.91 (dt, *J* = 15.9, 5.3 Hz, 1H), 5.97 (dt, *J* = 15.9, 1.7 Hz, 1H), 4.74 (dd, *J* = 5.3, 1.8 Hz, 2H), 3.75 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 166.2, 148.6, 140.8, 135.1, 133.8, 133.1, 130.2,

125.8, 123.6, 77.3, 77.2, 77.0, 76.0, 51.9. HRMS: calculated for $[C_{11}H_{12}N_2O_7S+H]^+$: 317.0438; found: 317.0433.

Synthesis of (*E*)-2-nitro-*N*-((4-oxopent-2-en-1-yl)oxy)benzenesulfonamide 1e

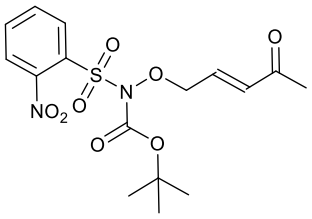


***tert*-Butyl (allyloxy)((2-nitrophenyl)sulfonyl)carbamate 8**



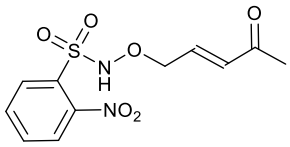
To a solution of *N*-(Allyloxy)-2-nitrobenzenesulfonamide **7** (1 equiv, 5 mmol, 1.29 g) in acetonitrile (0.3 M, 17 mL) in a 50 mL round bottom flask equipped with a Teflon-coated magnetic stirring bar and a glass stopper, di-tert-buthyl dicarbonate (1.1 equiv, 5.5 mmol, 1.20 g) was added followed by 4-(dimethylamino)pyridine (0.2 equiv, 1 mmol, 122 mg). The reaction was left stirring overnight. Subsequently, solvent was evaporated and the crude oil was purified by FC (eluent: hexanes/ethyl acetate 70:30) to obtain pure product **8** as a clear viscous oil (1.61 g, 90% yield). ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.14 – 8.12 (m, 1H), 7.79 – 7.76 (m, 1H), 7.74 – 7.70 (m, 2H), 6.03 – 5.96 (m, 1H), 5.43 – 5.38 (m, 1H), 5.35 – 5.30 (m, 1H), 4.63 (d, *J* = 6.7 Hz, 2H), 1.42 (s, 8H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 150.1, 148.5, 135.0, 132.0, 131.6, 131.3, 131.0, 124.5, 121.9, 86.5, 80.4, 27.8 (3C). HRMS calculated for $[C_{14}H_{18}N_2O_7S+H^+]$: 359.0907; found: 359.0903.

tert-butyl (_E_)-((2-nitrophenyl)sulfonyl)((4-oxopent-2-en-1-yl)oxy)carbamate 9



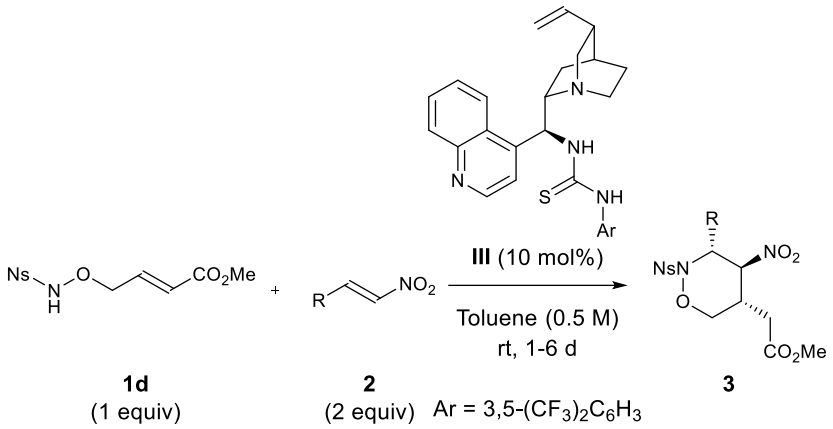
A solution of *tert*-butyl (allyloxy)((2-nitrophenyl)sulfonyl)carbamate **8** (1 equiv, 2 mmol, 716 mg) and a methyl vinyl ketone (5 equiv, 10 mmol, 0.83 mL) in dry dichloromethane (0.2 M, 10 mL) in a 25 mL Schlenk flask equipped with a condenser and a Teflon-coated magnetic stirring bar, was degassed three times employing freezepump-thaw method and flushed with dry Argon afterwards. As the solution warmed up to room temperature nitro Grela catalyst (2.5 mol%, 0.05 mmol, 33 mg) was added and the reaction mixture was heated to 45°C and was left stirring overnight. Afterwards, solvent was evaporated under reduced pressure and the crude product was purified by FC (eluent: hexanes/ethyl acetate 70:30) to obtain pure product **9** as a pale yellow viscous oil (584 mg, 73% yield). ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.22 – 8.15 (m, 1H), 7.84 – 7.81 (m, 1H), 7.79 – 7.75 (m, 2H), 6.83 (dt, *J* = 16.2, 5.8 Hz, 1H), 6.34 (dt, *J* = 16.2, 1.6 Hz, 1H), 4.85 (dd, *J* = 5.9, 1.6 Hz, 2H), 2.31 (s, 3H), 1.45 (s, 9H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 197.9, 150.0, 148.6, 138.1, 135.2, 133.4, 132.0, 131.9, 131.1, 124.6, 87.1, 77.9, 27.9 (3C), 27.4. HRMS calculated for [$C_{16}H_{20}N_2O_8S$+H^+]: 401.1013; found: 401.1014.

(_E_)-2-Nitro-N-((4-oxopent-2-en-1-yl)oxy)benzenesulfonamide 1d

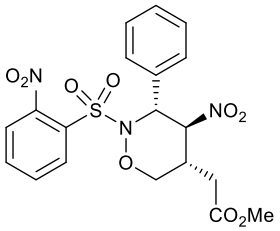


To a solution of *tert*-butyl (*E*)-((2-nitrophenyl)sulfonyl)((4-oxopent-2-en-1-yl)oxy)carbamate **9** (1 equiv, 1 mmol, 400 mg) in dichloromethane (0.2 M, 5 mL) in a 8 mL glass vial equipped with a magnetic stirring bar and a screw cap, trifluoroacetic acid (2 equiv, 2 mmol, 153 µL) was added. Reaction mixture was left stirring overnight and next it was transferred to a separatory funnel and was washed with saturated aqueous solution of sodium bicarbonate (10 mL). Aqueous layer was then extracted with dichloromethane (2 x 10 mL). Combined organic layers were dried over anhydrous magnesium sulfate, filtered off and evaporated under reduced pressure. Crude product was purified by FC (eluent: hexane/ethyl acetate 70:30). ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.27 (s, 1H), 8.21 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.92 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.86 – 7.80 (m, 14H), 6.75 (dt, *J* = 16.2, 5.4 Hz, 1H), 6.19 (dt, *J* = 16.2, 1.7 Hz, 1H), 4.75 (dd, *J* = 5.4, 1.7 Hz, 2H), 2.28 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 197.9, 148.6, 139.2, 135.1, 133.8, 133.1, 132.6, 130.2, 125.8, 76.2, 27.4. HRMS calculated for [$C_{11}H_{12}N_2O_6S$+H^+]: 301.0489; found: 301.0495.

4. Enantio- and diastereoselective synthesis of tetrahydro-1,2-oxazines 3 – general procedure

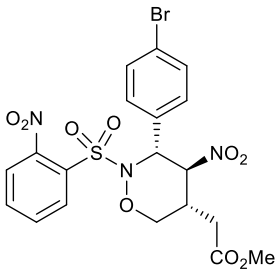


In an ordinary 4 mL glass vial, equipped with a teflon-coated magnetic stirring bar and a screw cap, catalyst **III** (0.1 equiv, 0.02 mmol, 11.2 mg) and the aminooxylating reagent **1d** (1 equiv, 0.2 mmol, 63 mg) were dissolved in toluene (1.6 mL). After 5 min., nitroolefin **2** (2 equiv, 0.4 mmol) was added and stirring was maintained for 24-144 h at ambient temperature. Reaction mixture was directly subjected to flash chromatography on silica gel (eluent: hexanes/ethyl acetate 70:30) to obtain pure product.



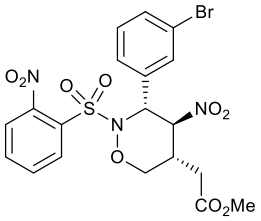
3da Methyl 2-((3*R*,4*S*,5*S*)-4-nitro-2-((2-nitrophenyl)sulfonyl)-3-phenyl-1,2-oxazinan-5-yl)acetate (Table 2, Entry 1)

Following general procedure, using nitroolefin **2a** and compound **1d** (reaction time 48 h), pure product **3da** was isolated by FC on silica gel (eluent: hexanes/ethyl acetate 70:30) in 95% yield as a white amorphous solid (>20:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.74 (td, *J* = 7.7, 1.4 Hz, 1H), 7.66 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.61 (td, *J* = 7.7, 1.3 Hz, 1H), 7.42 – 7.38 (m, 2H), 7.34 – 7.27 (m, 3H), 5.21 (d, *J* = 8.0 Hz, 1H), 5.03 (t, *J* = 8.6 Hz, 1H), 4.45 (dd, *J* = 12.1, 4.9 Hz, 1H), 3.95 (dd, *J* = 12.1, 8.9 Hz, 1H), 3.64 (s, 3H), 3.01 (qt, *J* = 9.1, 4.8 Hz, 1H), 2.37 (dd, *J* = 17.2, 4.8 Hz, 1H), 2.33 (dd, *J* = 17.2, 8.4 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 170.4, 148.6, 135.0, 132.2, 132.0, 131.6, 129.9, 129.7, 128.9 (2C), 128.7 (2C), 124.5, 89.7, 72.5, 65.3, 52.3, 35.9, 32.8. HRMS calculated for [$C_{19}H_{19}N_3O_9S+H^+$]: 466.0915; found: 466.0911. The *er* was determined by HPLC using a chiral Chiralpack IA column [hexane:*i*-PrOH, 90:10]; column temperature 30 °C; flow rate 1.0 mL/min; detection wavelength = 216 nm; τ_{major} = 61.6 min, τ_{minor} = 53.2 min, (>99.5:0.5 er); $[\alpha]_D^{20}$ = +10.6 (*c* = 1.0, $CHCl_3$).



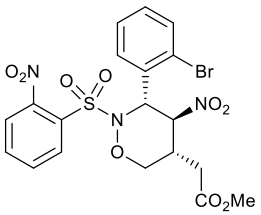
3db Methyl 2-((3*R*,4*S*,5*S*)-3-(4-bromophenyl)-4-nitro-2-((2-nitrophenyl)sulfonyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 2)

Following general procedure, using nitroolefin **2b** and compound **1d** (reaction time 72 h), pure product **3db** was isolated by FC on silica gel (eluent: hexanes/ethyl acetate 70:30) in 78% yield as a pale orange amorphous solid (>20:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.91 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.78 (td, *J* = 7.7, 1.3 Hz, 1H), 7.68 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.66 (td, *J* = 7.7, 1.3 Hz, 1H), 7.46 – 7.41 (m, 2H), 7.31 – 7.26 (m, 2H), 5.16 (d, *J* = 8.2 Hz, 1H), 4.98 (dd, *J* = 9.3, 8.2 Hz, 1H), 4.43 (dd, *J* = 12.1, 4.9 Hz, 1H), 3.93 (dd, *J* = 12.1, 9.1 Hz, 1H), 3.65 (s, 3H), 3.00 (ddq, *J* = 13.8, 9.2, 4.8 Hz, 1H), 2.38 (dd, *J* = 17.2, 4.6 Hz, 1H), 2.33 (dd, *J* = 17.2, 8.5 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 170.3, 148.6, 135.2, 132.2 (2C), 132.1, 131.7, 131.2, 130.4 (2C), 129.4, 124.6, 124.3, 89.6, 72.5, 64.7, 52.3, 35.9, 32.7. HRMS calculated for [$C_{19}H_{18}BrN_3O_9S+H^+$]: 544.0020; found: 544.0024. The *er* was determined by HPLC using a chiral Chiralpack IB column [hexane:*i*-PrOH, 80:20]; column temperature 30 °C; flow rate 1.0 mL/min; detection wavelength = 225 nm; τ_{major} = 31.5 min, τ_{minor} = 35.8 min, (99.4:0.6 er); $[\alpha]_D^{20}$ = +20.3 (*c* = 1.0, $CHCl_3$).



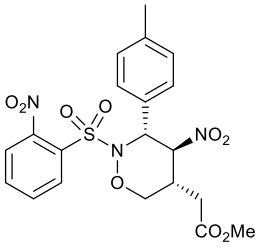
3dc Methyl 2-((3*R*,4*S*,5*S*)-3-(3-bromophenyl)-4-nitro-2-((2-nitrophenyl)sulfonyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 3)

Following general procedure, using nitroolefin **2c** and compound **1d** (reaction time 72 h), pure product **3dc** was isolated by FC on silica gel (eluent: hexanes/ethyl acetate 70:30) in 77% yield as a pale orange amorphous solid (>20:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.91 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.77 (td, *J* = 7.7, 1.4 Hz, 1H), 7.68 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.65 (td, *J* = 7.7, 1.2 Hz, 1H), 7.51 (t, *J* = 1.8 Hz, 1H), 7.46–7.43 (m, 1H), 7.38–7.36 (m, 1H), 7.20 (t, *J* = 7.9 Hz, 1H), 5.23 (d, *J* = 7.8 Hz, 1H), 4.98 (dd, *J* = 8.9, 7.8 Hz, 1H), 4.47 (dd, *J* = 12.1, 4.8 Hz, 1H), 3.94 (dd, *J* = 12.1, 8.6 Hz, 1H), 3.65 (s, 3H), 3.02 (qt, *J* = 8.5, 5.0 Hz, 1H), 2.40 – 2.30 (m, 2H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 170.3, 148.6, 135.3, 134.7, 133.0, 132.0, 131.7, 131.5, 130.5, 129.5, 127.4, 124.6, 122.9, 89.3, 72.5, 64.2, 52.3, 35.6, 32.8. HRMS calculated for [$C_{19}H_{18}BrN_3O_9S+H^+$]: 544.0020; found: 544.0028. The *er* was determined by HPLC using a chiral Chiralpack IA column [hexane:*i*-PrOH, 80:20]; column temperature 30 °C; flow rate 1.0 mL/min; detection wavelength = 219 nm; τ_{major} = 35.2 min, τ_{minor} = 21.7 min, (99.1:0.9 er); $[\alpha]_D^{20}$ = +1.4 (*c* = 1.0, $CHCl_3$).



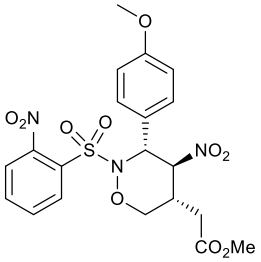
3dd Methyl 2-((3*R*,4*S*,5*S*)-3-(2-bromophenyl)-4-nitro-2-((2-nitrophenyl)sulfonyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 4)

Following general procedure, using nitroolefin **2d** and compound **1d** (reaction time 72 h), pure product **3dd** was isolated by FC on silica gel (eluent: hexanes/ethyl acetate 70:30) in 97% pale yellow oil (>20:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.76 (td, *J* = 7.7, 1.4 Hz, 1H), 7.71 – 7.66 (m, 2H), 7.68 – 7.63 (m, 1H), 7.56 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.31 (td, *J* = 7.6, 1.2 Hz, 1H), 7.20 (td, *J* = 7.7, 1.6 Hz, 1H), 5.95 (bs, 1H), 5.15 (bs, 1H), 4.43 (dd, *J* = 12.2, 4.3 Hz, 1H), 3.97 (dd, *J* = 12.2, 6.9 Hz, 1H), 3.63 (s, 3H), 3.13 (dtt, *J* = 9.0, 6.9, 4.6 Hz, 1H), 2.40 (dd, *J* = 17.1, 8.8 Hz, 1H), 2.31 (dd, *J* = 17.1, 4.9 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 170.4, 148.7, 135.1, 133.9, 132.6, 132.0, 131.8, 131.0, 130.2, 129.8, 128.0, 124.5, 123.9, 86.6, 72.1, 62.0, 52.3, 35.1, 33.3. HRMS calculated for [$C_{19}H_{18}BrN_3O_9S+H^+$]: 544.0020; found: 544.0011. The *er* was determined by HPLC using a chiral Chiralpack IB column [hexane:*i*-PrOH, 80:20]; column temperature 30 °C; flow rate 1.0 mL/min; detection wavelength = 210 nm; τ_{major} = 32.6 min, τ_{minor} = 36.7 min, (>99.5:0.5 er); $[\alpha]_D^{20}$ = +8.3 (*c* = 1.0, $CHCl_3$).



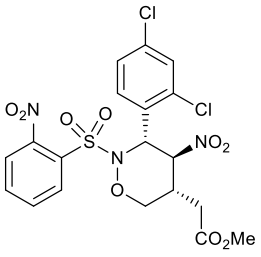
3de Methyl 2-((3*R*,4*S*,5*S*)-4-nitro-2-((2-nitrophenyl)sulfonyl)-3-(*p*-tolyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 5)

Following general procedure, using nitroolefin **2e** and compound **1d** (reaction time 72 h), pure product **3de** was isolated by FC on silica gel (eluent: hexanes/ethyl acetate 70:30) in 82% yield as a white amorphous solid (>20:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.74 (td, *J* = 7.7, 1.3 Hz, 1H), 7.66 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.60 (td, *J* = 7.8, 1.2 Hz, 1H), 7.29 – 7.25 (m, 2H), 7.09 – 7.07 (m, 2H), 5.11 (d, *J* = 8.4 Hz, 1H), 5.01 (dd, *J* = 9.5, 8.4 Hz, 1H), 4.43 (dd, *J* = 12.1, 4.9 Hz, 1H), 3.93 (dd, *J* = 12.1, 9.3 Hz, 1H), 3.65 (s, 3H), 3.00 (qt, *J* = 9.3, 4.7 Hz, 1H), 2.39 (dd, *J* = 17.1, 4.4 Hz, 1H), 2.33 (dd, *J* = 17.2, 8.7 Hz, 1H), 2.30 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 170.3, 148.7, 139.9, 134.9, 132.0, 131.5, 129.6, 129.6 (2C), 128.8, 128.8 (2C), 124.5, 90.0, 72.5, 65.5, 52.3, 36.2, 32.8, 21.4. HRMS calculated for [$C_{20}H_{21}N_3O_9S+H^+$]: 480.1071; found: 480.1077. The *er* was determined by HPLC using a chiral Chiralpack IA column [hexane:*i*-PrOH, 80:20]; column temperature 30 °C; flow rate 1.0 mL/min; detection wavelength = 225 nm; τ_{major} = 26.8min, τ_{minor} = 22.7 min, (>99.5:0.5 er); $[\alpha]_D^{20}$ = +11.6 (*c* = 1.0, $CHCl_3$).



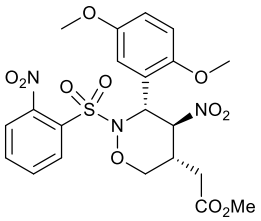
3df Methyl 2-((3*R*,4*S*,5*S*)-3-(4-methoxyphenyl)-4-nitro-2-((2-nitrophenyl)sulfonyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 6)

Following general procedure, using nitroolefin **2f** and compound **1d** (reaction time 120 h), pure product **3df** was isolated by FC on silica gel (eluent: hexanes/ethyl acetate 70:30) in 76% yield as a pale yellow amorphous solid (>20:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.73 (td, *J* = 7.7, 1.4 Hz, 1H), 7.66 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.60 (td, *J* = 7.7, 1.3 Hz, 1H), 7.32 – 7.27 (m, 2H), 6.80 – 6.75 (m, 2H), 5.04 (d, *J* = 8.8 Hz, 1H), 5.00 (t, *J* = 9.3 Hz, 1H), 4.41 (dd, *J* = 12.1, 5.1 Hz, 1H), 3.93 (dd, *J* = 12.1, 9.8 Hz, 1H), 3.77 (s, 3H), 3.66 (s, 3H), 2.99 (qt, *J* = 9.4, 4.6 Hz, 1H), 2.41 (dd, *J* = 17.1, 4.2 Hz, 1H), 2.33 (dd, *J* = 17.1, 8.7 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 170.3, 160.7, 148.6, 134.9, 131.9, 131.5, 130.4 (2C), 129.7, 124.5, 123.3, 114.3 (2C), 90.3, 72.6, 65.6, 55.4, 52.3, 36.5, 32.7. HRMS calculated for [$C_{20}H_{21}N_3O_{10}S$+H^+]: 496.1020; found: 496.1029. The *er* was determined by HPLC using a chiral Chiralpack IA column [hexane:*i*-PrOH, 80:20]; column temperature 30 °C; flow rate 1.0 mL/min; detection wavelength = 225 nm; τ_{major} = 35.7min, τ_{minor} = 29.7 min, (98.4:1.6 er); $[\alpha]_D^{20}$ = +26.5 (*c* = 1.0, $CHCl_3$).



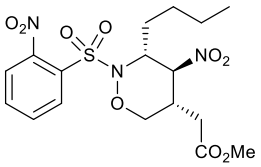
3dg Methyl 2-((3*R*,4*S*,5*S*)-3-(2,4-dichlorophenyl)-4-nitro-2-((2-nitrophenyl)sulfonyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 7)

Following general procedure, using nitroolefin **2g** and compound **1d** (reaction time 24 h), pure product **3dg** was isolated by FC on silica gel (eluent: hexanes/ethyl acetate 70:30) in 93% yield as a white amorphous solid (>20:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.05 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.79 (td, *J* = 7.8, 1.3 Hz, 1H), 7.71 (td, *J* = 7.8, 1.2 Hz, 1H), 7.67 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.40 (d, *J* = 2.1 Hz, 1H), 7.27 – 7.24 (m, 1H), 5.86 (bs, 1H), 5.10 (t, *J* = 7.2 Hz, 1H), 4.43 (dd, *J* = 12.1, 4.5 Hz, 1H), 3.95 (dd, *J* = 12.1, 7.2 Hz, 1H), 3.64 (s, 3H), 3.10 (dtd, *J* = 9.1, 7.4, 4.7 Hz, 1H), 2.38 (dd, *J* = 17.1, 8.6 Hz, 1H), 2.32 (dd, *J* = 17.1, 5.0 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 170.3, 148.6, 136.3, 135.3, 134.6, 132.2, 131.8, 131.0, 130.3, 129.6, 129.5, 127.9, 124.6, 86.4, 72.2, 59.8, 52.3, 35.1, 33.2. HRMS calculated for [$C_{19}H_{17}Cl_2N_3O_9S$+H^+]: 534.0135; found: 534.0141. The *er* was determined by HPLC using a chiral Chiralpack IA column [hexane:*i*-PrOH, 80:20]; column temperature 30 °C; flow rate 1.0 mL/min; detection wavelength = 223 nm; τ_{major} = 19.5 min, τ_{minor} = 22.3 min, (99.5:0.5 er); $[\alpha]_D^{20}$ = +16.0 (*c* = 1.0, $CHCl_3$).



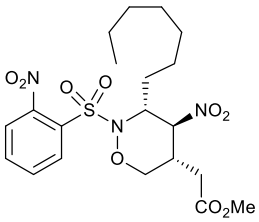
3dh Methyl 2-((3*R*,4*S*,5*S*)-3-(2,5-dimethoxyphenyl)-4-nitro-2-((2-nitrophenyl)sulfonyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 8)

Following general procedure, using nitroolefin **2h** and compound **1d** (reaction time 144 h), pure product **3dh** was isolated by FC on silica gel (eluent: hexanes/ethyl acetate 70:30) in 87% yield as a brown oil (>20:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.74 (td, *J* = 7.7, 1.4 Hz, 1H), 7.66 (td, *J* = 7.7, 1.3 Hz, 1H), 7.63 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.02 (d, *J* = 3.0 Hz, 1H), 6.82 (dd, *J* = 8.9, 3.0 Hz, 1H), 6.77 (d, *J* = 8.9 Hz, 1H), 5.82 (bs, 1H), 5.20 (t, *J* = 5.9 Hz, 1H), 4.44 (dd, *J* = 12.1, 4.2 Hz, 1H), 3.93 (dd, *J* = 12.1, 6.0 Hz, 1H), 3.82 (s, 3H), 3.71 (s, 3H), 3.60 (s, 3H), 3.09 – 3.02 (m, 1H), 2.39 (dd, *J* = 17.0, 9.0 Hz, 1H), 2.27 (dd, *J* = 17.0, 5.1 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 170.8, 153.7, 151.1, 148.6, 134.8, 131.8, 131.6, 130.3, 124.3, 122.2, 115.7, 115.4, 112.2, 85.2, 72.2, 59.1, 56.3, 55.9, 52.1, 34.5, 33.7. HRMS calculated for [$C_{21}H_{23}N_3O_{11}S$+H^+]: 526.1126; found: 526.1116. The *er* was determined by HPLC using a chiral Chiralpack IA column [hexane:*i*-PrOH, 80:20]; column temperature 30 °C; flow rate 1.0 mL/min; detection wavelength = 296 nm; τ_{major} = 28.1 min, τ_{minor} = 23.7 min, (99.4:0.6 er); $[\alpha]_D^{20}$ = –18.1° (*c* = 1.0, $CHCl_3$).



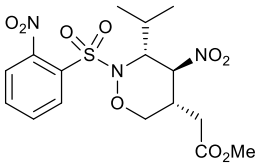
3di Methyl 2-((3*R*,4*S*,5*S*)-3-butyl-4-nitro-2-((2-nitrophenyl)sulfonyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 9)

Following general procedure, using nitroolefin **2i** and compound **1d** (reaction time 72 h), pure product **3di** was isolated by FC on silica gel (eluent: hexanes/ethyl acetate 70:30) in 93% yield as pale yellow oil (>20:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.10 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.79 (td, *J* = 7.7, 1.4 Hz, 1H), 7.72 (td, *J* = 7.8, 1.3 Hz, 1H), 7.68 (dd, *J* = 7.8, 1.3 Hz, 1H), 4.67 (t, *J* = 4.8 Hz, 1H), 4.65 – 4.62 (m, 1H), 4.31 (dd, *J* = 11.9, 4.4 Hz, 1H), 3.81 (dd, *J* = 11.9, 4.7 Hz, 1H), 3.69 (s, 3H), 3.08 – 3.00 (m, 1H), 2.62 (dd, *J* = 16.9, 8.8 Hz, 1H), 2.55 (dd, *J* = 16.9, 5.7 Hz, 1H), 2.05 – 1.90 (m, 2H), 1.56 – 1.48 (m, 1H), 1.47 – 1.41 (m, 1H), 1.41 – 1.35 (m, 2H), 0.92 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 170.9, 148.6, 135.1, 132.0, 131.8, 130.1, 124.5, 84.3, 72.4, 60.3, 52.4, 34.3, 32.9, 30.1, 27.9, 22.4, 13.9. HRMS calculated for [$C_{17}H_{23}N_3O_9S$+H^+]: 446.1228; found: 446.1232. The *er* was determined by HPLC using a chiral Chiralpack IG column [hexane:*i*-PrOH, 80:20]; column temperature 30 °C; flow rate 1.0 mL/min; detection wavelength = 214 nm; τ_{major} = 29.6 min, τ_{minor} = 26.5 min, (98.3:1.7 er); $[\alpha]_D^{20}$ = –55.1° (*c* = 1.0, $CHCl_3$).



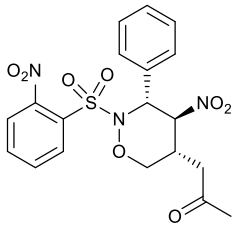
3dj Methyl 2-((3*R*,4*S*,5*S*)-3-heptyl-4-nitro-2-((2-nitrophenyl)sulfonyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 10)

Following general procedure, using nitroolefin **2j** and compound **1d** (reaction time 72 h), pure product **3dj** was isolated by FC on silica gel (eluent: hexanes/ethyl acetate 70:30) in 66% yield as pale yellow oil (>20:1 dr). ^{1}H NMR (700 MHz,) δ 8.10 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.78 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.72 (td, *J* = 7.7, 1.3 Hz, 1H), 7.68 (dd, *J* = 7.9, 1.3 Hz, 1H), 4.67 (t, *J* = 4.8 Hz, 1H), 4.63 (td, *J* = 6.6, 4.6 Hz, 1H), 4.32 (dd, *J* = 11.9, 4.4 Hz, 1H), 3.81 (dd, *J* = 11.9, 4.8 Hz, 1H), 3.69 (s, 3H), 3.07 – 3.00 (m, 1H), 2.61 (dd, *J* = 16.9, 8.8 Hz, 1H), 2.55 (dd, *J* = 16.9, 5.7 Hz, 1H), 2.03 – 1.89 (m, 2H), 1.56 – 1.48 (m, 1H), 1.49 – 1.40 (m, 1H), 1.37 – 1.22 (m, 10H), 0.89 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 170.9, 148.7, 135.1, 132.0, 131.7, 130.1, 124.5, 84.3, 72.4, 60.4, 52.4, 34.3, 32.9, 31.8, 31.1, 30.4, 29.1, 25.8, 22.7, 14.2. HRMS calculated for [$C_{20}H_{29}N_3O_9S+H^+$]: 488.1697; found: 488.1705. The *er* was determined by HPLC using a chiral Chiralpack IG column [hexane:*i*-PrOH, 80:20]; column temperature 30 °C; flow rate 1.0 mL/min; detection wavelength = 225 nm; τ_{major} = 26.2 min, τ_{minor} = 23.1 min, (99.0:1.0 er); $[\alpha]_D^{20}$ = –58.7° (*c* = 1.0, $CHCl_3$).



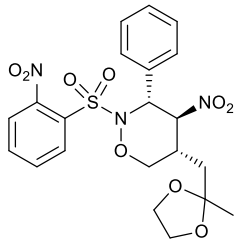
3dk Methyl 2-((3*R*,4*S*,5*S*)-3-isopropyl-4-nitro-2-((2-nitrophenyl)sulfonyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 11)

Following general procedure, using nitroolefin **2k** and compound **1d** (reaction time 72 h in 40 °C), pure product **3dk** was isolated by FC on silica gel (eluent: hexanes/ethyl acetate 70:30) in 74% yield as pale yellow oil (>20:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.08 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.77 (td, *J* = 7.7, 1.4 Hz, 1H), 7.72 (td, *J* = 7.7, 1.3 Hz, 1H), 7.64 (dd, *J* = 7.9, 1.3 Hz, 1H), 4.80 (dd, *J* = 7.2, 4.7 Hz, 1H), 4.63 (dd, *J* = 7.7, 4.7 Hz, 1H), 4.49 (dd, *J* = 10.7, 5.7 Hz, 1H), 3.82 (dd, *J* = 10.8, 6.5 Hz, 1H), 3.70 (s, 3H), 3.10 – 3.02 (m, 1H), 2.57 (dd, *J* = 17.1, 7.8 Hz, 1H), 2.52 (dd, *J* = 17.1, 5.4 Hz, 1H), 2.23 – 2.15 (m, 1H), 1.09 (d, *J* = 6.7 Hz, 3H), 1.03 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 170.7, 148.9, 134.8, 131.8, 131.2, 130.8, 124.3, 82.7, 71.9, 64.7, 52.3, 33.6, 32.4, 31.4, 19.4, 19.1. HRMS calculated for [$C_{16}H_{21}N_3O_9S+H^+$]: 432.1071; found: 432.1065. The *er* was determined by HPLC using a chiral Chiralpack IA column [hexane:*i*-PrOH, 80:20]; column temperature 30 °C; flow rate 1.0 mL/min; detection wavelength = 223 nm; τ_{major} = 15.3 min, τ_{minor} = 16.7 min, (>99.5:0.5 er); $[\alpha]_D^{20}$ = –130.3° (*c* = 1.0, $CHCl_3$).

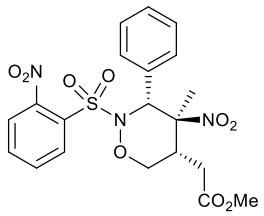


3ea 1-((3*R*,4*S*,5*S*)-4-Nitro-2-((2-nitrophenyl)sulfonyl)-3-phenyl-1,2-oxazinan-5-yl)propan-2-one (Scheme 2)

Following general procedure, using nitroolefin **2a** and compound **1e** (reaction time 24 h), pure product **3ea** was isolated by FC on silica gel (eluent: hexanes/diethyl ether 30:70) in 89% yield as a white amorphous solid (18:1:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.74 (td, *J* = 7.7, 1.4 Hz, 1H), 7.66 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.63 (td, *J* = 7.7, 1.3 Hz, 1H), 7.44 – 7.38 (m, 2H), 7.34 – 7.28 (m, 3H), 5.29 (d, *J* = 7.6 Hz, 1H), 4.98 (dd, *J* = 8.7, 7.6 Hz, 1H), 4.43 (dd, *J* = 12.0, 4.8 Hz, 1H), 3.85 (dd, *J* = 12.0, 8.3 Hz, 1H), 3.05 (qt, *J* = 8.3, 4.8 Hz, 1H), 2.50 (dd, *J* = 18.7, 4.9 Hz, 1H), 2.43 (dd, *J* = 18.6, 8.1 Hz, 1H), 1.99 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 204.5, 148.6, 135.0, 132.6, 132.0, 131.7, 129.7, 129.7, 128.9 (2C), 128.6 (2C), 124.5, 89.2, 72.7, 64.9, 41.8, 34.6, 30.2. HRMS calculated for [$C_{19}H_{19}N_3O_8S$+H^+]: 450.0966; found: 450.0977. $[\alpha]_D^{20}$ = +5.6° (*c* = 1.0, $CHCl_3$). In order to determine the er, the product was converted to the 1,3-dioxolane **10**.



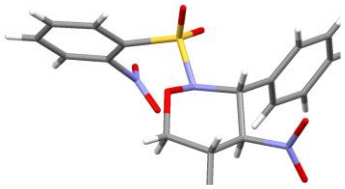
10 (3*R*,4*S*,5*S*)-5-((2-Methyl-1,3-dioxolan-2-yl)methyl)-4-nitro-2-((2-nitrophenyl)sulfonyl)-3-phenyl-1,2-oxazinane. To a solution of **3ea** (1 equiv, 0.02 mmol, 9 mg) in toluene (1 mL) in a 5 mL round bottom flask equipped with a Teflon-coated magnetic stirring bar and a Dean-Stark apparatus, ethylene glycol (0.12 mL) followed by pyridinium p-toluenesulfonate (0.2 equiv 0.004 mmol, 1.0 mg) was added. Reaction mixture was refluxed for 2 h with vigorous stirring. Subsequently, it was cooled to room temperature and saturated aqueous solution of sodium bicarbonate (10 mL) was added. Contents of the flask were transferred to a separatory funnel and the product was extracted with diethyl ether (3x10 mL). Combined organic layers were washed with brine (15 mL), dried over magnesium sulfate, filtered off and concentrated under reduced pressure to obtain **10** which was directly subjected to HPLC analysis. ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.73 (td, *J* = 7.7, 1.4 Hz, 1H), 7.66 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.60 (ddd, *J* = 7.9, 7.5, 1.3 Hz, 1H), 7.38 (dd, *J* = 7.9, 1.7 Hz, 2H), 7.32 – 7.26 (m, 3H), 5.08 (d, *J* = 8.7 Hz, 1H), 4.90 (dd, *J* = 9.9, 8.7 Hz, 1H), 4.51 (dd, *J* = 12.3, 5.2 Hz, 1H), 3.93 – 3.82 (m, 5H), 2.78 (tddd, *J* = 9.7, 8.6, 5.2, 3.3 Hz, 1H), 1.72 (dd, *J* = 14.9, 3.4 Hz, 1H), 1.66 (dd, *J* = 14.9, 8.6 Hz, 1H), 1.22 (s, 3H). 13C NMR (176 MHz, $CDCl_3$) δ 148.7, 134.9, 132.1, 132.0, 131.6, 129.9, 129.7, 129.0 (2C), 128.8 (2C), 124.5, 108.7, 91.7, 74.1, 66.2, 64.8, 64.5, 37.6, 36.1, 24.0. HRMS calculated for [$C_{21}H_{23}N_3O_9S$+H^+]: 494.1228; found: 494.1231. The *er* was determined by HPLC using a chiral Chiralpack IA column [hexane:*i*-PrOH, 80:20]; column temperature 30 °C; flow rate 1.0 mL/min; detection wavelength = 223 nm; τ_{major} = 19.9 min, τ_{minor} = 21.3 min, (88:12 er).



3dl Methyl 2-((3*R*,4*S*,5*S*)-4-methyl-4-nitro-2-((2-nitrophenyl)sulfonyl)-3-phenyl-1,2-oxazinan-5-yl)acetate (Scheme 2)

Following general procedure, using nitroolefin **2l** and compound **1d** (reaction time 96 h), pure product **3dl** was isolated by FC on silica gel (eluent: hexanes/ethyl acetate 70:30) in 90% yield as pale yellow oil (>20:1 dr). ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.9 Hz, 1H), 7.74 (td, *J* = 7.7, 1.3 Hz, 1H), 7.66 – 7.60 (m, 2H), 7.42 – 7.38 (m, 2H), 7.35 – 7.30 (m, 1H), 7.31 – 7.26 (m, 2H), 5.71 (s, 1H), 4.38 (dd, *J* = 12.0, 4.5 Hz, 1H), 3.91 (dd, *J* = 12.0, 6.9 Hz, 1H), 3.65 (s, 3H), 3.45 – 3.38 (m, 1H), 2.38 (dd, *J* = 16.7, 10.7 Hz, 1H), 2.16 (dd, *J* = 16.7, 3.2 Hz, 1H), 1.59 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 170.9, 148.7, 134.9, 132.0, 131.9, 131.6, 129.9 (2C), 129.8, 129.5, 128.3 (2C), 124.3, 93.0, 72.6, 67.9, 52.3, 52.0, 38.8, 32.3. HRMS calculated for [$C_{20}H_{21}N_3O_9S+H^+$]: 480.1071; found: 480.1082. The *er* was determined by HPLC using a chiral Chiralpack IA column [hexane:*i*-PrOH, 80:20]; column temperature 30 °C; flow rate 1.0 mL/min; detection wavelength = 215 nm; τ_{major} = 21.1min, τ_{minor} = 17.4 min, (95.4:4.6 er); $[\alpha]_D^{20}$ = –57.6 (*c* = 1.0, $CHCl_3$).

5. Crystal and X-ray data for methyl 2-((3*R*,5*S*)-4-nitro-2-((2-nitrophenyl)sulfonyl)-3-phenyl-1,2-oxazinan-5-yl)acetate (3da)



Formula $C_{19}H_{19}N_3O_9S$, monoclinic, space group $P2_1$, Z = 2, cell constants a = 5.9946(2) Å, b = 13.3006(5) Å, c = 13.1317(5) Å, β = 93.111(3)°, V = 1045.47(7) Å^3. The data was collected on a Rigaku Synergy, Pilatus 300K diffractometer at 100 K using PhotonJet micro-focus X-ray Source Cu-Kα (λ =1.54178 Å) as a source of radiation. The integration of the data yielded a total of 10198 reflections to a θ angle of 79.3°, of which 3787 were independent (Rint =5.48%,) and 3401 were greater than $2\sigma(F^2)$. The final anisotropic full-matrix least-squares refinement on F^2 with 290 variables converged at R_1 = 5.80%, for the observed data and wR_2 = 16.09% for all data. The hydrogen atoms were placed in calculated positions and refined isotropically by using a riding model. The goodness-of-fit was 1.029.

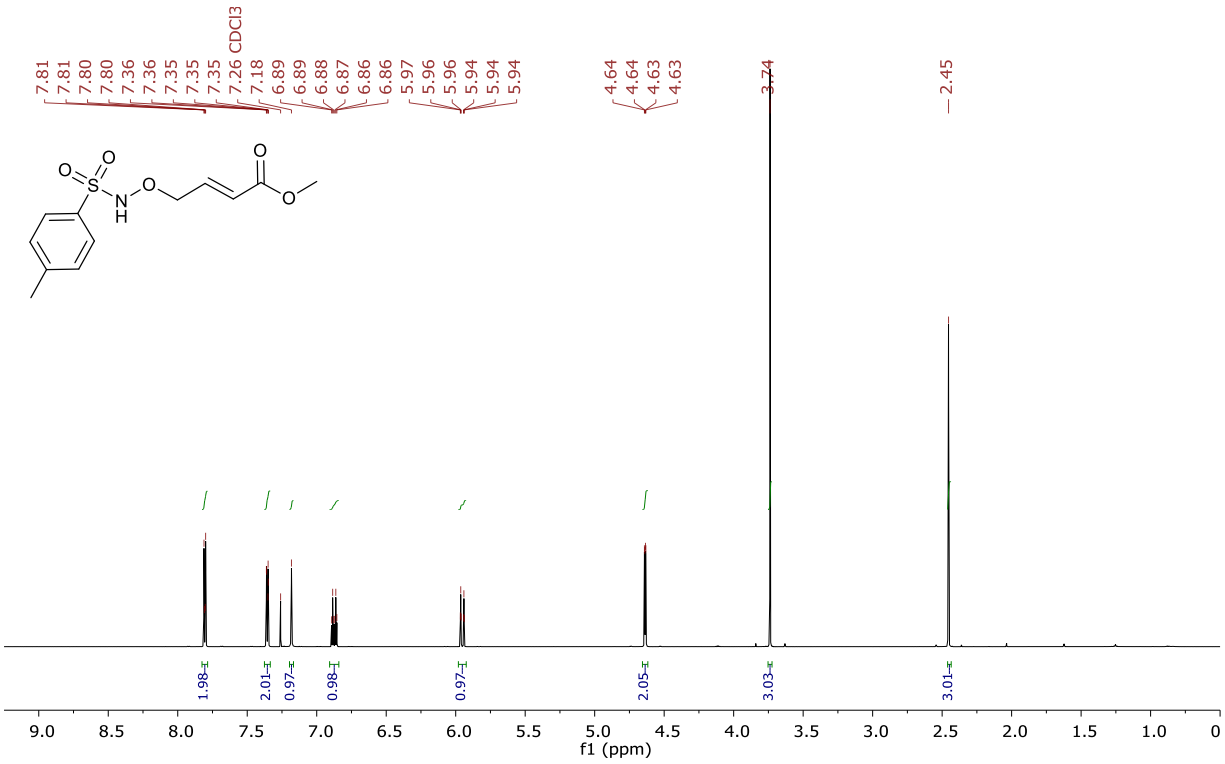
The absolute configuration of **3da** was determined from anomalous scattering, by calculating the Flack parameter: -0.02(3) (Classical Flack method preferred over Parsons because s.u. lower).

CCDC 1553098 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

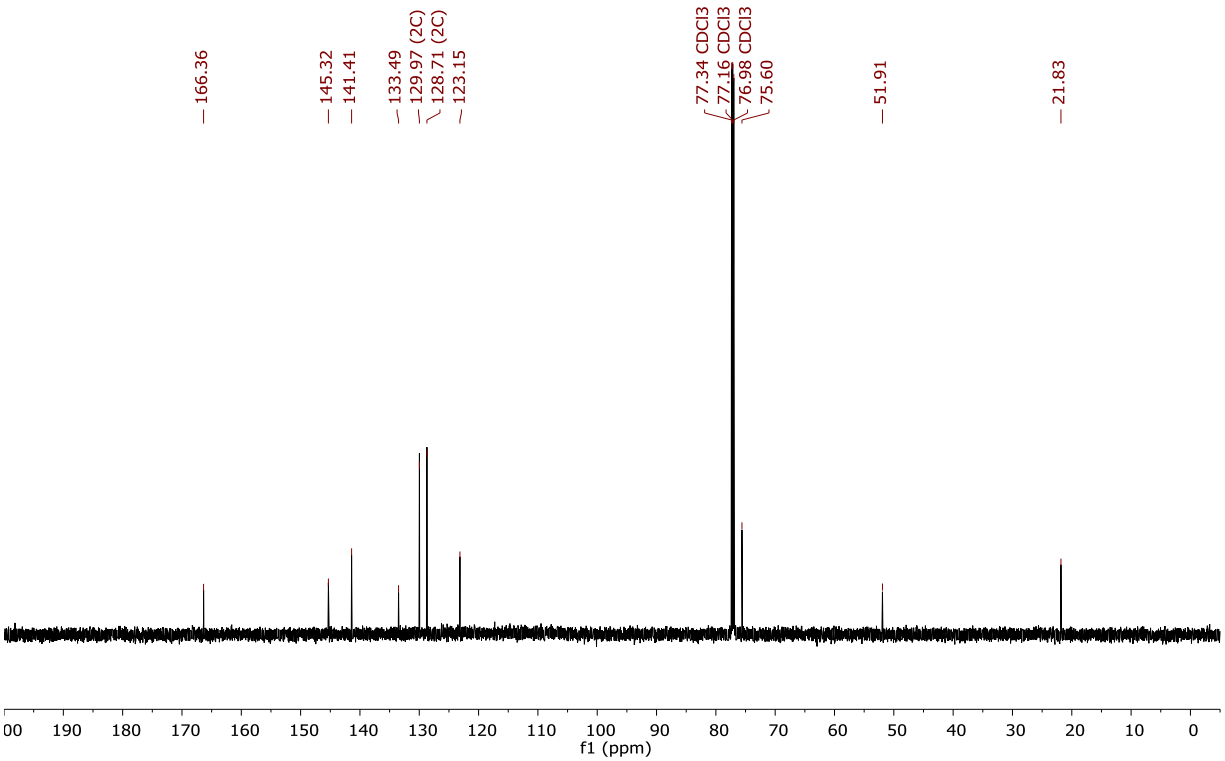
6. NMR data

Methyl (*E*)-4-(((4-methylphenyl)sulfonamido)oxy)but-2-enoate (1c)

^{1}H NMR

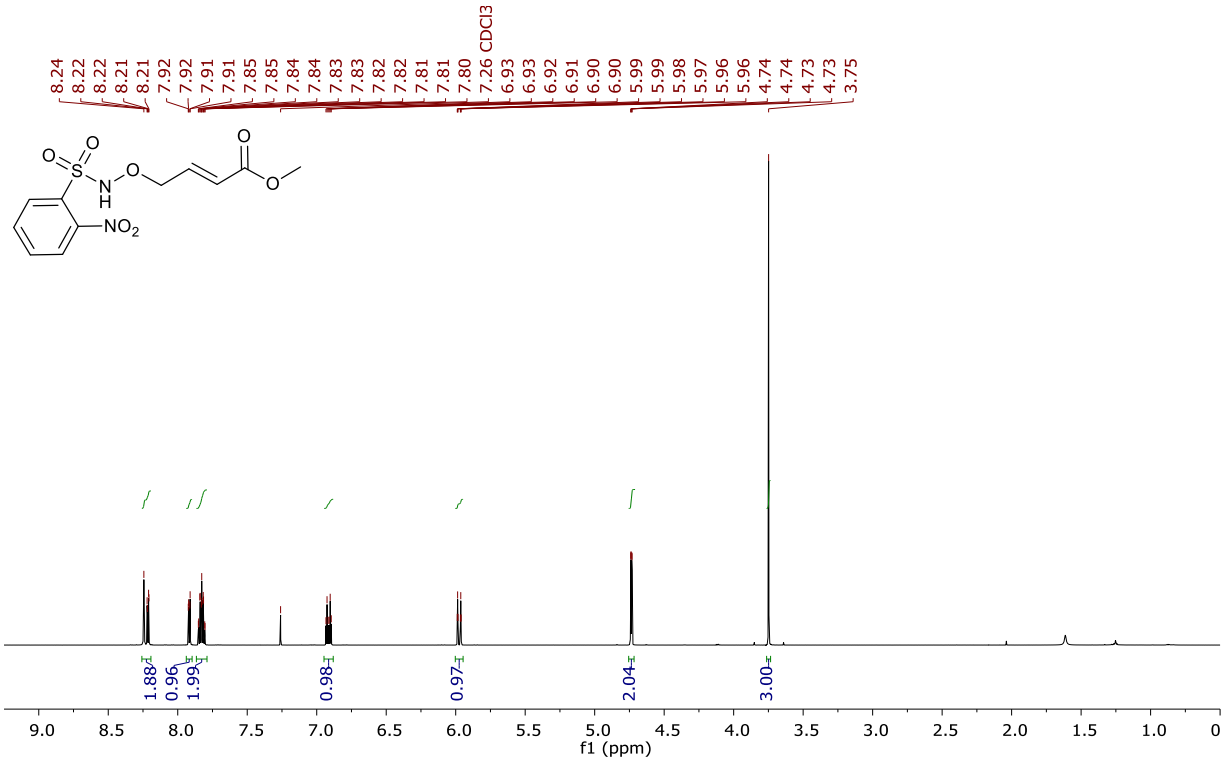


^{13}C NMR

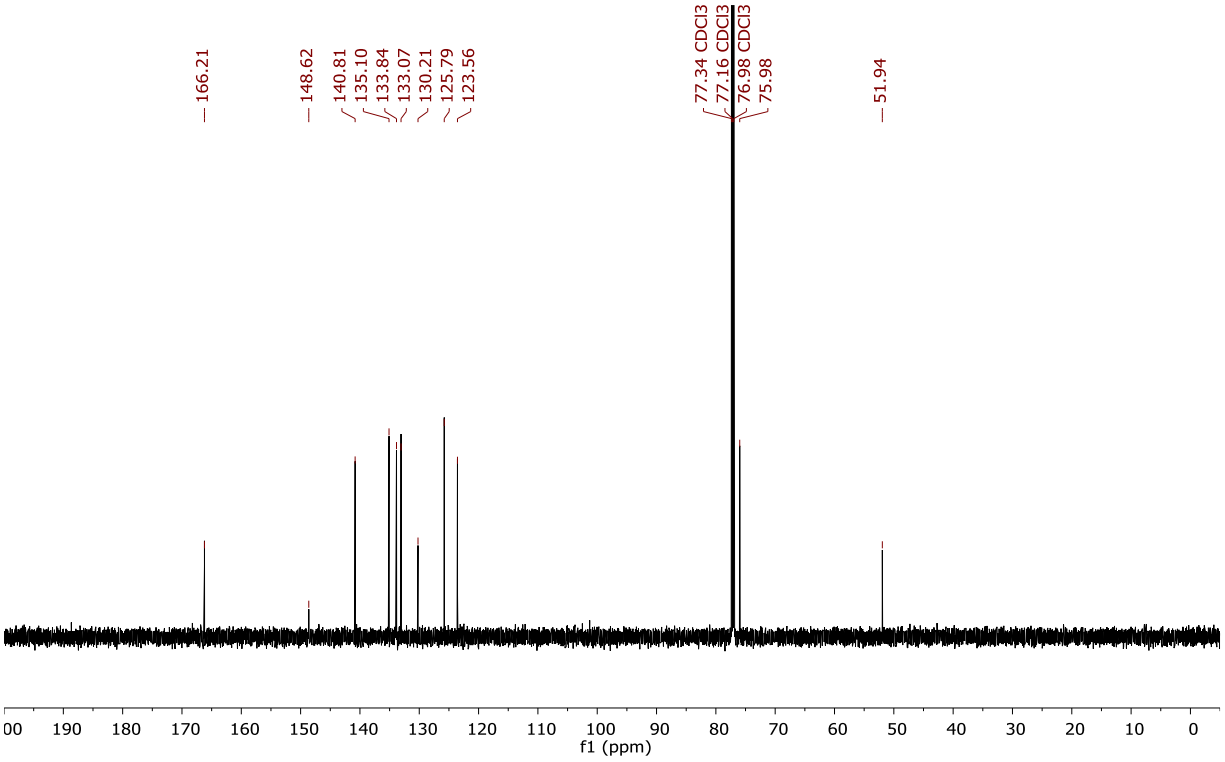


Methyl (*E*)-4-(((2-nitrophenyl)sulfonamido)oxy)but-2-enoate (1d)

^{1}H NMR

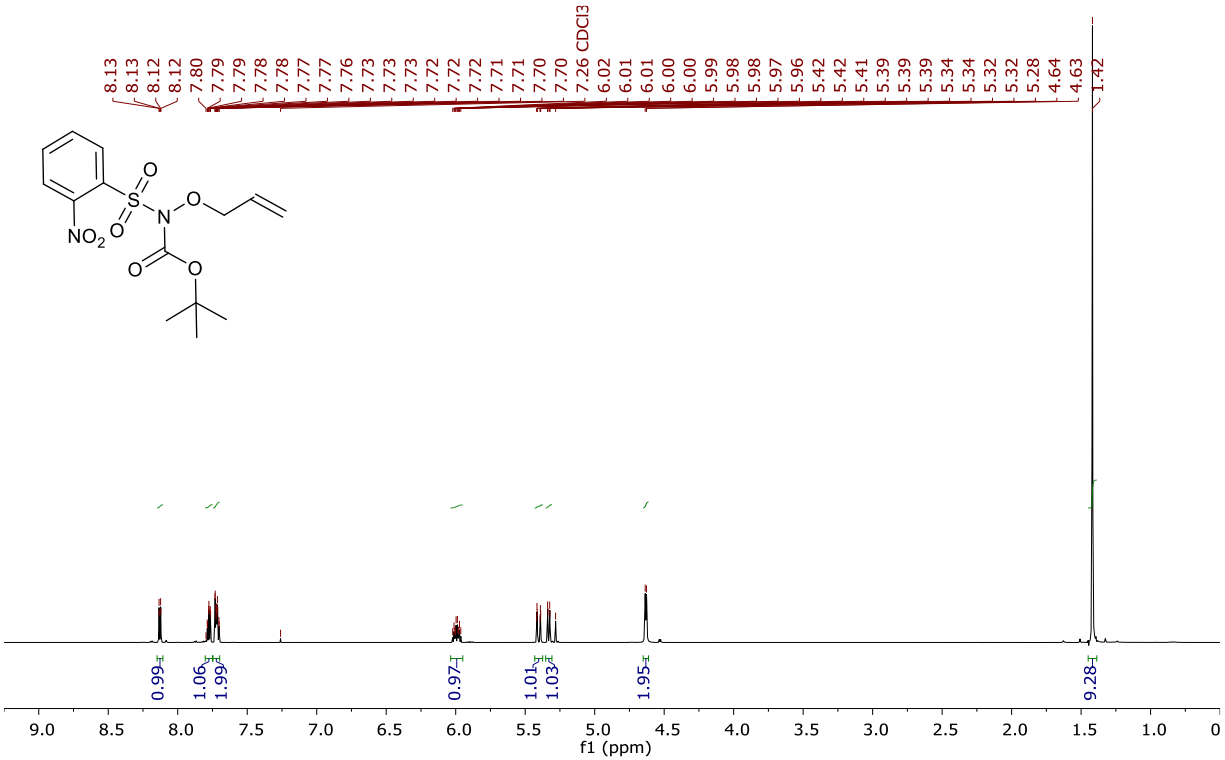


^{13}C NMR

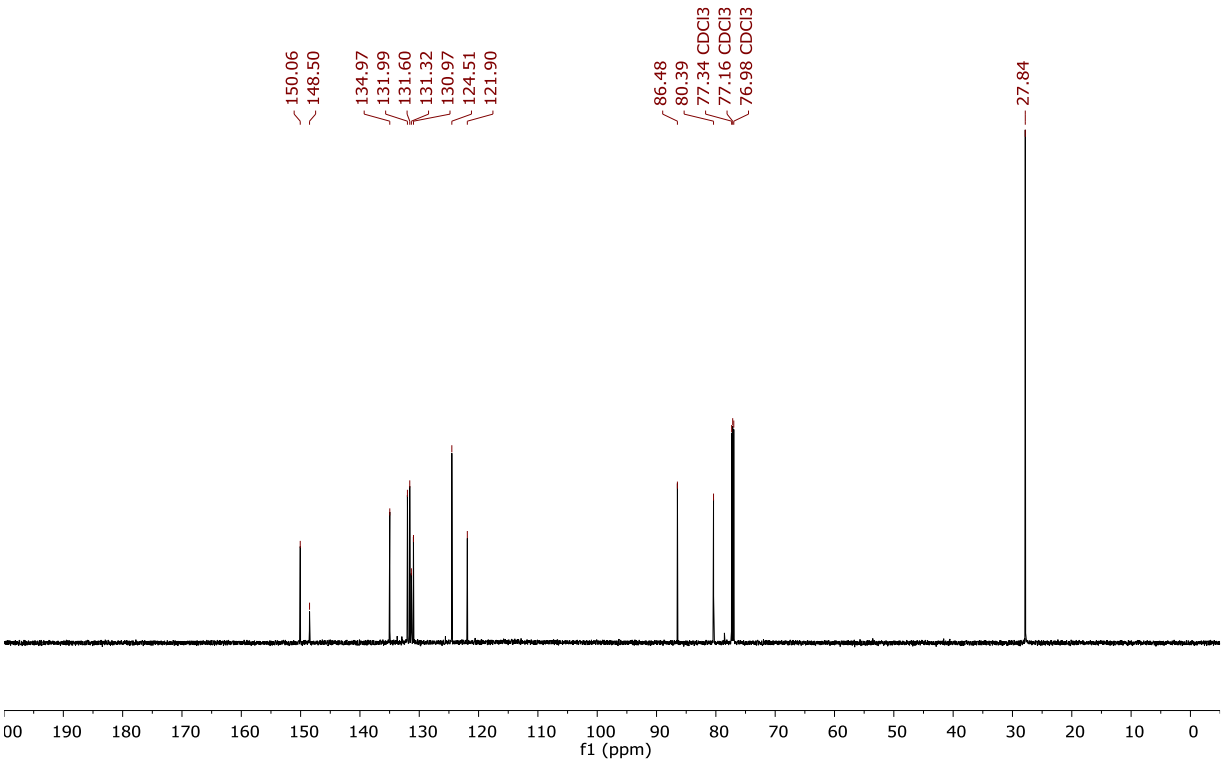


tert-Butyl (allyloxy)((2-nitrophenyl)sulfonyl)carbamate (8)

^{1}H NMR

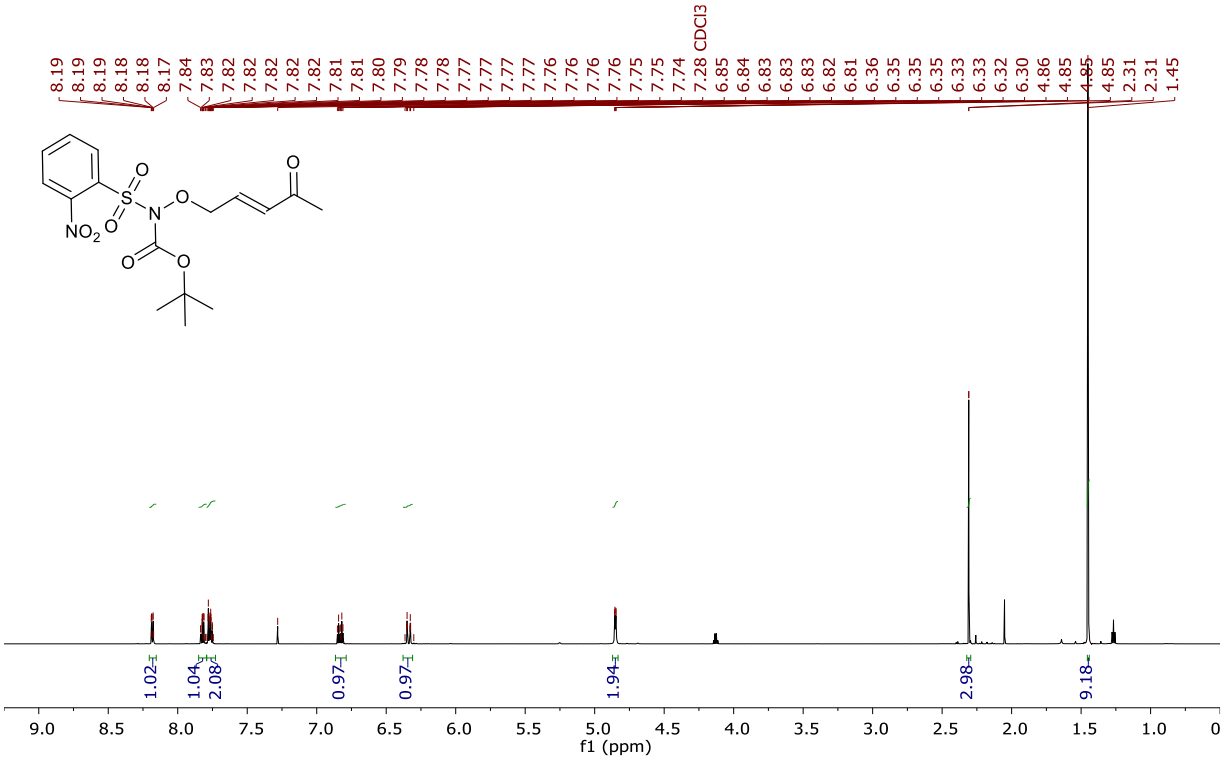


^{13}C NMR

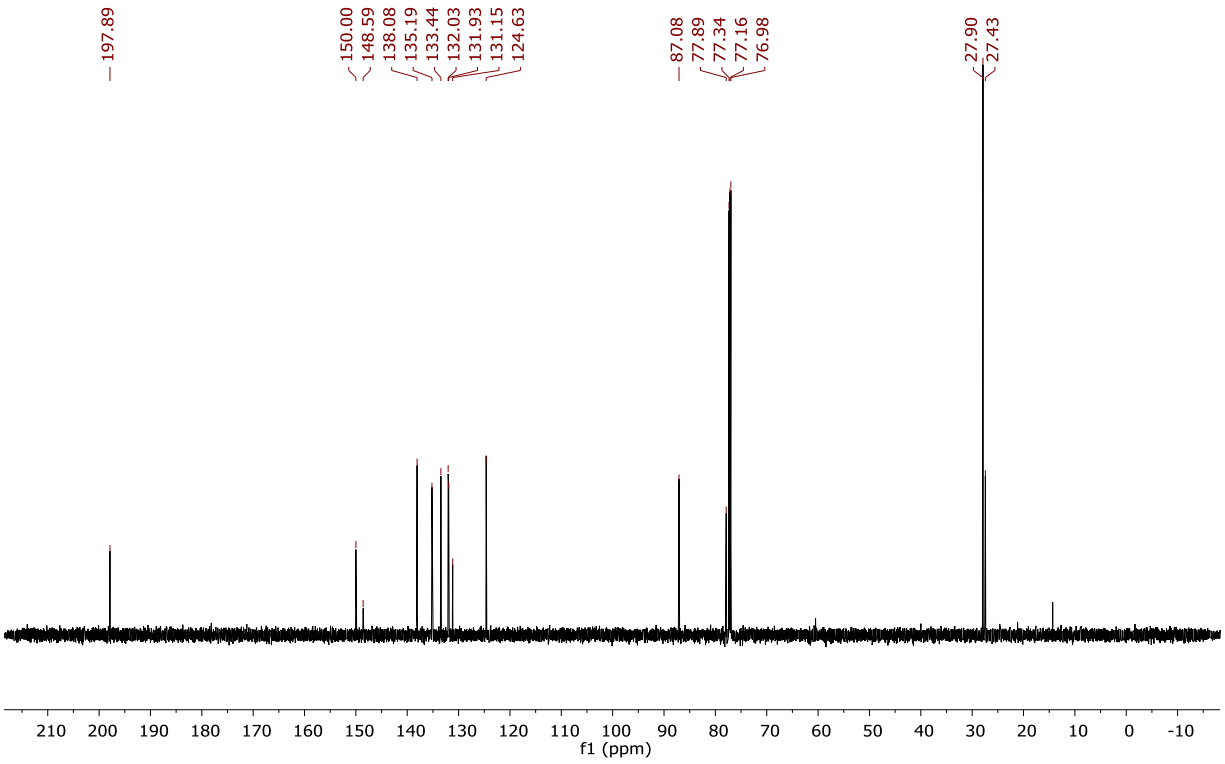


tert-Butyl (*E*)-((2-nitrophenyl)sulfonyl)((4-oxopent-2-en-1-yl)oxy)carbamate (9)

^{1}H NMR

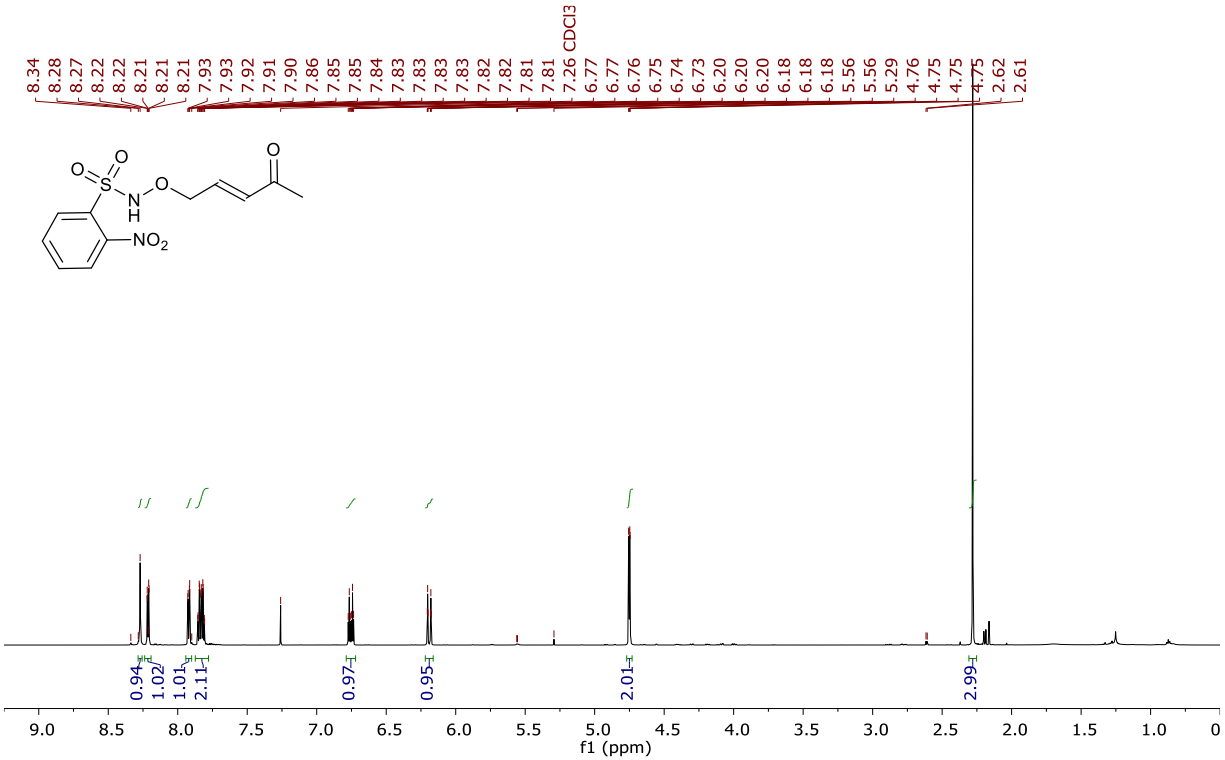


^{13}C NMR

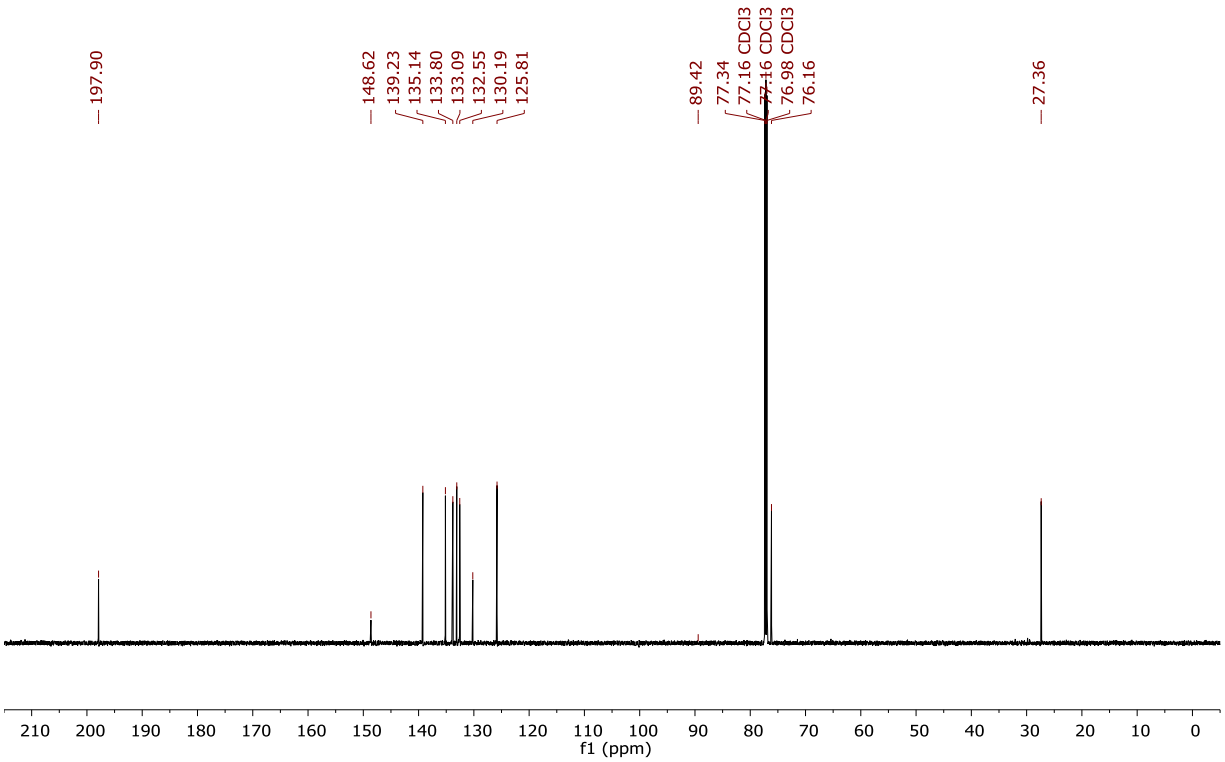


(*E*)-2-Nitro-*N*-((4-oxopent-2-en-1-yl)oxy)benzenesulfonamide (1e)

^{1}H NMR

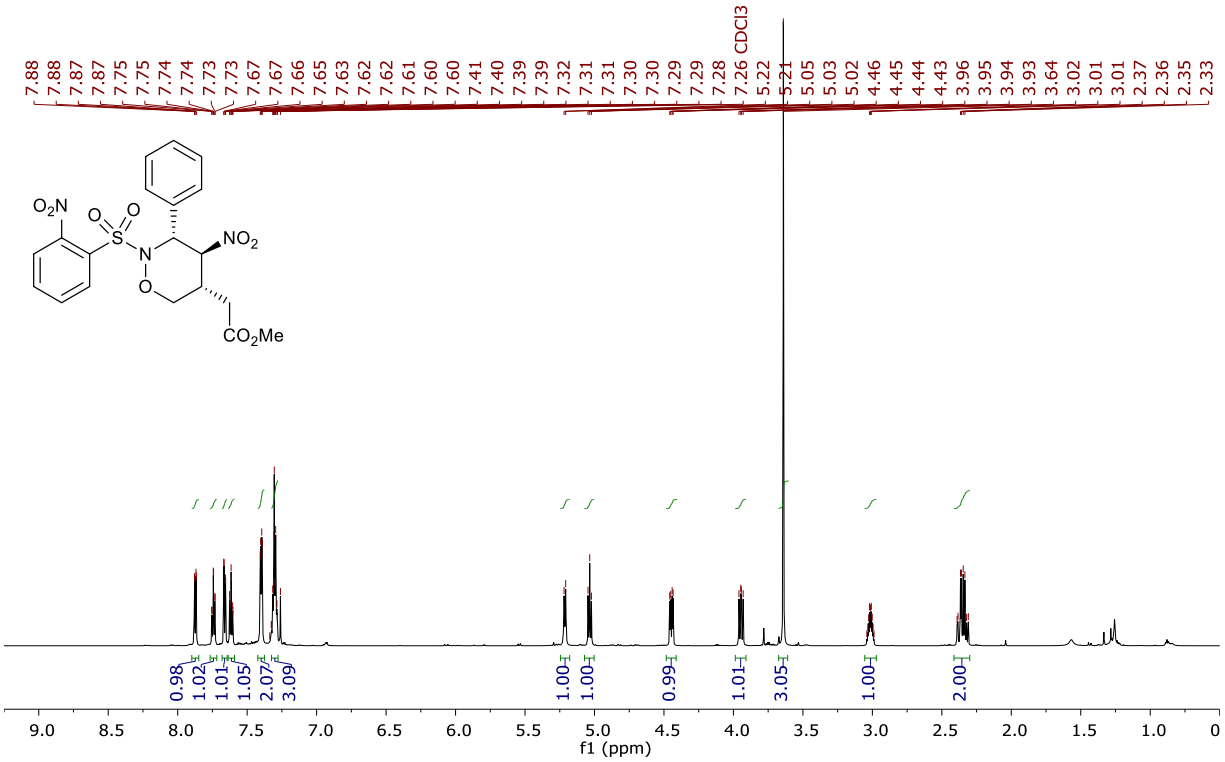


^{13}C NMR

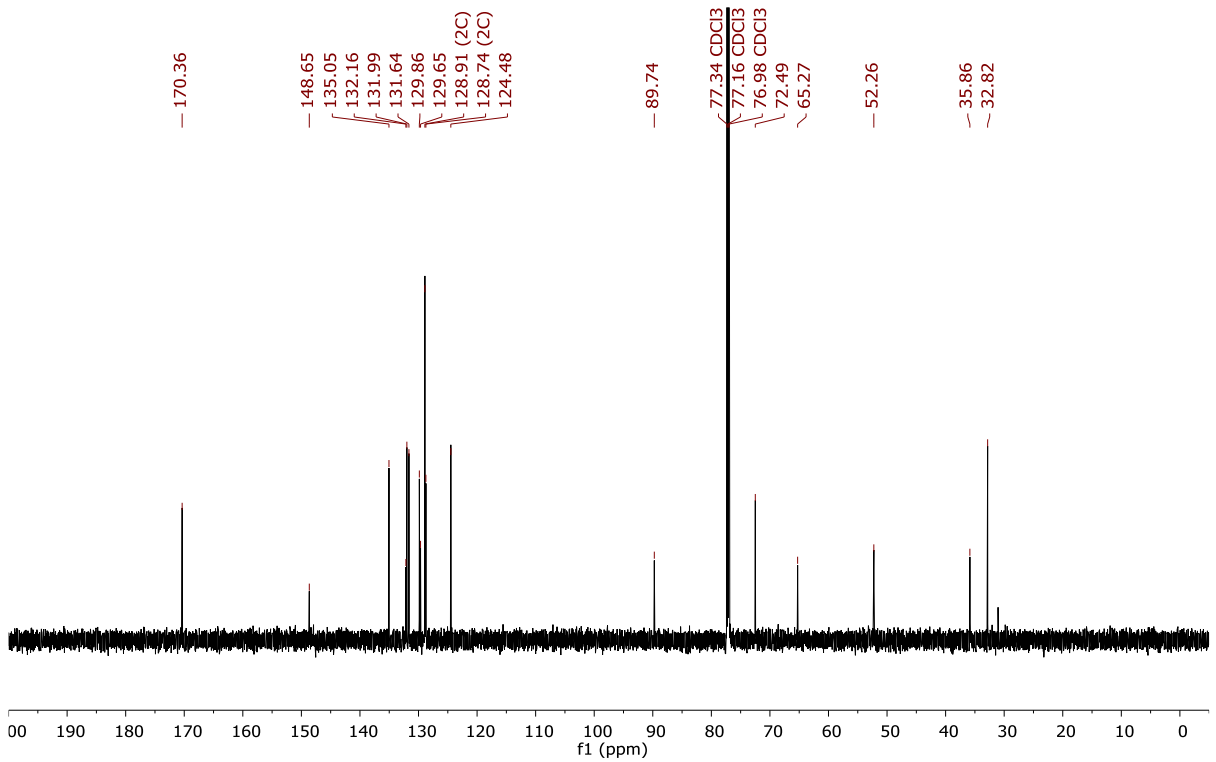


3da Methyl 2-((3*R*,4*S*,5*S*)-4-nitro-2-((2-nitrophenyl)sulfonyl)-3-phenyl-1,2-oxazinan-5-yl)acetate (Table 2, Entry 1)

^{1}H NMR

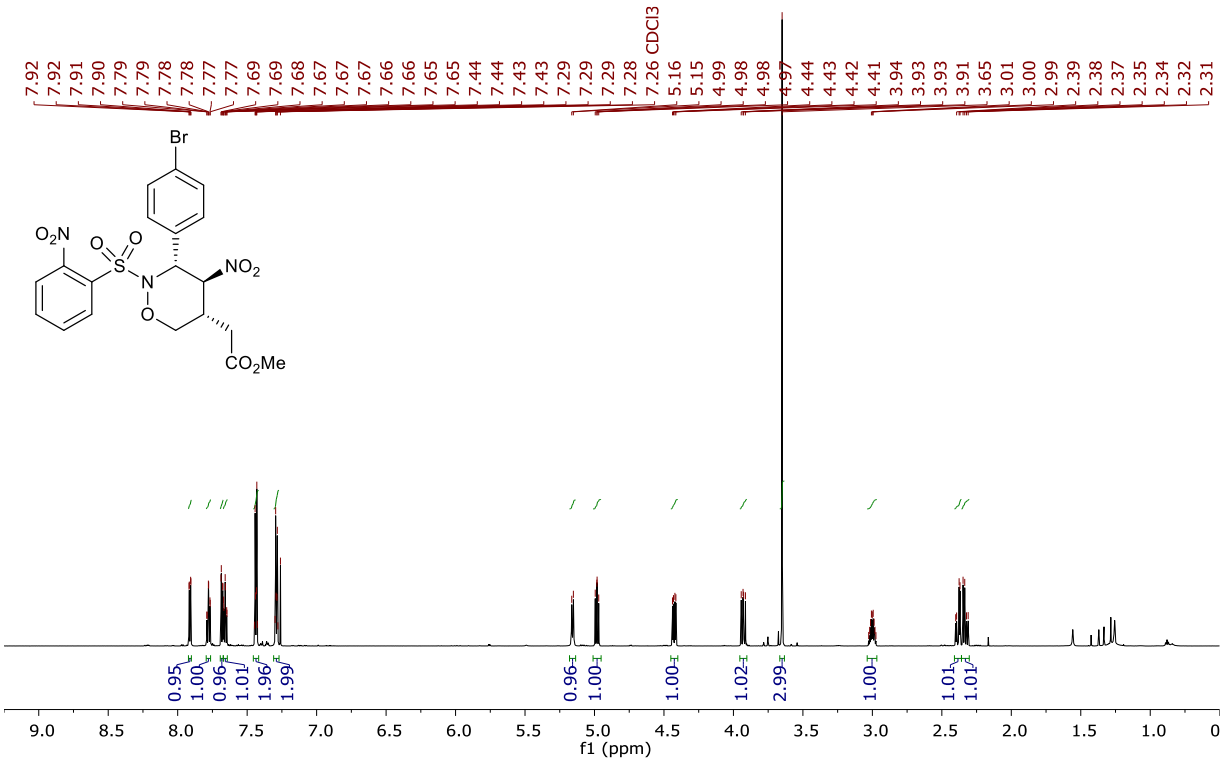


^{13}C NMR

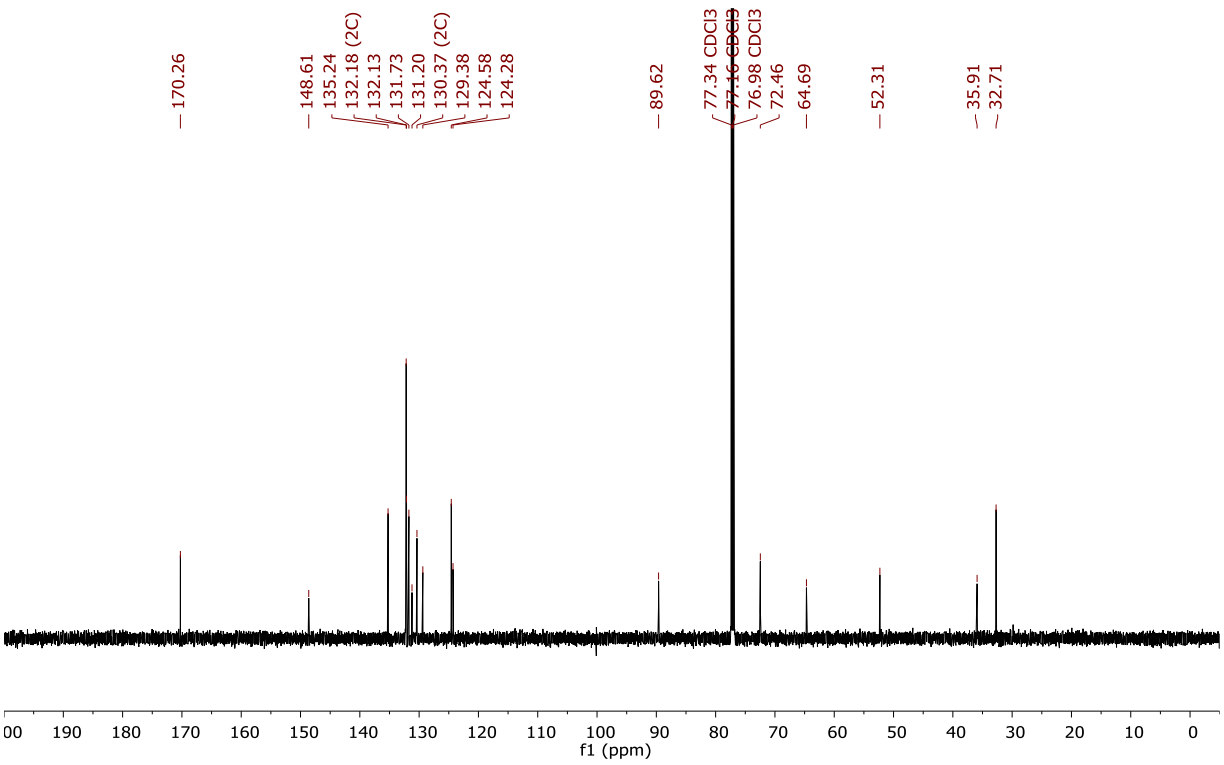


3db Methyl 2-((3*R*,4*S*,5*S*)-3-(4-bromophenyl)-4-nitro-2-((2-nitrophenyl)sulfonyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 2)

^{1}H NMR

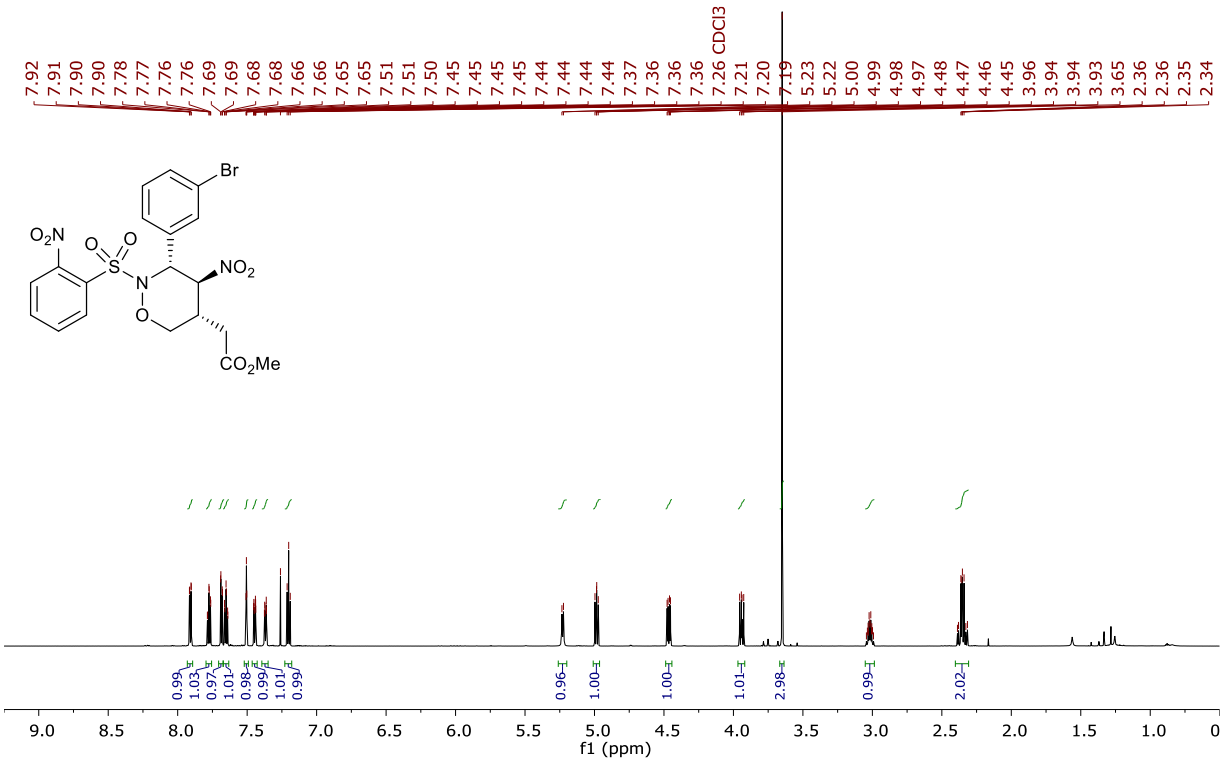


^{13}C NMR

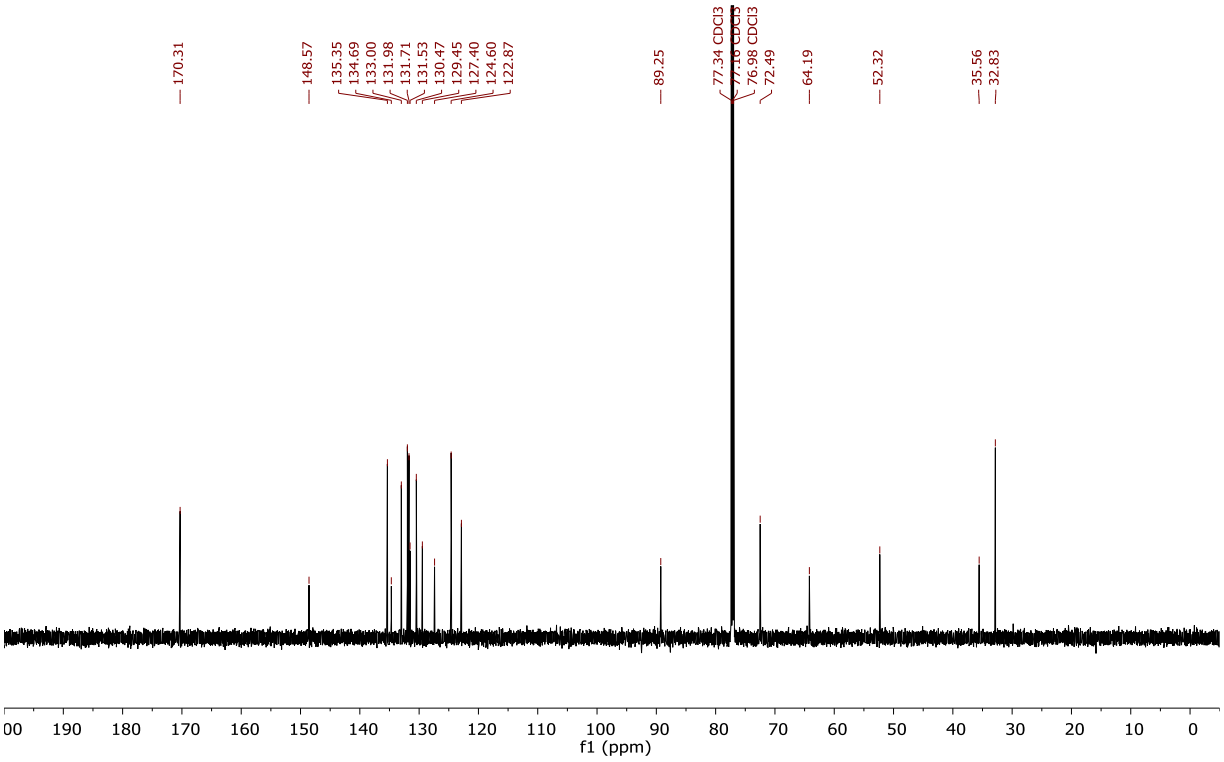


3dc Methyl 2-((3*R*,4*S*,5*S*)-3-(3-bromophenyl)-4-nitro-2-((2-nitrophenyl)sulfonyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 3)

^{1}H NMR

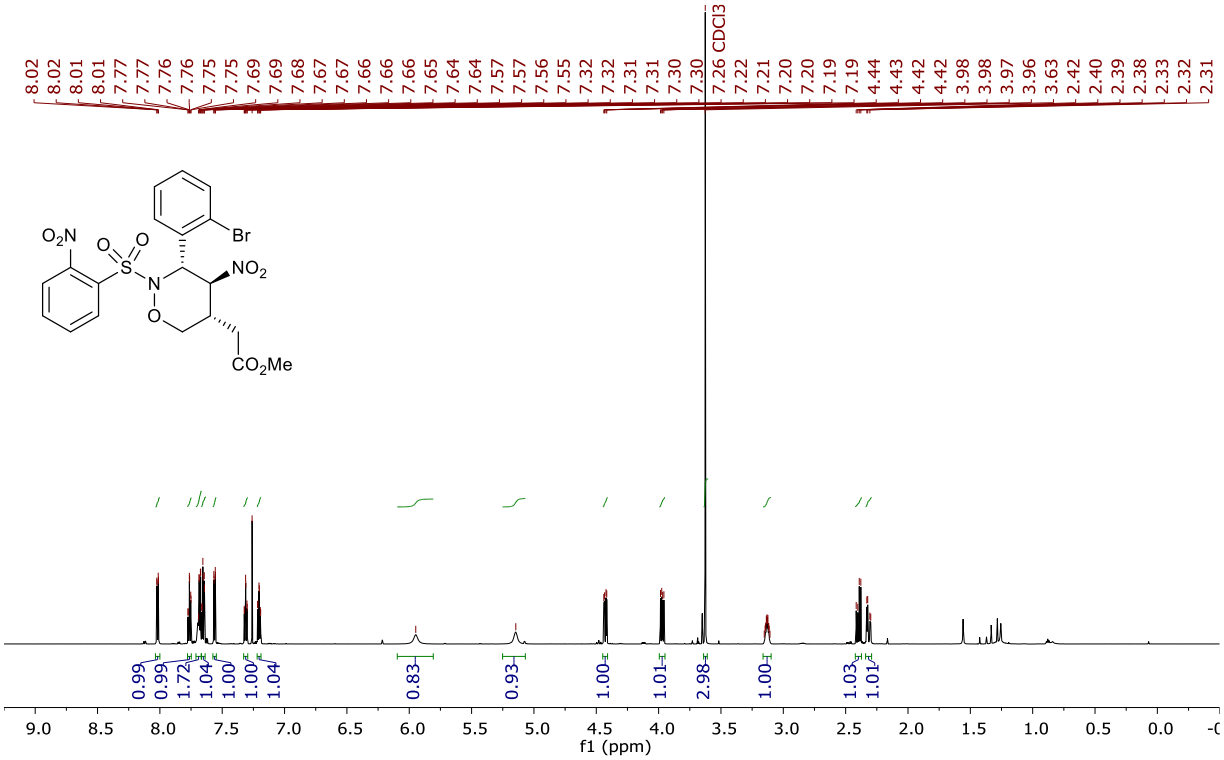


^{13}C NMR

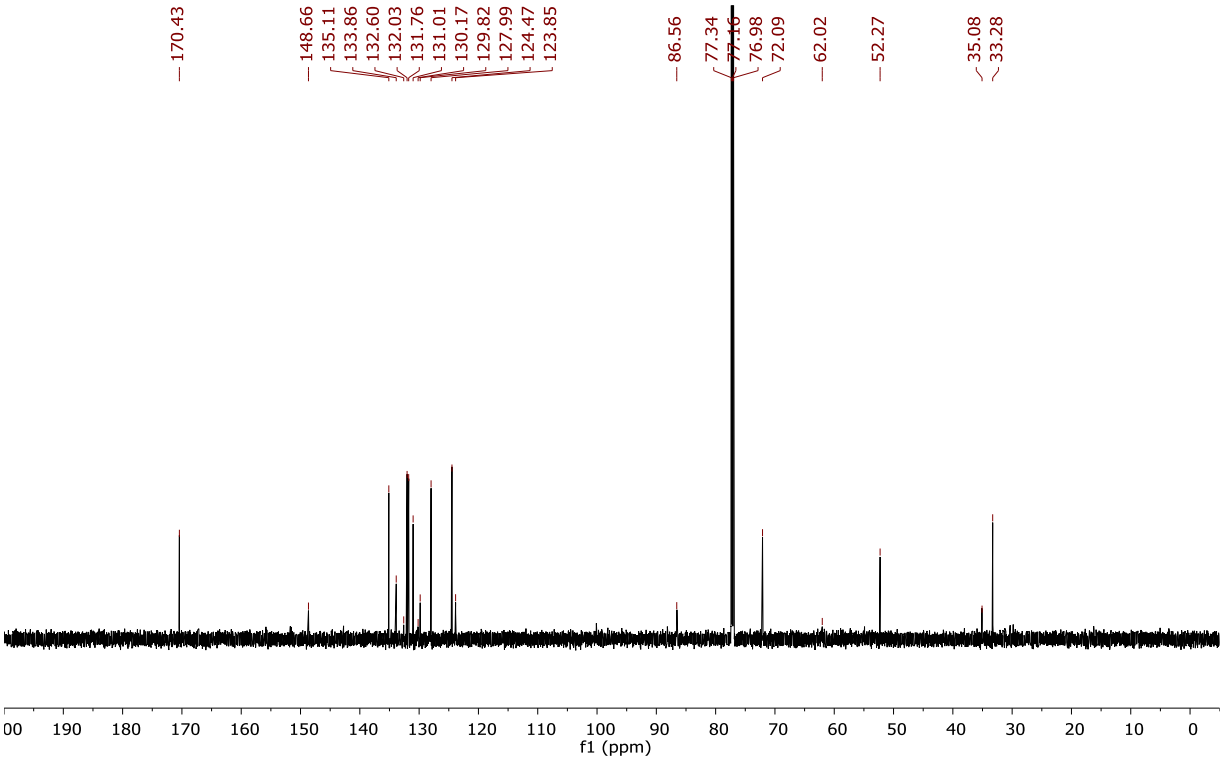


3dd Methyl 2-((3*R*,4*S*,5*S*)-3-(2-bromophenyl)-4-nitro-2-((2-nitrophenyl)sulfonyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 4)

^{1}H NMR

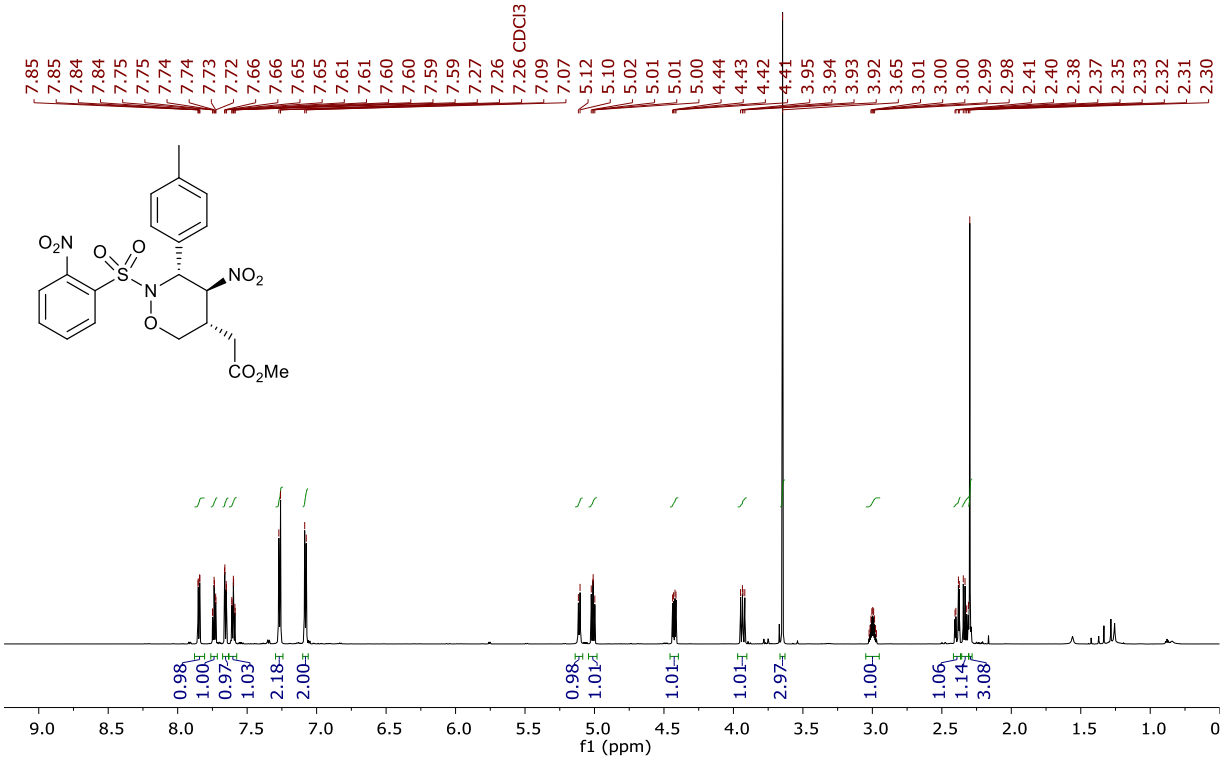


^{13}C NMR

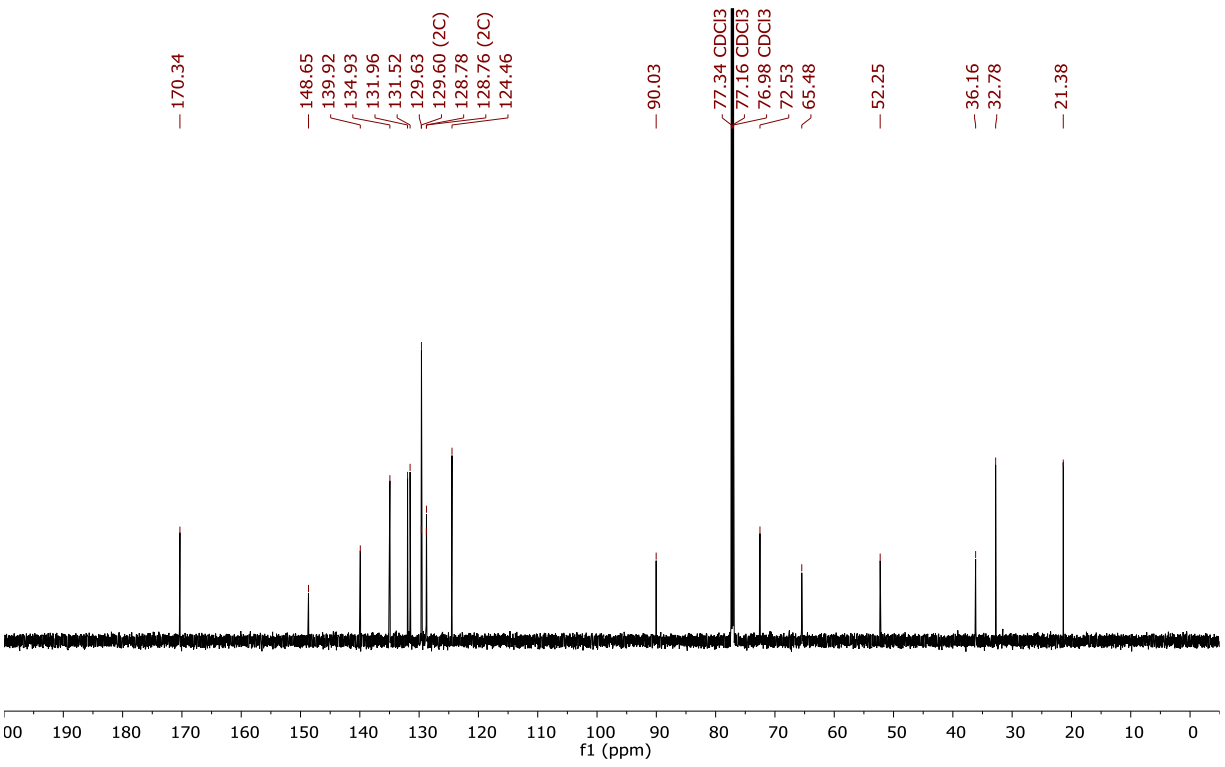


3de Methyl 2-((3*R*,4*S*,5*S*)-4-nitro-2-((2-nitrophenyl)sulfonyl)-3-(*p*-tolyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 5)

^{1}H NMR

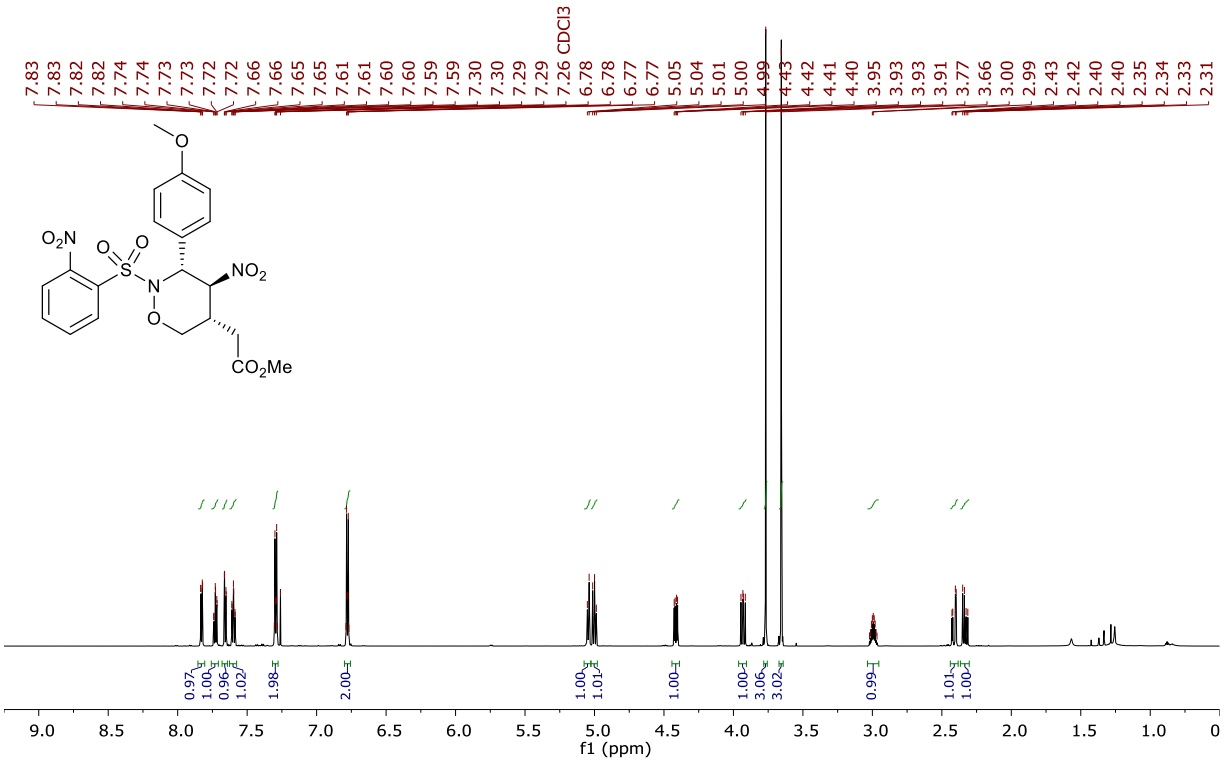


^{13}C NMR

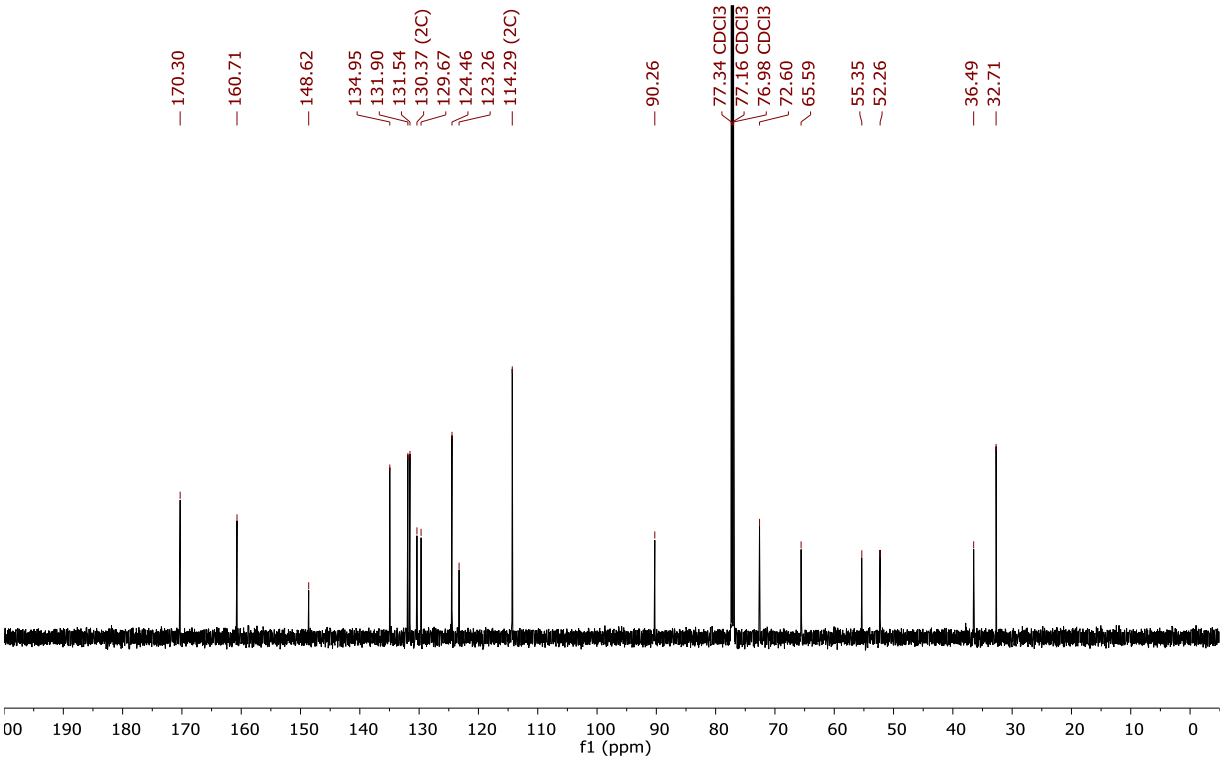


3df Methyl 2-((3*R*,4*S*,5*S*)-3-(4-methoxyphenyl)-4-nitro-2-((2-nitrophenyl)sulfonyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 6)

^{1}H NMR

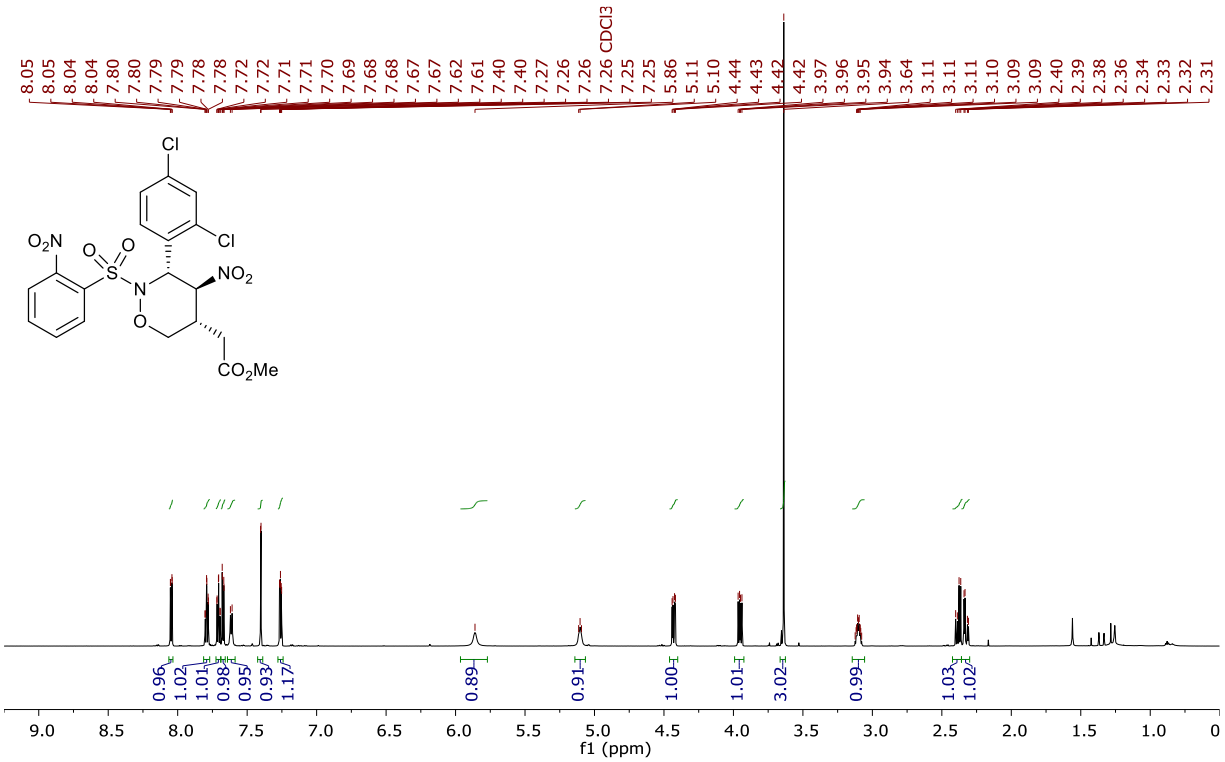


^{13}C NMR

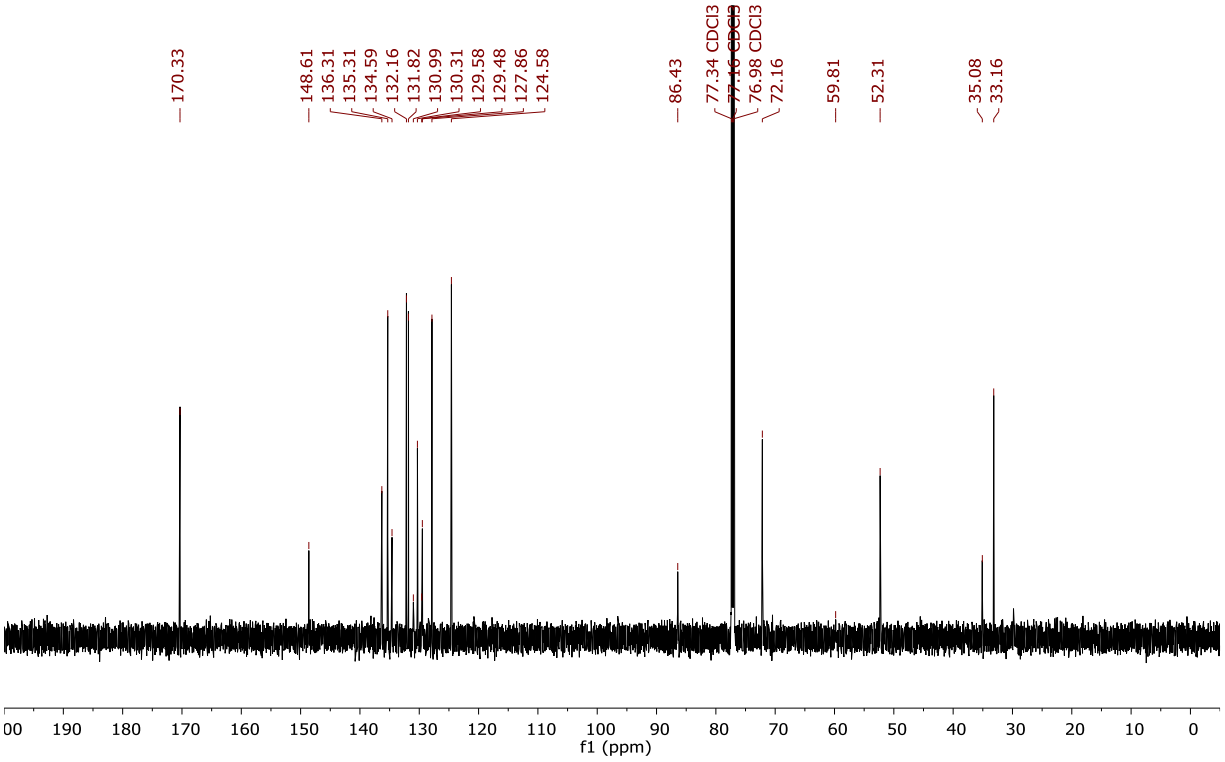


3dg Methyl 2-((3*R*,4*S*,5*S*)-3-(2,4-dichlorophenyl)-4-nitro-2-((2-nitrophenyl)sulfonyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 7)

^{1}H NMR

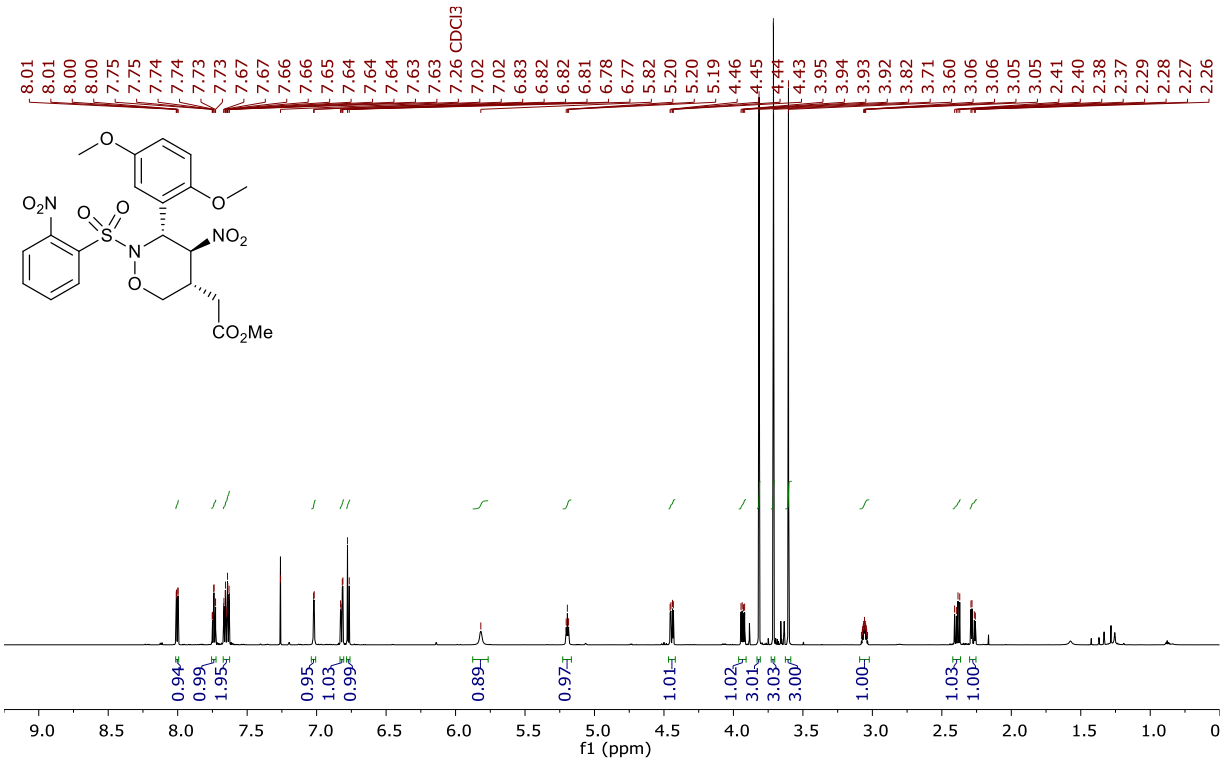


^{13}C NMR

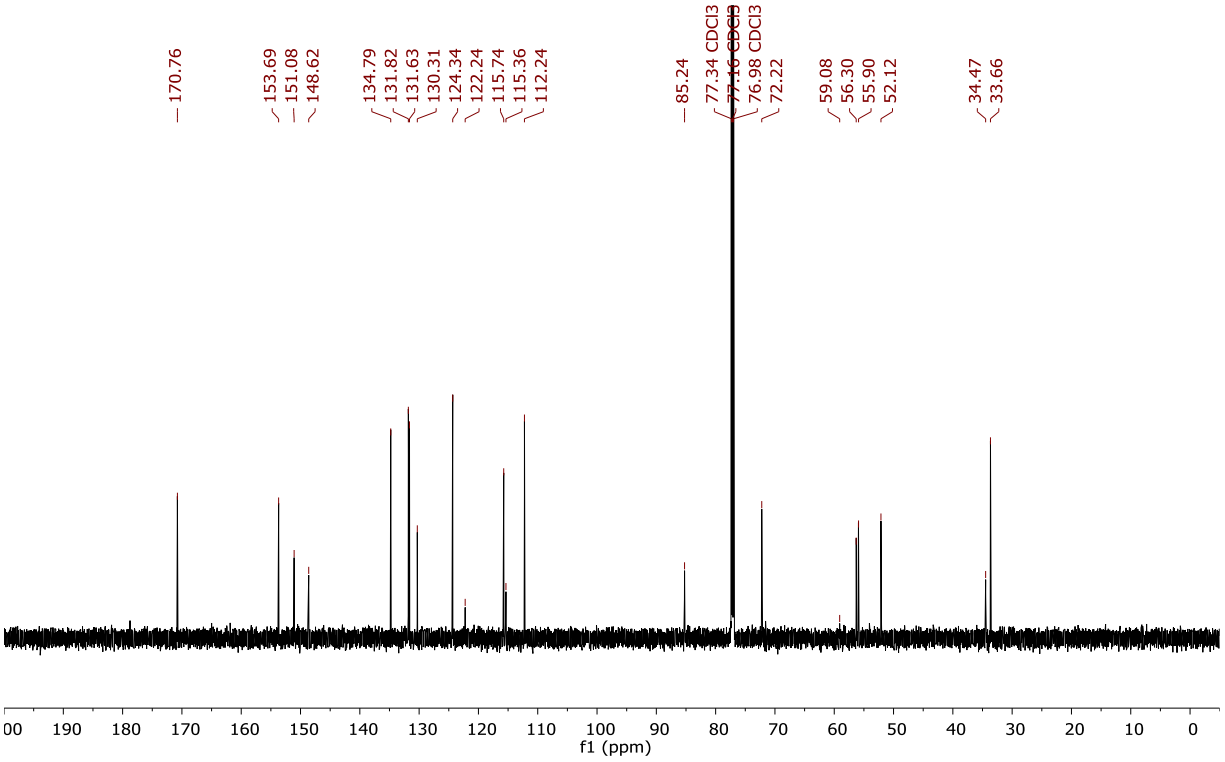


3dh Methyl 2-((3*R*,4*S*,5*S*)-3-(2,5-dimethoxyphenyl)-4-nitro-2-((2-nitrophenyl)sulfonyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 8)

^{1}H NMR

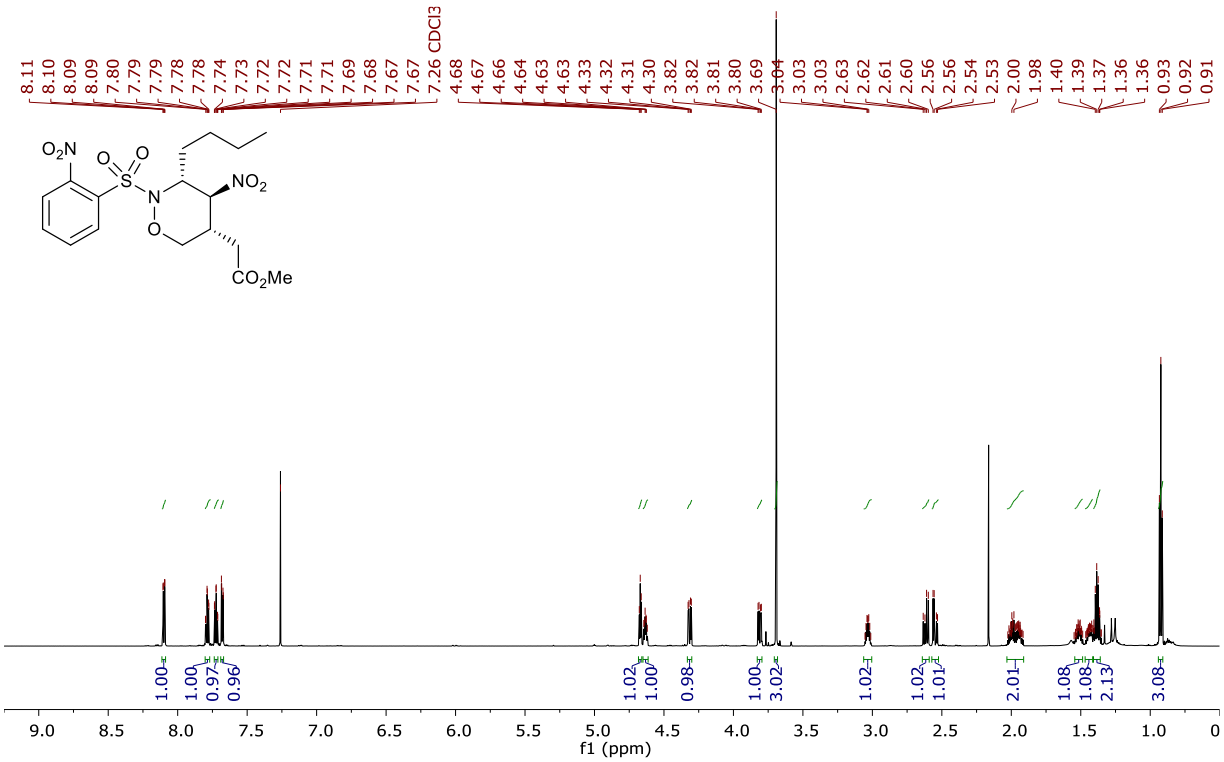


^{13}C NMR

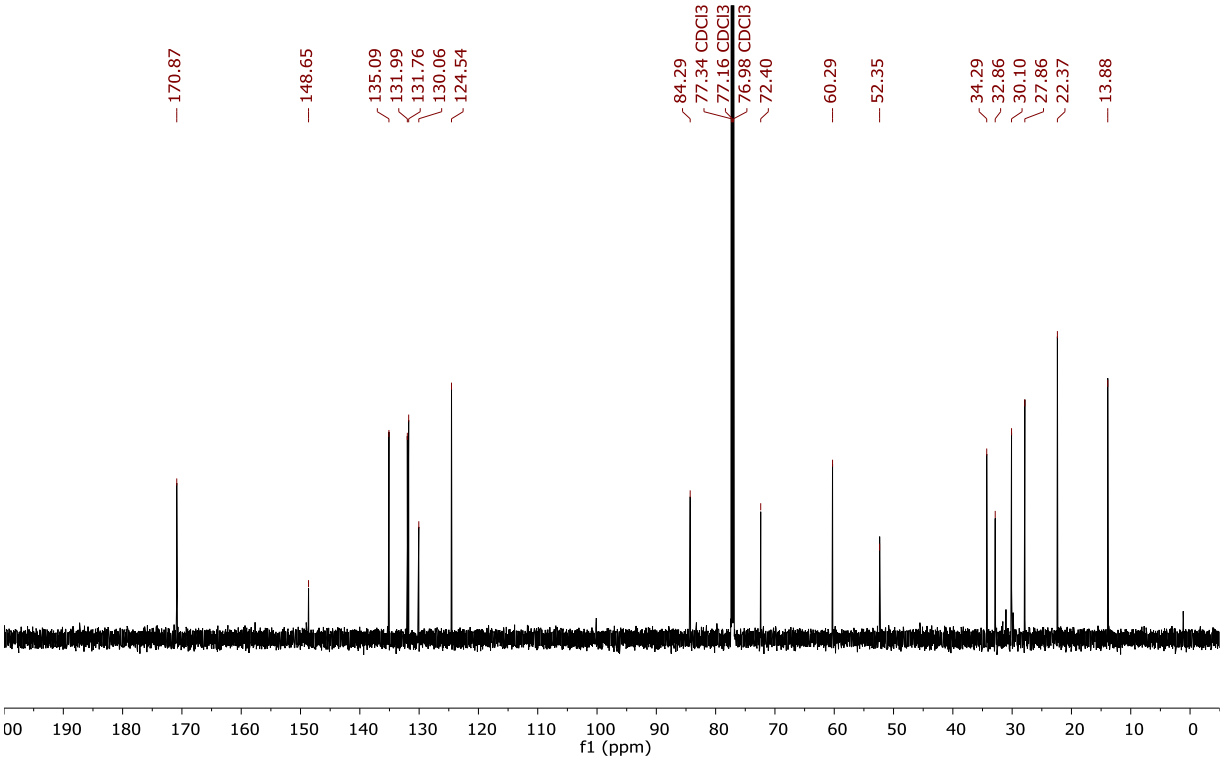


3di Methyl 2-((3*R*,4*S*,5*S*)-3-butyl-4-nitro-2-((2-nitrophenyl)sulfonyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 9)

^{1}H NMR

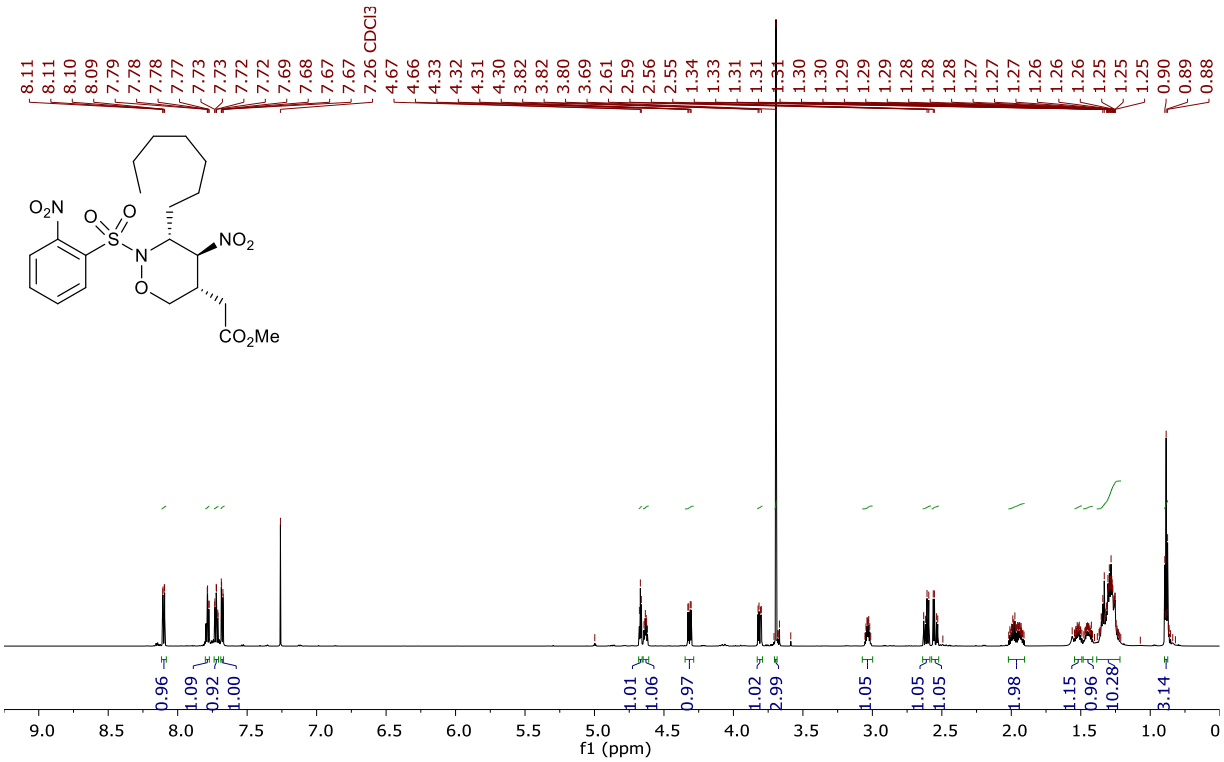


^{13}C NMR

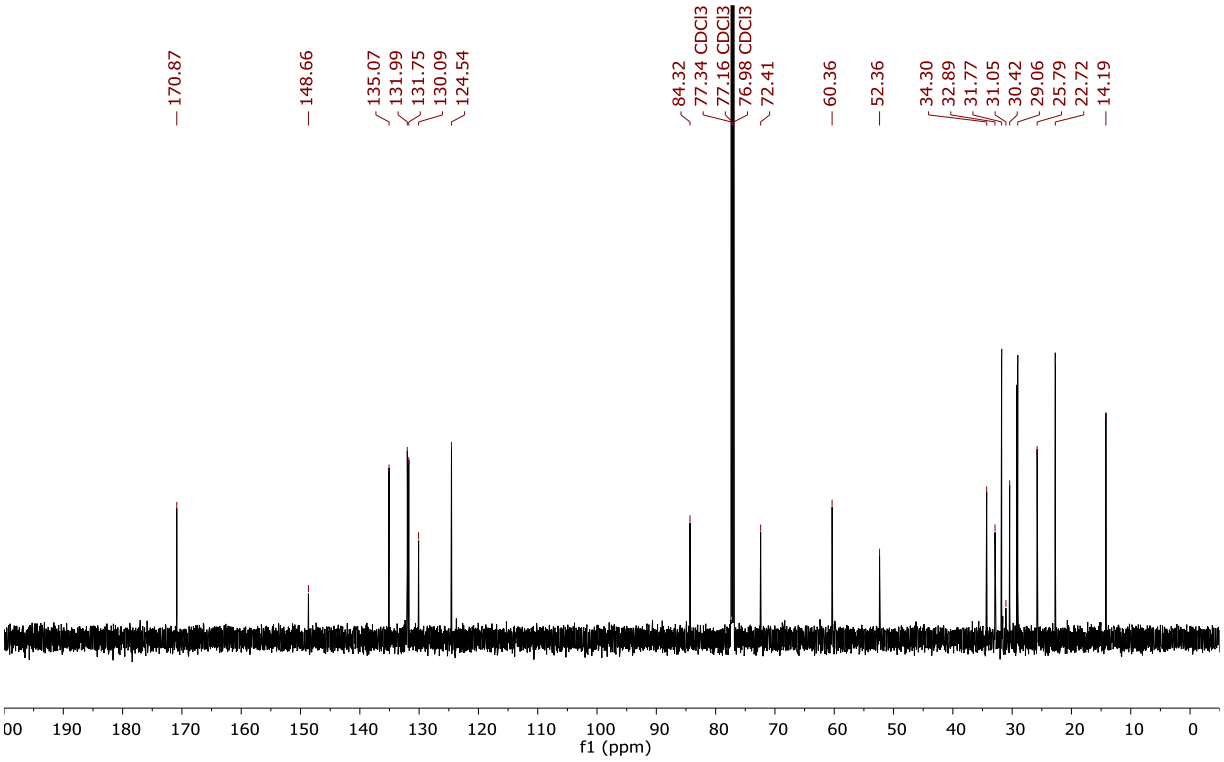


3dj Methyl 2-((3*R*,4*S*,5*S*)-3-heptyl-4-nitro-2-((2-nitrophenyl)sulfonyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 10)

^{1}H NMR

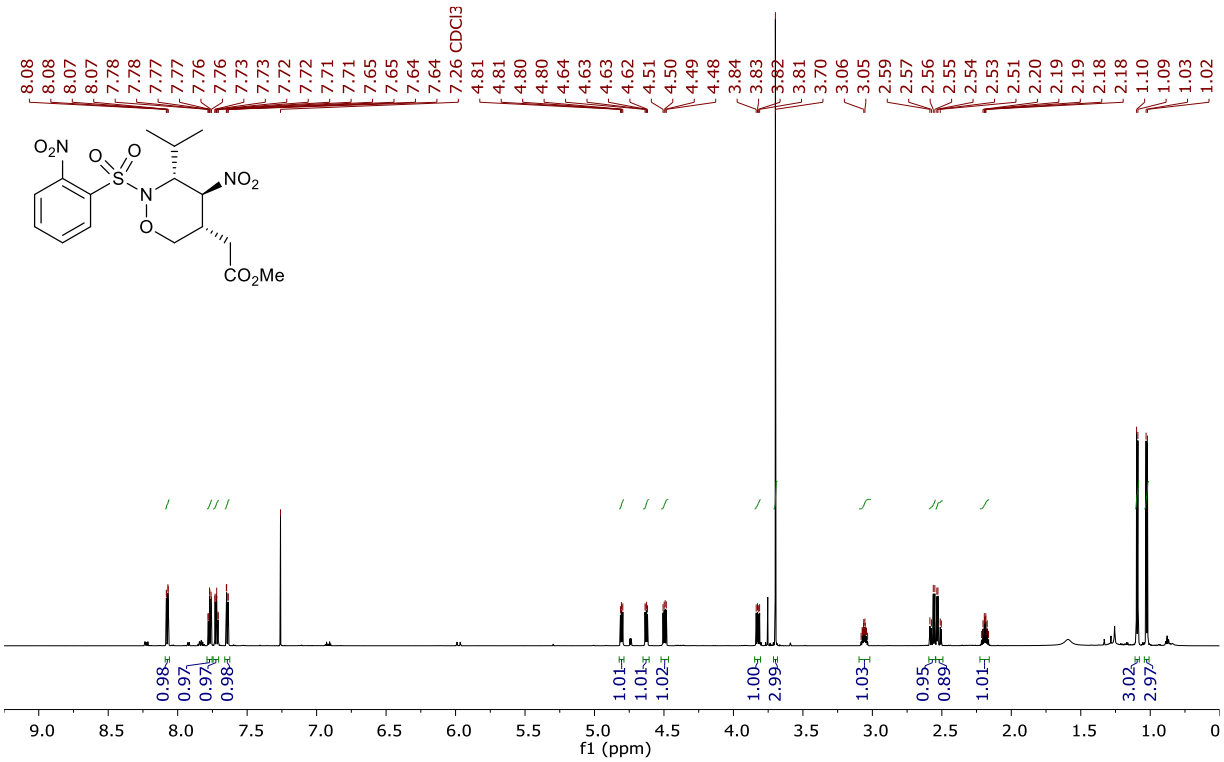


^{13}C NMR

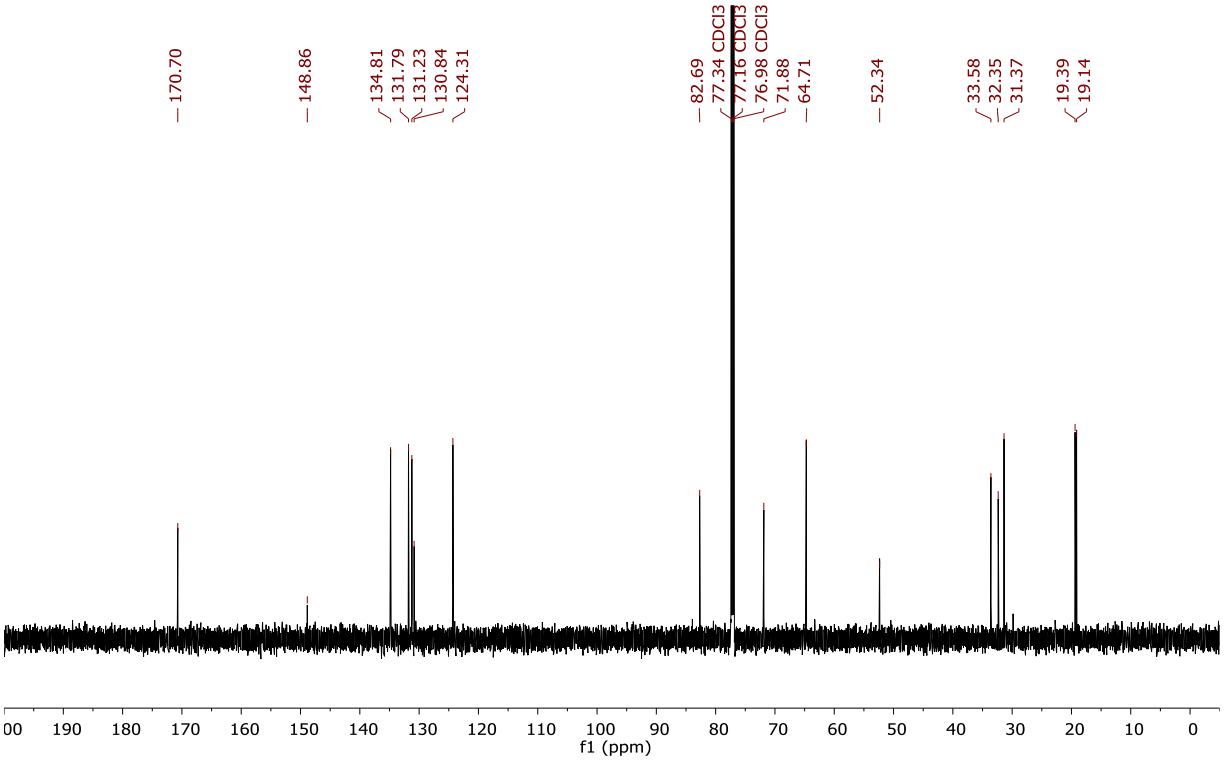


3dk Methyl 2-((3*R*,4*S*,5*S*)-3-isopropyl-4-nitro-2-((2-nitrophenyl)sulfonyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 11)

^{1}H NMR

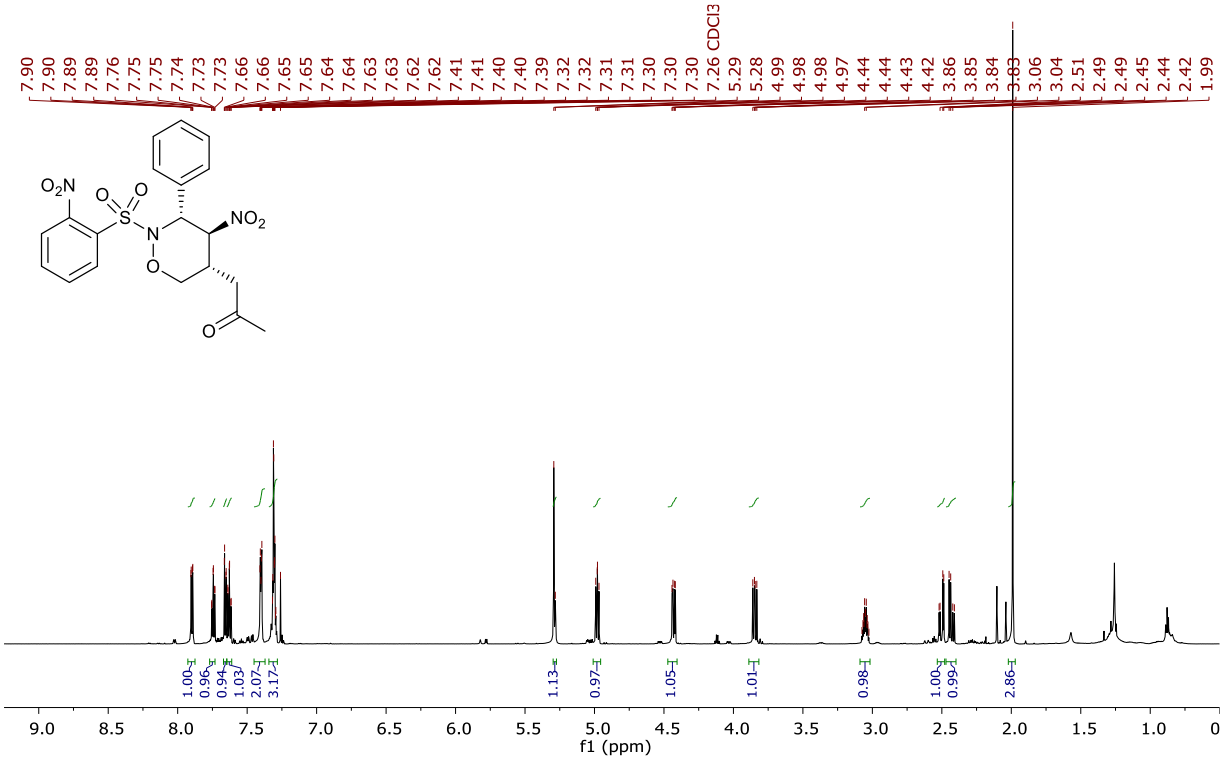


^{13}C NMR

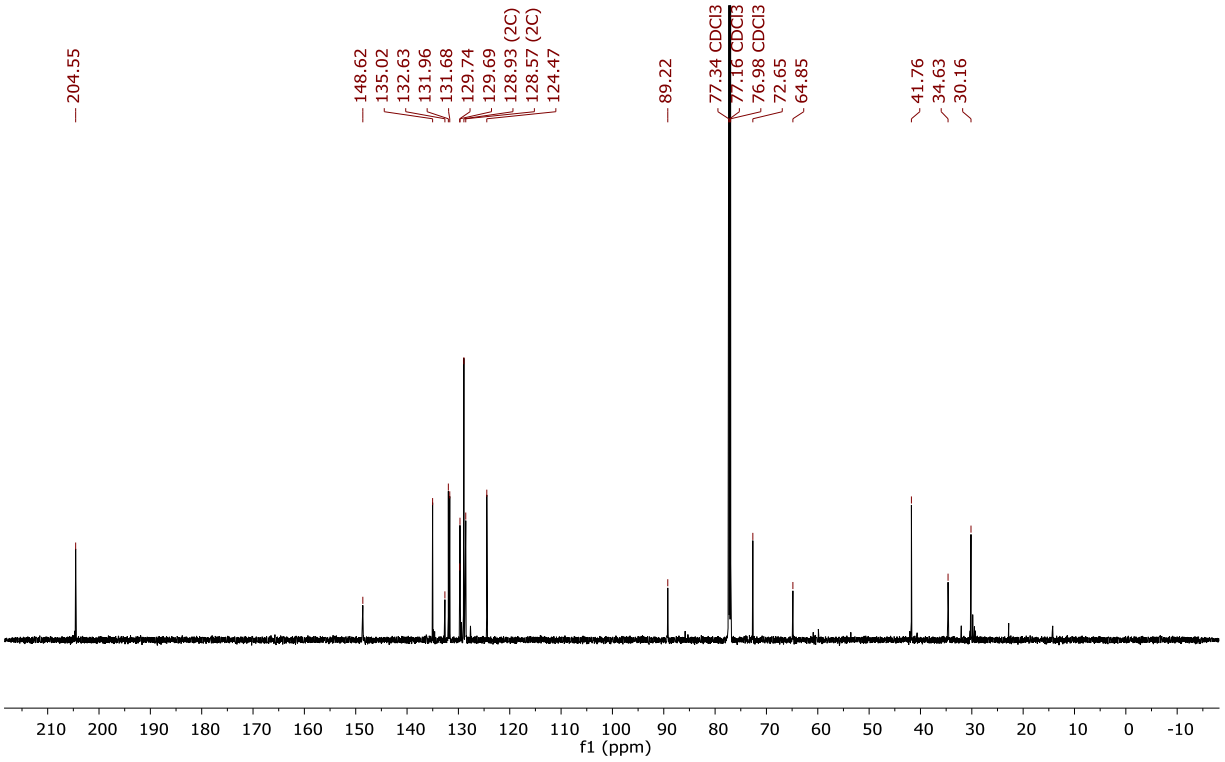


3ea 1-((3*R*,4*S*,5*S*)-4-Nitro-2-((2-nitrophenyl)sulfonyl)-3-phenyl-1,2-oxazinan-5-yl)propan-2-one (Scheme 2)

^{1}H NMR

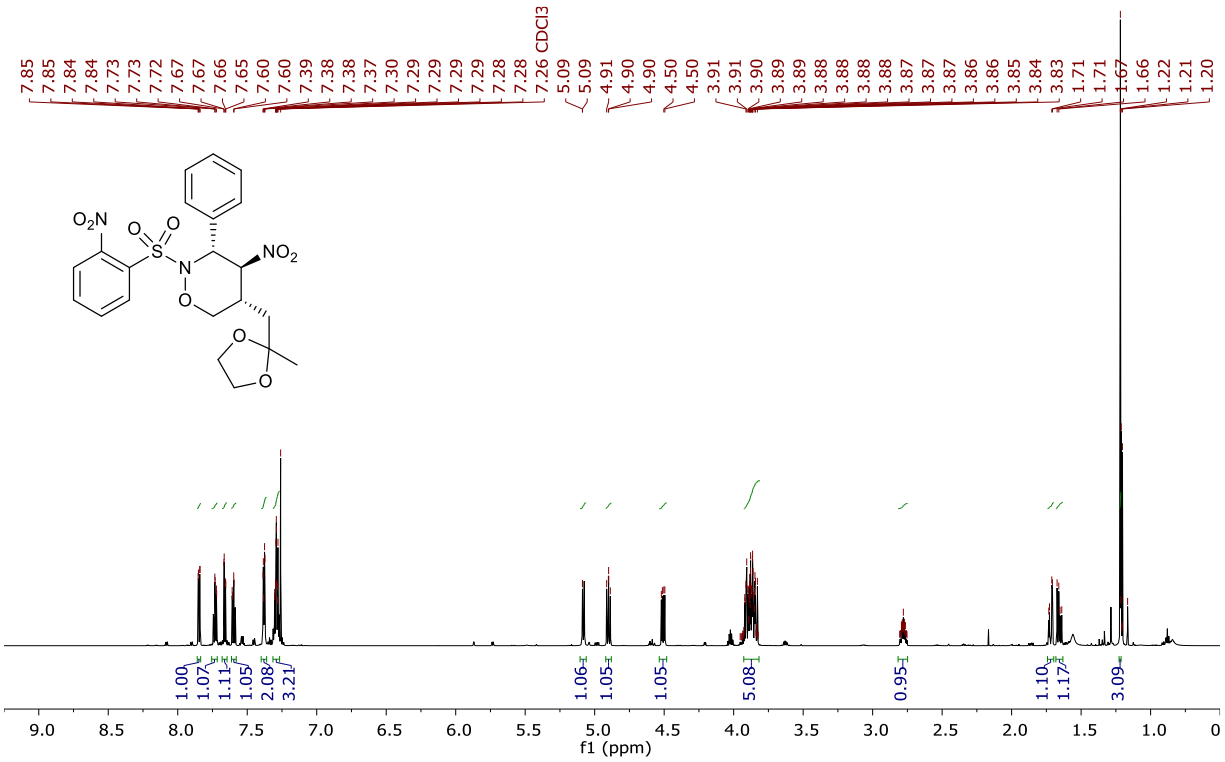


^{13}C NMR

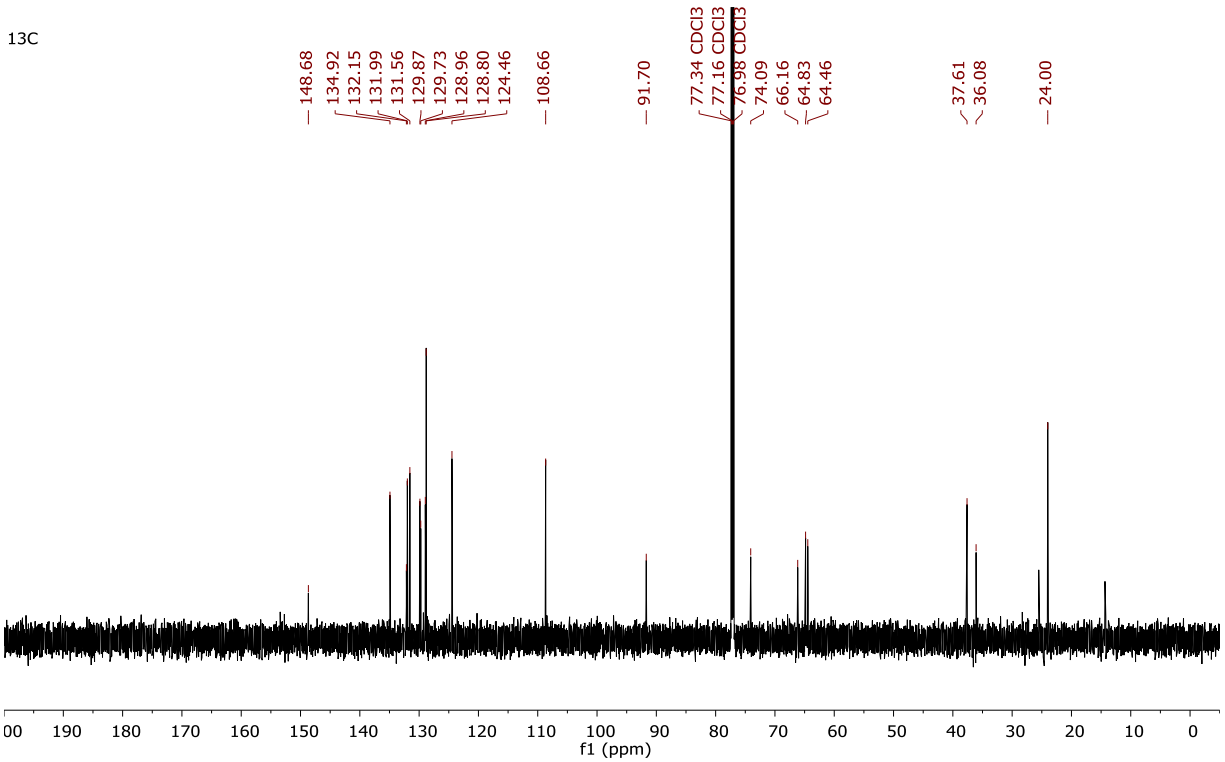


10 (3*R*,4*S*,5*S*)-5-((2-Methyl-1,3-dioxolan-2-yl)methyl)-4-nitro-2-((2-nitrophenyl)sulfonyl)-3-phenyl-1,2-oxazinane

^{1}H NMR

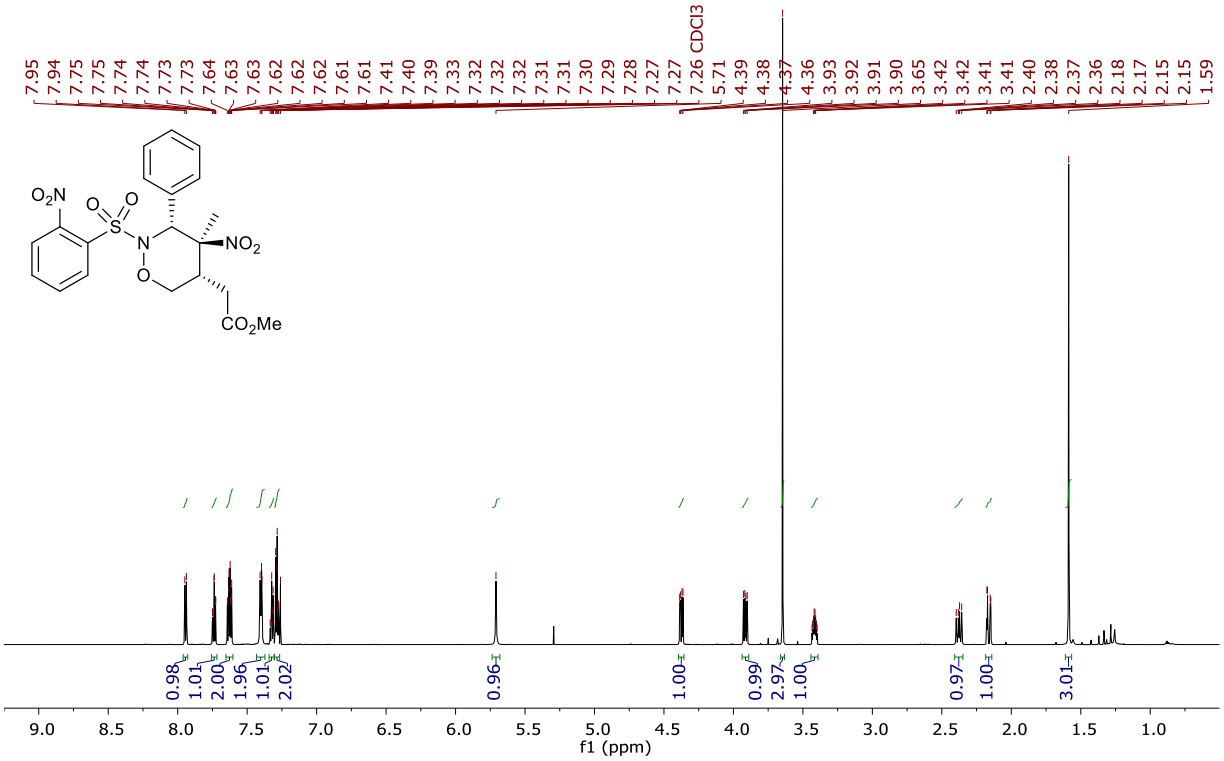


^{13}C NMR

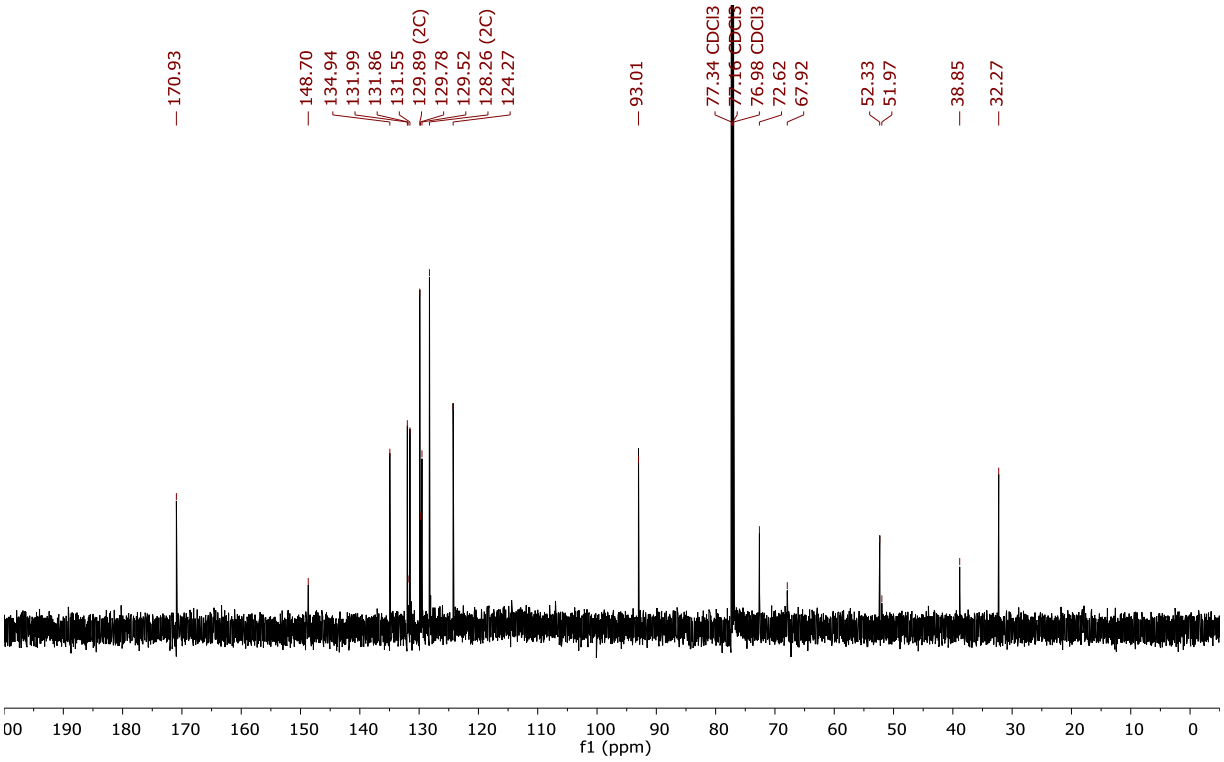


3dl Methyl 2-((3*R*,4*S*,5*S*)-4-methyl-4-nitro-2-((2-nitrophenyl)sulfonyl)-3-phenyl-1,2-oxazinan-5-yl)acetate (Scheme 2)

^{1}H NMR



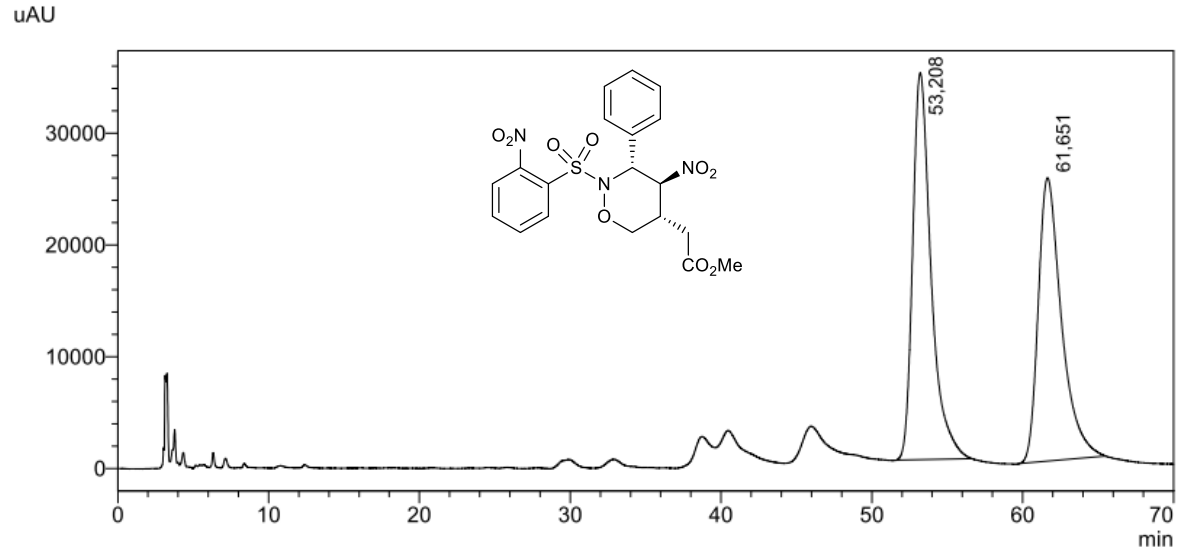
^{13}C NMR



7. HPLC traces

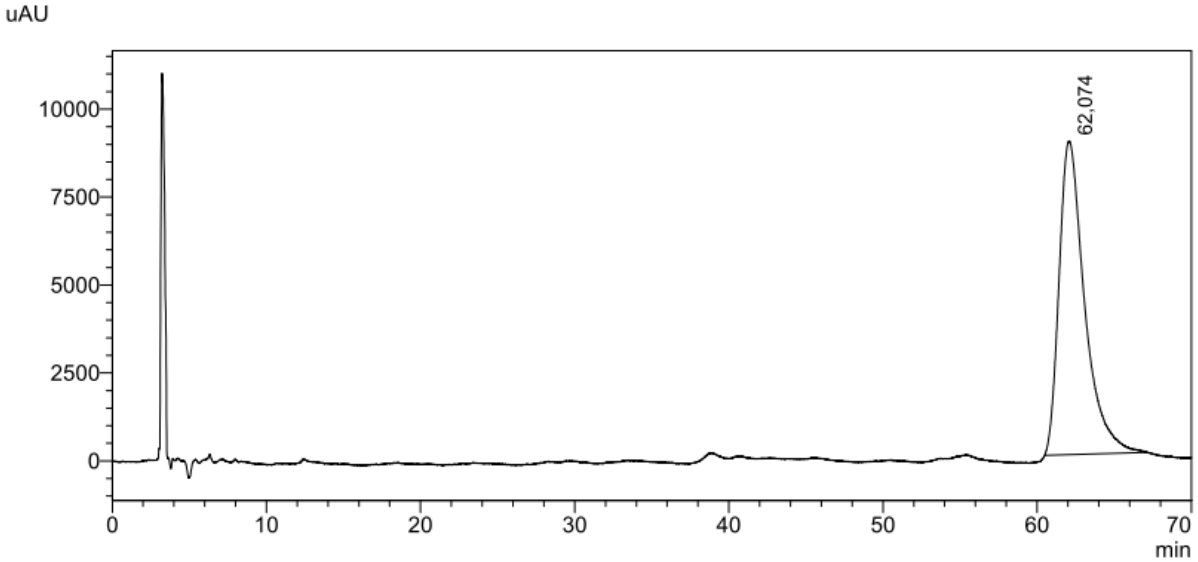
3da Methyl 2-((3*R*,4*S*,5*S*)-4-nitro-2-((2-nitrophenyl)sulfonyl)-3-phenyl-1,2-oxazinan-5-yl)acetate (Table 2, Entry 1)

Racemic sample



Peak#	Ret. Time	Area%
1	53,208	51,952
2	61,651	48,048
Total		100,000

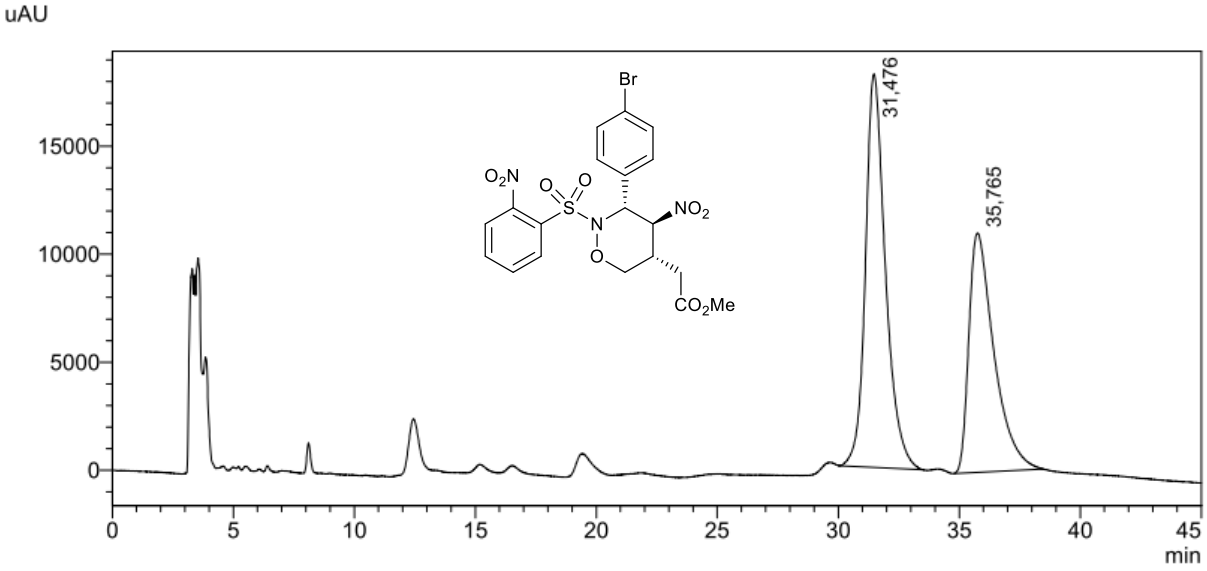
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	62,074	100,000
Total		100,000

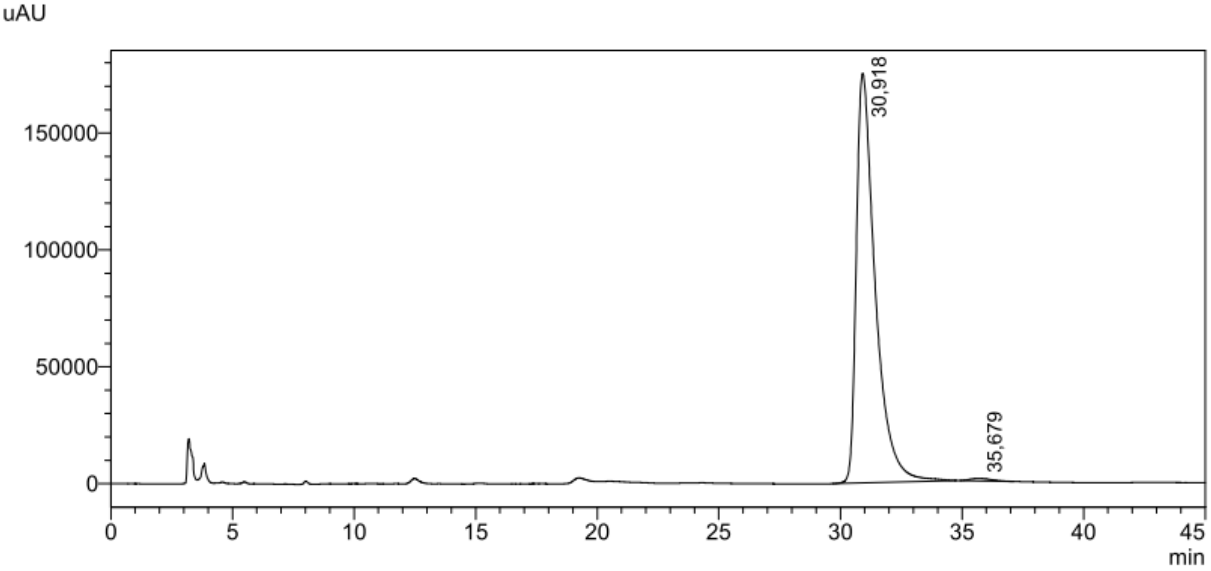
3db Methyl 2-((3*R*,4*S*,5*S*)-3-(4-bromophenyl)-4-nitro-2-((2-nitrophenyl)sulfonyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 2)

Racemic Sample



Peak#	Ret. Time	Area%
1	31,476	56,716
2	35,765	43,284
Total		100,000

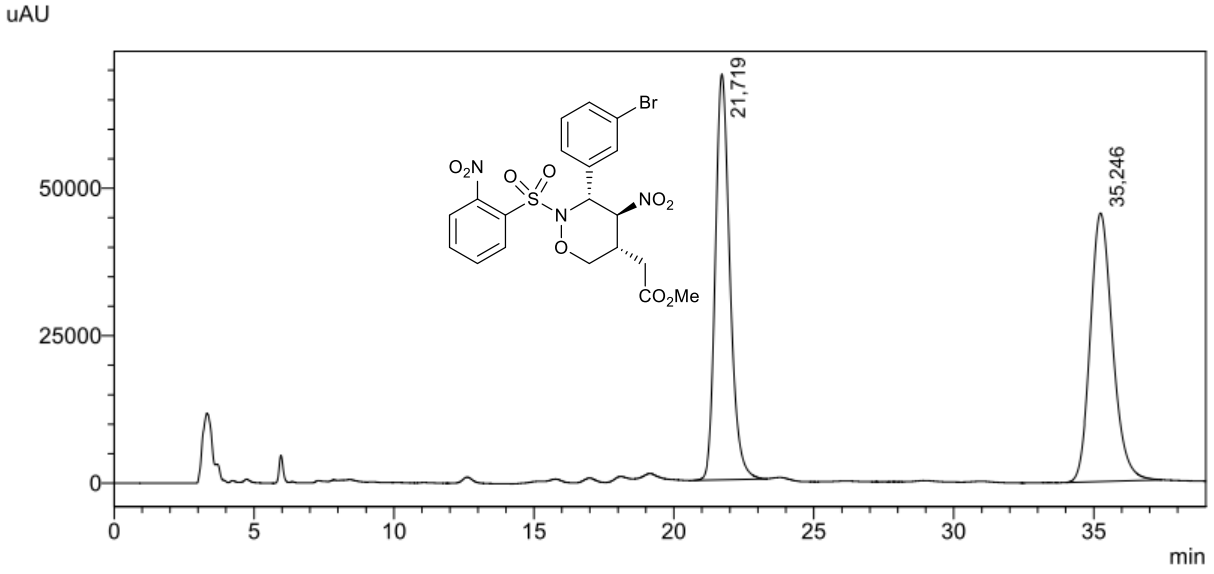
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	30,918	99,353
2	35,679	0,647
Total		100,000

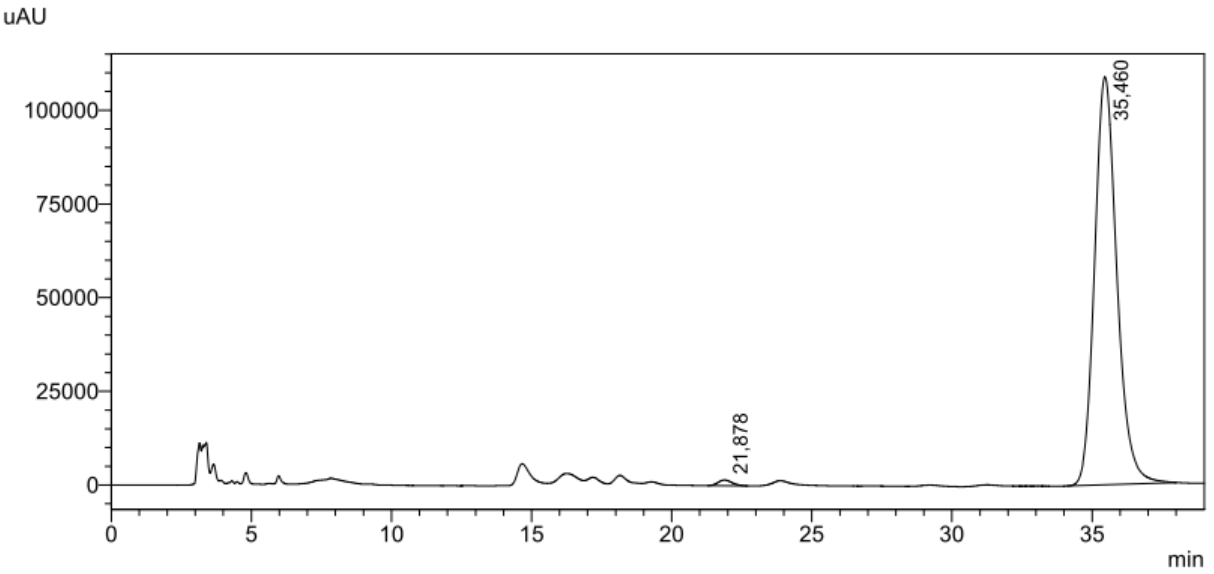
3dc Methyl 2-((3*R*,4*S*,5*S*)-3-(3-bromophenyl)-4-nitro-2-((2-nitrophenyl)sulfonyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 3)

Racemic Sample



Peak#	Ret. Time	Area%
1	21,719	49,674
2	35,246	50,326
Total		100,000

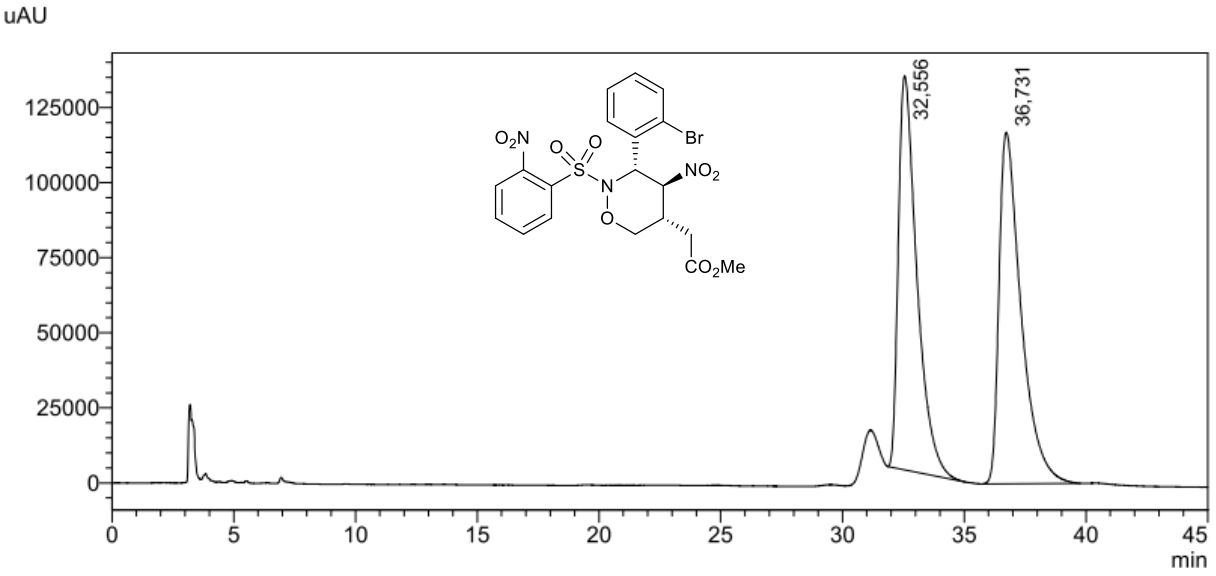
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	21,878	0,876
2	35,460	99,124
Total		100,000

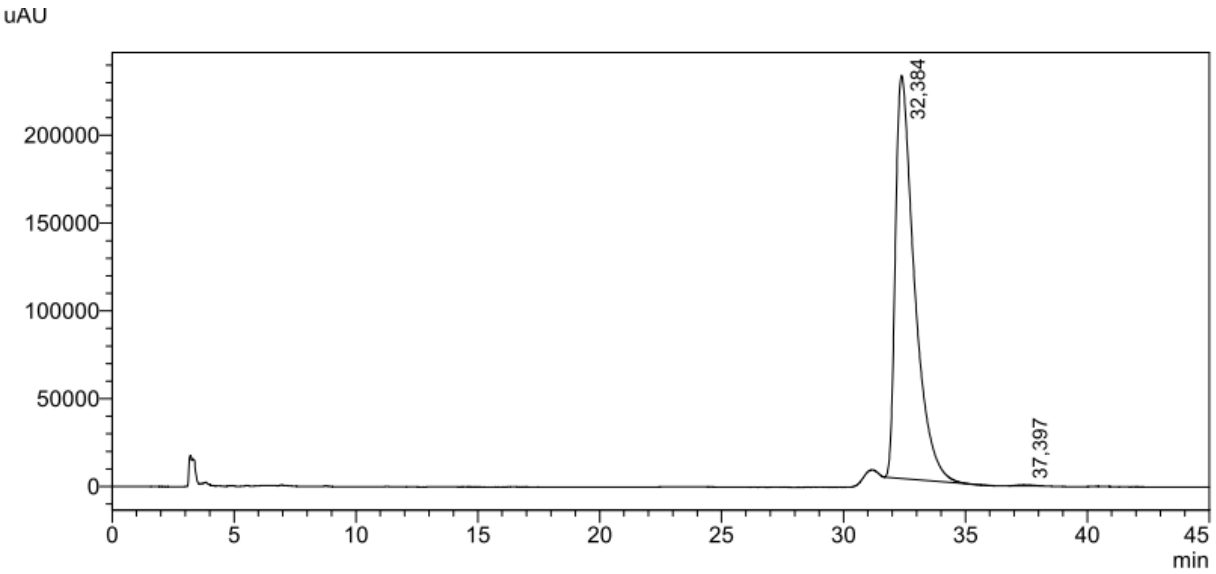
3dd Methyl 2-((3*R*,4*S*,5*S*)-3-(2-bromophenyl)-4-nitro-2-((2-nitrophenyl)sulfonyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 4)

Racemic Sample



Peak#	Ret. Time	Area%
1	32,556	48,592
2	36,731	51,408
Total		100,000

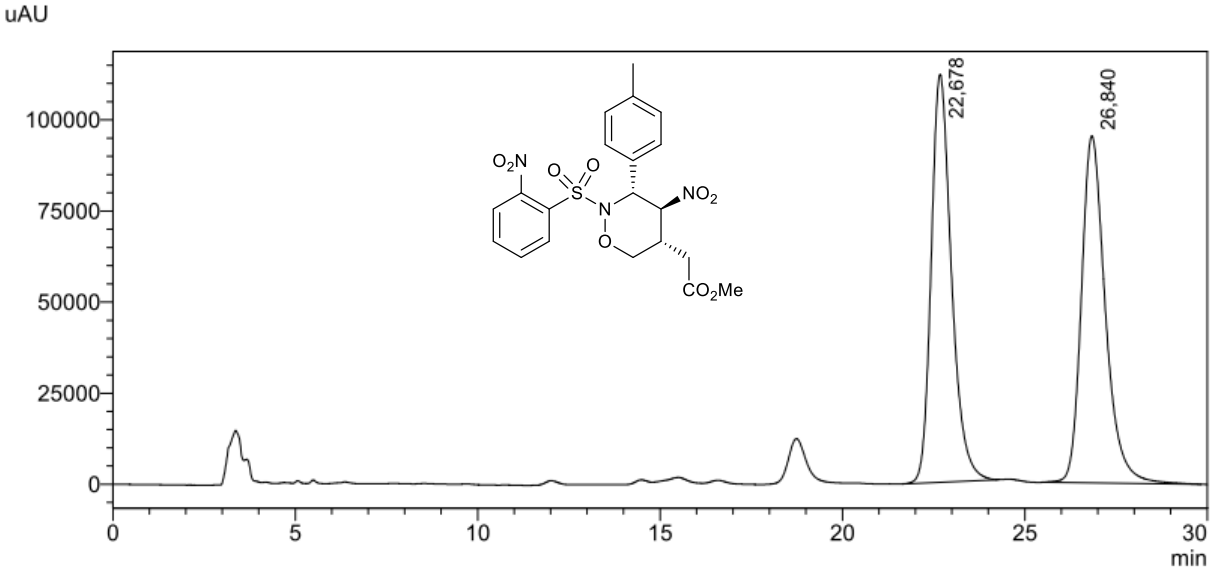
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	32,384	99,779
2	37,397	0,221
Total		100,000

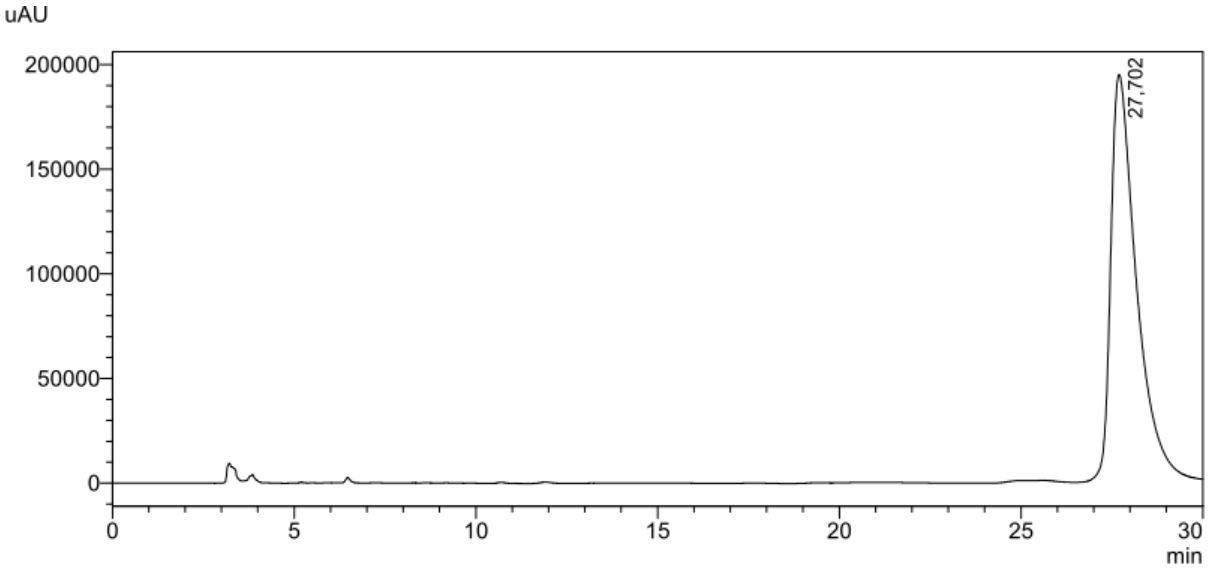
3de Methyl 2-((3*R*,4*S*,5*S*)-4-nitro-2-((2-nitrophenyl)sulfonyl)-3-(*p*-tolyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 5)

Racemic Sample



Peak#	Ret. Time	Area%
1	22,678	49,805
2	26,840	50,195
Total		100,000

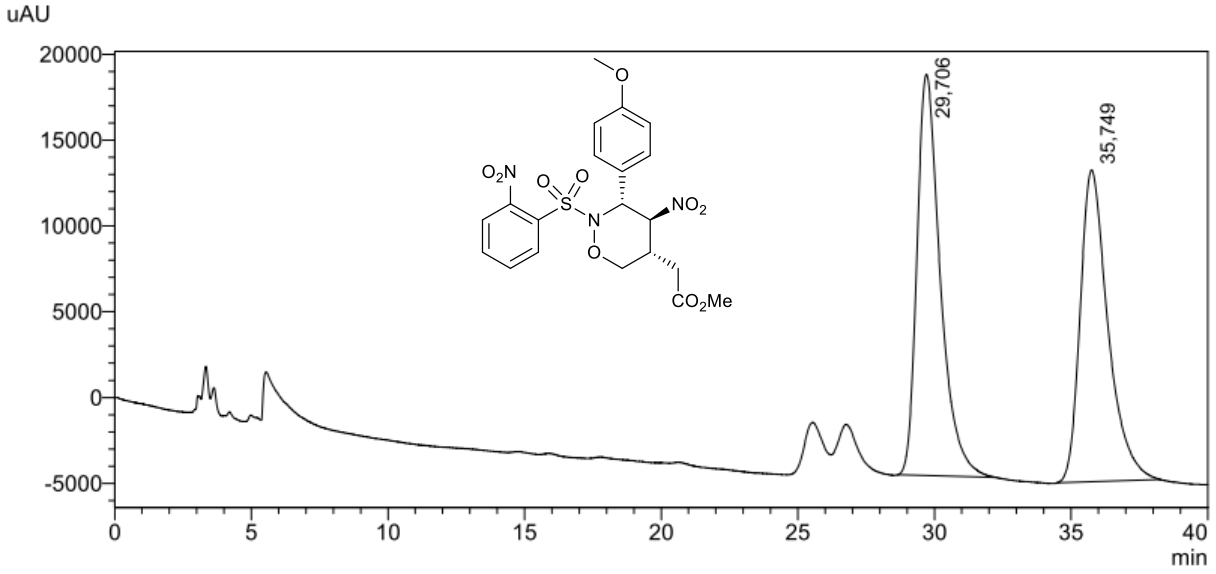
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	27,702	100,000
Total		100,000

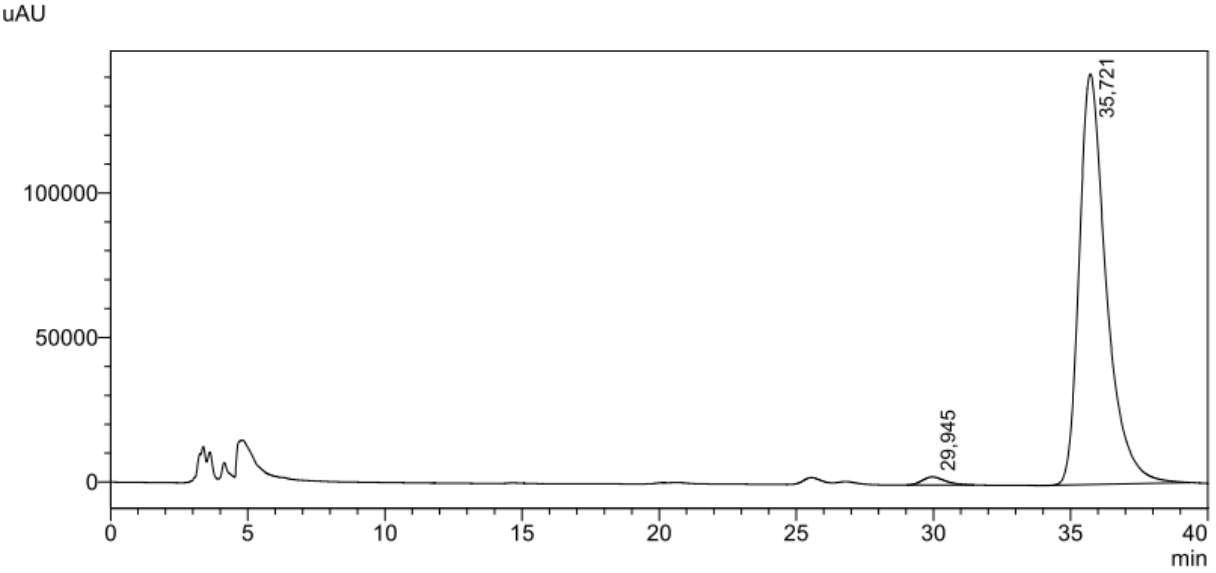
3df Methyl 2-((3*R*,4*S*,5*S*)-3-(4-methoxyphenyl)-4-nitro-2-((2-nitrophenyl)sulfonyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 6)

Racemic Sample



Peak#	Ret. Time	Area%
1	29,706	51,935
2	35,749	48,065
Total		100,000

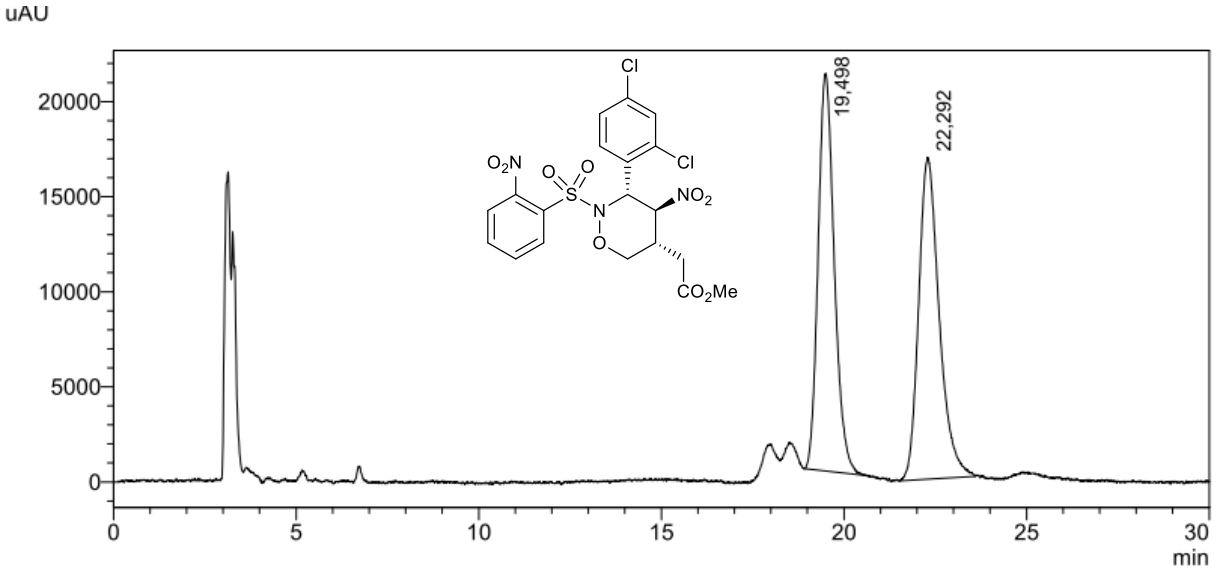
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	29,945	1,603
2	35,721	98,397
Total		100,000

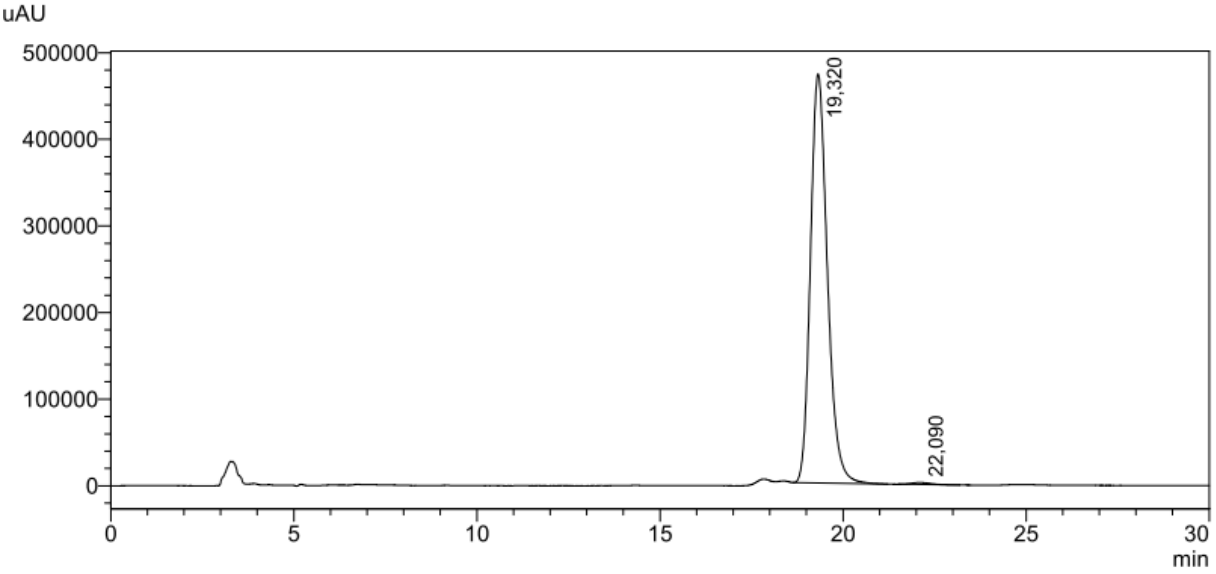
3dg Methyl 2-((3*R*,4*S*,5*S*)-3-(2,4-dichlorophenyl)-4-nitro-2-((2-nitrophenyl)sulfonyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 7)

Racemic Sample



Peak#	Ret. Time	Area%
1	19,498	49,252
2	22,292	50,748
Total		100,000

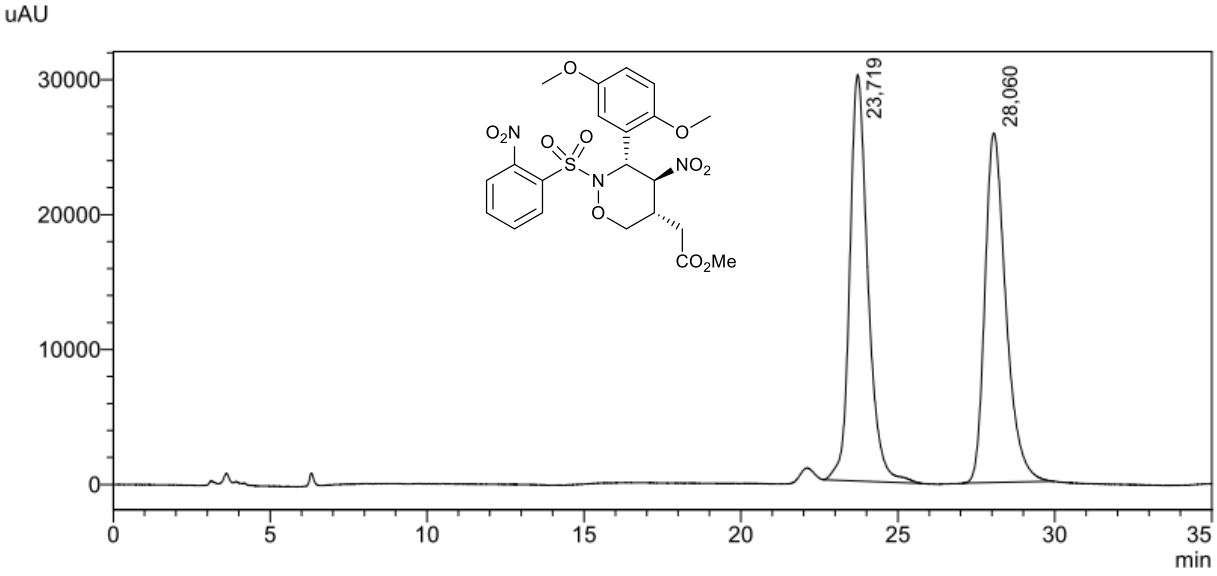
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	19,320	99,470
2	22,090	0,530
Total		100,000

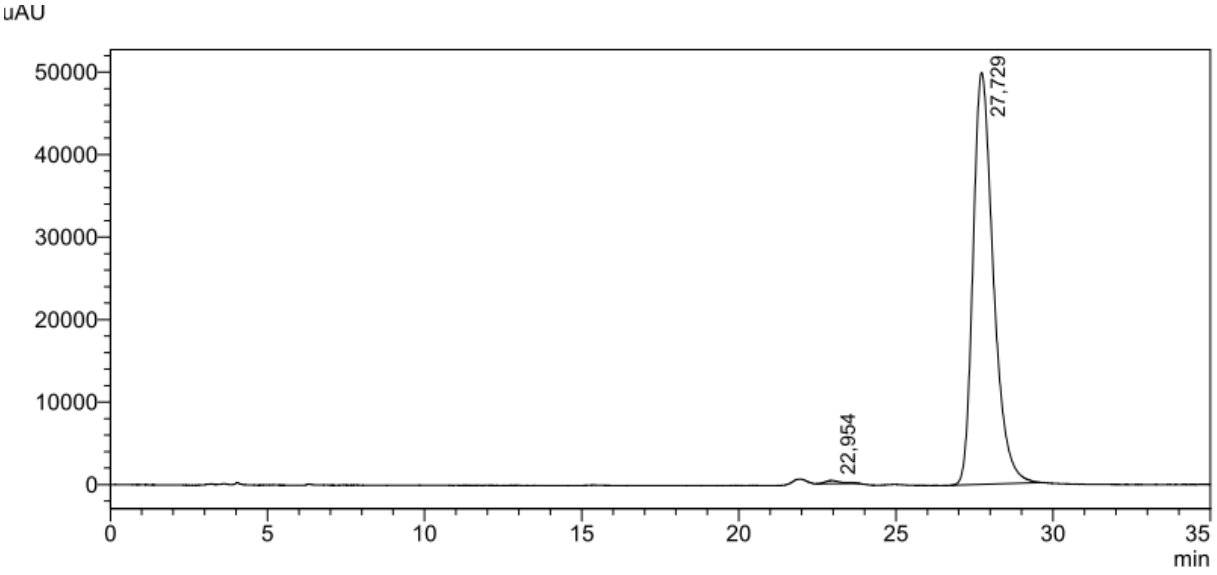
3dh Methyl 2-((3*R*,4*S*,5*S*)-3-(2,5-dimethoxyphenyl)-4-nitro-2-((2-nitrophenyl)sulfonyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 8)

Racemic Sample



Peak#	Ret. Time	Area%
1	23,719	50,139
2	28,060	49,861
Total		100,000

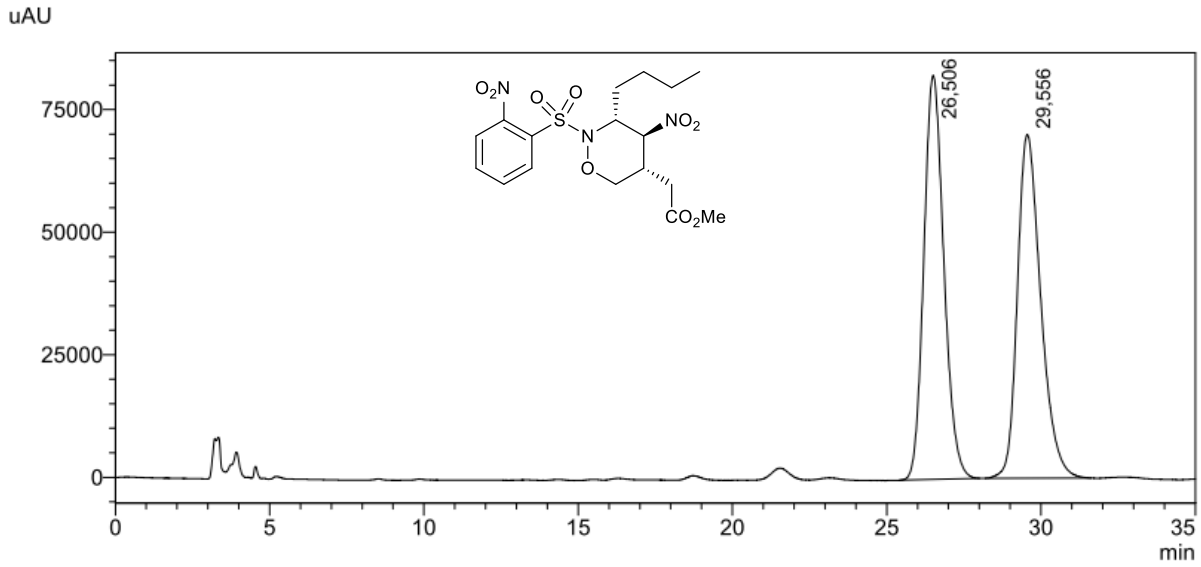
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	22,954	0,643
2	27,729	99,357
Total		100,000

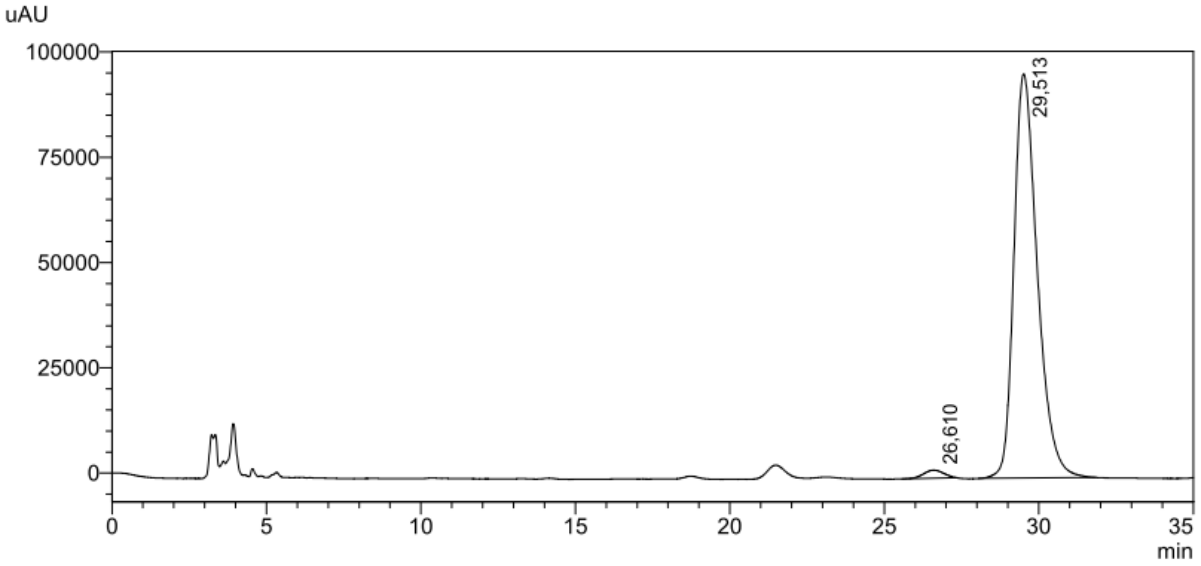
3di Methyl 2-((3*R*,4*S*,5*S*)-3-butyl-4-nitro-2-((2-nitrophenyl)sulfonyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 9)

Racemic Sample



Peak#	Ret. Time	Area%
1	26,506	50,192
2	29,556	49,808
Total		100,000

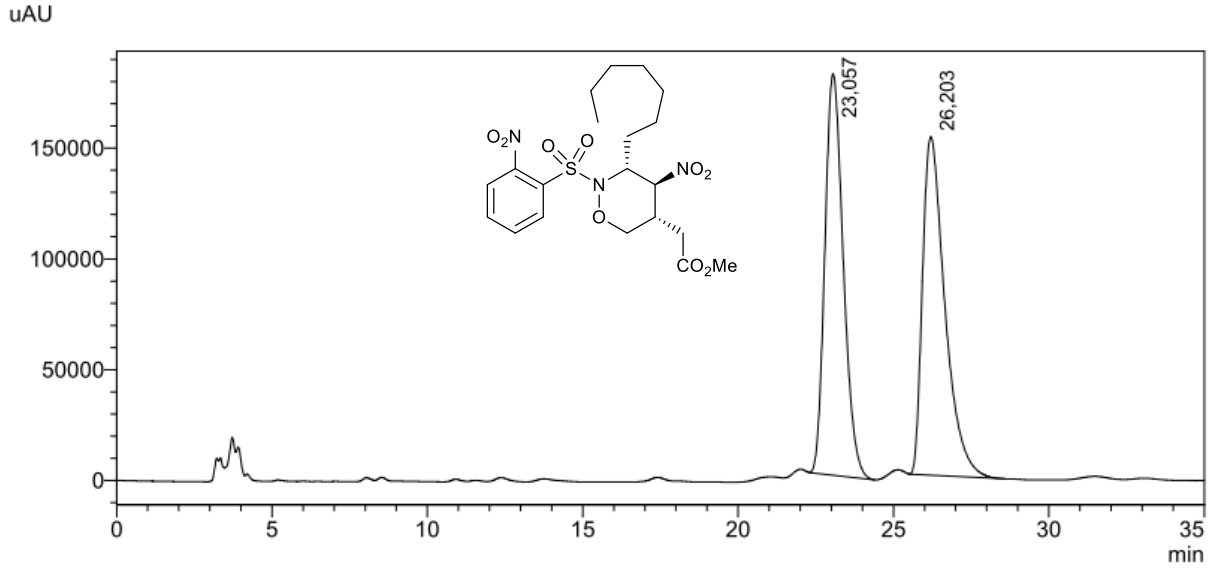
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	26,610	1,692
2	29,513	98,308
Total		100,000

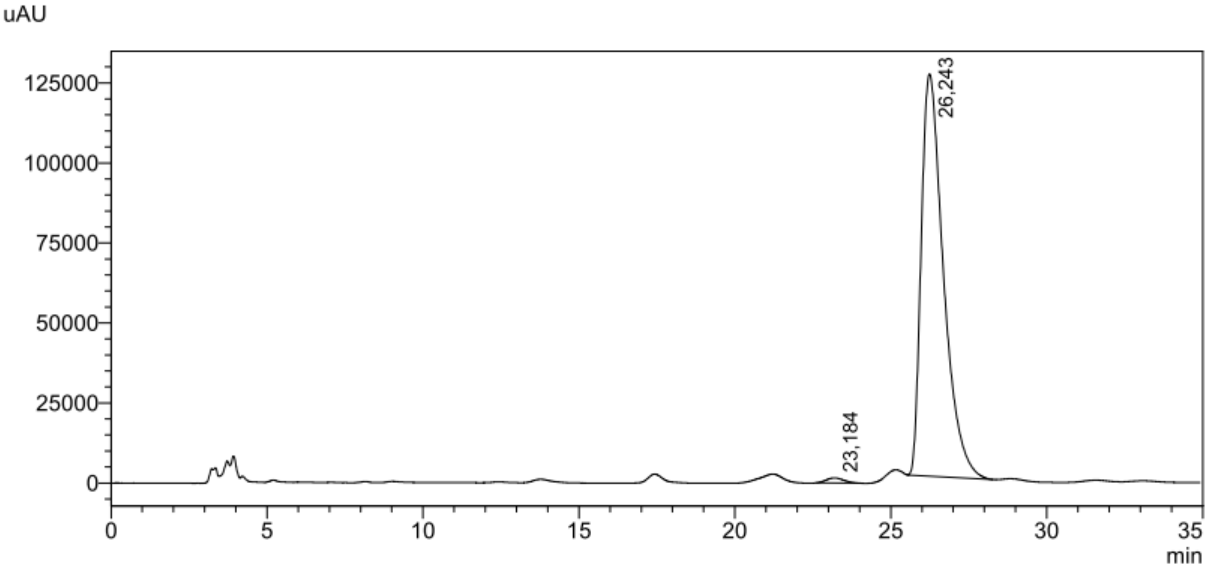
3dj Methyl 2-((3*R*,4*S*,5*S*)-3-heptyl-4-nitro-2-((2-nitrophenyl)sulfonyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 10)

Racemic Sample



Peak#	Ret. Time	Area%
1	23,057	49,316
2	26,203	50,684
Total		100,000

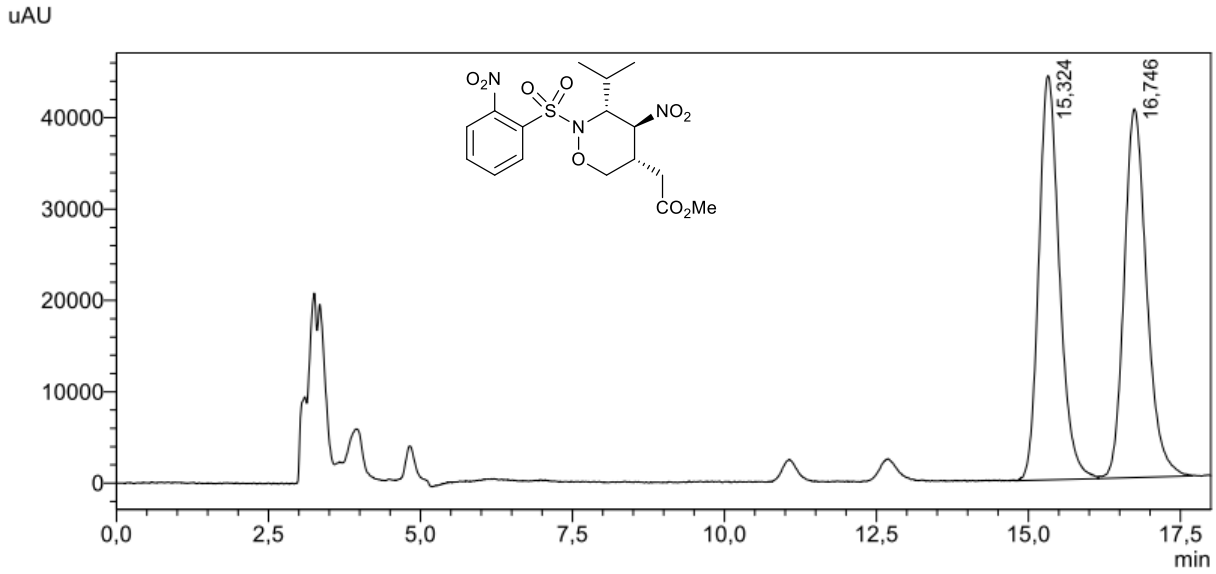
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	23,184	0,965
2	26,243	99,035
Total		100,000

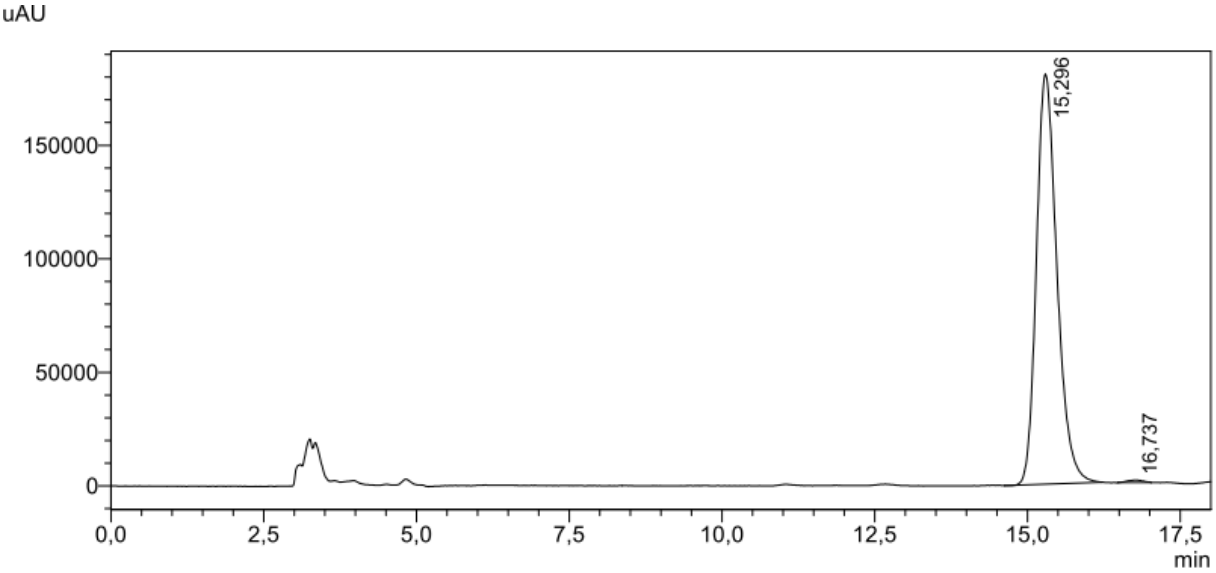
3dk Methyl 2-((3*R*,4*S*,5*S*)-3-isopropyl-4-nitro-2-((2-nitrophenyl)sulfonyl)-1,2-oxazinan-5-yl)acetate (Table 2, Entry 11)

Racemic Sample



Peak#	Ret. Time	Area%
1	15,324	50,049
2	16,746	49,951
Total		100,000

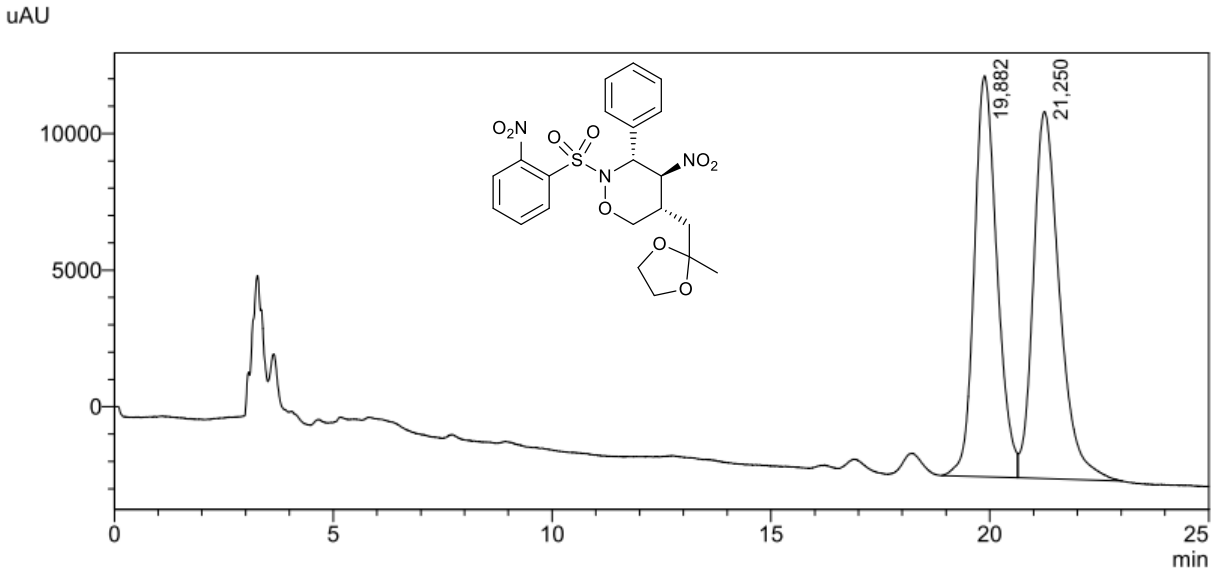
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	15,296	99,548
2	16,737	0,452
Total		100,000

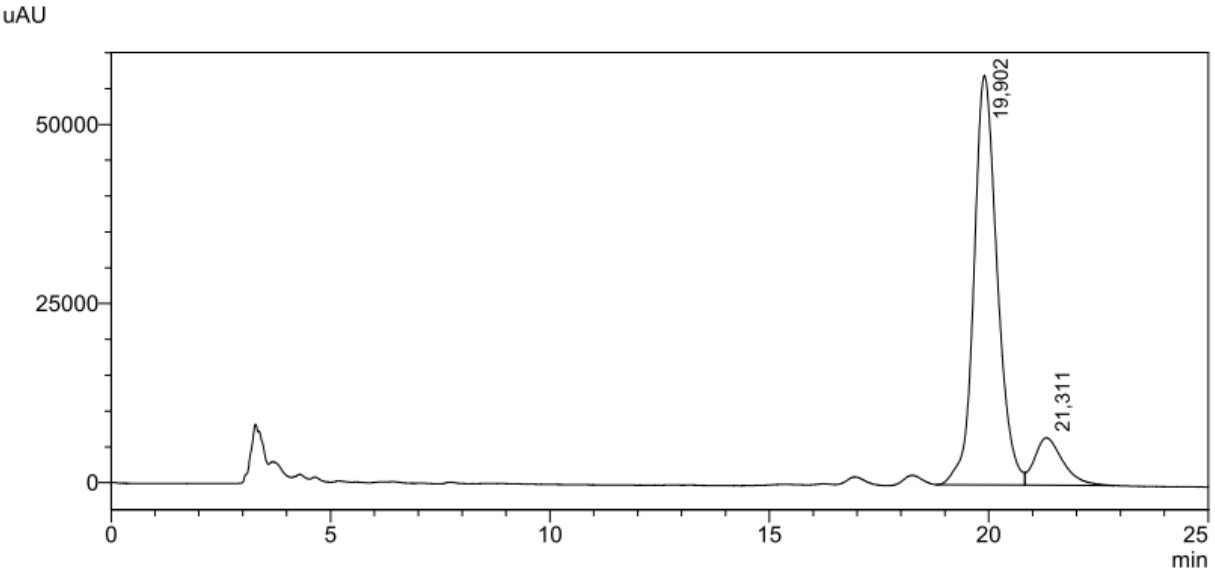
10 (3*R*,4*S*,5*S*)-5-((2-Methyl-1,3-dioxolan-2-yl)methyl)-4-nitro-2-((2-nitrophenyl)sulfonyl)-3-phenyl-1,2-oxazinane

Racemic Sample



Peak#	Ret. Time	Area%
1	19,882	48,570
2	21,250	51,430
Total		100,000

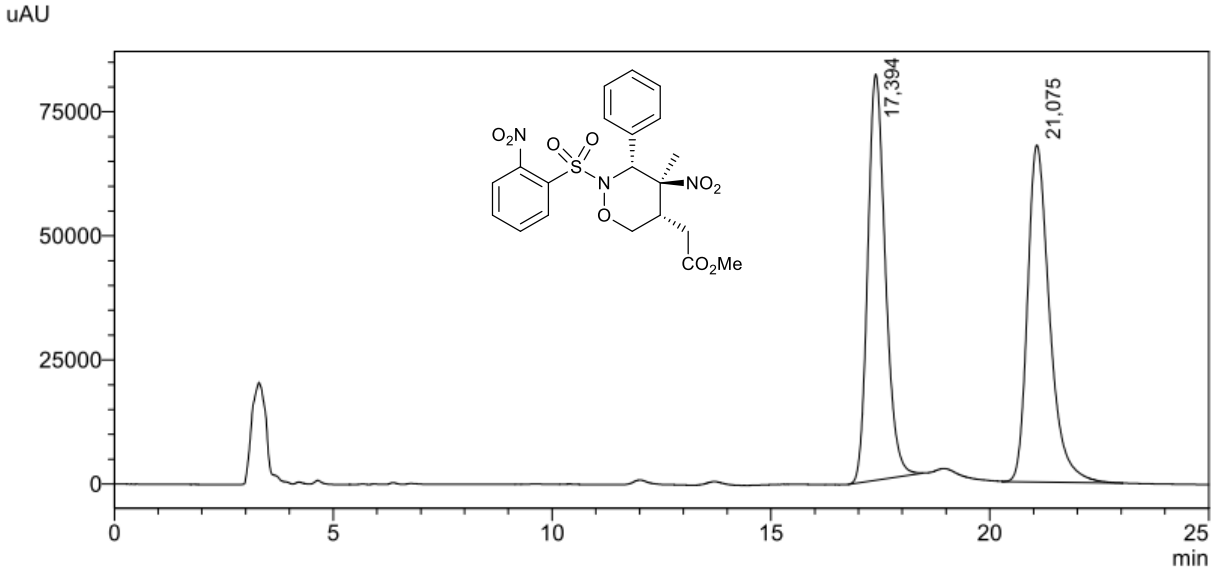
Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	19,902	87,636
2	21,311	12,364
Total		100,000

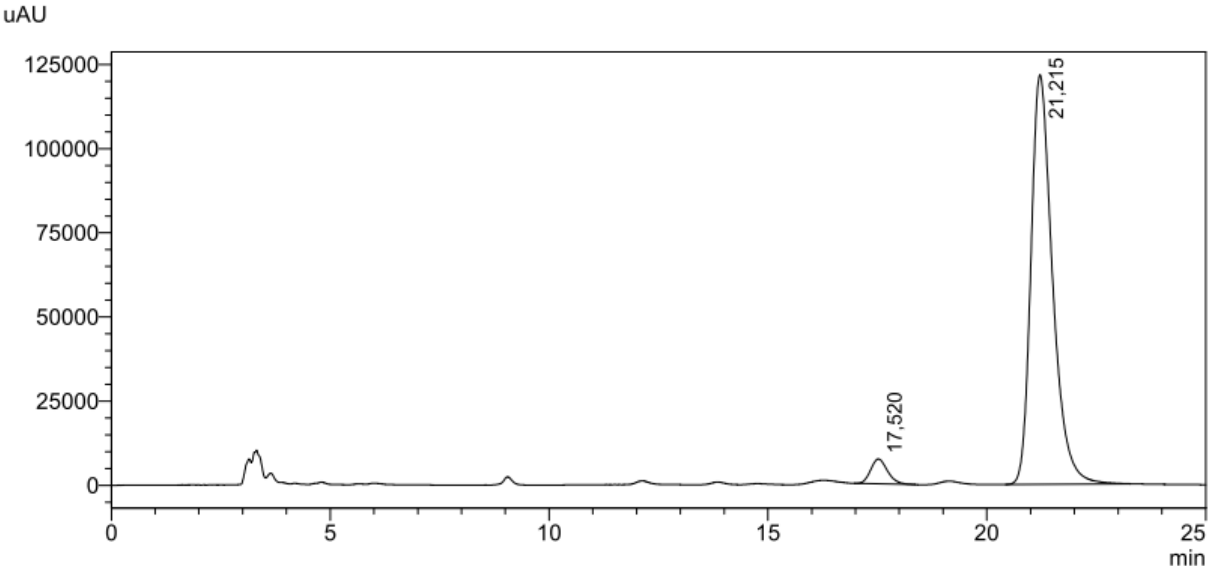
3dl Methyl 2-((3*R*,4*S*,5*S*)-4-methyl-4-nitro-2-((2-nitrophenyl)sulfonyl)-3-phenyl-1,2-oxazinan-5-yl)acetate (Scheme 2)

Racemic Sample



Peak#	Ret. Time	Area%
1	17,394	49,027
2	21,075	50,973
Total		100,000

Enantiomerically enriched sample



Peak#	Ret. Time	Area%
1	17,520	4,558
2	21,215	95,442
Total		100,000