Catalytic Asymmetric Formal [4+1] Annulation Leading to Optically Active *cis*-Isoxazoline *N*-Oxides

SUPPORTING INFORMATION

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I. General Information

Analytical thin layer chromatography (TLC) was performed using Merck 60 F254 precoated silica gel plate (0.2 mm thickness). Subsequent to elution, plates were visualized using UV radiation (254 nm) on Spectroline Model ENF-24061/F 254 nm. Further visualization was possible by staining with basic solution of potassium permanganate or acidic solution of ceric molybdate.

Flash column chromatography was performed using Merck silica gel 60 with freshly distilled solvents. Columns were typically packed as slurry and equilibrated with the appropriate solvent system prior to use. Proton nuclear magnetic resonance spectra (^{1}H-NMR) were recorded on Bruker AMX 400 spectrophotometer ($CDCl_3$ as solvent). Chemical shifts for ^{1}H NMR spectra are reported as δ in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0) and relative to the signal of chloroform-d (δ 7.26, singlet). Multiplicities were given as: s (singlet), d (doublet), t (triplet), dd (doublets of doublet) or m (multiplets). The number of protons (n) for a given resonance is indicated by nH. Coupling constants are reported as a *J* value in Hz. Carbon nuclear magnetic resonance spectra (^{13}C-NMR) are reportedas δ in units of parts per million (ppm) downfield from SiMe4 (δ 0.0) and relative to the signal of chloroform-d (δ 77.0, triplet).

Enantioselectivities were determined by High Performance Liquid Chromatography (HPLC) analysis (Shimadzu, LC-20AD) employing a Chiralcel OD-H or AD-H. Optical rotations were measured in $CHCl_3$ on a Schmidt + Haensdch polarimeter (Polartronic MH8) with a 10 cm cell (c given in g/100 mL).

High resolution mass spectrometry (HRMS) was recorded on Finnigan MAT 95 × P spectrometer.

α-Iodoaldehyde[1] and 2-nitroacrylate[2] substrates were prepared according to the procedure of literatures, catalyst **4a**,[3] **4b**,[3] **4c**,[3] **4d**[4] and **4f**[5] were synthesized following documented methods. Catalyst **4e**,[6] **4g**,[6] **4h**[7] and **4i**[5] were prepared with modified method of literatures.

II. General procedure of catalytic [4+1] annulation reaction

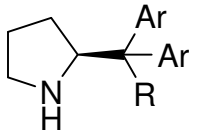
α-Iodoaldehyde (0.8 mmol, 4.0 equivalent), (S)-2-(azidodiphenylmethyl)pyrrolidine (**4e**, 0.04 mmol, 0.2 equivalent) were dissolved in 2.0 mL toluene at room temperature (23 ^{o}C), then 2-Nitroacrylate derivatives (0.2 mmol) and triethyl amine (0.22 mmol) were added successively. The reaction progress was monitored by TLC analysis. Upon consumption of 2-nitroacrylate

derivatives, the crude reaction mixture was applied to silica gel and the desired products were obtained by flash chromatography (hexane/ethyl acetate, 10:1 to 2:1).

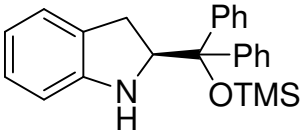
Racemic adducts were synthesized using 2-(diphenyl(trimethylsilyloxy)methyl)pyrrolidine as catalyst.

Optimization of reaction conditions

1) Catalyst screening



4a R = OTMS, Ar = Ph
4b R = OTMS, Ar = 3,5-CF_3-Ph
4c R = OTMS, Ar = 4-MePh
4d R = OMe, Ar = Ph
4e R = N_3, Ar = Ph
4g R = NHAc, Ar = Ph



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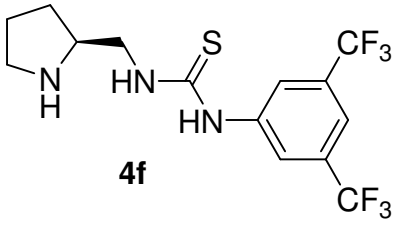
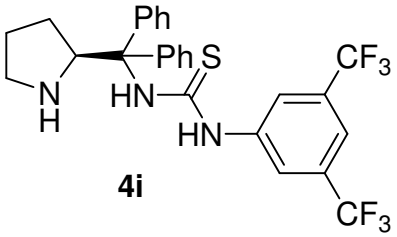
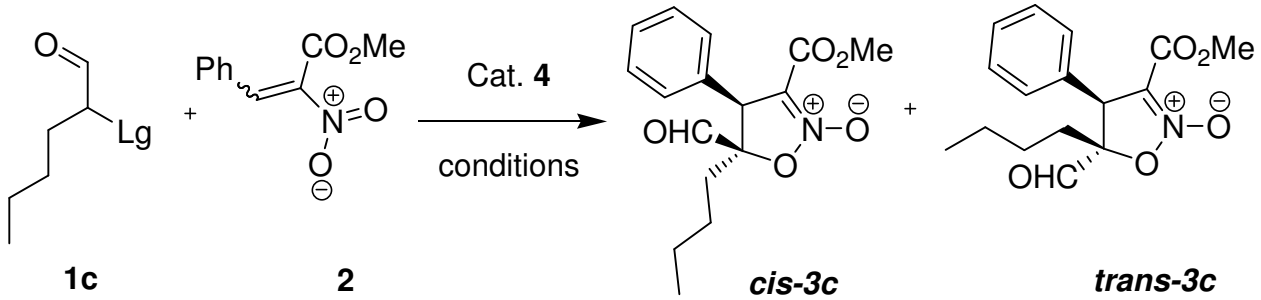


4f



4i

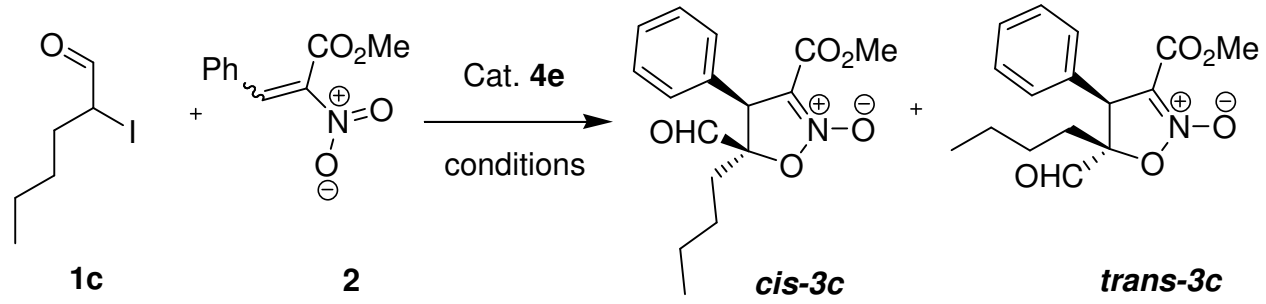


1c **2** ***cis-3c*** ***trans-3c***

entry	**4**	Lg	solvent	additive	*t* (h)	yield (%)[b]	*cis*/*trans*[c]	*ee* (%)[d]
1	**4a**	Cl	TBME	DIPEA	48	50	1:1.4	70
2	**4b**	Cl	TBME	DIPEA	96	18	n.d.	0
3	**4a**	Br	TBME	DIPEA	24	90	1.3:1	99
4	**4a**	I	TBME	DIPEA	5	79	1.8:1	96
5	**4a**	I	toluene	DIPEA	5	77	4.5:1	96
6	**4c**	I	toluene	DIPEA	5	78	2.2:1	95
7	**4d**	I	toluene	DIPEA	3	60	6:1	95
8	**4e**	I	toluene	DIPEA	7	83	9:1	98
9	**4f**	I	toluene	DIPEA	24	20	3:1	n.d.
10	**4g**	I	toluene	DIPEA	24	n.d.	n.d.	n.d.
11	**4h**	I	toluene	DIPEA	24	n.d.	n.d.	n.d.
12	**4i**	I	toluene	DIPEA	24	n.d.	n.d.	n.d.

[a] Unless noted, reactions were performed at rt on a 0.1 mmol scale, in 0.5 mL toluene, with a molar ratio of α-iodohexanal/2-nitroacyrate/DIPEA/**4** = 4:1:1.1:0.2. [b] The sum of both isomers. [c] Analysis of crude ^{1}H NMR. [d] Determined by HPLC for *cis*-isomer. n.r.= no reaction, n.d.= no determination.

2) Survey of additive

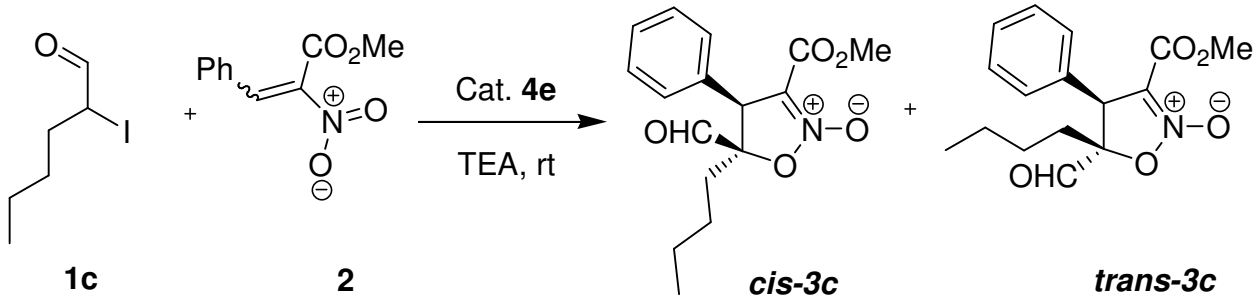


1c **2** ***cis-3c*** ***trans-3c***

entry	additive	*t* (h)	yield (%)[b]	*cis*/*trans*[c]	*ee* (%) [d]
1	DIPEA	7	83	9:1	98
2	TEA	8	89	11:1	>99
3	2,6-lutidine	48	85	7:1	96
4	NaOAc	48	n.r.	n.d.	n.d.
5	Pyridine	48	47	8:1	96
6	DABCO	48	20	11:1	97
7[e]	TEA	10	80	11:1	>99

[a] Unless noted, reactions were performed at rt on a 0.1 mmol scale, in 0.5 mL toluene, with a molar ratio of α-iodohexanal/2-nitroacyrate/additive/**4** = 4:1:1.1:0.2. [b] The sum of both isomers. [c] Analysis of crude ^{1}H NMR. [d] Determined by HPLC for *cis*-isomer. [e] 1.0 equivalent TEA was employed. n.r.= no reaction, n.d.= no determination.

3) Concentration effect

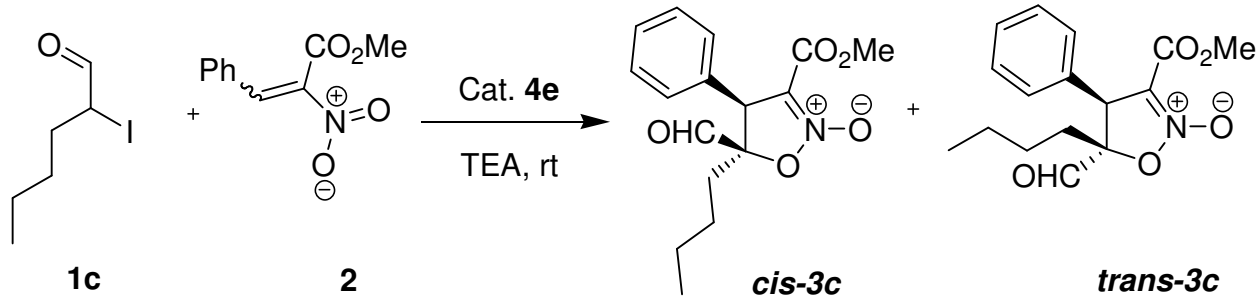


1c **2** ***cis-3c*** ***trans-3c***

entry	M **2**	*t* (h)	yield (%)[b]	*cis*/*trans*[c]	*ee* (%)[d]
1	0.5	8	89	11:1	>99
2	0.2	14	94	11:1	>99

[a] Unless noted, reactions were performed at rt on a 0.1mmol scale, in toluene, with a molar ratio of α-iodohexanal/2-nitroacyrate/TEA/**4** = 4:1:1.1:0.2. [b] The sum of both isomers. [c] Analysis of crude ^{1}H NMR. [d] Determined by HPLC for *cis*-isomer.

4) Solvent effect

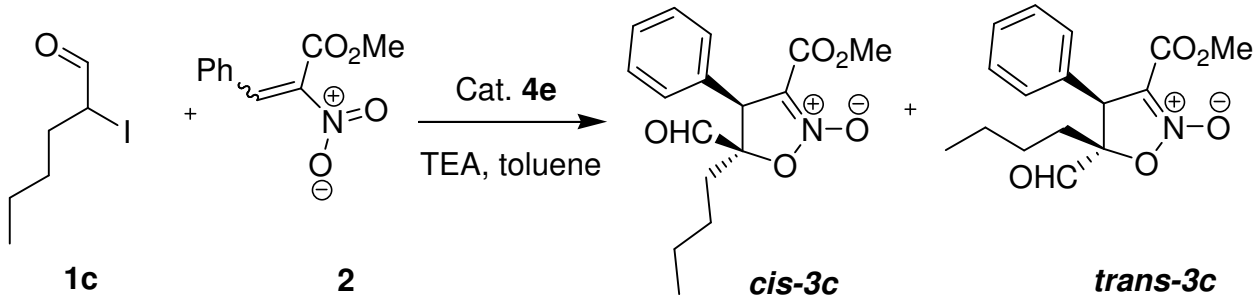


1c **2** ***cis-3c*** ***trans-3c***

entry	solvent	*t* (h)	yield (%)[b]	*cis*/*trans*[c]	*ee* (%)[d]
1	toluene	14	94	11:1	>99
2	benzene	14	82	11:1	>99
3	m-xylene	21	72	13:1	98
4	TBME	14	61	9:1	99

[a] Unless noted, reactions were performed at rt on a 0.1 mmol scale, at 0.1 M concentration, with a molar ratio of α-iodohexanal/2-nitroacyrate/TEA/**4** = 4:1:1.1:0.2. [b] The sum of both isomers. [c] Analysis of crude ^{1}H NMR. [d] Determined by HPLC for *cis*-isomer.

5) Catalyst loading and temperature effect



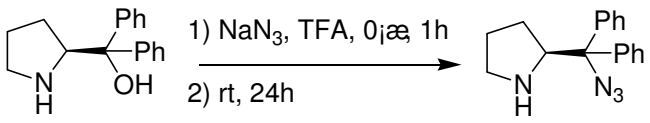
1c **2** ***cis-3c*** ***trans-3c***

entry	mol % of **4e**	T (°C)	*t* (h)	yield (%)[b]	*cis*/*trans*[c]	*ee* (%)[d]
1	20	23	14	94	11:1	>99
2	10	23	23	69	9:1	99
3	20	0	48	n.r.	n.d.	n.d.
4	20	30	24	92	7:1	95
5	10	30	24	62	10:1	95

[a] Unless noted, reactions were performed at rt on a 0.1 mmol scale, at 0.1 M concentration, with a molar ratio of α-iodohexanal/2-nitroacyrate/TEA/**4** = 4:1:1.1:0.2. [b] The sum of both isomers. [c] Analysis of crude ^{1}H NMR. [d] Determined by HPLC for *cis*-isomer. n.r.= no reaction, n.d.= no determination.

III. NMR and HPLC data

(*S*)-2-(Azidodiphenylmethyl)pyrrolidine (4e)

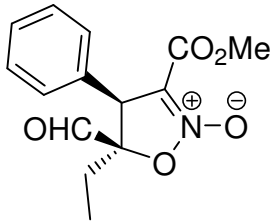


82% yield

Catalyst **4e** was synthesized using modified method of literature:[6] (*S*)-Diphenyl(pyrrolidin-2-yl)methanol (0.81 g, 3.2 mmol) was dissolved in 20 mL TFA, then cooled with ice bath. NaN_3 (1.25 g, 19.2 mmol) was potionwise added, then stirred at room temperature for 24 h. Reaction was quenched with saturated aquous Na_2CO_3 solution, extracted with dichloromethane, dried over Na_2SO_4, concentrated under vacco, then the residue was applied to column chromatography, gave 0.73 g solid product (Mp: 70-71 ^oC), with 82% yield.

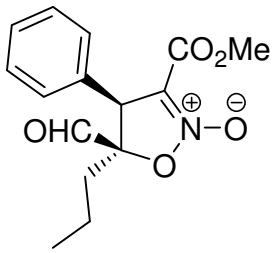
^1H NMR (400 MHz, $CDCl_3$): δ 1.61-1.75 (m, 5H), 2.98 (t, *J* = 8 Hz, 2H), 4.35 (t, *J* = 8 Hz, 1H), 7.22-7.49 (m, 8H), 7.52 (d, *J* = 7.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.1, 28.0, 47.3, 65.3, 75.2, 127.0, 127.2, 127.5, 128.0, 128.2, 128.5, 142.3, 142.7.

(4*S*,5*R*)-3-(Methoxycarbonyl)-5-formyl-4-phenyl-5-ethyl-4,5-dihydroisoxazole 2-oxide (3a)



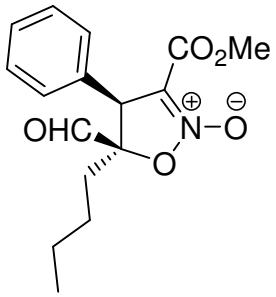
According to general procedure: 16 h, at room temperature, the product was obtained from flash chromatography (hexane/EtOAc = 10:1 to 2:1), as white solid 36 mg (Mp: 126-128 ^oC), 64% yield, 10:1 dr, 95% *ee*. HPLC analysis: Chiralcel OD-H (hexane/*i*-PrOH = 90/10, 1.0 mL/min), t_R (major) 11.66 min, t_R (minor) 16.57 min $[\alpha]^{22}_D$= +119.2° (c = 3.17, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 1.03 (t, *J* = 7.4 Hz, 3H), 2.07-2.17 (m, 2H), 3.72 (s, 3H), 4.55 (s, 1H), 7.14-7.16 (m, *J* = 6.8 Hz, 2H), 7.32-7.38 (m, 3H), 9.13 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 7.2, 28.9, 52.8, 57.0, 88.6, 110.4, 127.9, 129.1, 129.6, 133.1, 158.7, 196.7, HRMS (ESI) Calcd for $C_{14}H_{16}NO_5$ ($[M+H]^+$) 278.1028, found 278.1032.

(4*S*,5*R*)-3-(Methoxycarbonyl)-5-formyl-4-phenyl-5-propyl-4,5-dihydroisoxazole 2-oxide (3b)



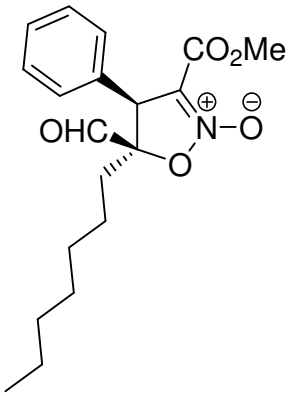
According to general procedure: 16 h, at room temperature, the product was obtained from flash chromatography (hexane/EtOAc = 10:1 to 2:1), as white solid 39 mg (Mp: 149-152 ^{o}C), 68% yield, 11:1 dr, 94% *ee*. HPLC analysis: Chiralcel OD-H (hexane/*i*-PrOH = 90/10, 1.0 mL/min), t_R (major) 9.35 min, t_R (minor) 18.61 min $[\alpha]^{22}_D$= +92.3° (c =1.65, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.97 (t, *J* = 7.3 Hz, 3H), 1.30-1.39 (m, 1H), 1.53-1.59 (m, 1H), 2.01-2.10 (m, 2H), 3.73 (s, 3H), 4.54 (s, 1H), 7.14-7.15 (m, *J* = 6.9 Hz, 2H), 7.32-7.36 (m, 3H), 9.13 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2, 16.3, 38.1, 52.8, 57.4, 88.4, 110.4, 127.9, 129.2, 129.6, 133.3, 158.1, 196.8, HRMS (ESI) Calcd for $C_{15}H_{18}NO_5$ ($[M+H]^+$) 292.1185, found 292.1179.

(4*S*,5*R*)-3-(Methoxycarbonyl)-5-formyl-4-phenyl-5-butyl-4,5-dihydroisoxazole 2-oxide (3c)



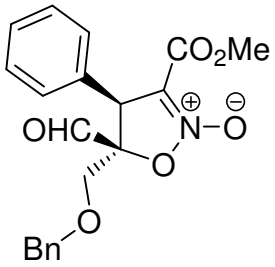
According to general procedure: 14 h, at room temperature, the product was obtained from flash chromatography (hexane/EtOAc = 10:1 to 2:1), as white solid 57 mg (Mp: 145-147 ^{o}C), 94% yield, 11:1 dr, >99% *ee*. HPLC analysis: Chiralcel OD-H (hexane/*i*-PrOH = 90/10, 1.0 mL/min), t_R (major) 8.48 min, t_R (minor) 17.81 min $[\alpha]^{22}_D$= +108.3° (c =1.70, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.91 (t, *J* = 7.2 Hz, 3H), 1.33-1.38 (m, 3H), 1.45-1.54 (m, 1H), 2.02-2.12 (m, 2H), 3.73 (s, 3H), 4.55 (s, 1H), 7.14-7.15 (m, *J* = 6.6 Hz, 2H), 7.34-7.36 (m, 3H), 9.13 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.7, 22.8, 24.8, 35.8, 52.8, 57.3, 88.5, 110.4, 127.9, 129.2, 129.6, 133.3, 158.7, 196.8, HRMS (ESI) Calcd for $C_{16}H_{20}NO_5$ ($[M+H]^+$) 306.1341, found 306.1343.

(*4S*,5*R*)-3-(Methoxycarbonyl)-5-formyl-4-phenyl-5-heptyl-4,5-dihydroisoxazole 2-oxide (3d)



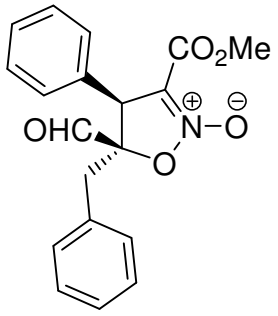
According to general procedure: 16 h, at room temperature, the product was obtained from flash chromatography (hexane/EtOAc = 10:1 to 2:1), as white solid 58 mg (Mp: 82-85 ^{o}C), 84% yield, 9:1 dr, 92% *ee*. HPLC analysis: Chiralcel OD-H (hexane/*i*-PrOH = 90/10, 1.0 mL/min), t_R (major) 8.96 min, t_R (minor) 23.50 min $[\alpha]^{22}_D$= +94.9° (c =4.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (t, *J* = 7.0 Hz, 3H), 1.26-1.29 (m, 9H), 1.51-1.54 (m, 1H), 2.02-2.11 (m, 2H), 3.72 (s, 3H), 4.55 (s, 1H), 7.13-7.15 (m, *J* = 6.6 Hz, 2H), 7.31-7.35 (m, 3H), 9.12 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1, 22.6, 22.8, 28.9, 29.6, 31.6, 36.0, 52.8, 57.3, 88.5, 110.4, 127.9, 129.2, 129.6, 133.1, 158.7, 196.8, HRMS (ESI) Calcd for $C_{19}H_{26}NO_5$ ($[M+H]^+$) 348.1811, found 348.1811.

(4*S*,5*S*)- 5-(Benzyloxymethyl)- 5-formyl -3-(Methoxycarbonyl)-4-phenyl-4,5-dihydroisoxazole 2-oxide (3e)



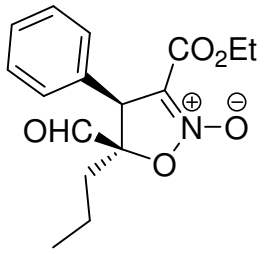
According to general procedure: 14 h, at room temperature, the product was obtained from flash chromatography (hexane/EtOAc = 10:1 to 2:1), as sticky oil 55 mg, 75% yield, 18:1 dr, 99% *ee*. HPLC analysis: Chiralcel OD-H (hexane/*i*-PrOH = 90/10, 1.0 mL/min), t_R (major) 22.48 min, t_R (minor) 29.62 min $[\alpha]^{22}_D$= +44.6° (c = 2.60, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.72 (s, 3H), 3.82-3.94 (dd, *J* = 8, 36 Hz, 2H), 4.65-4.66 (m, *J* = 4 Hz, 2H), 7.13-7.15 (m, *J* = 8.0 Hz, 2H), 7.32-7.38 (m, 8H), 9.14 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.8, 53.9, 70.6, 74.1, 86.7, 110.1, 127.8, 128.0, 128.2, 128.6, 129.2, 129.7, 132.9, 136.9, 158.6, 195.1, HRMS (ESI) Calcd for $C_{20}H_{20}NO_6$ ($[M+H]^+$) 370.1291, found 370.1299.

(4*S*,5*R*)-5-Benzyl-4-phenyl)-5-formyl-3-(methoxycarbonyl)-4,5-dihydroisoxazole 2-oxide (3f)



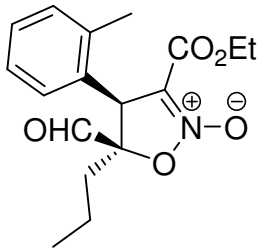
According to general procedure: 24 h, at room temperature, the product was obtained from flash chromatography (hexane/EtOAc = 4:1 to 2:1), as sticky oil 47 mg, 70% yield, 8:1 dr, 99% *ee*. HPLC analysis: Chiralcel OD-H (hexane/*i*-PrOH = 95/05, 1.0 mL/min), t_R (major) 25.77 min, t_R (minor) 43.81 min. $[\alpha]^{21}_D$= +60.8° (c = 1.40, $CHCl_3$). ^{1}H NMR (400 MHz, ^{1}H $CDCl_3$): δ 3.28 (s, 2H), 3.63 (s, 3H), 4.63 (s, 1H), 7.15-7.16 (d, *J* = 2.7 Hz, 2H), 7.31-7.35 (m, 8H), 9.14 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 40.9, 52.7, 56.3, 87.6, 110.0, 127.8, 128.0, 128.7, 129.2, 129.2, 129.7, 130.3, 132.5, 132.9, 158.2, 196.6. HRMS (ESI) Calcd for $C_{19}H_{18}NO_5$ ($[M+H]^+$) 340.1185, found 340.1179.

(*4S*,5*R*)-3-(Ethoxycarbonyl)-5-formyl-4-phenyl-5-propyl-4,5-dihydroisoxazole 2-oxide (3g)



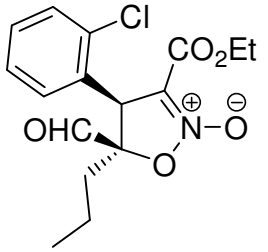
According to general procedure: 16 h, at room temperature, the product was obtained from flash chromatography (hexane/EtOAc = 10:1 to 2:1), as white solid 38 mg (Mp: 113-114 ^{o}C), 87% yield, 9:1 dr, 91% *ee*. HPLC analysis: Chiralcel OD-H (hexane/*i*-PrOH = 90/10, 1.0 mL/min), t_R (major) 8.44 min, t_R (minor) 19.44 min $[\alpha]^{22}_D$= +90.1° (c = 3.80, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.97 (t, *J* = 7.2 Hz, 3H), 1.11 (t, *J* = 7.2 Hz, 3H), 1.31-1.39 (m, 1H), 1.52-1.61 (m, 1H), 1.99-2.14 (m, 2H), 4.12-4.22 (m, 2H), 4.54 (s, 1H), 7.14 (t, *J* = 6.4 Hz, 2H), 7.31-7.37 (m, 3H), 9.16 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9, 14.2, 16.3, 38.1, 57.6, 62.0, 88.3, 110.4, 127.9, 129.1, 133.3, 158.1, 196.9, HRMS (ESI) Calcd for $C_{16}H_{20}NO_5$ ($[M+H]^+$) 306.1341, found 306.1344.

(4*S*,5*R*)-3-(Ethoxycarbonyl)-5-formyl-5-propyl-4-o-tolyl-4,5-dihydroisoxazole 2-oxide (3h)



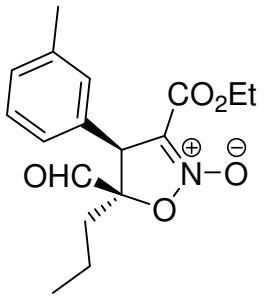
According to general procedure: 24 h, at room temperature, the product was obtained from flash chromatography (hexane/EtOAc = 10:1 to 2:1), as white solid 52 mg (Mp: 75-77 °C), 81% yield, 11:1 dr, 97% *ee*. HPLC analysis: Chiralcel OD-H (hexane/*i*-PrOH = 90/10, 1.0 mL/min), t_R (major) 6.37 min, t_R (minor) 22.00 min. $[\alpha]^{22}_D$= +59.9° (c = 4.50, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.97 (t, *J* = 7.2 Hz, 3H), 1.12 (t, *J* = 7.2 Hz, 3H), 1.29-1.38 (m, 1H), 1.53-1.62 (m, 1H), 2.00-2.236 (m, 2H), 2.32 (s, 3H), 4.13-4.21 (m, 2H),4.77 (s, 1H), 7.10-7.13 (q, *J* = 1.6 Hz, 1H), 7.19 (d, *J* = 5.2 Hz, 3H), 9.11 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9, 14.2, 16.4, 38.5, 52.9, 62.0, 88.2, 110.8, 126.6, 127.0, 128.9, 131.5, 131.8, 158.0, 197.3. HRMS (ESI) Calcd for $C_{17}H_{22}NO_5$ ($[M+H]^+$) 320.1498, found 320.1494.

(4*S*,5*R*)-4-(2-Chlorophenyl)-3-(ethoxycarbonyl)-5-formyl-5-propyl-4,5-dihydroisoxazole 2-oxide (3i)



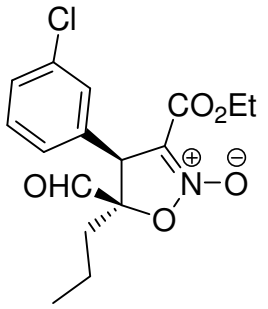
According to general procedure: 16 h, at room temperature, the product was obtained from flash chromatography (hexane/EtOAc = 10:1 to 2:1), as white solid 43 mg (Mp: 78-79 °C), 64% yield, >20:1 dr, 96% *ee*. HPLC analysis: Chiralcel OD-H (hexane/*i*-PrOH = 90/10, 1.0 mL/min), t_R (major) 8.78 min, t_R (minor) 30.14 min. $[\alpha]^{22}_D$= +46.1° (c = 3.507, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.99 (t, *J* = 7.2 Hz, 3H), 1.12 (t, *J* = 7.3 Hz, 3H), 1.33-1.41 (m, 1H), 1.55-1.62 (m, 1H), 2.07-2.24 (m, 2H), 4.13-4.22 (m, 2H), 5.24 (s, 1H), 7.16-7.18 (m, 1H), 7.27 (t, *J* = 3.0 Hz, 2H), 7.41-7.44 (m, 1H), 9.13 (d, *J* = 0.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8, 14.2, 16.3, 38.0, 52.8, 62.1, 88.0, 109.8, 127.8, 128.4, 130.3, 130.6, 131.5, 133.8, 157.9, 195.5. HRMS (ESI) Calcd for $C_{16}H_{19}NO_5Cl$ ($[M+H]^+$) 340.0952, found 340.0956.

(4*S*,5*R*)-3-(Ethoxycarbonyl)-5-formyl-5-propyl-4-m-tolyl-4,5-dihydroisoxazole 2-oxide (3j)



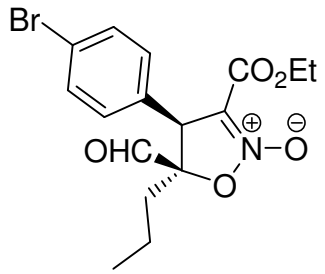
According to general procedure: 16 h, at room temperature, the product was obtained from flash chromatography (hexane/EtOAc = 10:1 to 2:1), as white solid 51 mg (Mp: 111-113 °C), 80% yield, 11:1 dr, 92% *ee*. HPLC analysis: Chiralcel OD-H (hexane/*i*-PrOH = 90/10, 1.0 mL/min), t_R (major) 6.39 min, t_R (minor) 15.20 min. $[\alpha]^{22}_D$= +66.9° (c = 4.80, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.97 (t, *J* = 7.2 Hz, 3H), 1.14 (t, *J* = 7.2 Hz, 3H), 1.33-1.35 (m, 1H), 1.54-1.58 (m, 1H), 1.98-2.13 (m, 2H), 2.32 (s, 3H), 4.13-4.23 (m, 2H), 4.49 (s, 1H), 6.94 (s, 2H), 7.11 (d, *J* = 7.6 Hz, 1H), 7.23 (t, *J* = 8.0 Hz, 1H), 9.15 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9, 14.2, 16.3, 21.4, 38.1, 57.5, 62.0, 88.2, 110.5, 125.0, 128.4, 129.4, 129.9, 133.2, 139.5, 158.2, 196.9. HRMS (ESI) Calcd for $C_{17}H_{22}NO_5$ ($[M+H]^+$) 320.1498, found 320.1496.

(4*S*,5*R*)-4-(3-Chlorophenyl)-3-(ethoxycarbonyl)-5-formyl-5-propyl-4,5-dihydroisoxazole 2-oxide (3k)



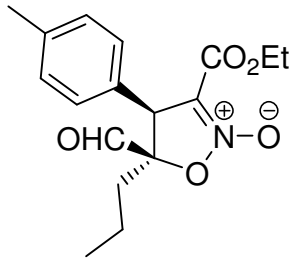
According to general procedure: 9 h, at room temperature, the product was obtained from flash chromatography (hexane/EtOAc = 10:1 to 2:1), as white solid 43 mg (Mp: 106-108 °C), 63% yield, >20:1 dr, > 96% *ee*. HPLC analysis: Chiralcel OD-H (hexane/*i*-PrOH = 90/10, 1.0 mL/min), t_R (major) 8.30 min, t_R (minor) 21.12 min. $[\alpha]^{22}_D$= +40.7° (c = 1.70, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.97 (t, *J* = 7.3 Hz, 3H), 1.15 (t, *J* = 7.1 Hz, 3H), 1.33-1.36 (m, 1H), 1.54-1.60 (m, 1H), 1.98-2.12 (m, 2H), 4.14-4.24 (m, 2H), 4.50 (s, 1H), 7.03 (d, *J* = 3.4 Hz, 1H), 7.15 (s, 1H), 7.29 (d, *J* = 4.8 Hz, 2H), 9.22 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9, 14.2, 16.3, 38.3, 57.1, 62.2, 88.2, 110.0, 126.0, 128.1, 129.4, 130.8, 135.5, 135.6, 157.9, 196.8. HRMS (ESI) Calcd for $C_{16}H_{19}NO_5Cl$ ($[M+H]^+$) 340.0952, found 340.0956.

(*4S*,*5R*)-4-(4-Bromophenyl)-3-(ethoxycarbonyl)-5-formyl-5-propyl-4,5-dihydroisoxazole 2-oxide (3l)



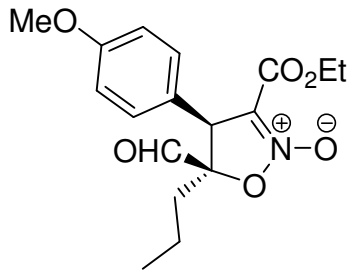
According to general procedure: 16 h, at room temperature, the product was obtained from flash chromatography (hexane/EtOAc = 10:1 to 2:1), as white solid 60 mg (Mp: 99-101 °C), 78% yield, 14:1 dr, 94% *ee*. HPLC analysis: Chiralcel OD-H (hexane/*i*-PrOH = 90/10, 1.0 mL/min), t_R (major) 8.58 min, t_R (minor) 26.68 min. $[\alpha]^{24}_D$= +44.4° (c =2.40, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.96 (t, *J* = 7.2 Hz, 3H), 1.14 (t, *J* = 7.2 Hz, 3H), 1.25-1.36 (m, 1H), 1.52-1.59 (m, 1H), 1.97-2.13 (m, 2H), 4.14-4.22 (m, 2H), 4.50 (s, 1H), 7.03 (d, *J* = 8.4 Hz, 2H), 7.48 (t, *J* = 8.4 Hz, 2H), 9.18 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9, 14.2, 16.3, 38.2, 57.0, 62.2, 88.2, 110.1, 123.3, 129.5, 132.5, 132.7, 158.0, 196.9. HRMS (ESI) Calcd for $C_{16}H_{19}NO_5Br$ ($[M+H]^+$) 384.0447, found 384.0446.

(4*S*,5*R*)-3-(Ethoxycarbonyl)-5-formyl-5-propyl-4-p-tolyl-4,5-dihydroisoxazole 2-oxide (3m)



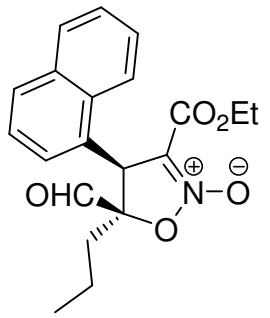
According to general procedure: 16 h, at room temperature, the product was obtained from flash chromatography (hexane/EtOAc = 10:1 to 2:1), as white solid 52 mg (Mp: 93-96 °C), 81% yield, 10:1 dr, 92% *ee*. HPLC analysis: Chiralcel OD-H (hexane/*i*-PrOH = 90/10, 1.0 mL/min), t_R (major) 6.73 min, t_R (minor) 15.74 min. $[\alpha]^{22}_D$ = +69.8° (c =4.20, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.96 (t, *J* = 7.2 Hz, 3H), 1.13 (t, *J* = 7.2 Hz, 3H), 1.33-1.39 (m, 1H), 1.53-1.63 (m, 1H), 1.98-2.15 (m, 2H), 2.34 (s, 3H), 4.16-4.24 (m, 2H), 4.53 (s, 1H), 7.03-7.05 (q, *J* = 7.6 Hz, 2H), 7.17 (d, *J* = 7.6 Hz, 2H), 9.17 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9, 14.2, 16.3, 38.0, 57.2, 62.0, 88.3, 110.5, 127.7, 130.1, 130.2, 139.0, 158.2, 197.1. HRMS (ESI) Calcd for $C_{17}H_{22}NO_5$ ($[M+H]^+$) 320.1498, found 320.1495.

(4*S*,5*R*)-3-(Ethoxycarbonyl)-5-formyl-4-(4-methoxyphenyl)-5-propyl-4,5-dihydroisoxazole 2-oxide (3n)



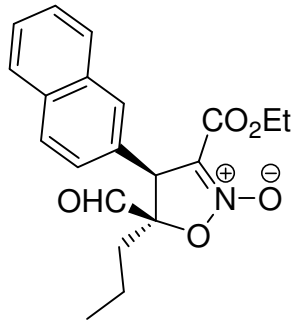
According to general procedure: 24 h, at room temperature, the product was obtained from flash chromatography (hexane/EtOAc = 10:1 to 2:1), as white solid 49 mg (Mp: 88-89 °C), 73% yield, 13:1 dr, 91% *ee*. HPLC analysis: Chiralcel OD-H (hexane/*i*-PrOH = 90/10, 1.0 mL/min), t_R (major) 11.31 min, t_R (minor) 27.46 min. $[\alpha]^{22}_D$ = +69.1° (c = 4.50, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.96 (t, *J* = 7.2 Hz, 3H), 1.13 (t, *J* = 7.2 Hz, 3H), 1.30-1.36 (m, 1H), 1.51-1.58 (m, 1H), 1.95-2.12 (m, 2H), 3.78 (s, 3H), 4.13-4.22 (m, 2H), 4.49 (s, 1H), 6.85 (d, *J* = 8.8 Hz, 2H), 7.05 (d, *J* = 8.8 Hz, 2H), 9.15 (d, *J* = 0.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9, 14.2, 16.3, 38.0, 55.3, 56.8, 62.0, 88.3, 110.5, 114.9, 125.0, 129.1, 158.2, 160.0, 197.1. HRMS (ESI) Calcd for $C_{17}H_{22}NO_6$ ($[M+H]^+$) 336.1447, found 336.1443.

(4*S*,5*R*)-3-(Ethoxycarbonyl)-5-formyl-4-(naphthalen-1-yl)-5-propyl-4,5-dihydroisoxazole 2-oxide (3o)



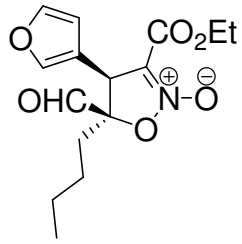
According to general procedure: 16 h, at room temperature, the product was obtained from flash chromatography (hexane/EtOAc = 10:1 to 2:1), as white solid 44 mg (Mp: 114-115 °C), 62% yield, 12:1 dr, 94% *ee*. HPLC analysis: Chiralcel OD-H (hexane/*i*-PrOH = 90/10, 1.0 mL/min), t_R (major) 10.47 min, t_R (minor) 31.92 min. $[\alpha]^{22}_D$= +5.7° (c = 3.20, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.97-1.04 (m, 6H), 1.36-1.43 (m, 1H), 1.60-1.68 (m, 1H), 2.17-2.33 (m, 2H), 4.08-4.14 (m, 2H), 5.43 (s, 1H), 7.37 (d, *J* = 7.2 Hz, 1H), 7.45 (t, *J* = 7.2Hz, 1H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.64 (t, *J* = 8.0 Hz, 1H), 7.83-7.92 (m, 3H), 8.98(s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8, 14.2, 16.4, 38.0, 51.8, 62.0, 88.0, 110.5, 122.3, 125.30, 125.33, 126.5, 127.3, 129.3, 129.9, 130.9, 134.2, 158.1, 195.5. HRMS (ESI) Calcd for $C_{20}H_{22}NO_5$ ($[M+H]^+$) 356.1498, found 356.1496.

(4*S*,5*R*)-5-Formyl-3-(methoxycarbonyl)-4-(naphthalen-2-yl)-5-propyl-4,5-dihydroisoxazole 2-oxide (3p)



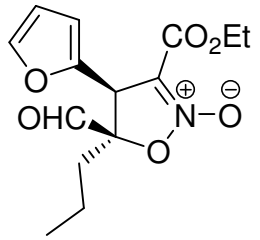
According to general procedure: 12 h, at room temperature, the product was obtained from flash chromatography (hexane/EtOAc = 8:1 to 2:1), as white solid 50 mg (Mp: 164-165 ^{o}C), 74% yield, 11:1 dr, 87% *ee*. After recrystallization, >99% *ee*. HPLC analysis: Chiralcel OD-H (hexane/*i*-PrOH = 90/10, 1.0 mL/min), t_R (major) 11.68 min, t_R (minor) 33.67 min. $[\alpha]^{23}_D$= +126.7° (c = 2.00, $CHCl_3$). ^{1}H NMR (400 MHz,^{1}H $CDCl_3$): δ 0.99 (t, *J* = 7.4 Hz, 3H), 1.34-1.40 (m, 1H), 1.55-1.63 (m, 1H), 2.07-2.16 (m, 2H), 3.71 (s, 3H), 4.71 (s, 1H), 7.23 (d, *J* = 8.4 Hz, 1H), 7.52 (t, *J* = 4.5 Hz, 2H), 7.64 (s, 1H), 7.81-7.86 (m, 3H), 9.15 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2, 16.3, 38.2, 52.9, 57.5, 88.6, 110.4, 125.0, 126.9, 127.0, 127.3, 127.8, 128.0, 129.8, 130.5, 133.3, 133.4, 158.7, 196.7. HRMS (ESI) Calcd for $C_{19}H_{20}NO_5$ ($[M+H]^+$) 342.1341, found 342.1344.

(4*S*,5*R*)-3-(Ethoxycarbonyl)-5-formyl-4-(furan-3-yl)-5-butyl-4,5-dihydroisoxazole 2-oxide (3q)



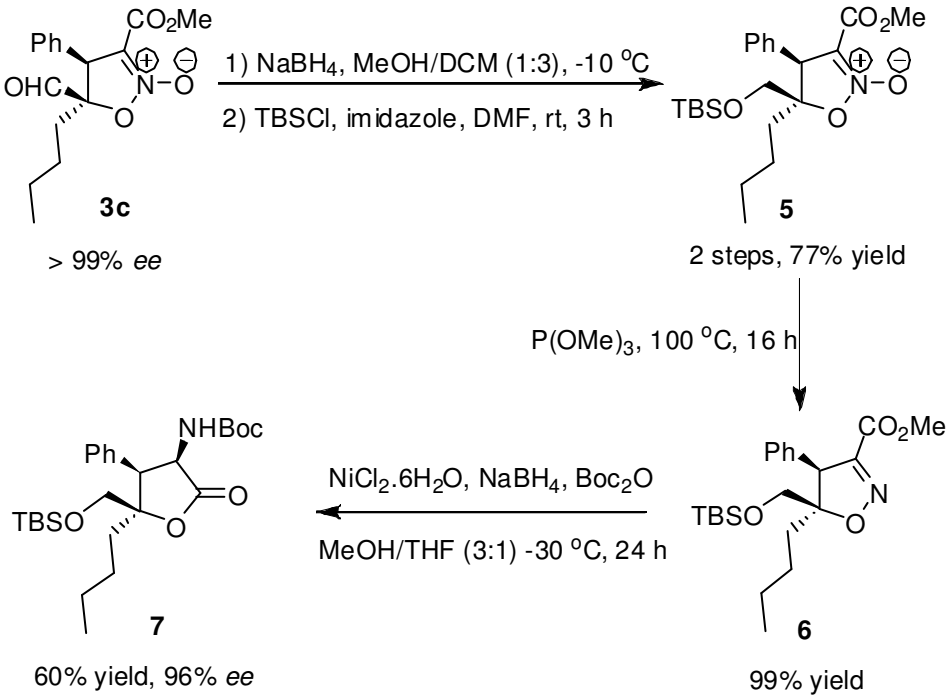
According to general procedure: 16 h, at room temperature, the product was obtained from flash chromatography (hexane/EtOAc = 10:1 to 6:1), as white solid 41 mg (Mp: 68-69 ^{o}C), 67% yield, >20:1 dr, 85% *ee*. HPLC analysis: Chiralcel OD-H (hexane/*i*-PrOH = 90/10, 1.0 mL/min), t_R (major) 8.38 min, t_R (minor) 18.39 min. $[\alpha]^{22}_D$= +30.8° (c = 1.70, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.91 (t, *J* = 7.2 Hz, 3H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.30-1.41 (m, 3H), 1.47-1.51 (m, 1H), 1.98-2.08 (m, 2H), 4.22-4.26 (m, 2H), 4.53 (s, 1H), 6.25 (s, 1H), 7.37 (s 1H), 7.41(s, 1H), 9.34 (s, 1H). ^{13}C NMR (400 MHz, $CDCl_3$): δ 13.7, 14.0, 22.8, 24.8, 35.0, 48.1, 62.1, 87.9, 109.4, 109.5, 117.9, 140.9, 144.7, 158.0, 196.8, HRMS (ESI) Calcd for $C_{15}H_{20}NO_6$ ($[M+H]^+$) 309.1230, found 309.1228.

(4*S*,5*R*)-3-(Ethoxycarbonyl)-5-formyl-4-(furan-2-yl)-5-propyl-4,5-dihydroisoxazole 2-oxide (3r)



According to general procedure: 16 h, at room temperature, the product was obtained from flash chromatography (hexane/EtOAc = 8:1 to 2:1), as white solid 36 mg (Mp: 103-105 ^{o}C), 61% yield, 11:1 dr, 84% *ee*. HPLC analysis: Chiralcel OD-H (hexane/*i*-PrOH = 90/10, 1.0 mL/min), t_R (major) 9.18 min, t_R (minor) 15.85 min. $[\alpha]^{22}D$= +12.5° (c = 2.50, $CHCl_3$). ^{1}H NMR (400 MHz, CDCl3): δ 0.96 (t, *J* = 7.6 Hz, 3H), 1.19 (t, *J* = 6.8 Hz, 3H), 1.35-1.40 (m, 1H), 1.48-1.59 (m, 1H), 1.92-2.11 (m, 2H), 4.17-4.29 (m, 2H), 4.70 (s, 1H), 6.28 (d, *J* = 3.2 Hz, 1H), 6.33-6.35 (dd, J_1 = 3.2 Hz, J_2 = 22.0 Hz, 1H), 7.36 (d, *J* = 1.2 Hz, 1H), 9.35 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0, 14.2, 16.2, 37.4, 50.7, 62.1, 87.6, 107.7, 110.1, 111.2, 143.5, 145.9, 157.9, 196.2, HRMS (ESI) Calcd for $C_{14}H_{18}NO_6$ ($[M+H]^+$) 296.1134, found 296.1135.

Tansformation of *cis*-isoxazoline *N*-oxides into densely functionalized 2-amino-γ-lactone



(4*S*,5*R*)-5-Butyl-5-((tert-butyldimethylsilyloxy)methyl)-3-(methoxycarbonyl)-4-phenyl-4,5-dihydroisoxazole 2-oxide (5)

To the solution of **3c** (100 mg, 0.33 mmol) in MeOH/DCM 2 mL (1:3) under -10 °C, was added $NaBH_4$ (25 mg, 0.66 mmol) portionwise. Reaction completed in 10 minutes, then quenched with 5 mL saturated aqueous ammonium chloride. After separation, and dry on anhydrous magnesium sulfate, the solvent was removed under reduced pressure. Obtained residue and imidazole (45 mg, 0.66 mmol) dissolved in 1.0 mL anhydrous DMF, then TBDMSCl (99 mg, 0.66 mmol) was added in one portion. Reaction finished in 5 h, with TLC monitor. Subsequent chromatography purification on silicon gel gave colorless oil in 77% yield for two steps.

^{1}H NMR (400 MHz, $CDCl_3$): δ -0.29 (s, 3H), -0.16 (s, 3H), 0.78 (s, 9H), 0.93 (t, *J* = 7.2 Hz, 3H), 1.33-1.52 (m, 4H), 1.94-1.96 (m, 2H), 3,23 (d, *J* = 10.5 Hz, 1H), 3,35 (d, *J* = 10.5 Hz, 1H), 3.68 (s, 3H), 4.40 (s, 1H), 7.14-7.17 (m, 2H), 7.30-7.32 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ -6.1, -6.0, 14.0, 18.0, 22.9, 24.9, 25.7, 35.5, 52.5, 55.9, 61.3, 86.7, 113.0, 128.2, 128.7, 135.1, 159.4.

(4*S*,5*R*)-Methyl 5-butyl-5-((tert-butyldimethylsilyloxy)methyl)-4-phenyl-4,5-dihydroisoxazole-3-carboxylate (6)

A solution of **4** (82 mg, 0.2 mmol) in 1.0 mL $P(OMe)_3$ was stirred at 100 ^oC for 16 h, with N_2 protection, hereafter diluted with Et_2O (5 mL), then 5 mL 1 M HCl was added at -10 ^oC. After separation, dried over magnesium sulfate, solution was concentrated in *vacuo*, then applied to silicon gel to give colorless oil in quantitative yield.

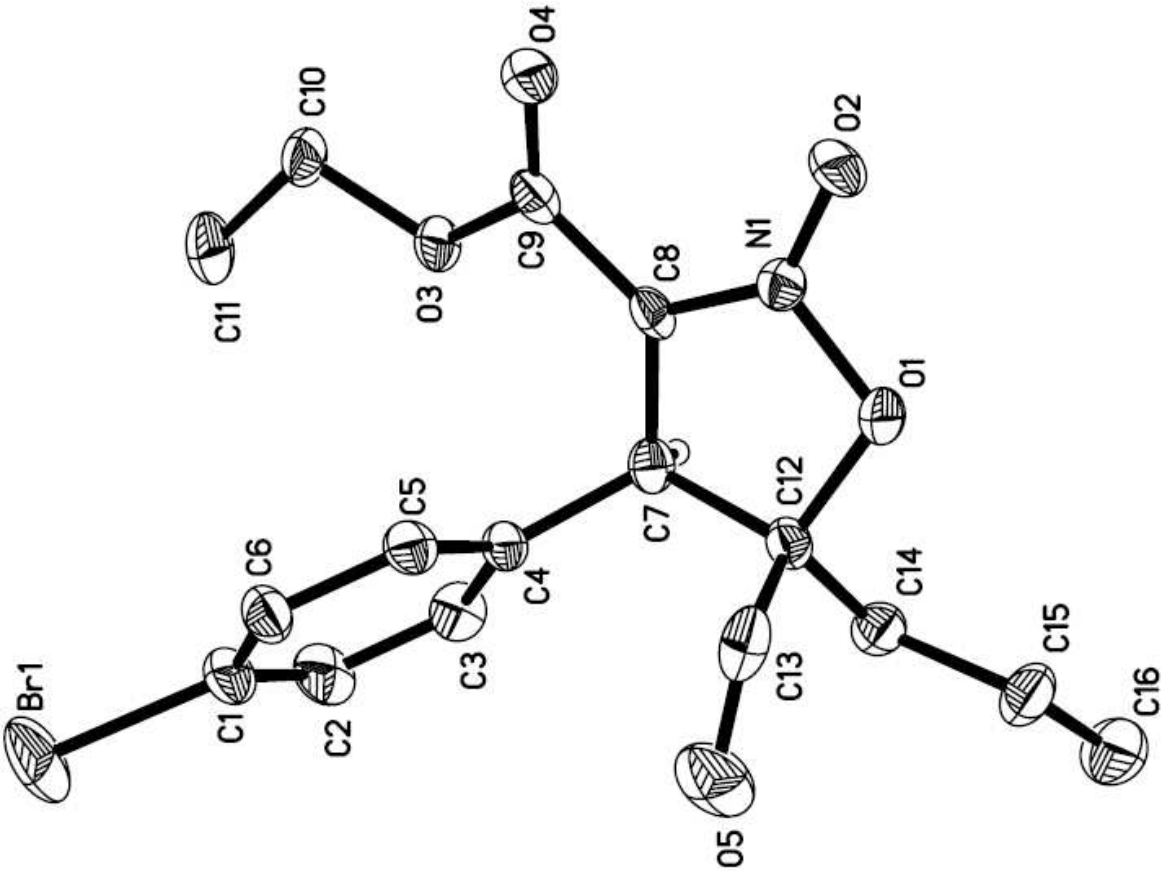
^1H NMR (400 MHz, $CDCl_3$): δ -0.33 (s, 3H), -0.17 (s, 3H), 0.77 (s, 9H), 0.93 (t, *J* = 7.2 Hz, 3H), 1.25-1.48 (m, 4H), 1.80-1.83 (m, 2H), 3,25 (d, *J* = 10.5 Hz, 1H), 3.46 (d, *J* = 10.5 Hz, 1H), 3.76 (s, 3H), 4.30 (s, 1H), 7.03 (d, *J* = 6.6 Hz, 2H), 7.26 -7.32 (m, 3H). ^{13}CH NMR (100 MHz, $CDCl_3$): δ -6.1, -6.0, 14.0, 18.0, 23.0, 25.1, 25.7, 36.0, 52.6, 58.9, 61.6, 94.7, 127.9, 128.6, 128.8, 133.8, 154.0, 160.8.

***tert*-Butyl (3R,4S,5R)-5-butyl-5-((tert-butyldimethylsilyloxy)methyl)-2-oxo-4-phenyltetrahydrofuran-3-ylcarbamate (7)**

$NiCl_2.6H_2O$ (0.33 mmol, 3 equiv), Boc_2O (0.33 mmol, 3 equiv) and **5** (0.11 mmol, 1 equiv) were suspended in a 3:1 mixture of MeOH/THF (0.8 mL) at -30 ^oC. After 10 min of stirring, $NaBH_4$ (1.1 mmol, 10 equiv) was added portionwise. The stirring was maintained at -30 ^oC for 24 h. After the reaction was completed, it was quenched with conc. NH_4OH (2 mL), extracted with dichloromethane, dried over magnesium sulfate and concentrated in *vacuo*. Silicon gel chromatography purification gave 31 mg colorless oil in 60% yield. 96% *ee*. HPLC analysis: Chiralcel IA-H (hexane/*i*-PrOH = 98/2, 1.0 mL/min), t_R (major) 6.87 min, t_R (minor) 8.36 min. $[\alpha]^{21}D$= +52.8° (c = 2.30, $CHCl_3$).

^1H NMR (400 MHz, $CDCl_3$): δ -0.25 (s, 3H), -0.11 (s, 3H), 0.80 (s, 9H), 0.92 (t, *J* = 7.2 Hz, 3H), 1.29 (s, 9H), 1.35-1.41 (m, 4H), 1.87-1.92 (m, 2H), 3.33 (d, *J* =12.0 Hz, 1H), 3.56 (d, *J* =12.0 Hz, 1H), 3.72 (d, *J* = 12.0 Hz, 1H), 4.89 (d, *J* = 8.0 Hz, 1H), 5.05 (t, *J* = 8.0 Hz, 1H), 7.07 (d, *J* =8.0 Hz, 2H), 7.26 -7.31 (m, 3H). ^{13}CH NMR (100 MHz, $CDCl_3$): δ -6.1, 14.0, 18.1, 23.0, 25.6, 25.7, 25.7, 28.1, 35.2, 52.5, 53.3, 62.7, 80.2, 88.8, 127.8, 128.6, 129.6, 133.9, 155.1, 174.9. HRMS (ESI) Calcd for $C_{26}H_{43}NO_5SiNa$ ($[M+Na]^+$) 500.2808, found 500.2805.

IV. Absolute configuration assignments of (4*S*,5*R*)-4-(4-Bromophenyl)-3-(ethoxycarbonyl)-5-formyl-5-propyl-4,5-dihydroisoxazole 2-oxide (3l)



V. Reference

1. a) Kanao, M.; Watanabe, Y.; Kimura, Y. *J. Med. Chem.* **1989**, *32*, 1326. b) Riehl, J. J.; Fougerousse, A. *Tetraheron Lett.* **1968**, *42*, 4415.
2. Fornicola, R.; Oblinger, E.; Montgomery, J. *J. Org. Chem*. **1998**, *63*, 3528.
3. Hayashi, Y.; Gotoh, H.; Hayashi, T.; Shoji, M. *Angew. Chem.* **2005**, *117*, 4284-4287; *Angew. Chem. Int. Ed*. **2005**, *44*, 4212.
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5. Cao, C.; Ye, M.; Sun, X.; Tang, Y. *Org. Lett.* **2006**, *8*, 2901.
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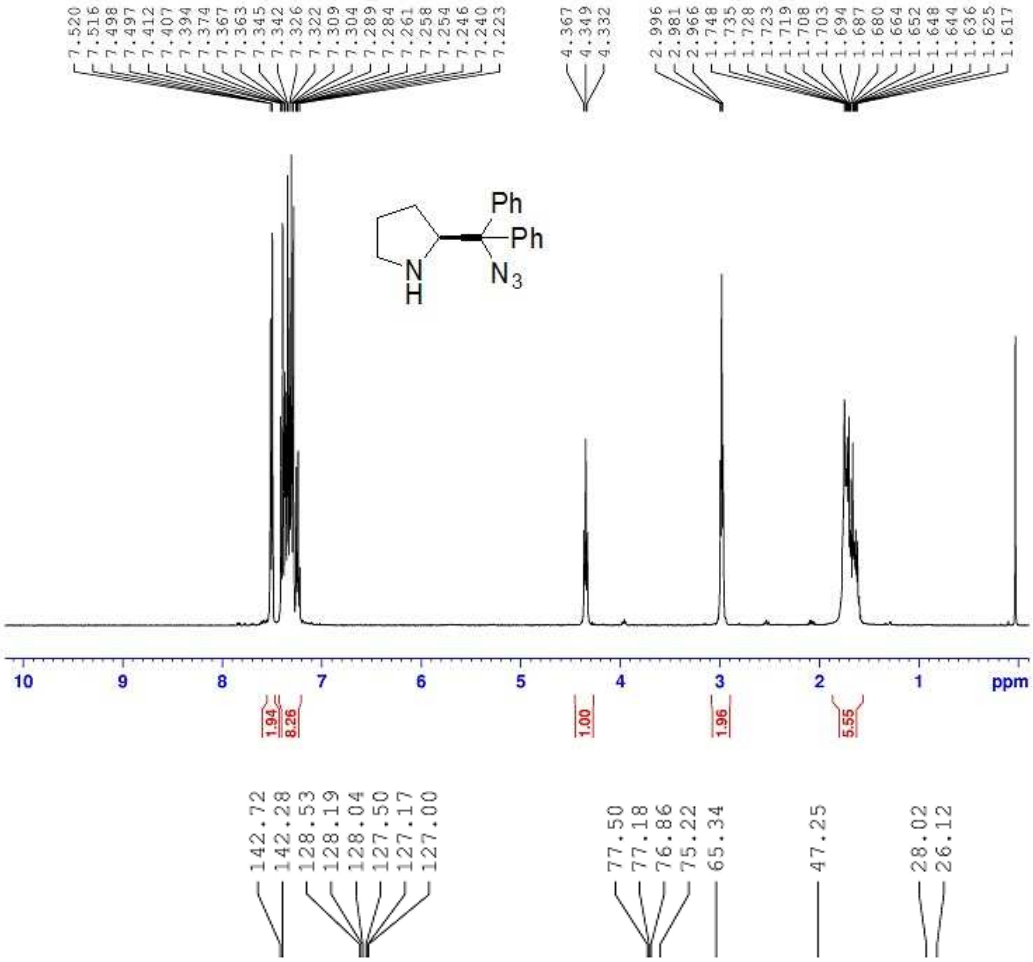
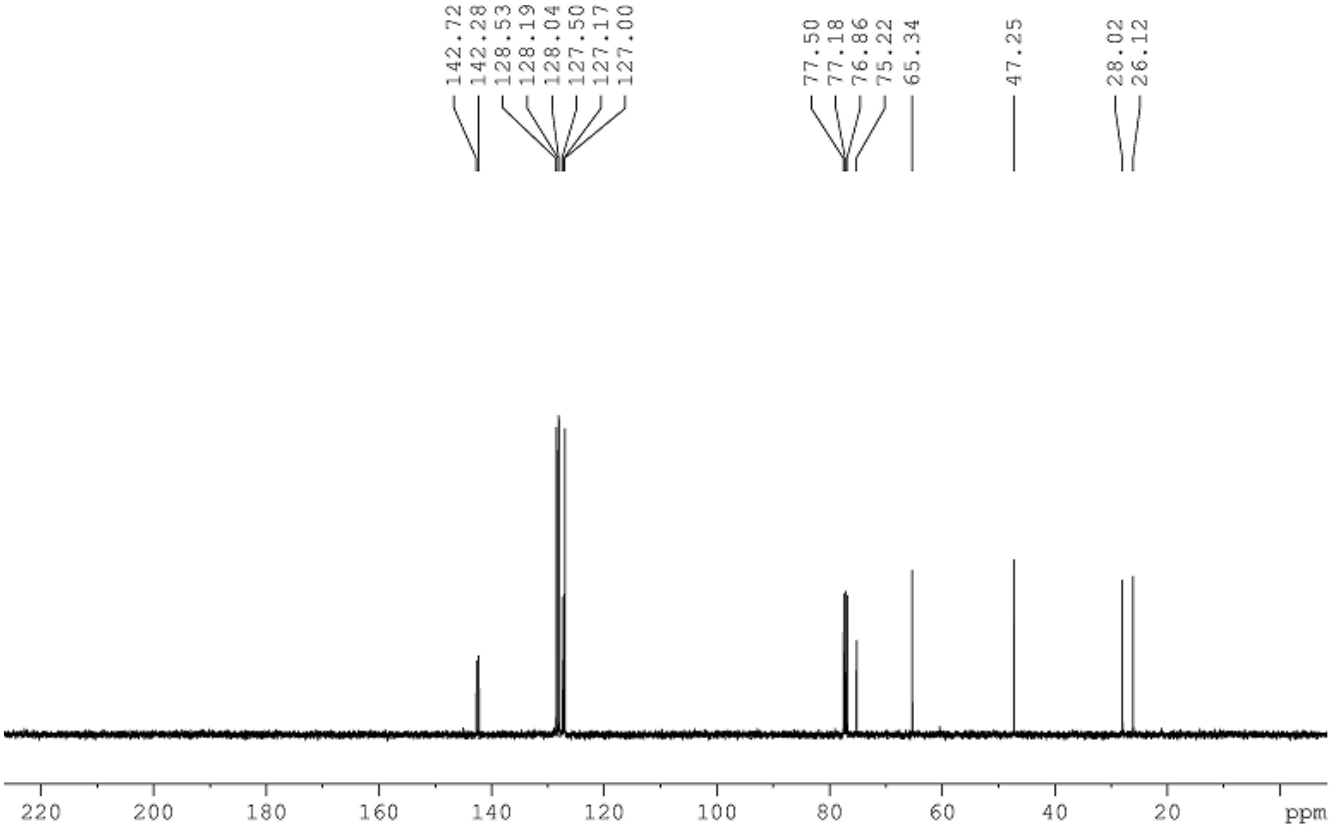
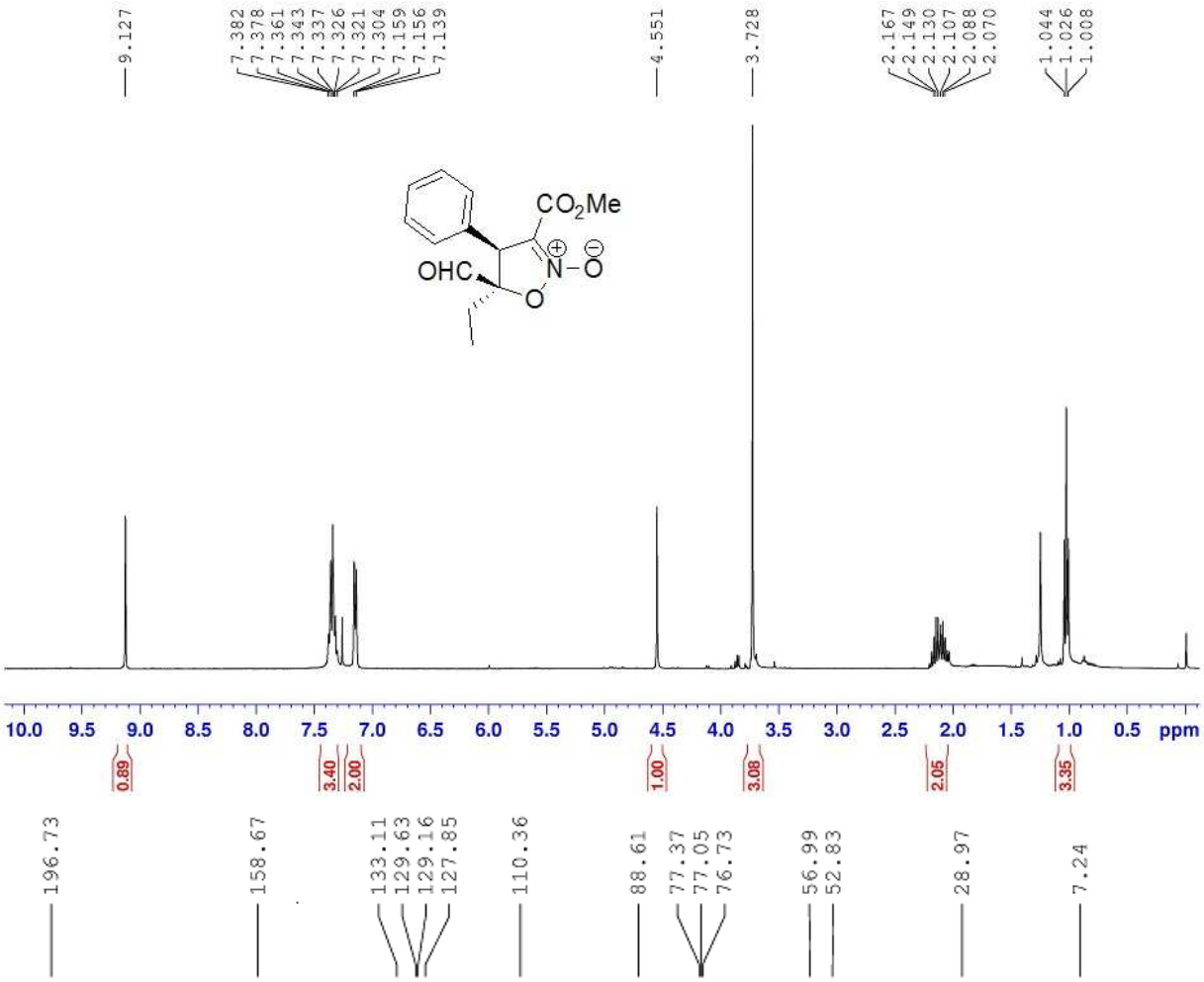
VI. ^{1}H NMR and ^{13}C NMR spectra

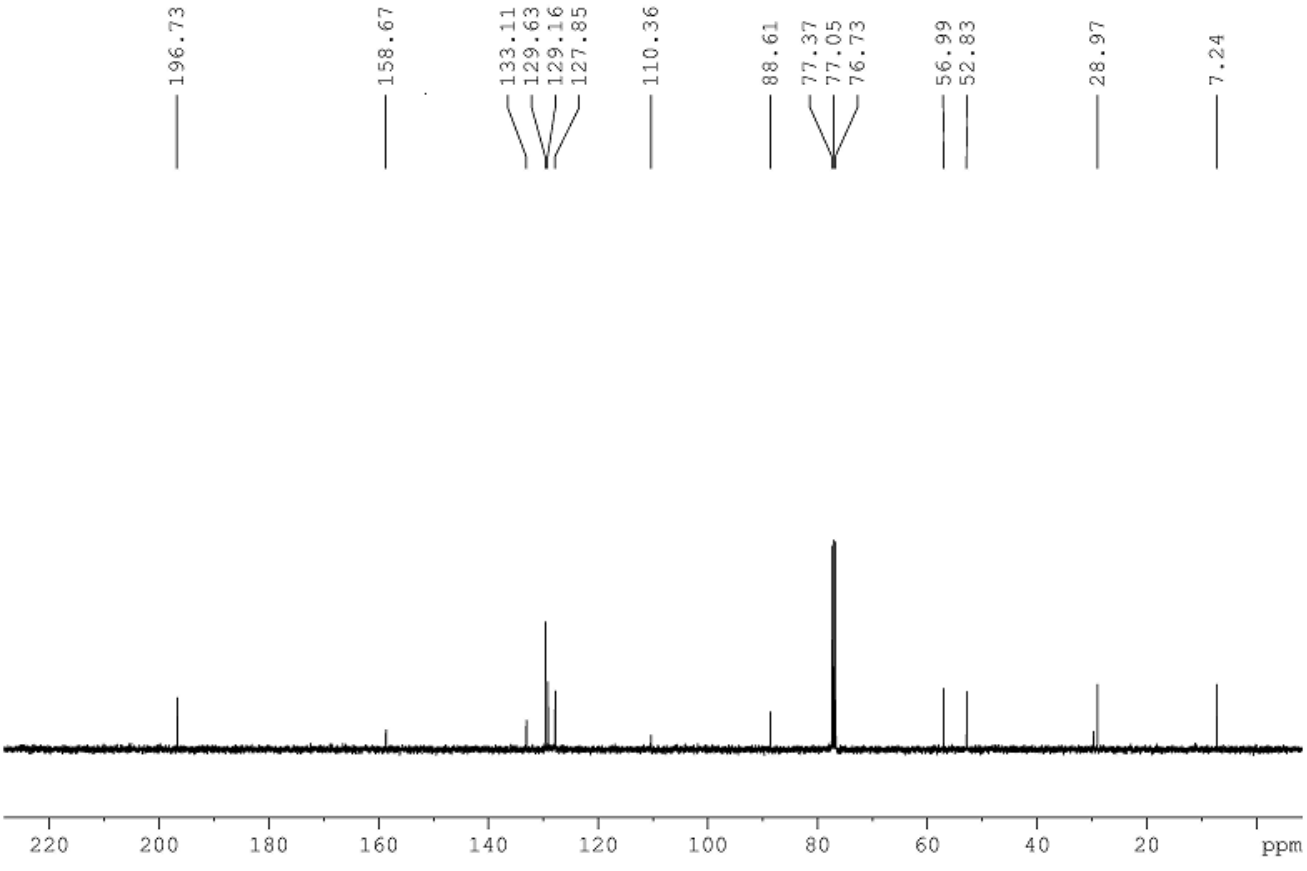
(*S*)-2-(Azidodiphenylmethyl)pyrrolidine (4e)



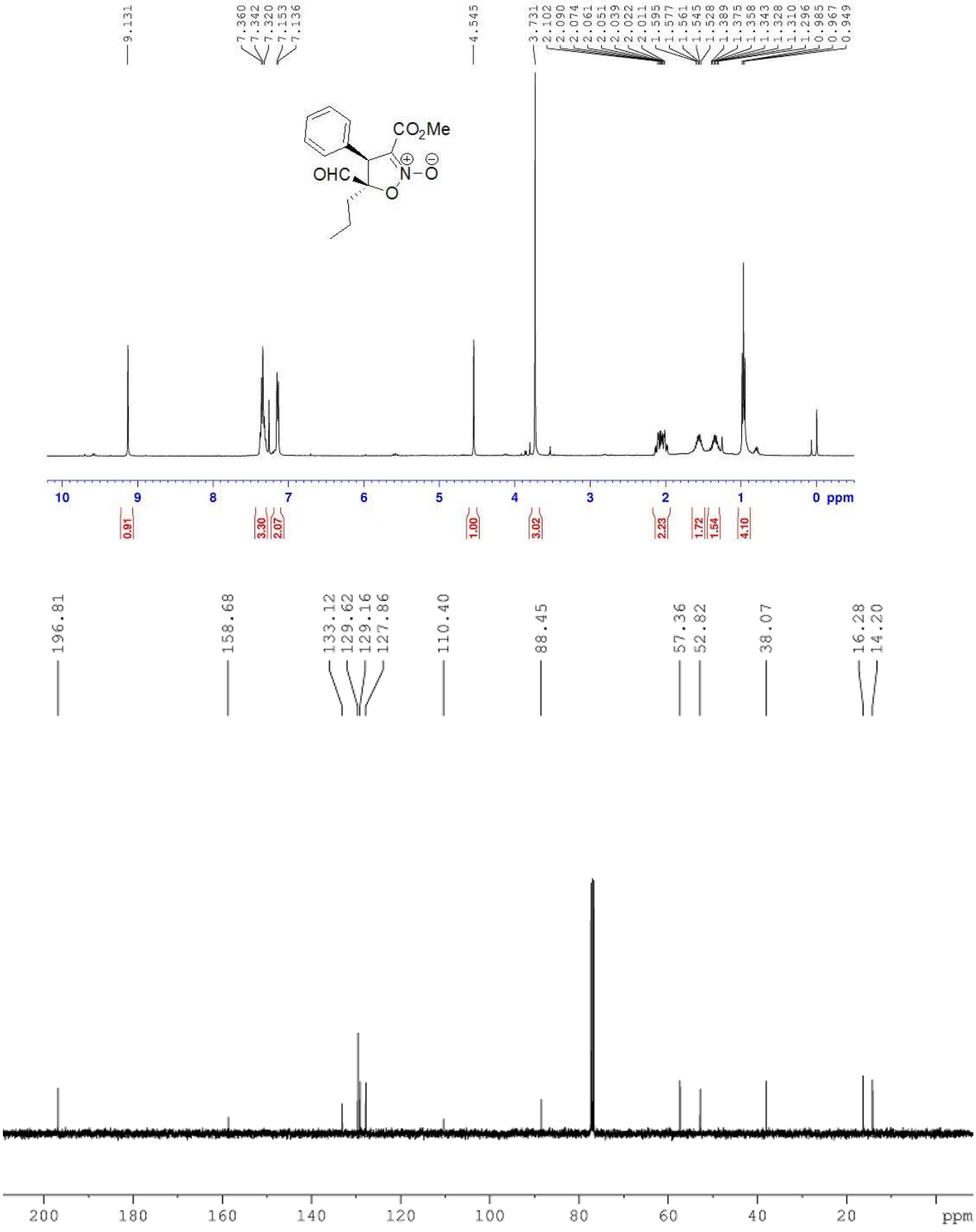


(4*S*,5*R*)-3-(Methoxycarbonyl)-5-formyl-4-phenyl-5-ethyl-4,5-dihydroisoxazole 2-oxide (3a)

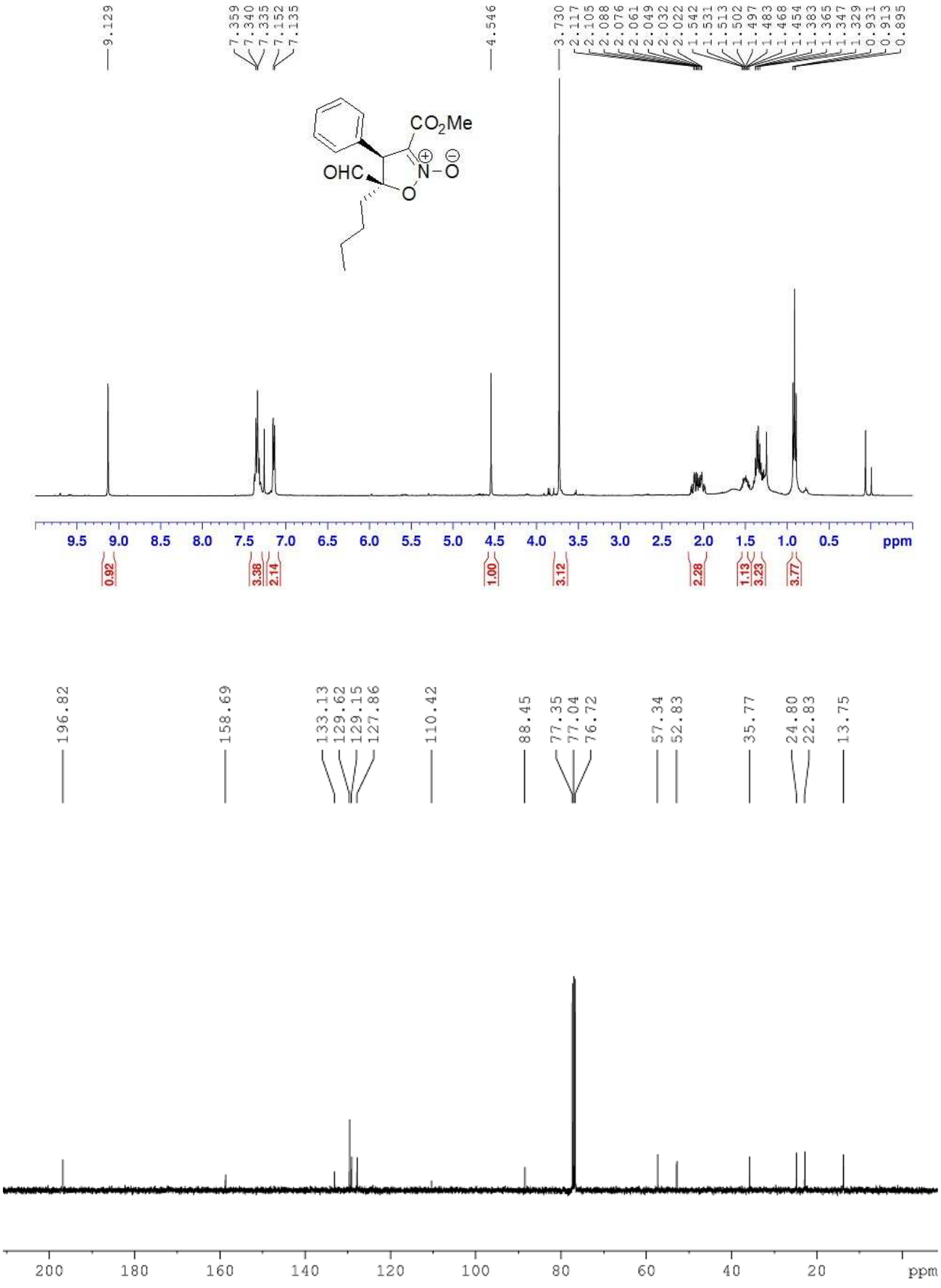




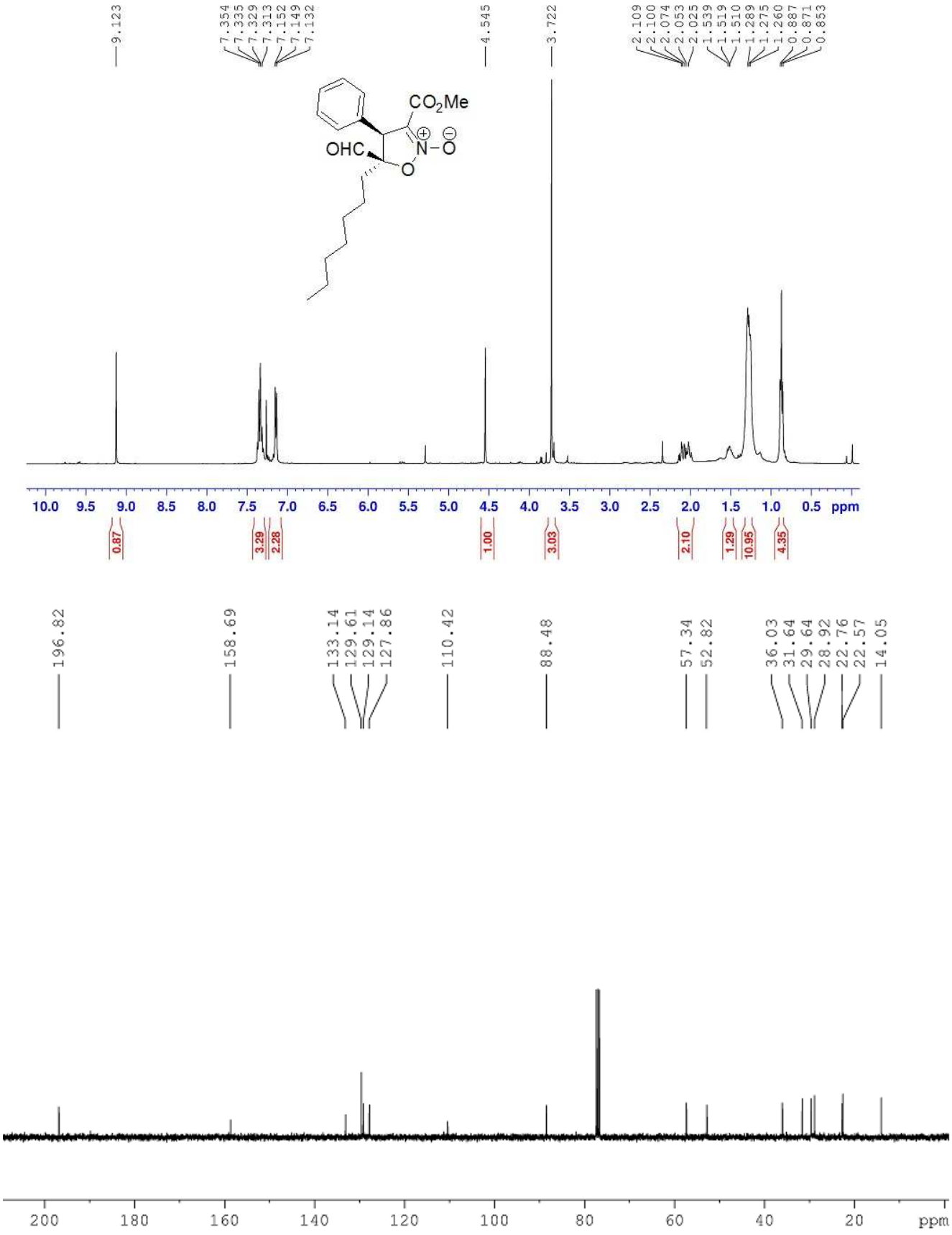
(4*S*,5*R*)-3-(Methoxycarbonyl)-5-formyl-4-phenyl-5-propyl-4,5-dihydroisoxazole 2-oxide (3b)



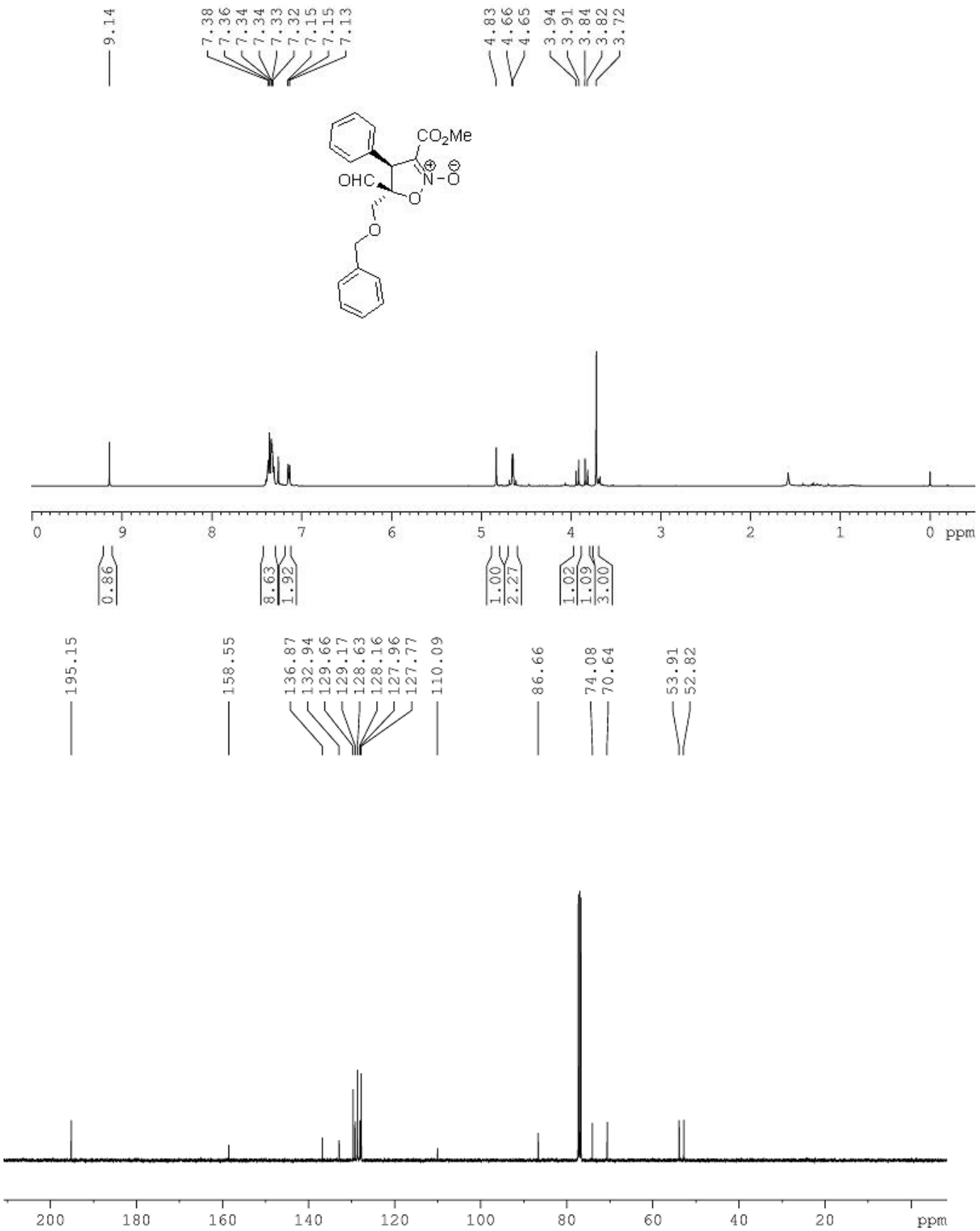
(4*S*,5*R*)-3-(Methoxycarbonyl)-5-formyl-4-phenyl-5-butyl-4,5-dihydroisoxazole 2-oxide (3c)



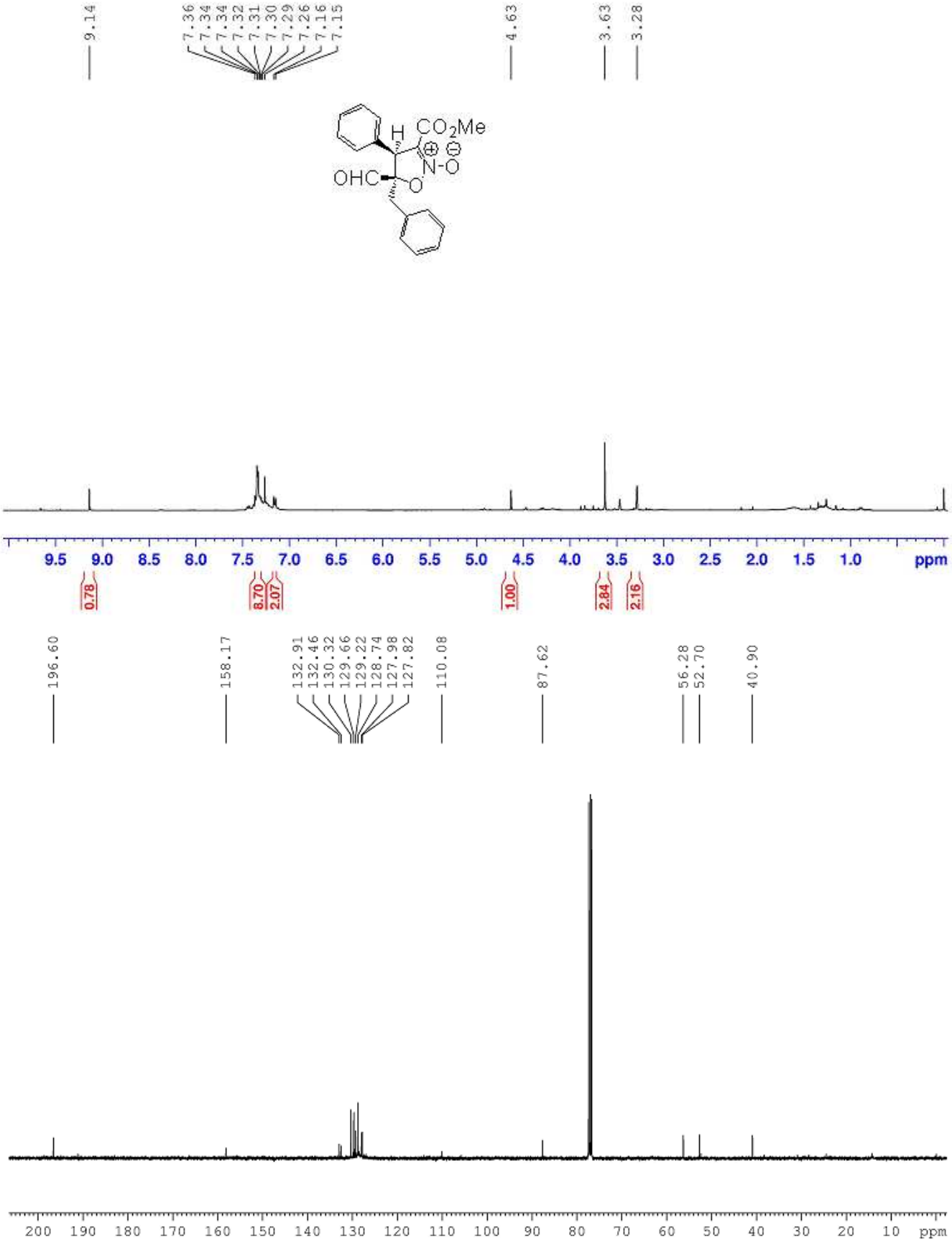
(4*S*,5*R*)-3-(Methoxycarbonyl)-5-formyl-4-phenyl-5-heptyl-4,5-dihydroisoxazole 2-oxide (3d)



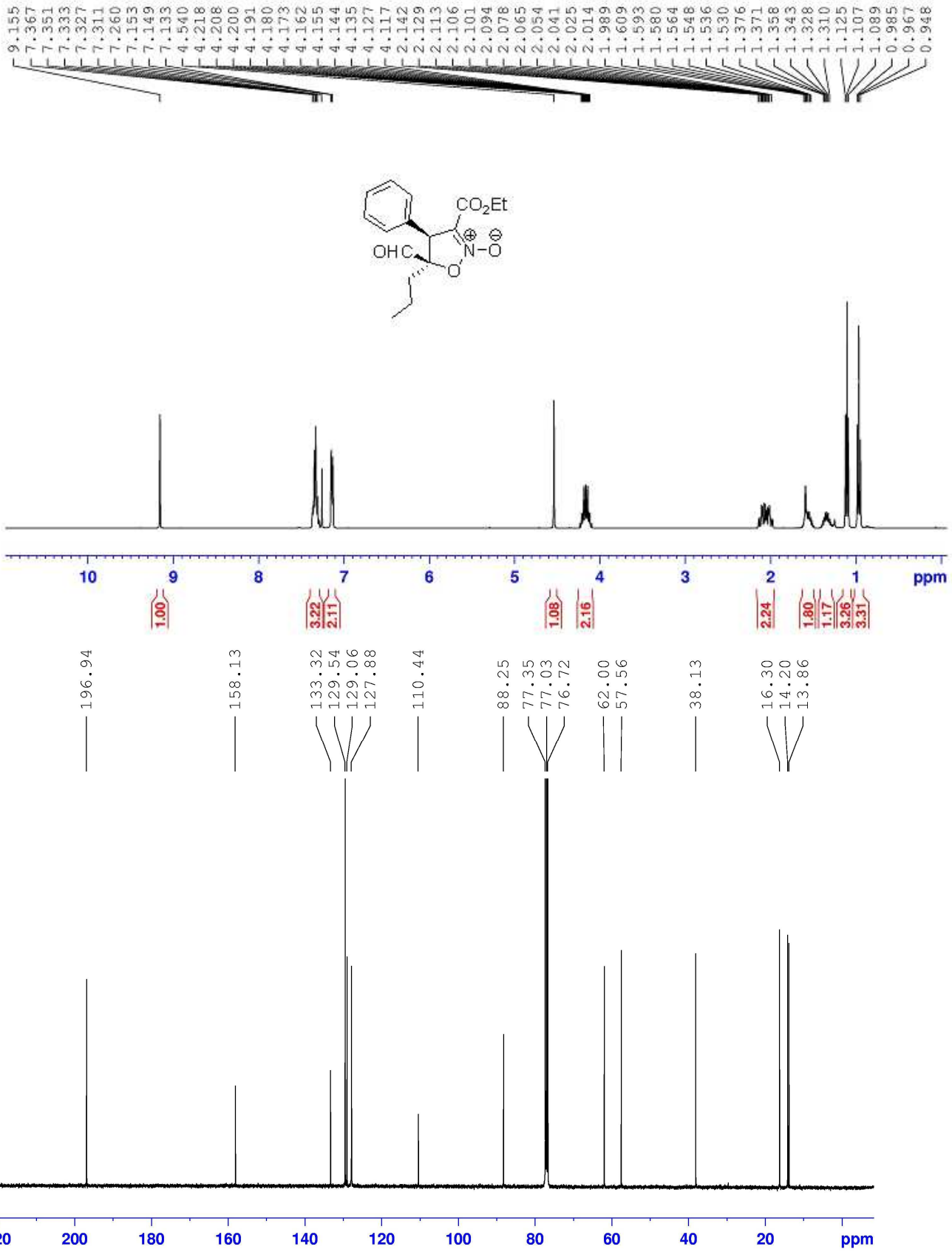
(4*S*,5*S*)-5-(Benzyloxymethyl)-5-formyl-3-(Methoxycarbonyl)-4-phenyl-4,5-dihydroisoxazole 2-oxide (3e)



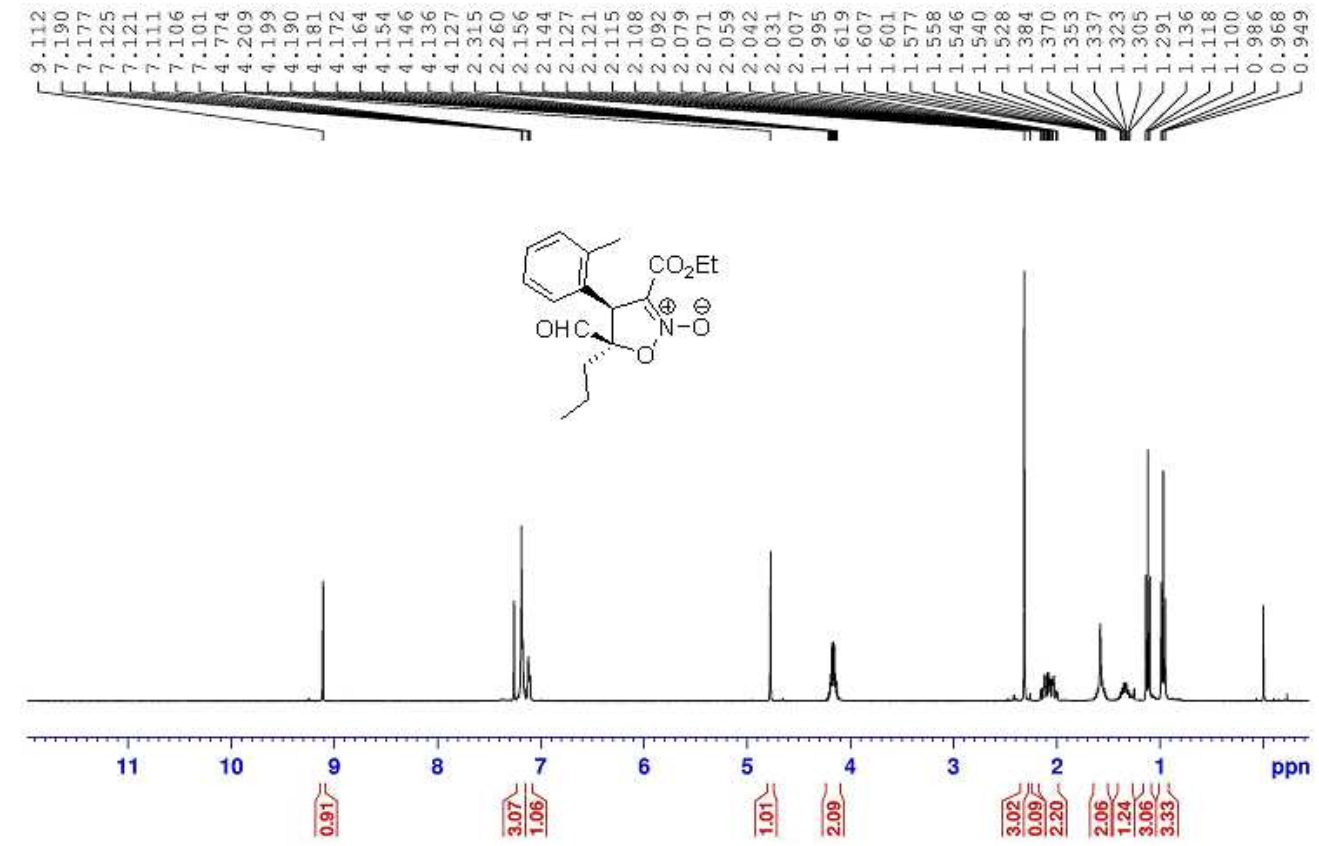
(*4S*,5*R*)-5-Benzyl-4-(4-chlorophenyl)-5-formyl-3-(methoxycarbonyl)-4,5-dihydroisoxazole 2-oxide (3f)

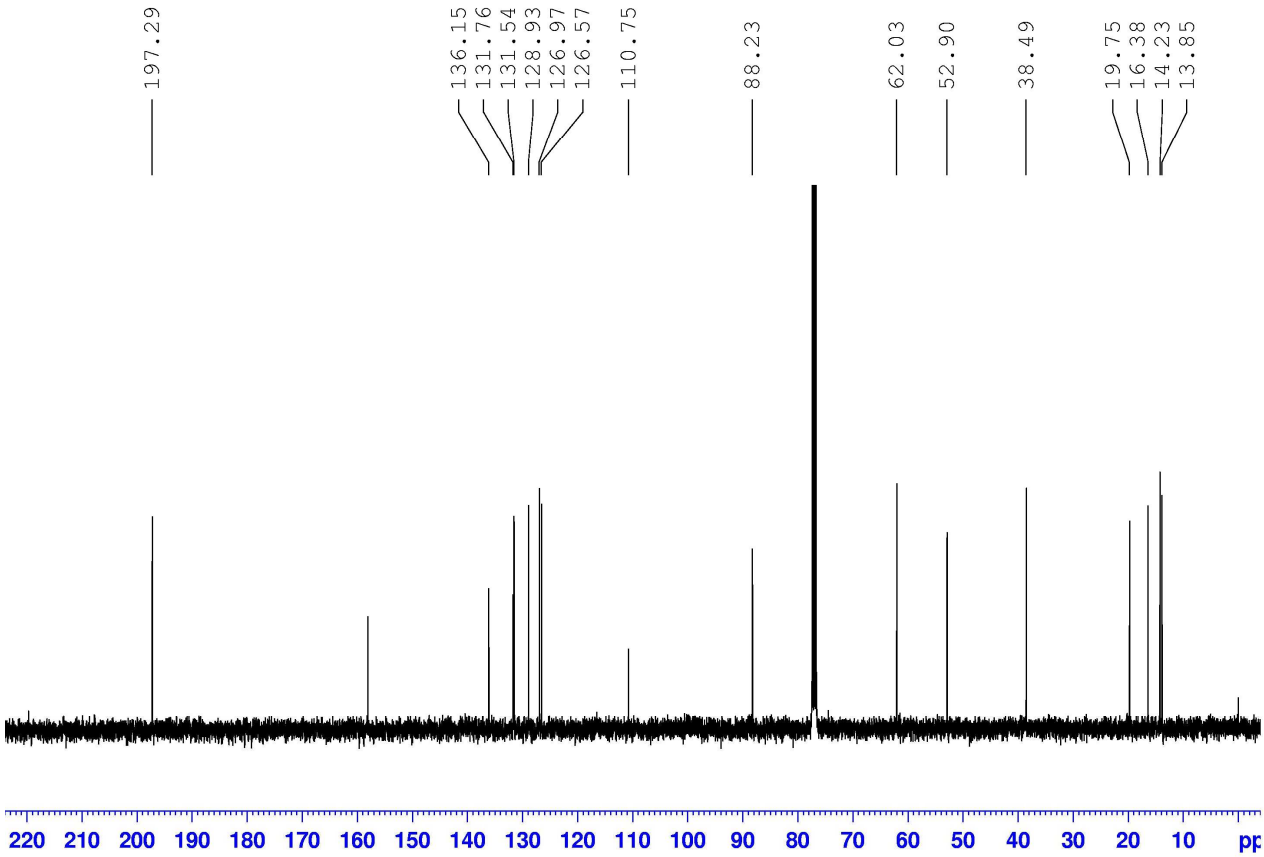


(4*S*,5*R*)-3-(Ethoxycarbonyl)-5-formyl-4-phenyl-5-propyl-4,5-dihydroisoxazole 2-oxide (3g)

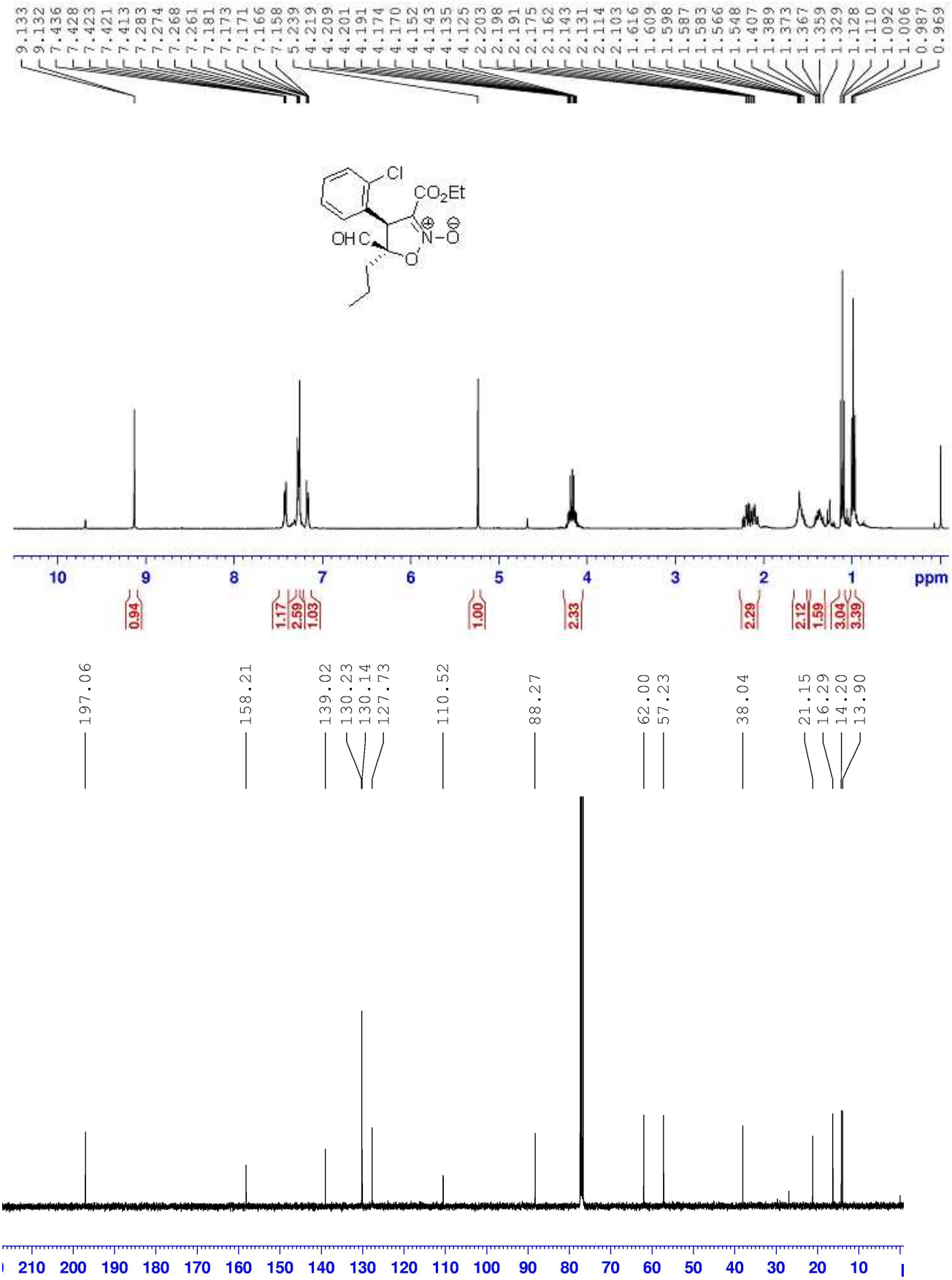


(4*S*,5*R*)-3-(Ethoxycarbonyl)-5-formyl-5-propyl-4-o-tolyl-4,5-dihydroisoxazole 2-oxide (3h)

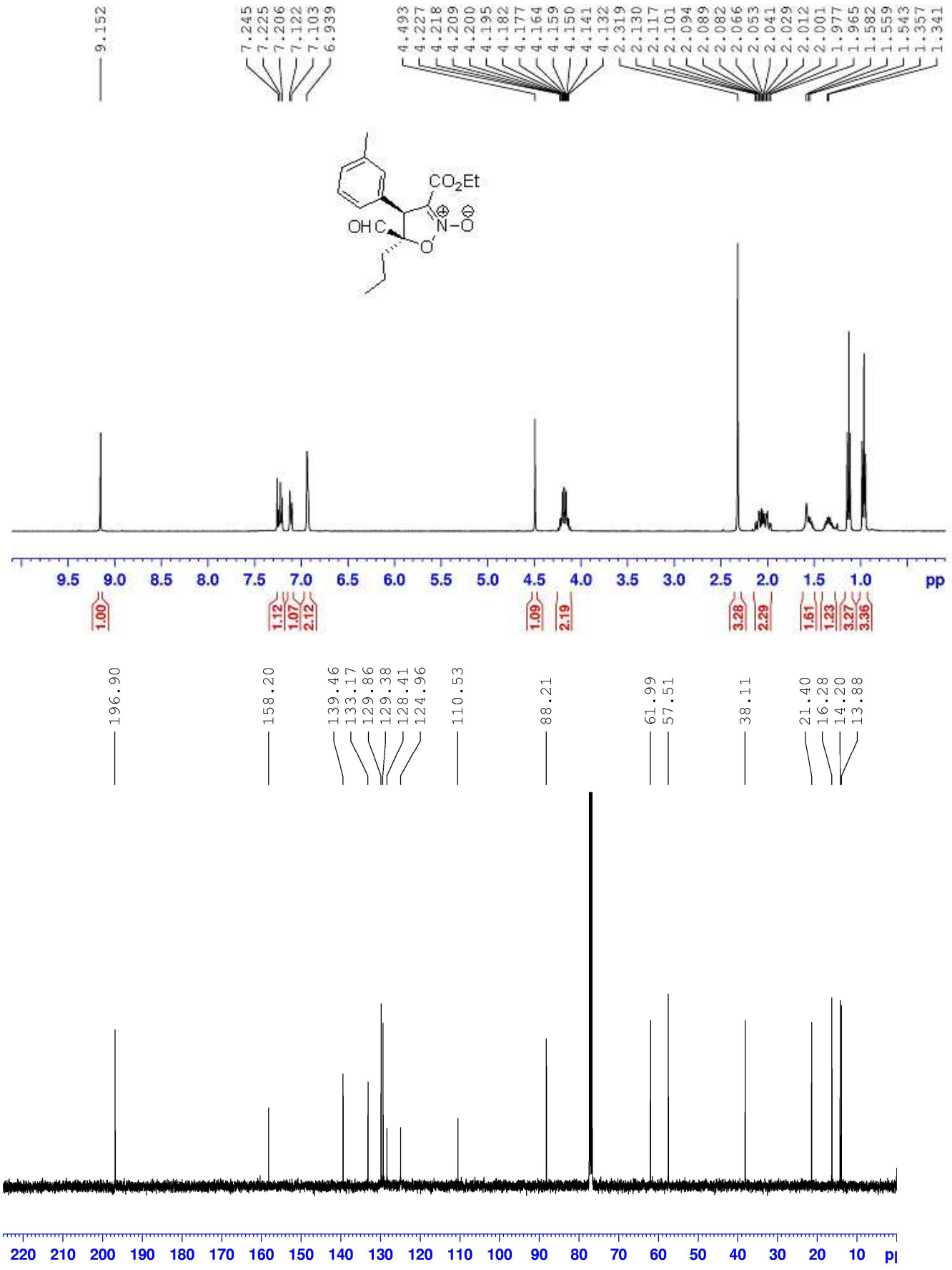




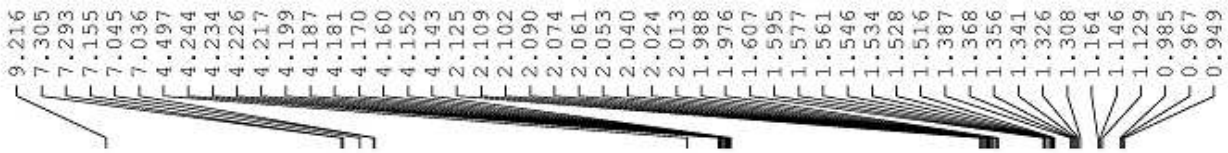
(4*S*,5*R*)-4-(2-Chlorophenyl)-3-(ethoxycarbonyl)-5-formyl-5-propyl-4,5-dihydroisoxazole 2-oxide (3i)

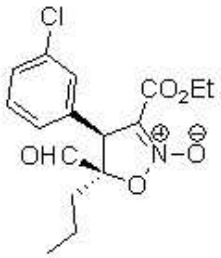


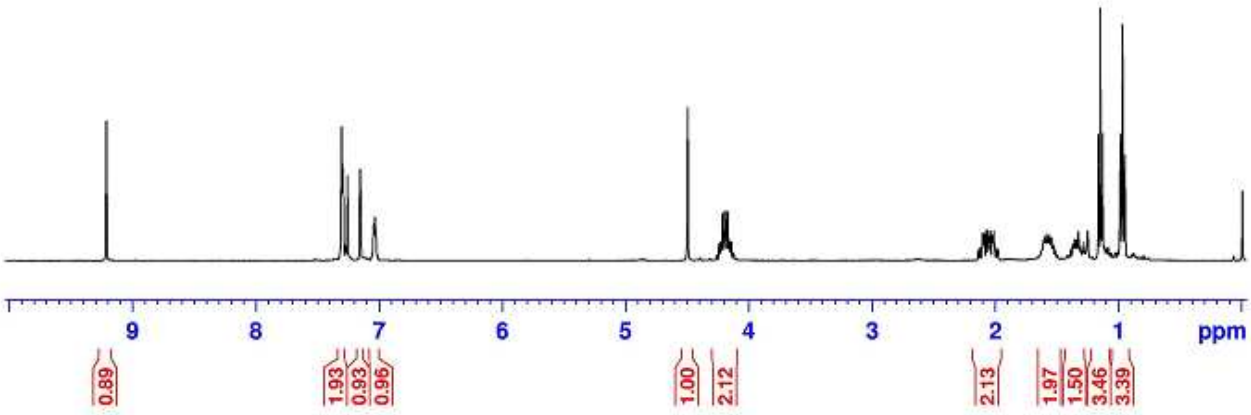
(4*S*,5*R*)-3-(Ethoxycarbonyl)-5-formyl-5-propyl-4-m-tolyl-4,5-dihydroisoxazole 2-oxide (3j)

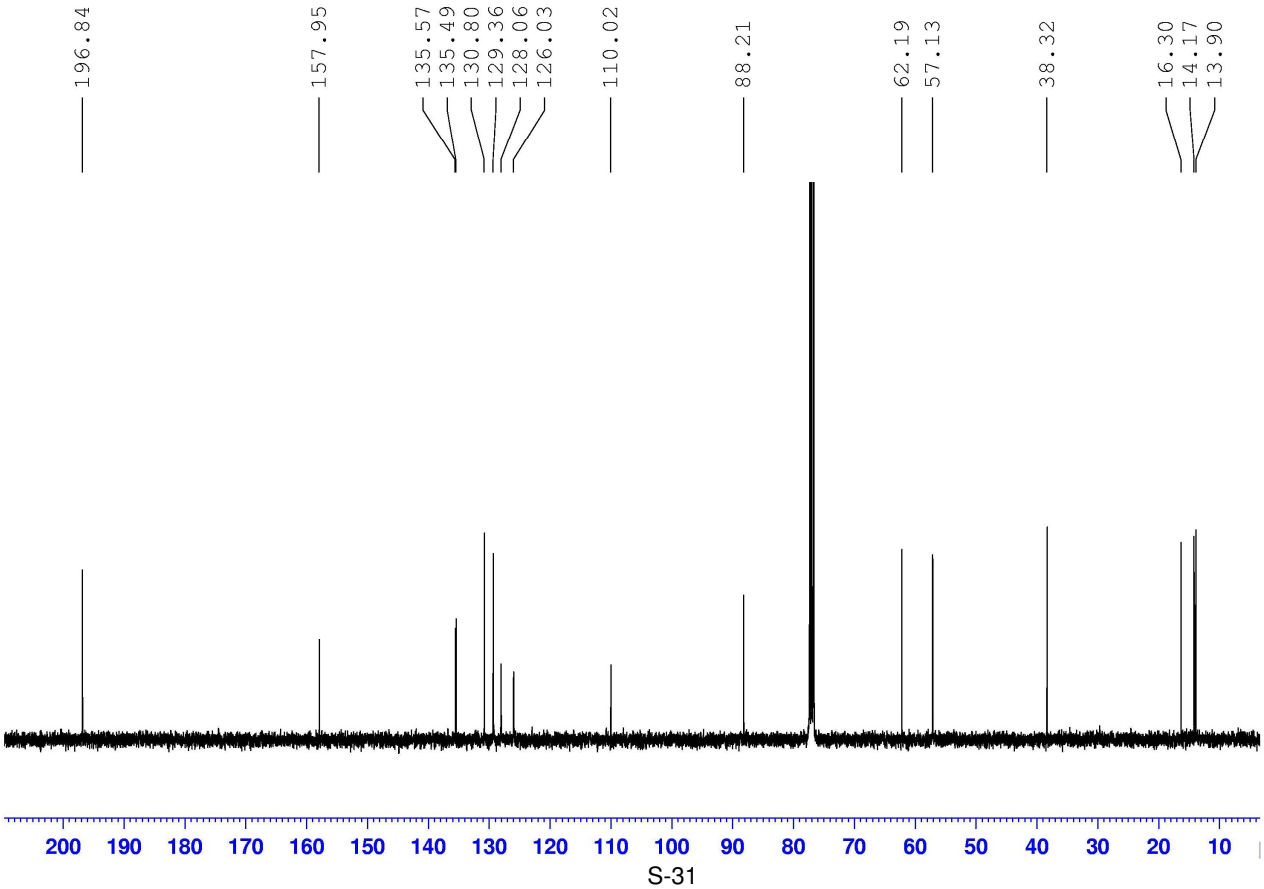


(4*S*,5*R*)-4-(3-Chlorophenyl)-3-(ethoxycarbonyl)-5-formyl-5-propyl-4,5-dihydroisoxazole 2-oxide (3k)

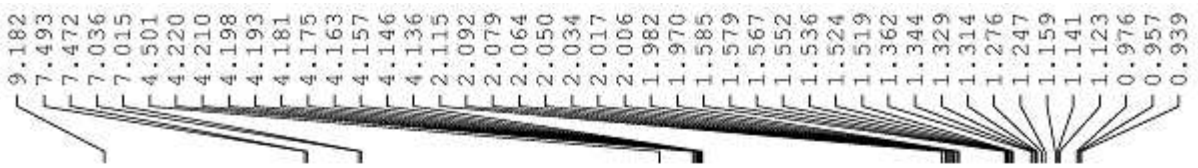


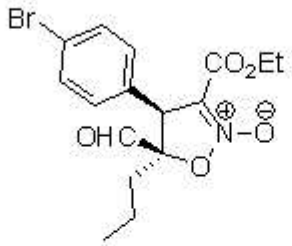


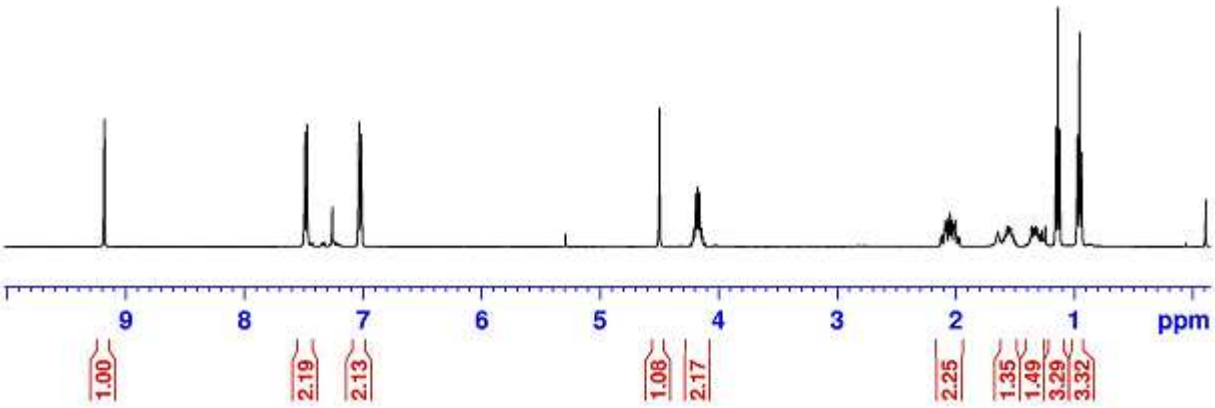


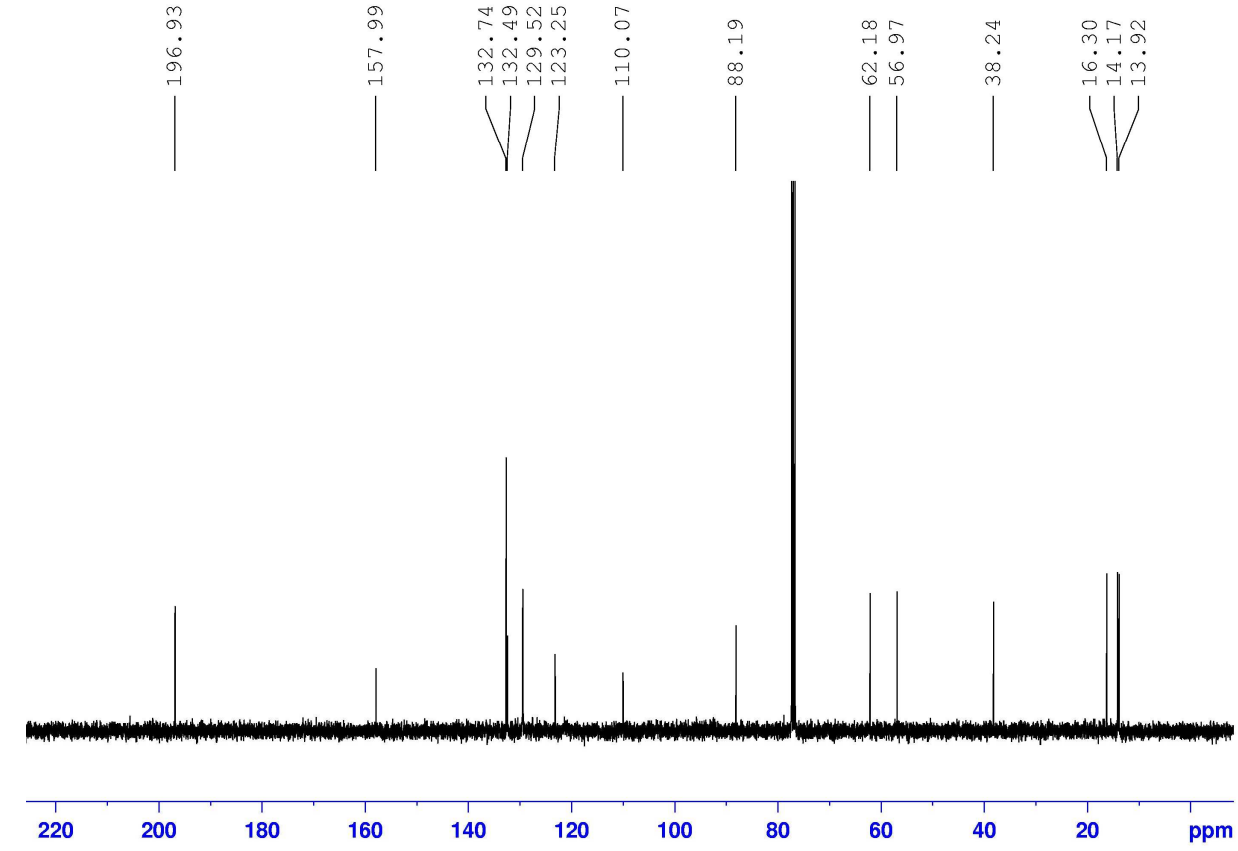


(4*S*,5*R*)-4-(4-Bromophenyl)-3-(ethoxycarbonyl)-5-formyl-5-propyl-4,5-dihydroisoxazole 2-oxide (3l)

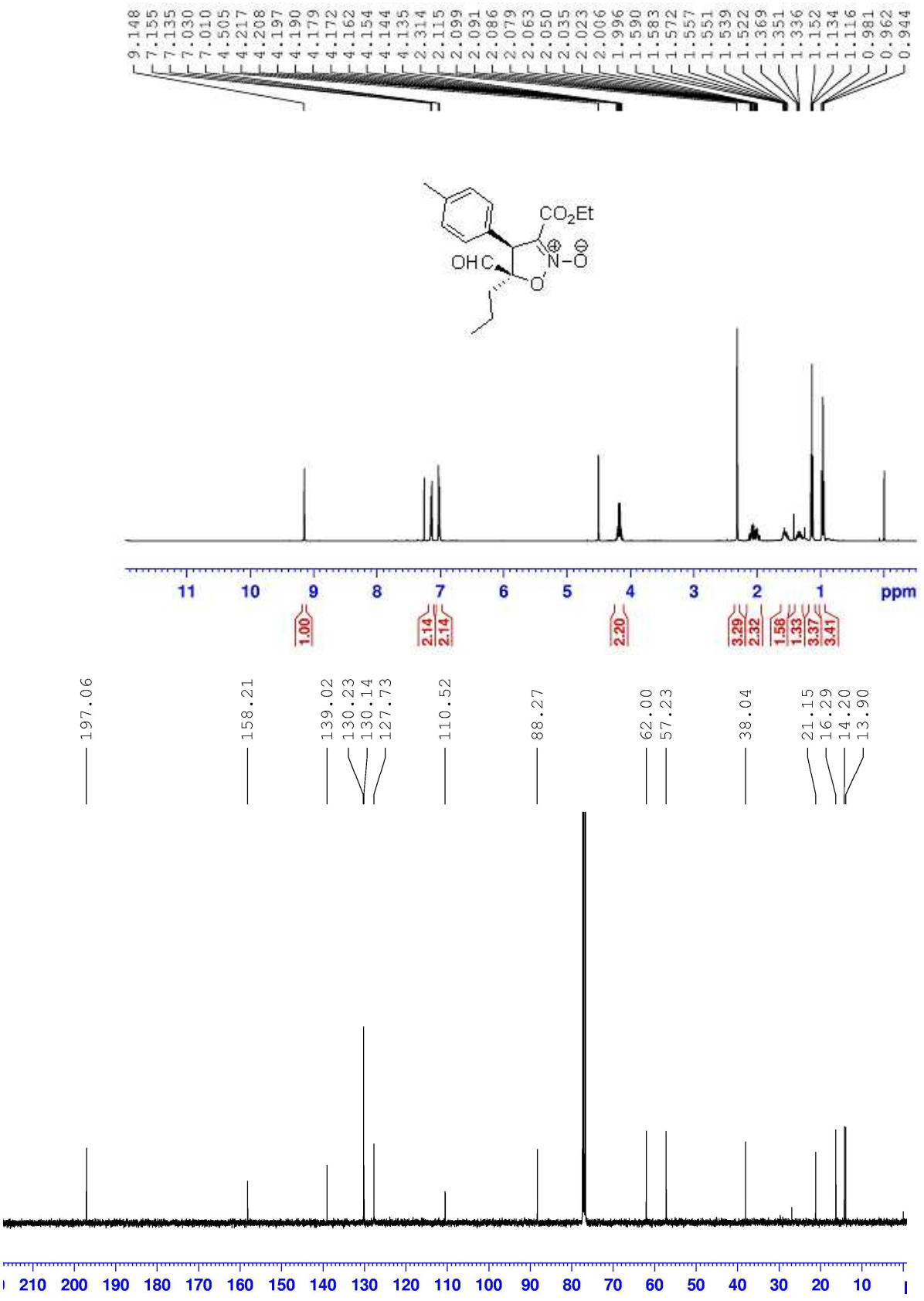




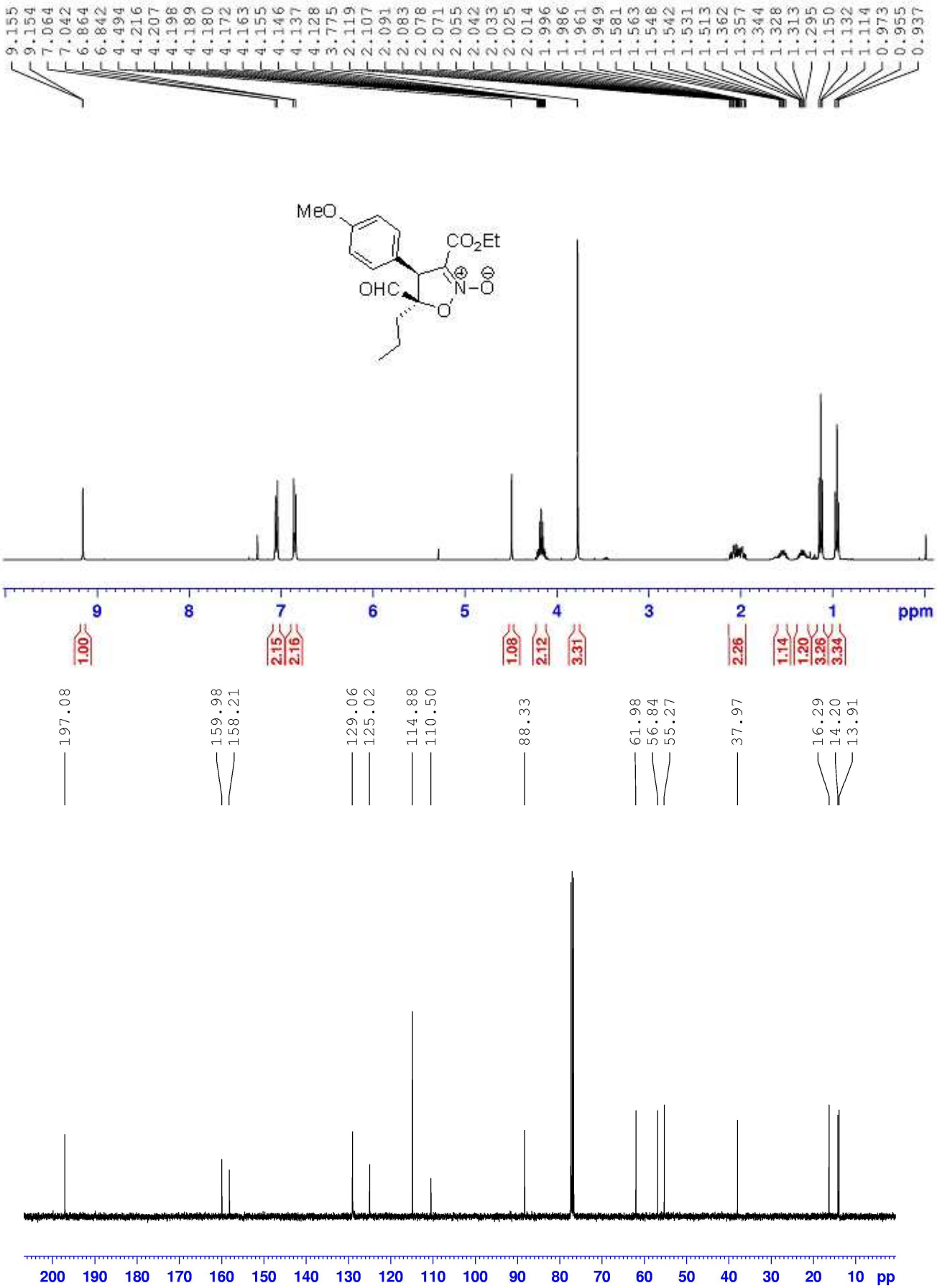




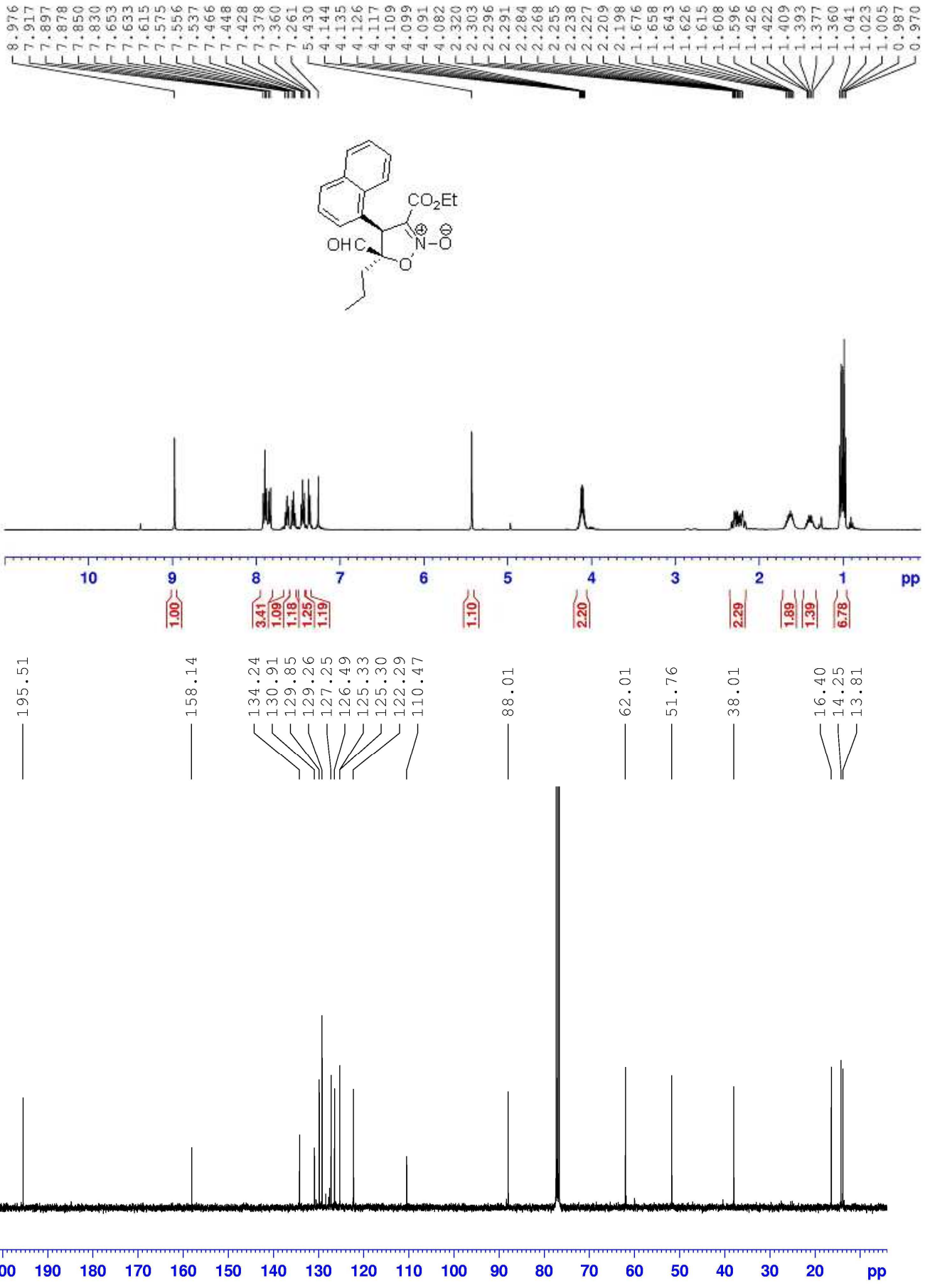
(4*S*,5*R*)-3-(Ethoxycarbonyl)-5-formyl-5-propyl-4-*p*-tolyl-4,5-dihydroisoxazole 2-oxide (3m)



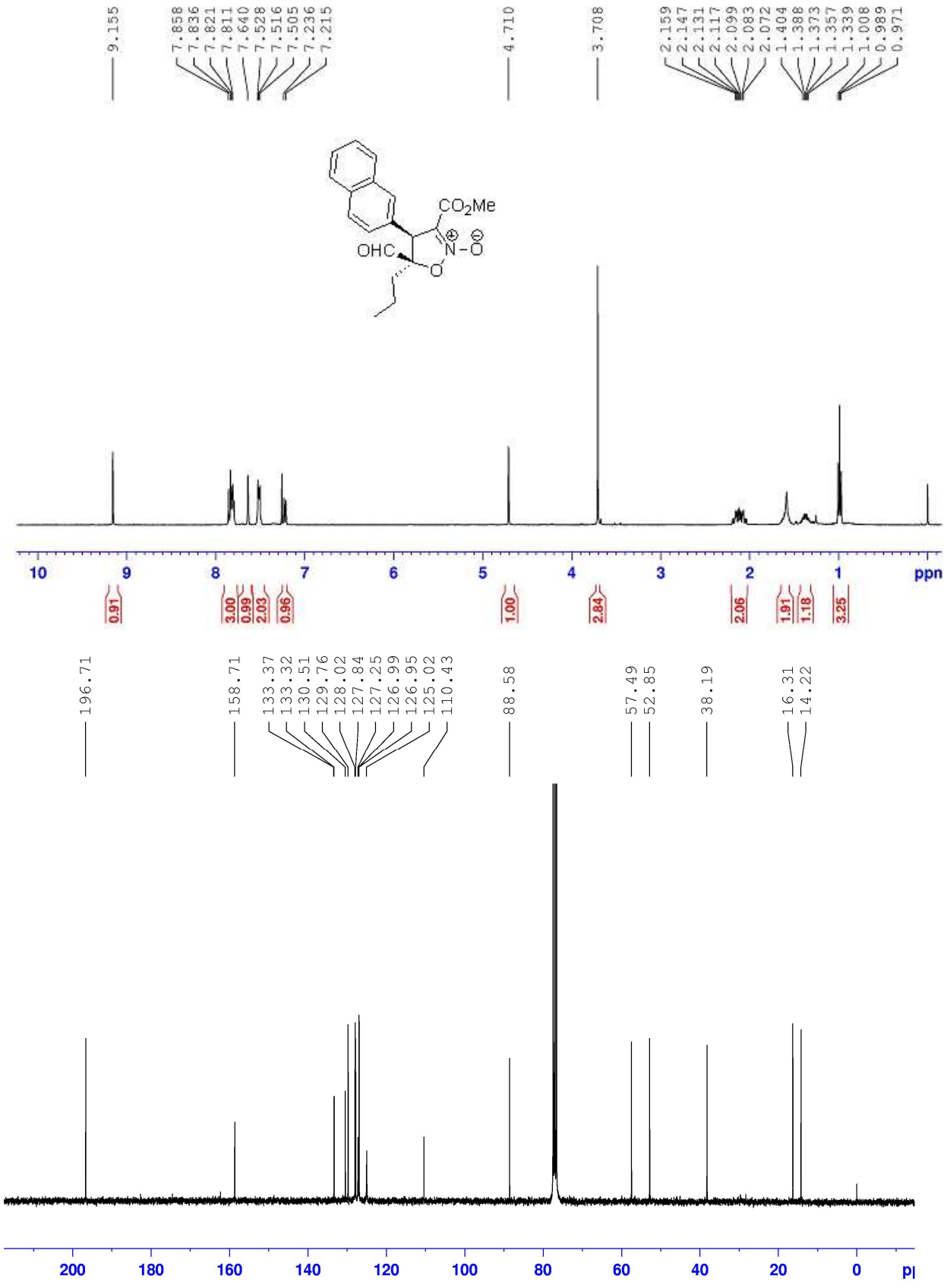
(4*S*,5*R*)-4-(4-Methoxyphenyl)-3-(ethoxycarbonyl)-5-formyl-5-propyl-4,5-dihydroisoxazole 2-oxide (3n)



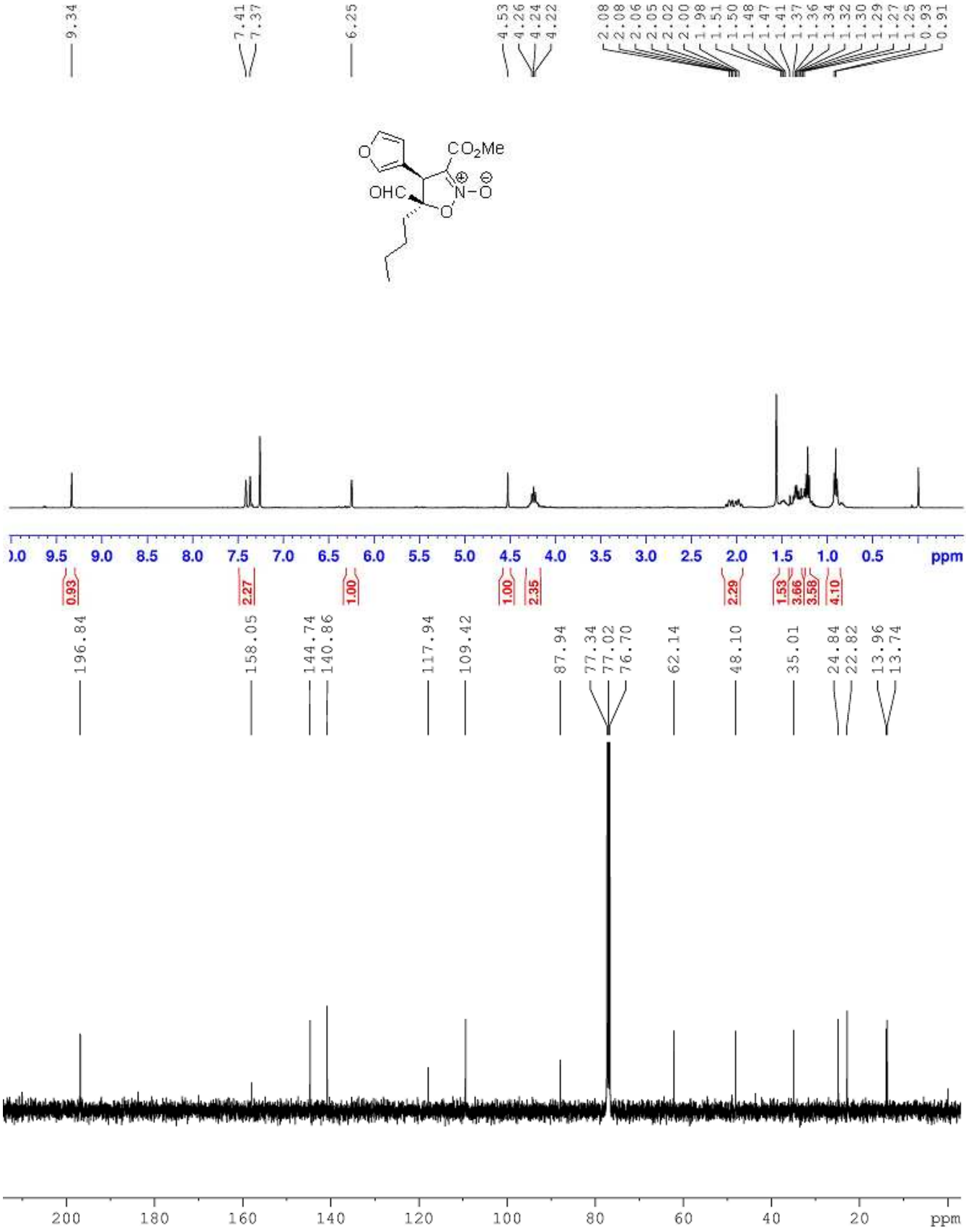
(4*S*,5*R*)-3-(Ethoxycarbonyl)-5-formyl-4-(naphthalen-1-yl)-5-propyl-4,5-dihydroisoxazole 2-oxide (3o)



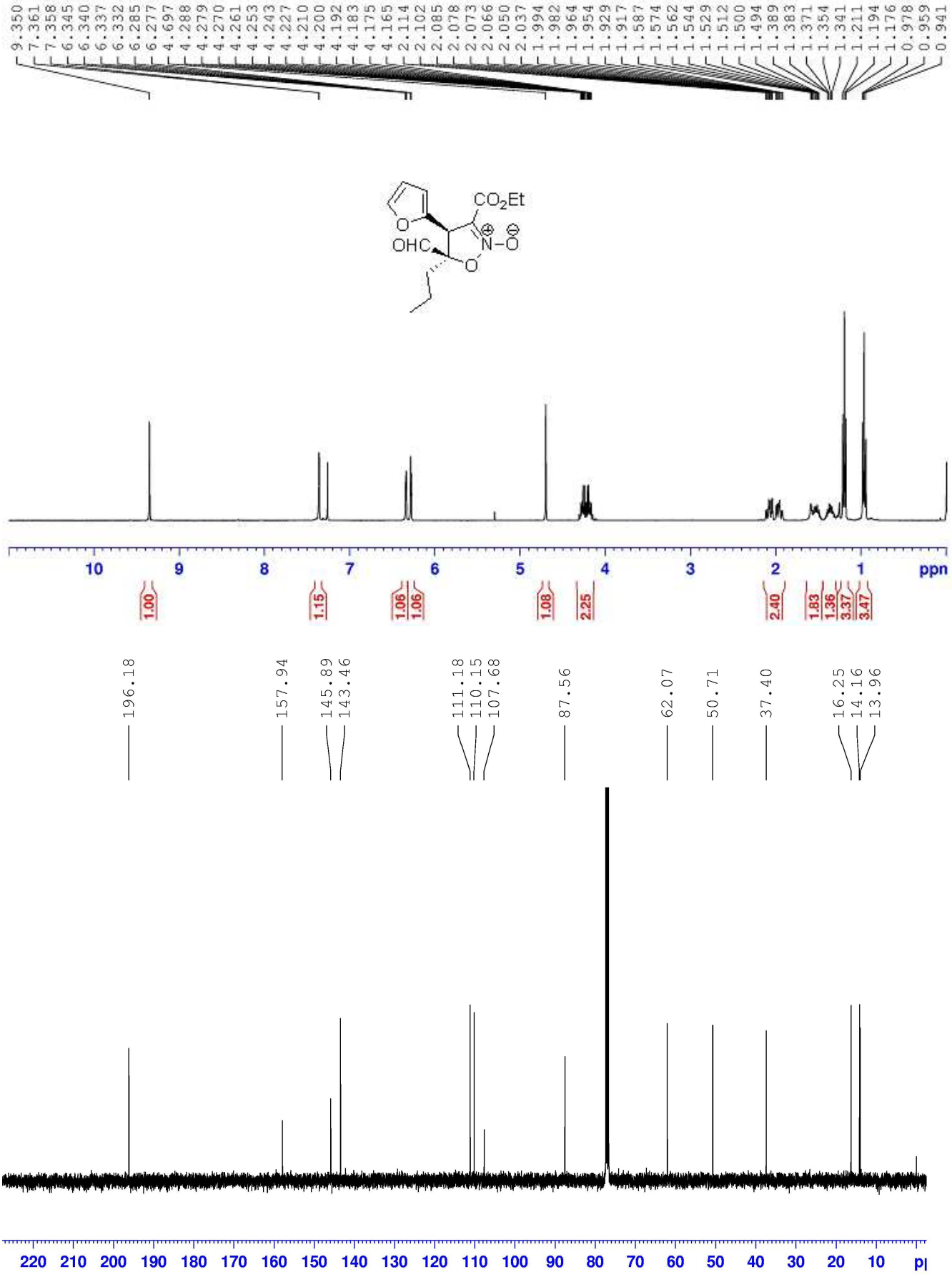
(4*S*,5*R*)-5-Formyl-3-(methoxycarbonyl)-4-(naphthalen-2-yl)-5-propyl-4,5-dihydroisoxazole 2-oxide (3p)



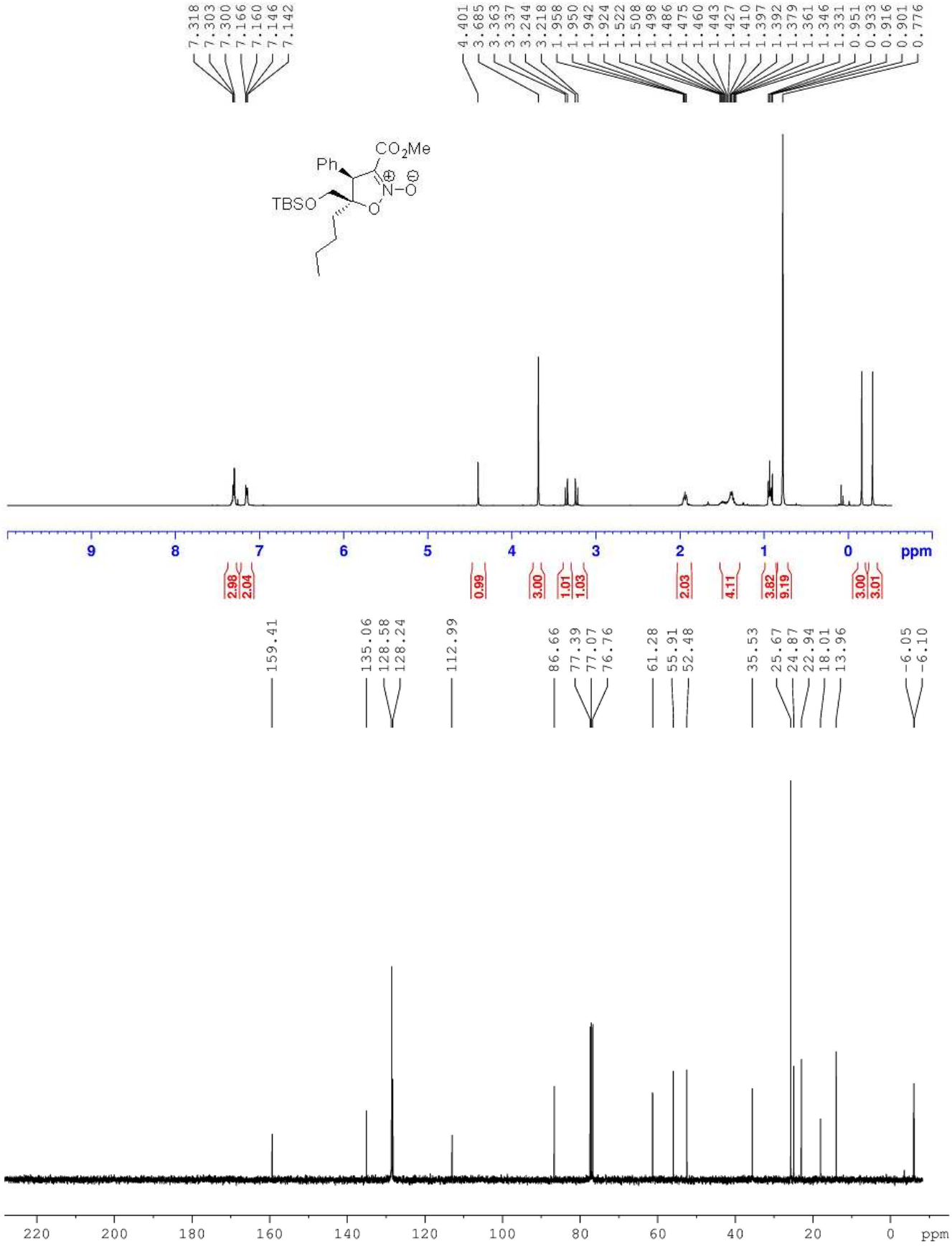
(4*S*,5*R*)-3-(Ethoxycarbonyl)-5-formyl-4-(furan-3-yl)-5-butyl-4,5-dihydroisoxazole-2-oxide (3q)



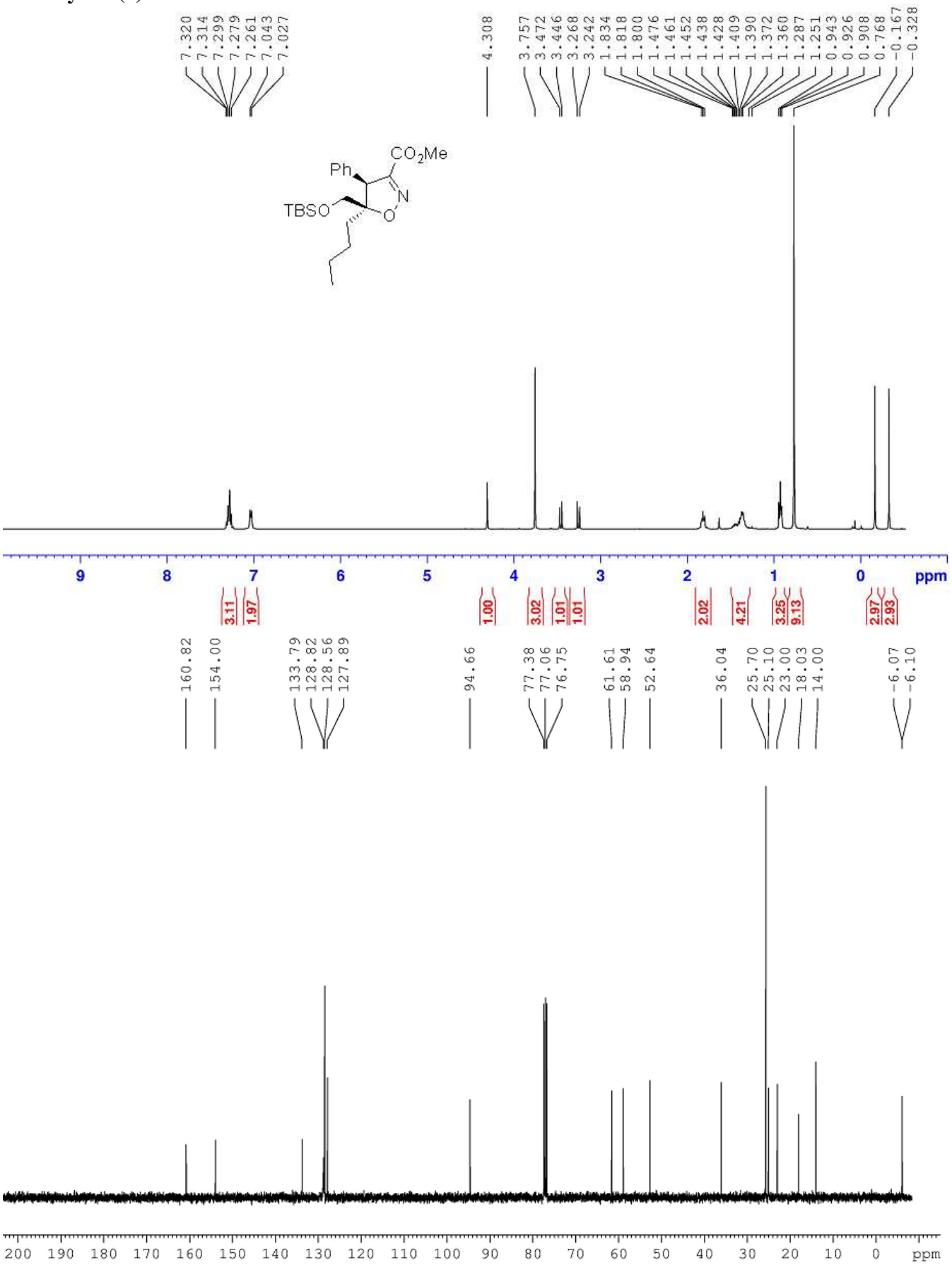
(4*S*,5*R*)-3-(Ethoxycarbonyl)-5-formyl-4-(furan-2-yl)-5-propyl-4,5-dihydroisoxazole 2-oxide (3r)



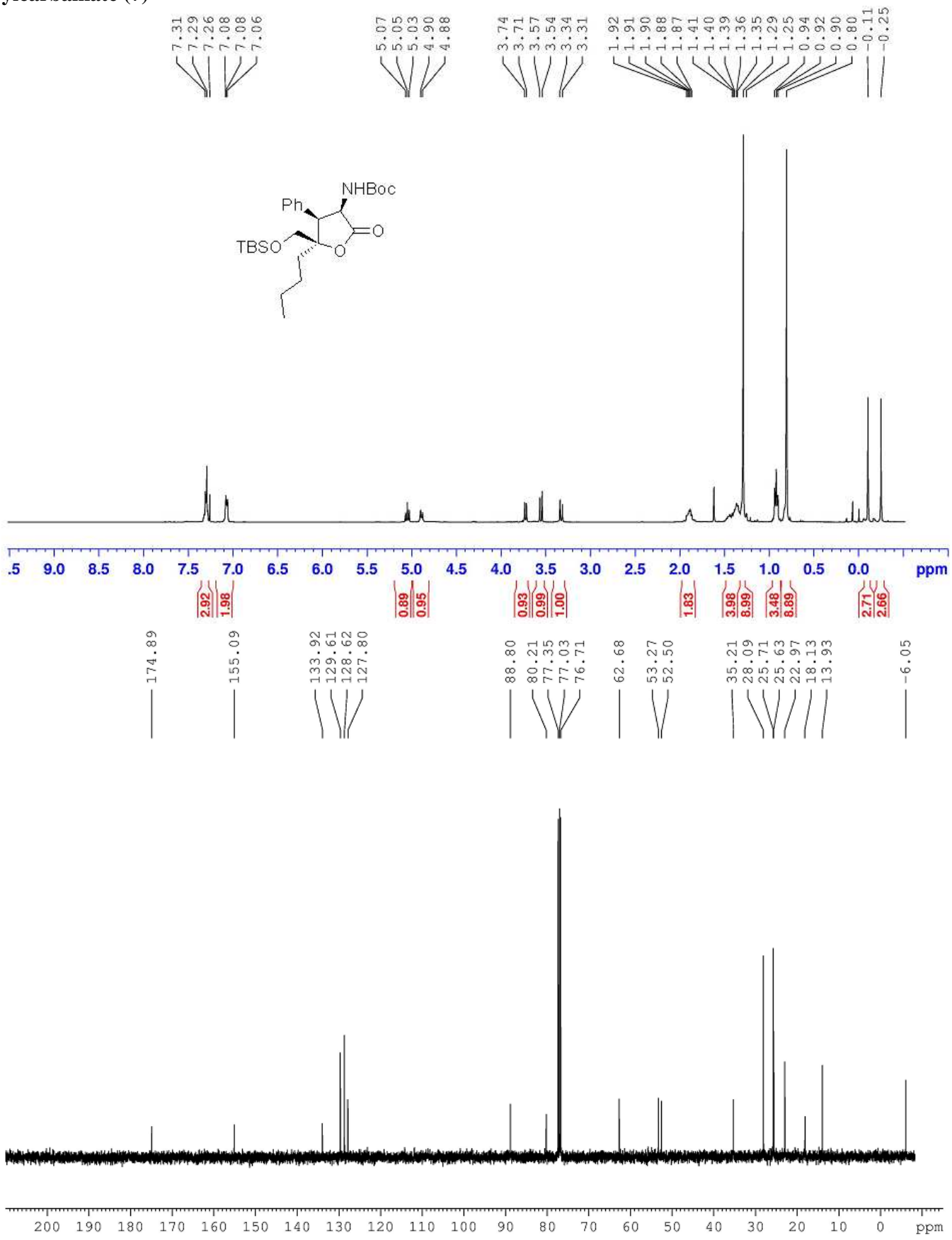
(4*S*,5*R*)-5-Butyl-5-((tert-butyldimethylsilyloxy)methyl)-3-(methoxycarbonyl)-4-phenyl-4,5-dihydroisoxazole 2-oxide (5)



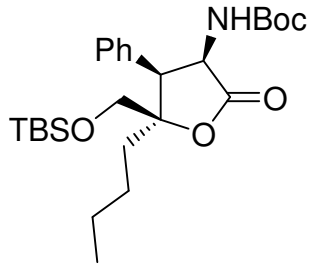
(4S,5R)-Methyl 5-butyl-5-((tert-butyldimethylsilyloxy)methyl)-4-phenyl-4,5-dihydroisoxazole-3-carboxylate (6)

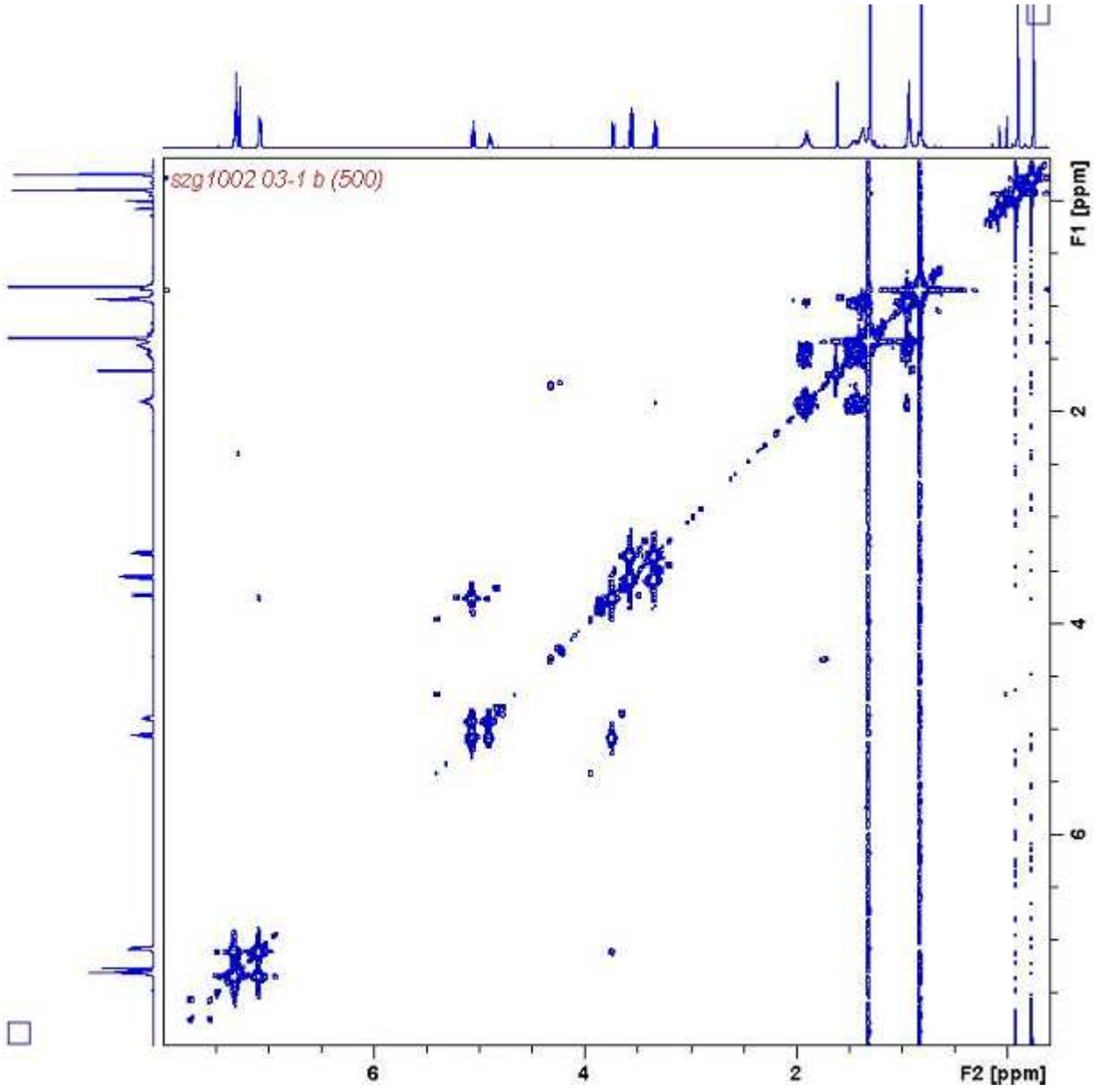


***tert*-Butyl (3*R*,4*S*,5*R*)-5-butyl-5-((tert-butyldimethylsilyloxy)methyl)-2-oxo-4-phenyltetrahydrofuran-3-ylcarbamate (7)**

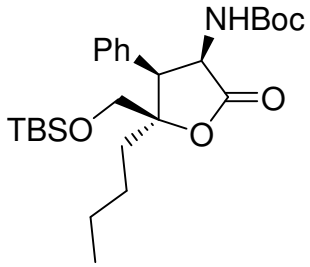


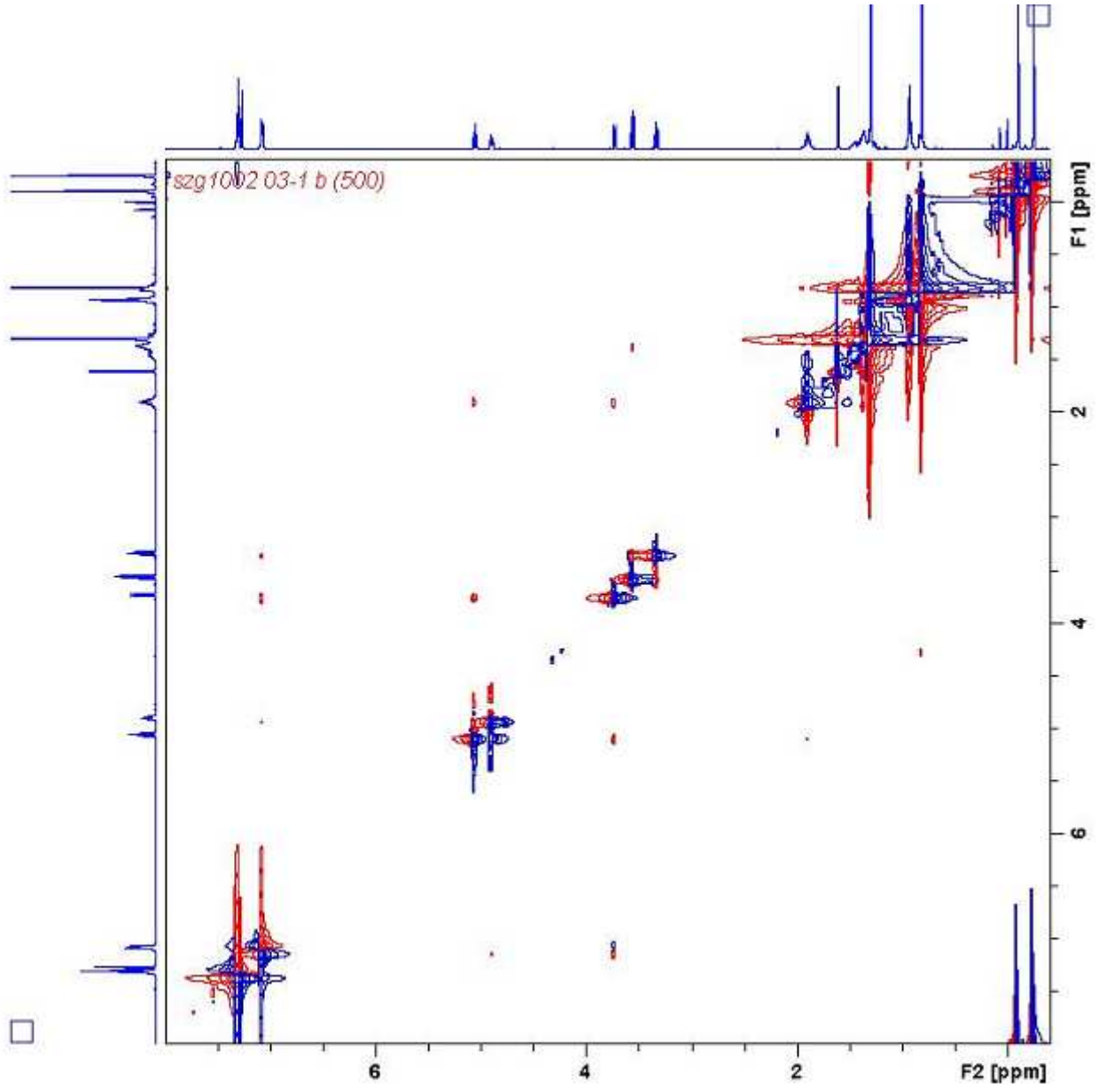
COSY spectrum of *tert*-butyl (3*R*,4*S*,5*R*)-5-butyl-5-((tert-butyldimethylsilyloxy)methyl)-2-oxo-4-phenyltetrahydrofuran-3-ylcarbamate (7)



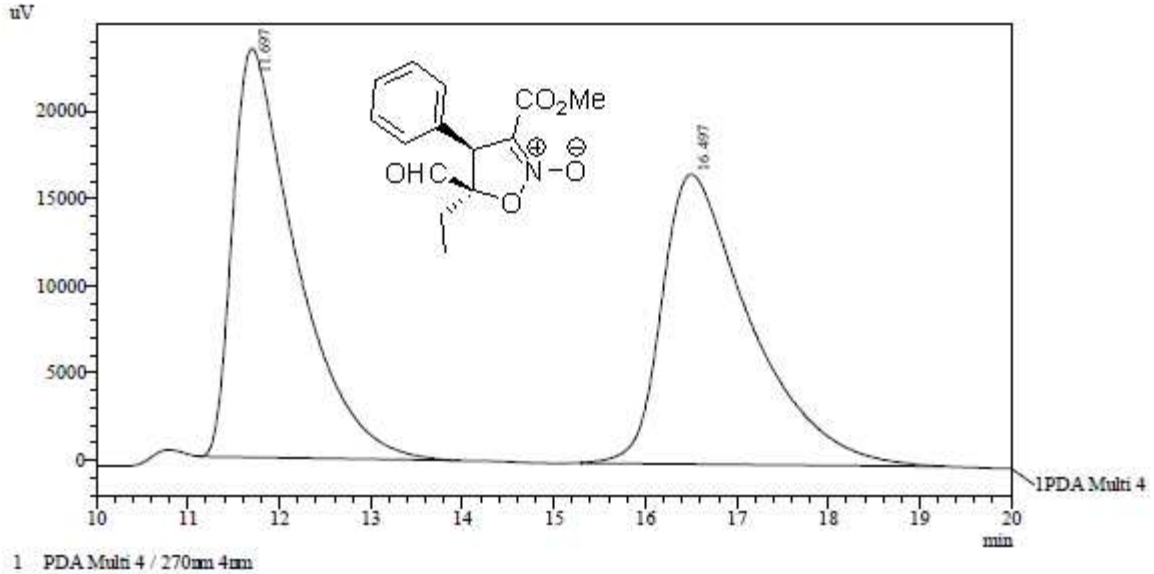


NOESY spectrum of *tert*-butyl (3*R*,4*S*,5*R*)-5-butyl-5-((tert-butyldimethylsilyloxy)methyl)-2-oxo-4-phenyltetrahydrofuran-3-ylcarbamate (7)





VII. HPLC spectra



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PeakTable

PDA Ch4 270nm 4nm

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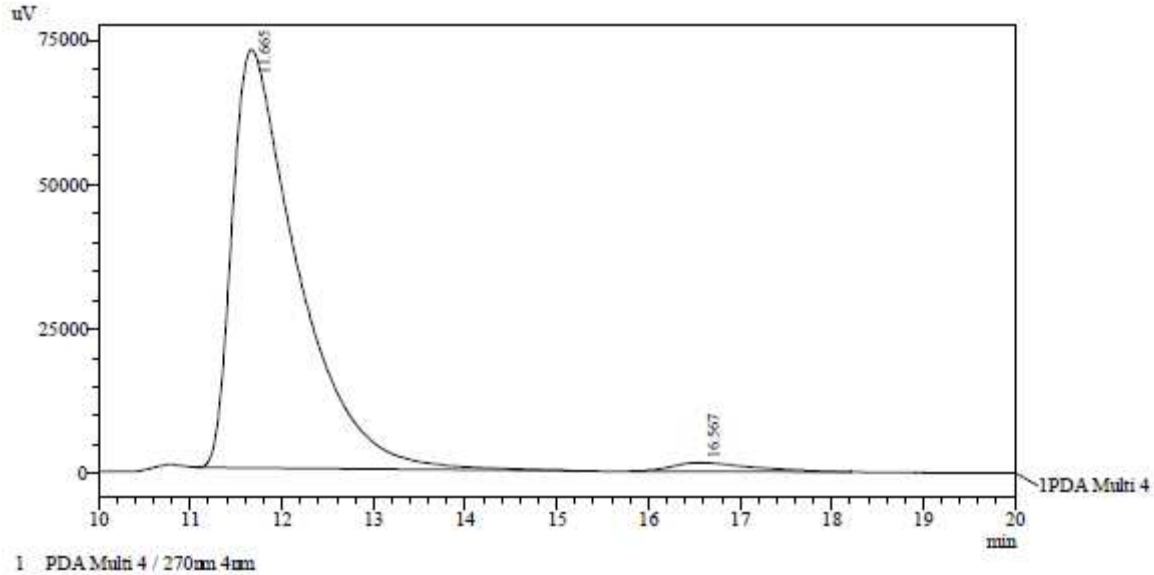

1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

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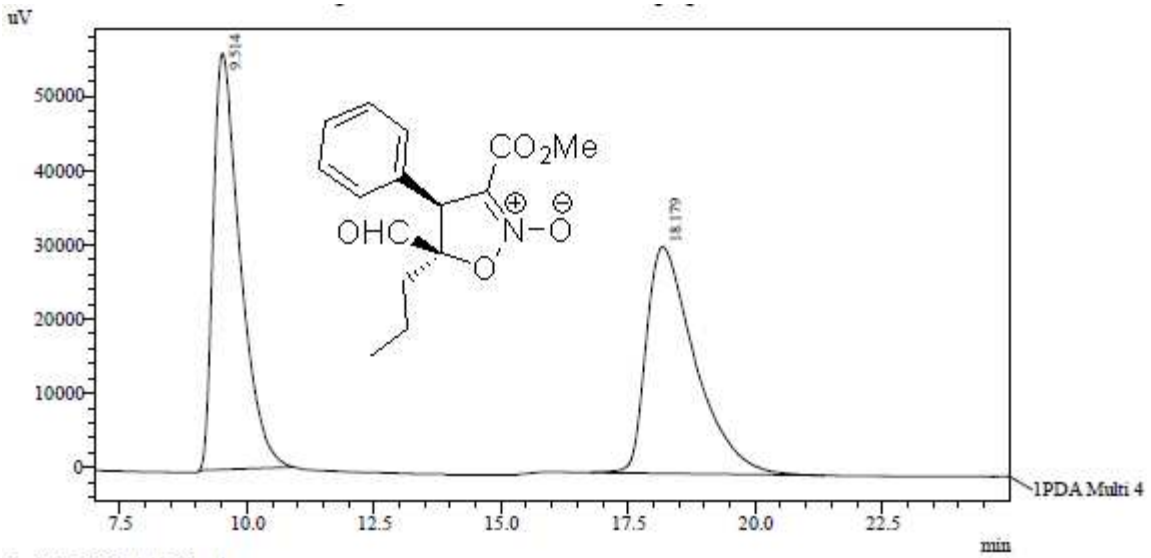
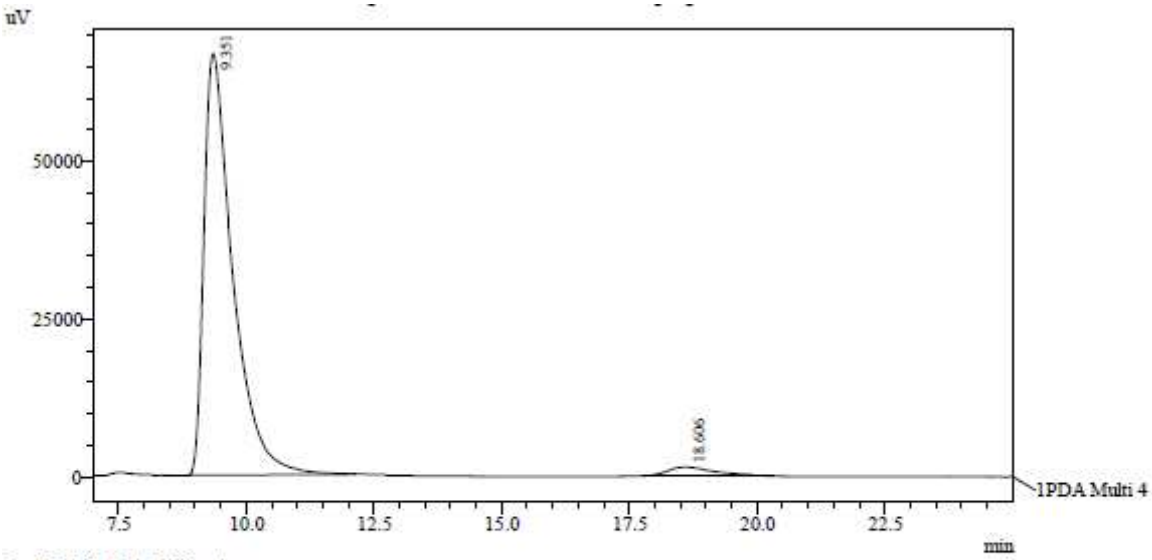


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.514	2070350	55984	50.379	64.762
2	18.179	2039169	30462	49.621	35.238
Total		4109519	86446	100.000	100.000

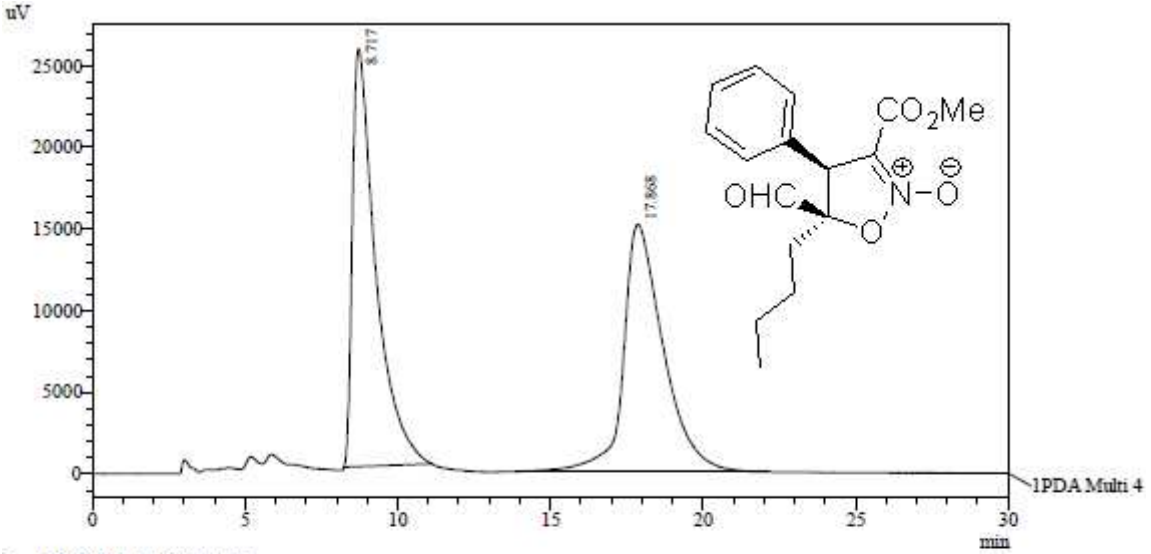


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.351	2614018	66726	96.809	97.968
2	18.606	86155	1384	3.191	2.032
Total		2700173	68110	100.000	100.000

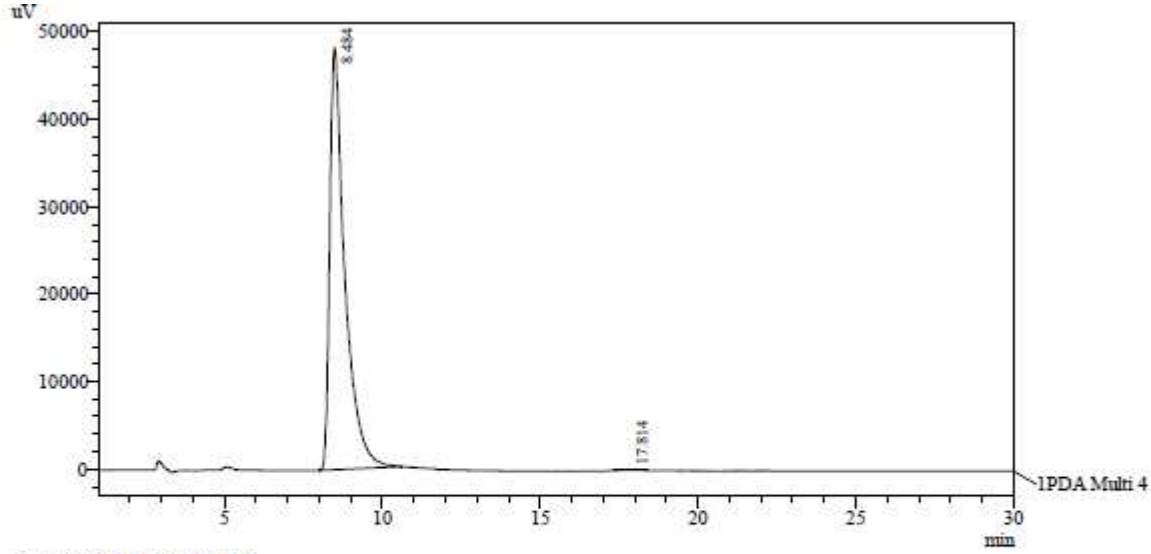


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.717	1369137	25618	49.936	62.852
2	17.868	1372620	15141	50.064	37.148
Total		2741757	40759	100.000	100.000

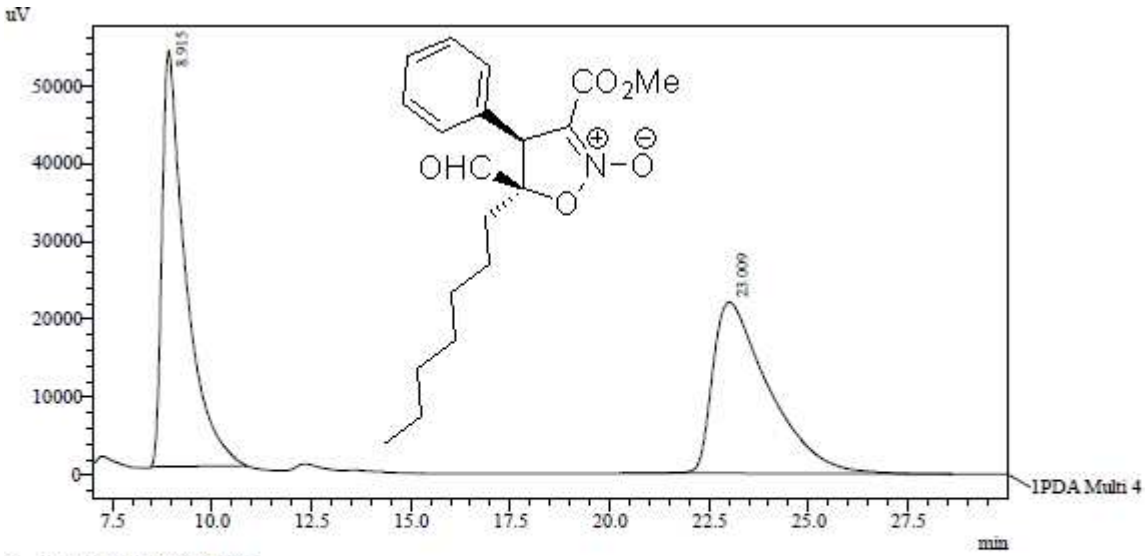


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.484	1612094	48220	99.782	99.792
2	17.814	3520	100	0.218	0.208
Total		1615614	48321	100.000	100.000

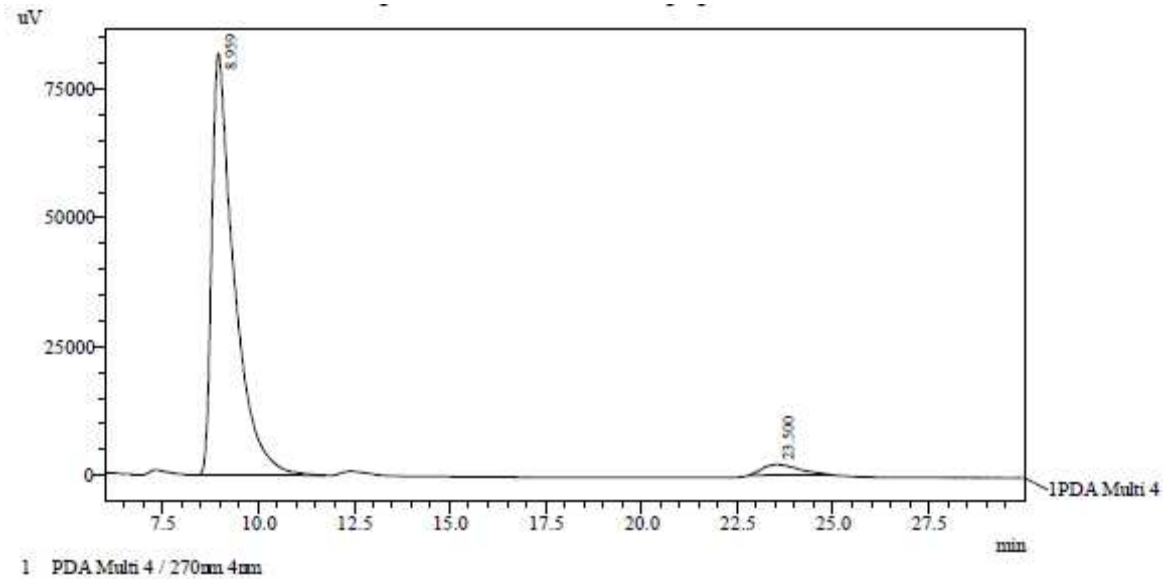


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.915	2212148	53382	50.627	70.851
2	23.009	2157322	21962	49.373	29.149
Total		4369470	75344	100.000	100.000

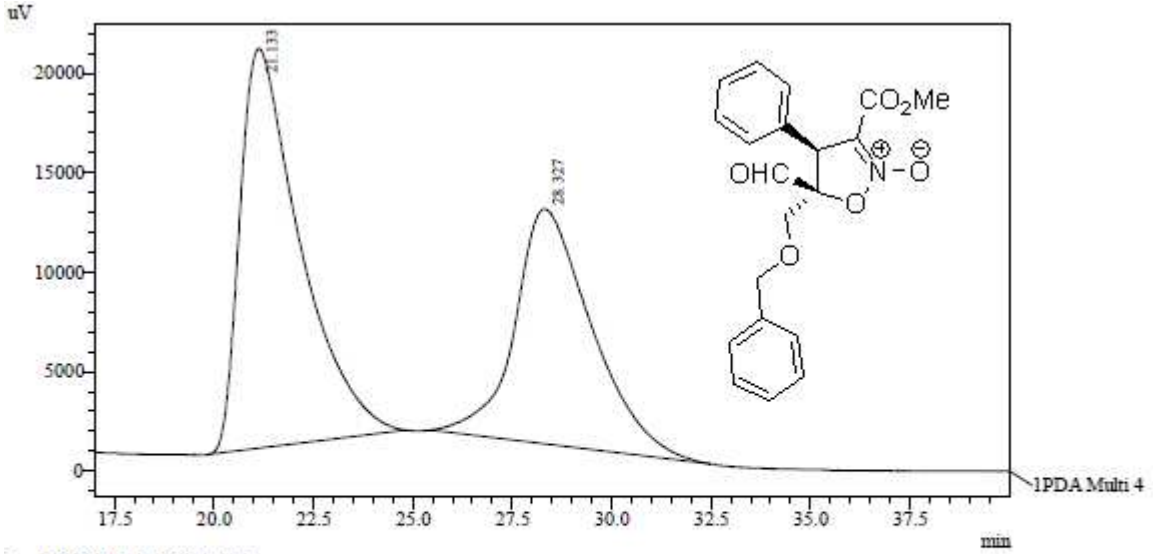


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.959	3315745	81852	96.121	97.566
2	23.500	133818	2042	3.879	2.434
Total		3449563	83894	100.000	100.000

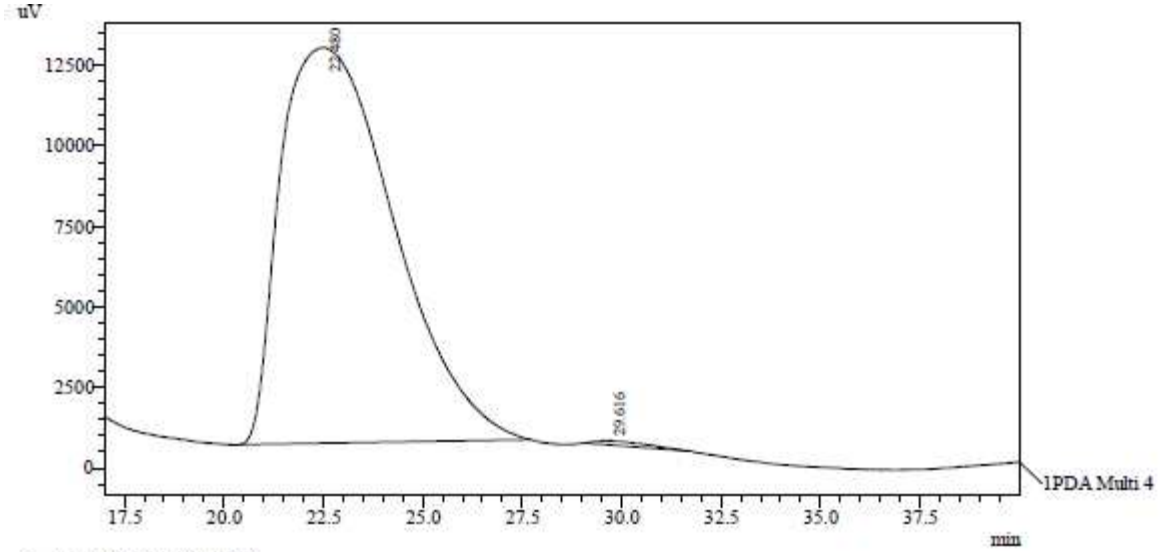


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.133	2114615	20098	56.996	62.985
2	28.327	1595495	11811	43.004	37.015
Total		3710110	31909	100.000	100.000

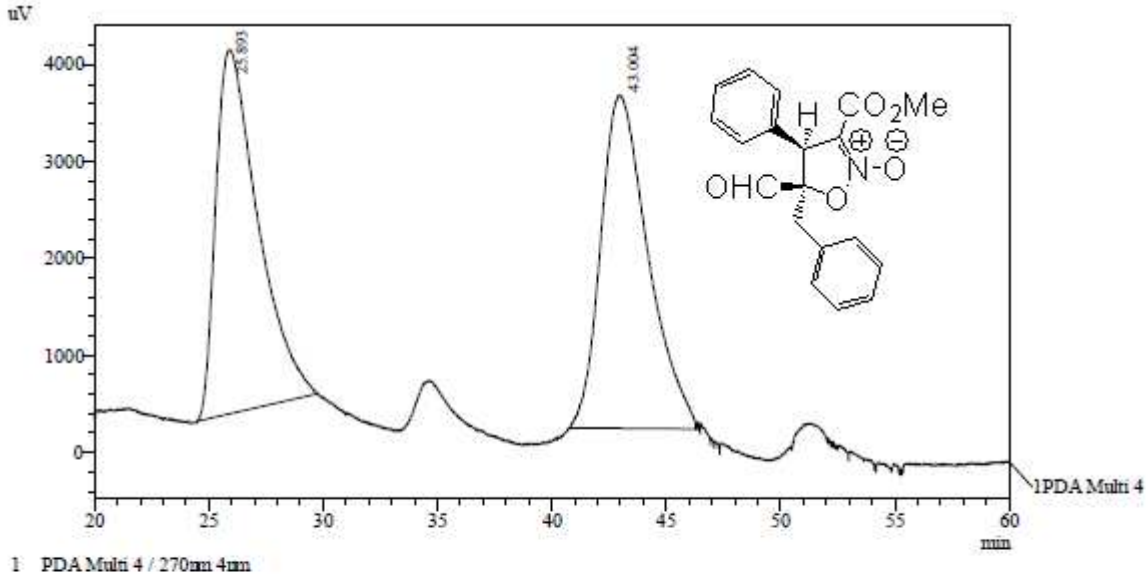


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.480	2441281	12282	99.470	98.940
2	29.616	13000	132	0.530	1.060
Total		2454281	12414	100.000	100.000

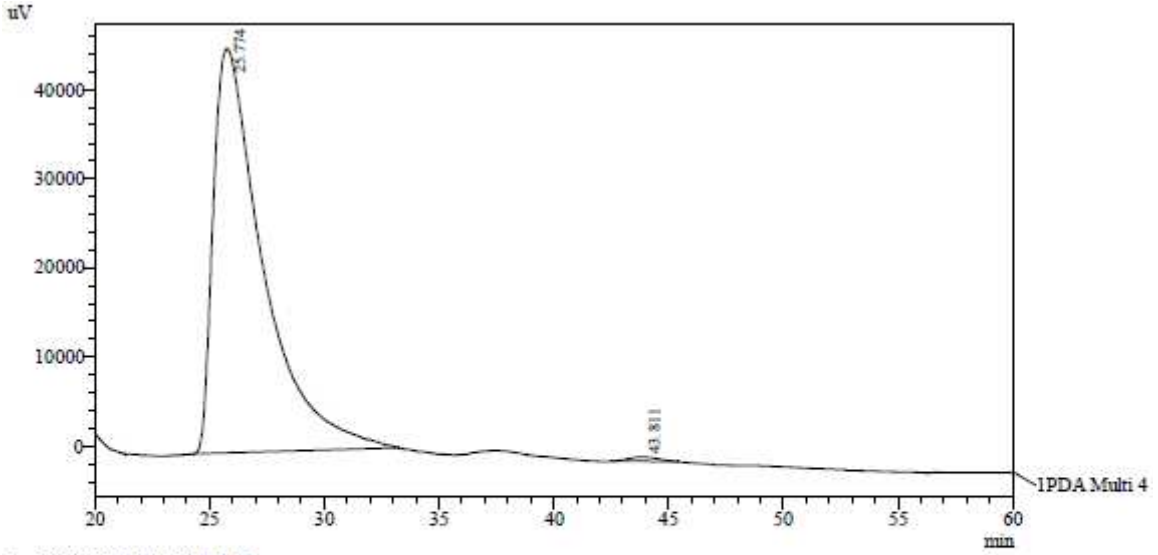


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.893	481221	3758	49.260	52.224
2	43.004	495683	3438	50.740	47.776
Total		976904	7196	100.000	100.000

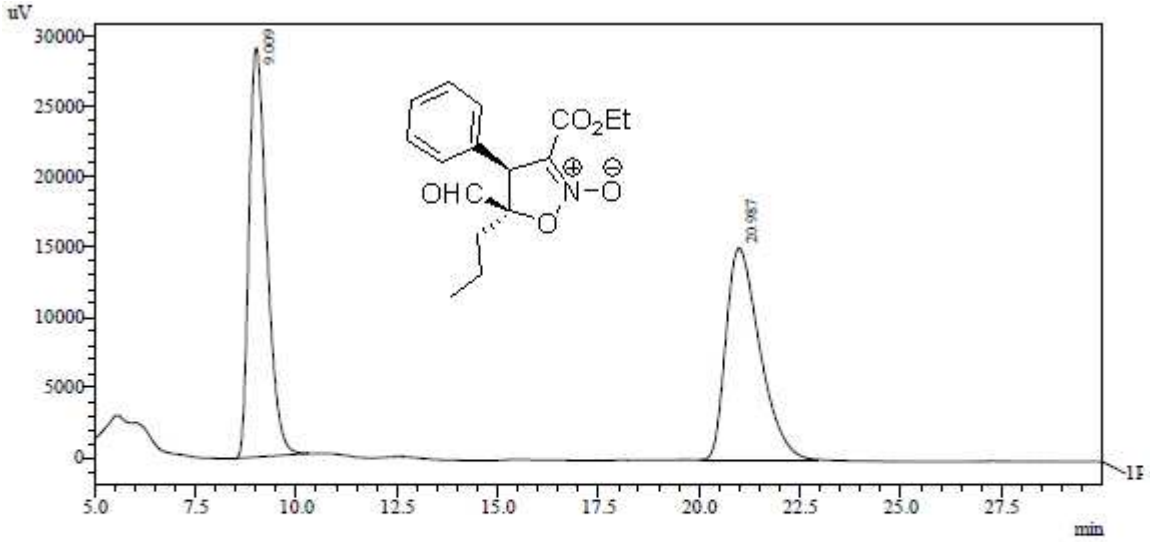


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.774	6820440	45330	99.363	98.974
2	43.811	43725	470	0.637	1.026
Total		6864165	45801	100.000	100.000

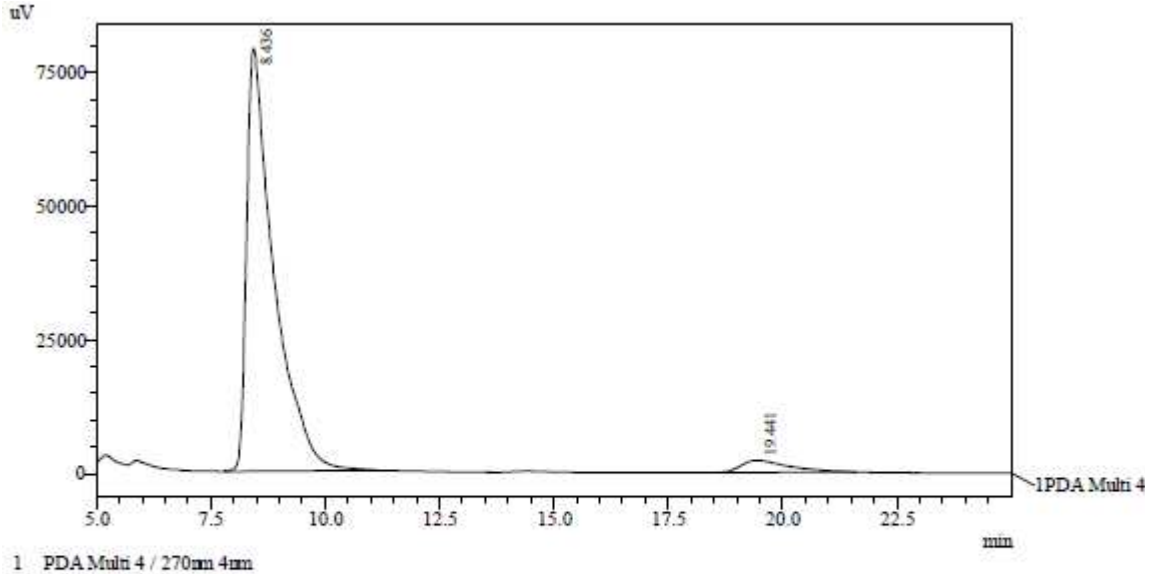


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.009	894207	29108	50.470	65.940
2	20.987	877555	15035	49.530	34.060
Total		1771762	44144	100.000	100.000

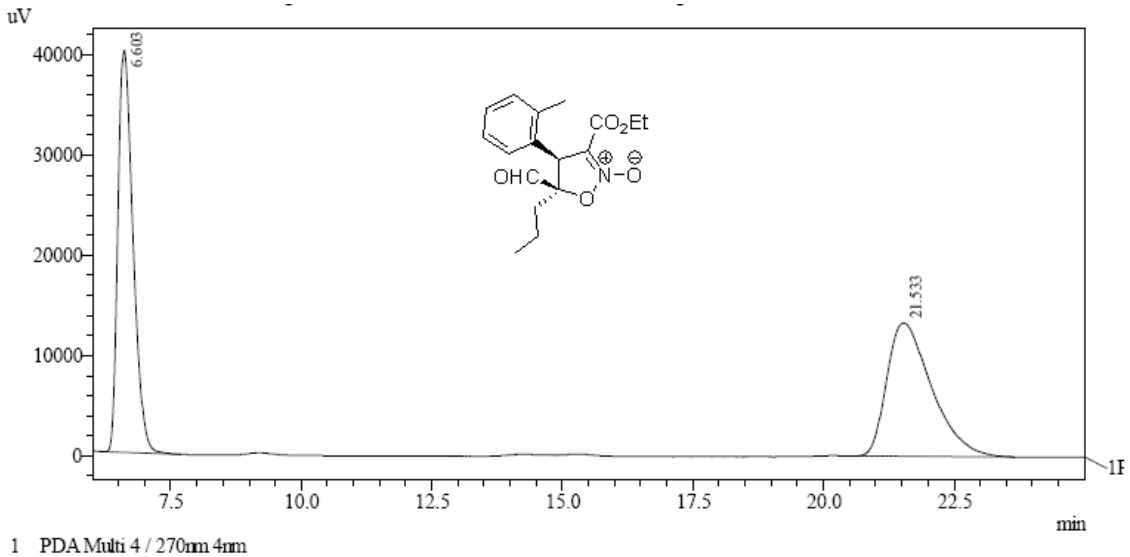


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.436	3278564	79043	95.326	97.232
2	19.441	160772	2250	4.674	2.768
Total		3439335	81293	100.000	100.000

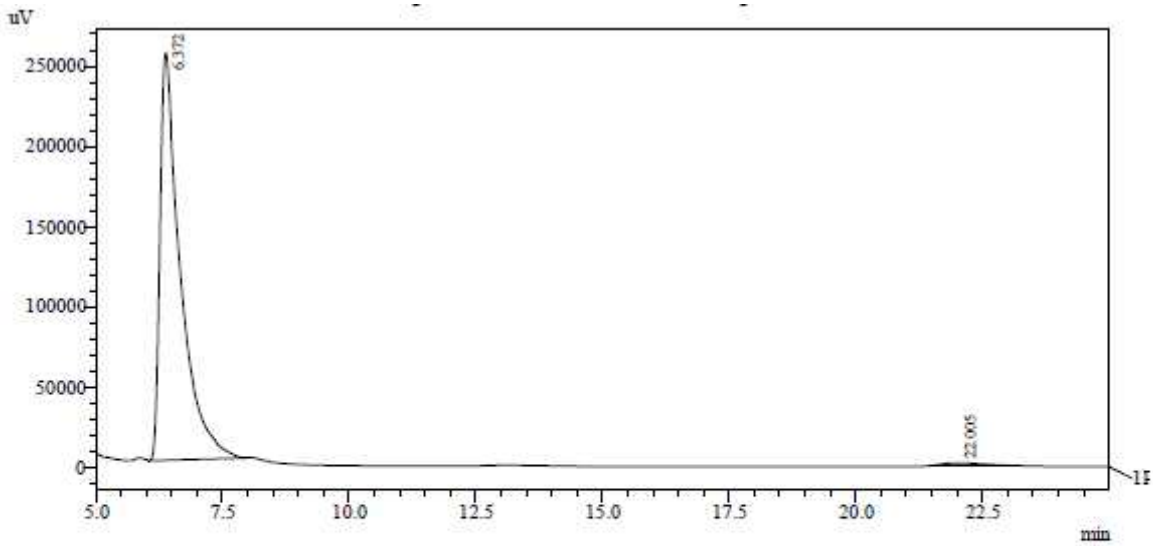


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.603	803461	40076	50.371	75.103
2	21.533	791617	13286	49.629	24.897
Total		1595078	53362	100.000	100.000

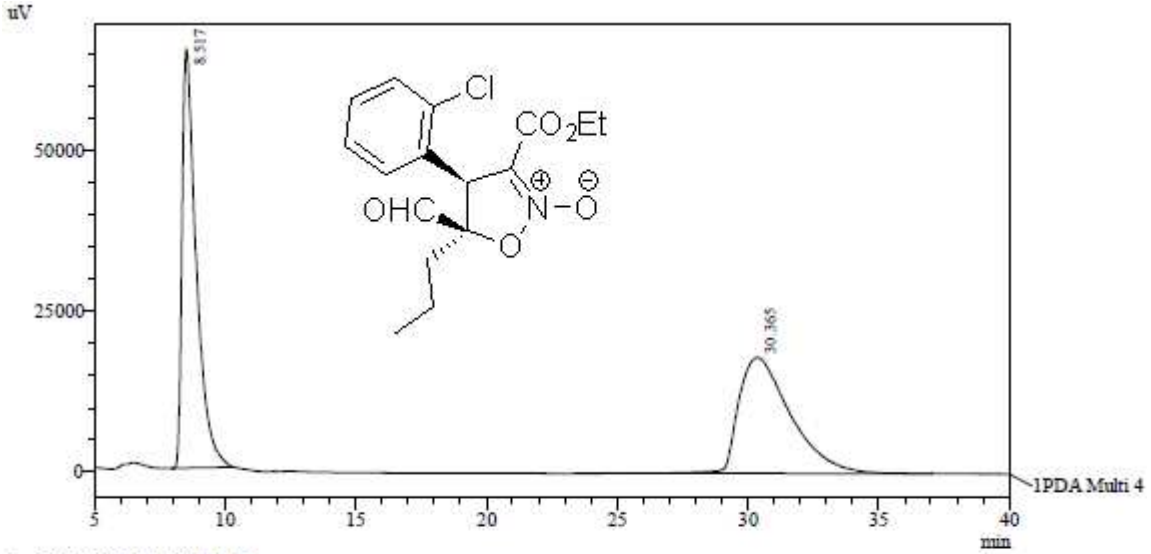


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.372	7072549	253935	98.708	99.286
2	22.005	92542	1825	1.292	0.714
Total		7165091	255761	100.000	100.000

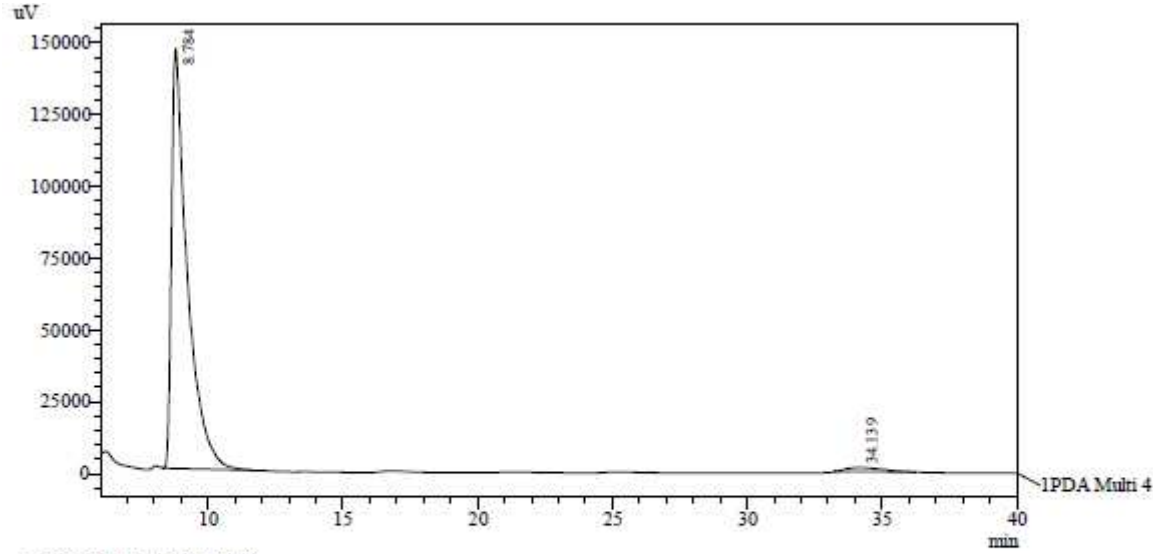


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.517	2471393	65081	49.915	78.343
2	30.365	2479785	17991	50.085	21.657
Total		4951177	83072	100.000	100.000

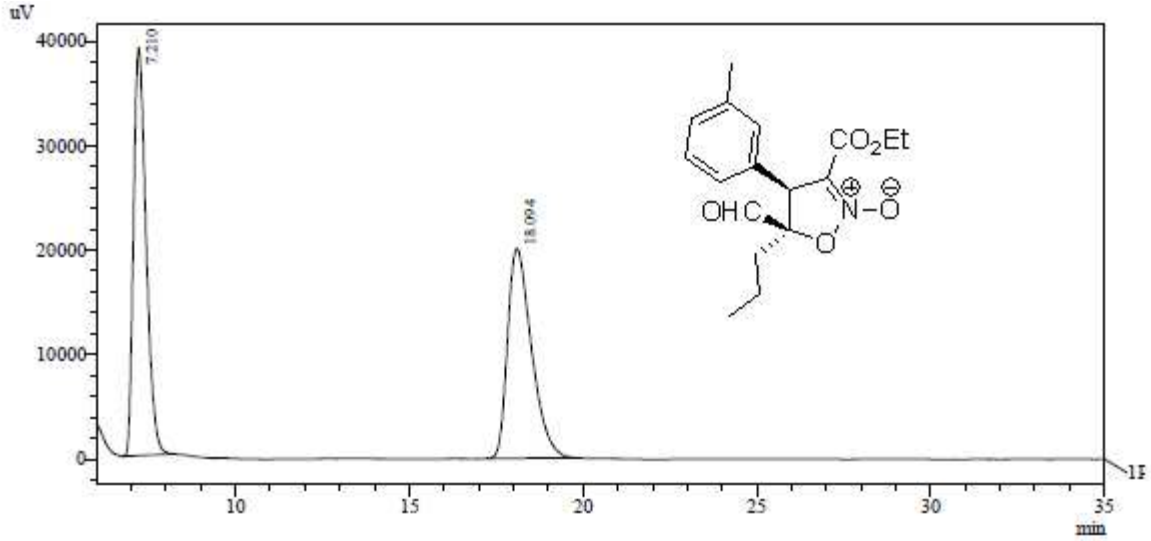


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.784	5946027	146129	97.854	99.040
2	34.139	130384	1416	2.146	0.960
Total		6076412	147545	100.000	100.000

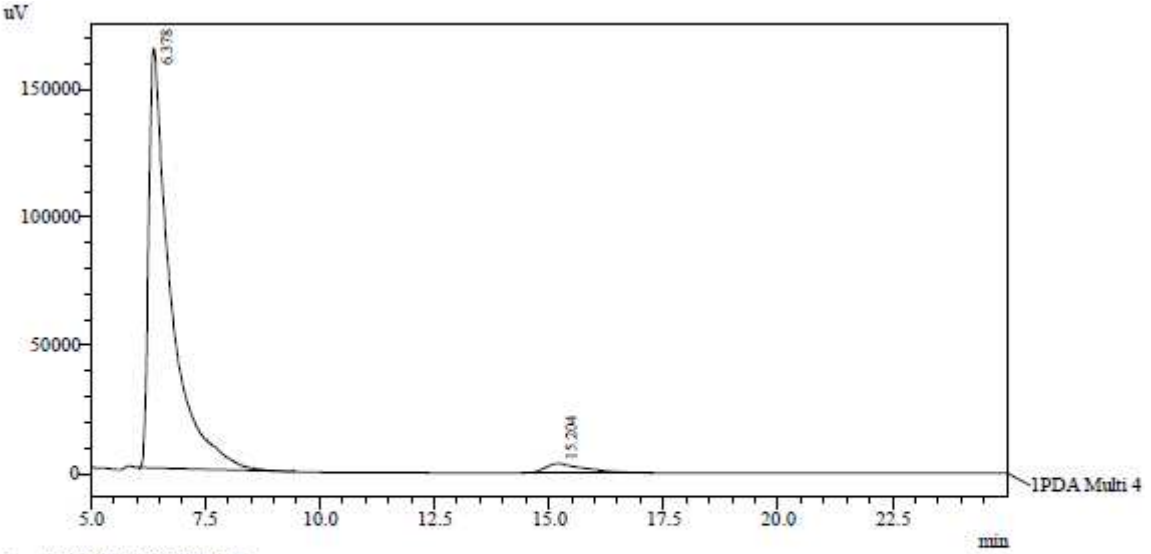


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.210	982058	39012	50.556	66.040
2	18.094	960459	20061	49.444	33.960
Total		1942517	59074	100.000	100.000

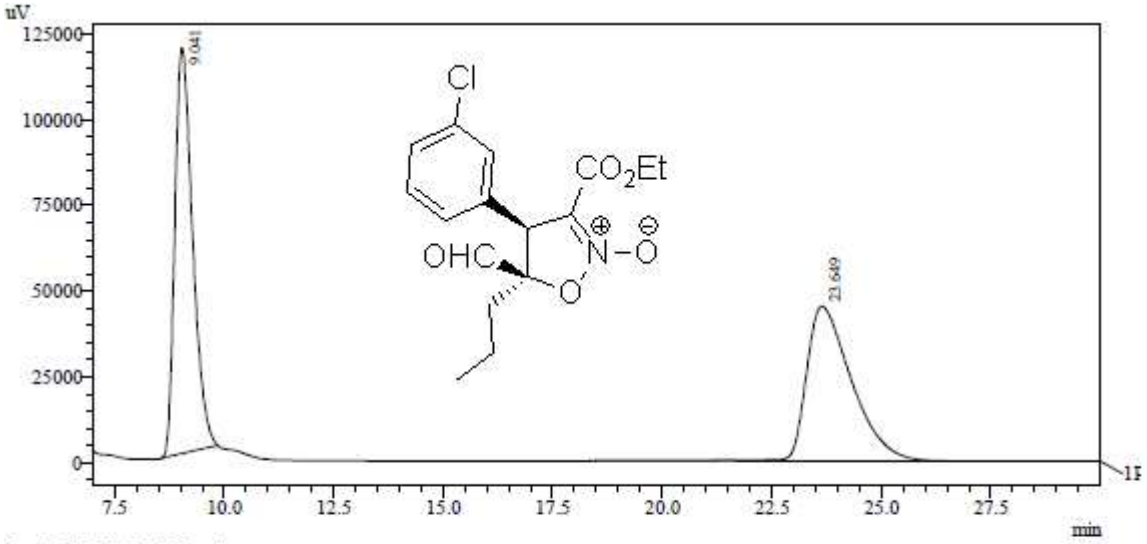


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.378	5429026	163733	96.211	97.880
2	15.204	213790	3546	3.789	2.120
Total		5642815	167278	100.000	100.000

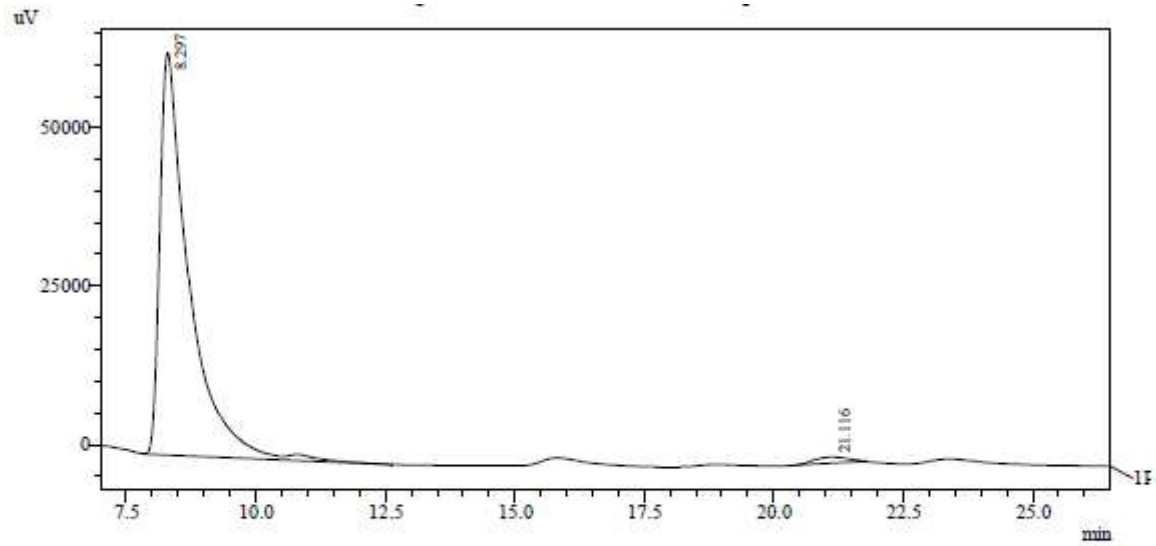


1 PDA Multi 1 / 220nm 4nm

PeakTable

PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.041	3329174	118389	50.695	72.399
2	23.649	3237944	45135	49.305	27.601
Total		6567118	163524	100.000	100.000

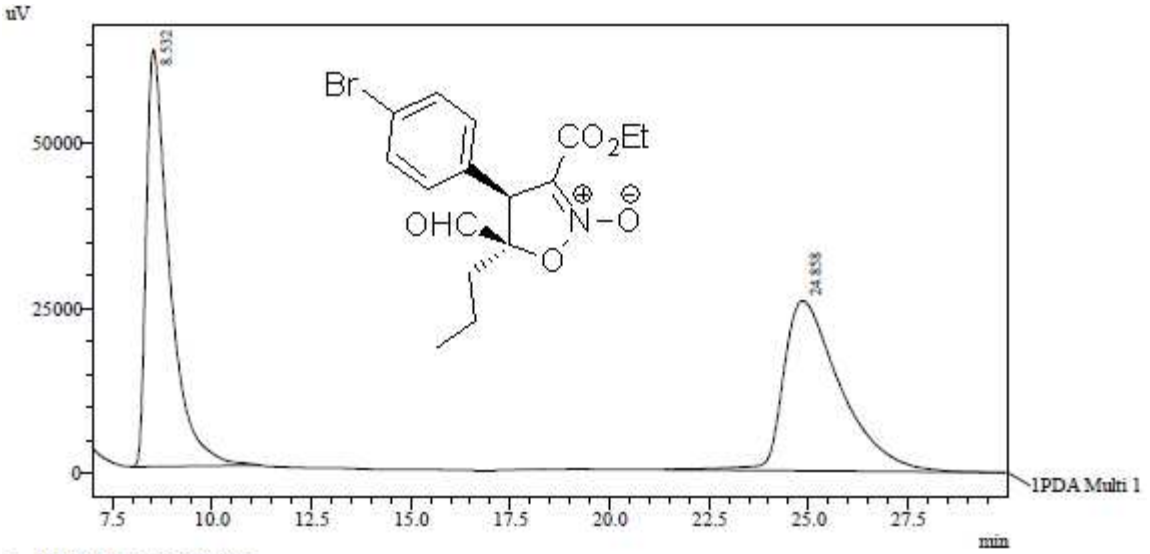


1 PDA Multi 1 / 220nm 4nm

PeakTable

PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.297	2458368	63404	98.222	98.472
2	21.116	44510	984	1.778	1.528
Total		2502879	64388	100.000	100.000

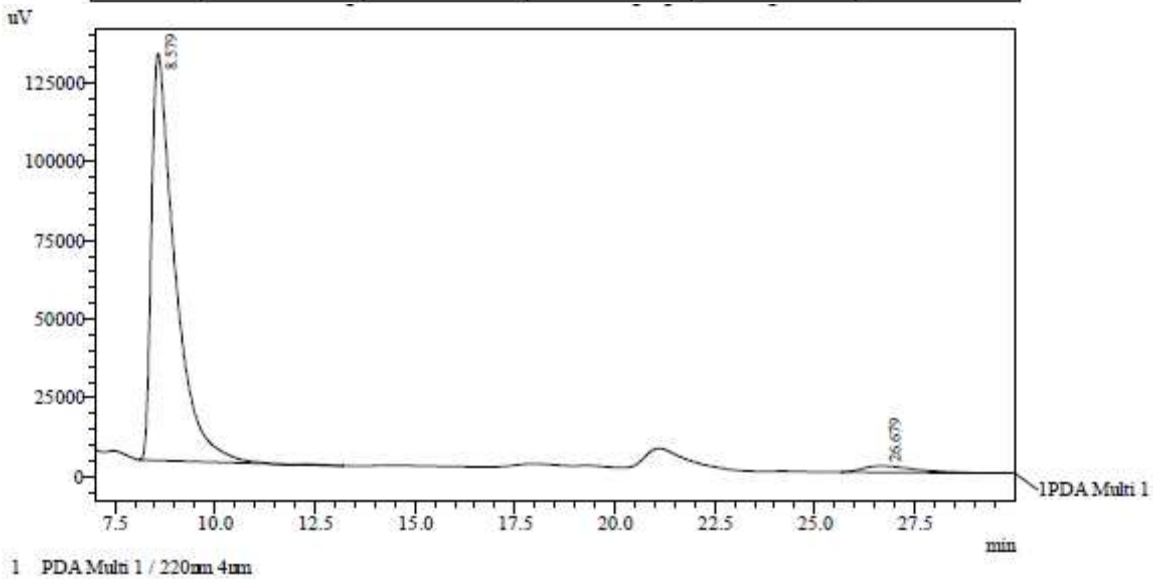


1 PDA Multi 1 / 220nm 4nm

PeakTable

PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.532	2575341	63133	50.085	71.012
2	24.858	2566621	25772	49.915	28.988
Total		5141962	88905	100.000	100.000

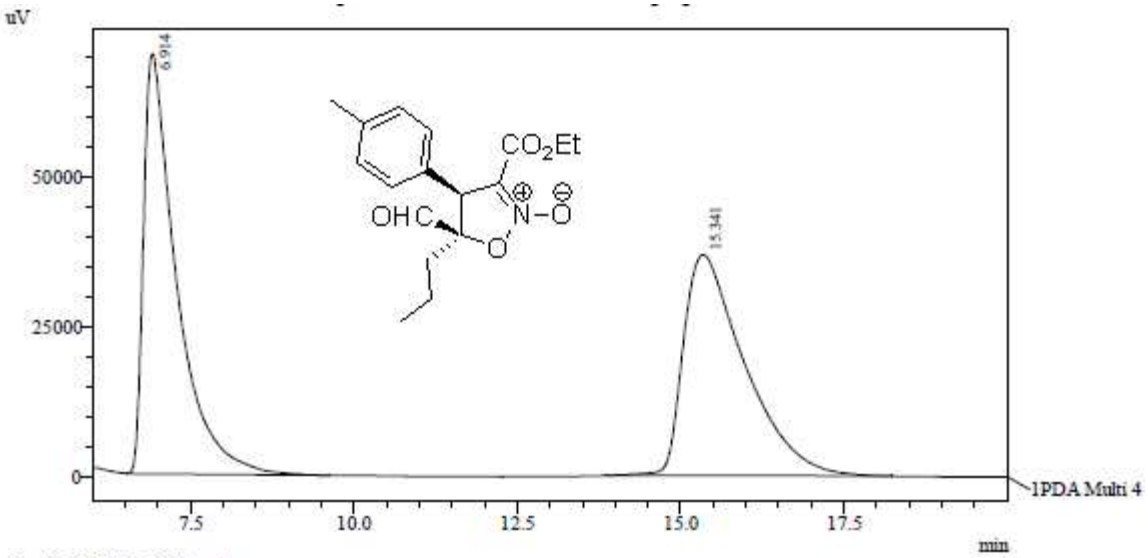


1 PDA Multi 1 / 220nm 4nm

PeakTable

PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.579	5289427	129161	96.755	98.466
2	26.679	177399	2012	3.245	1.534
Total		5466826	131173	100.000	100.000

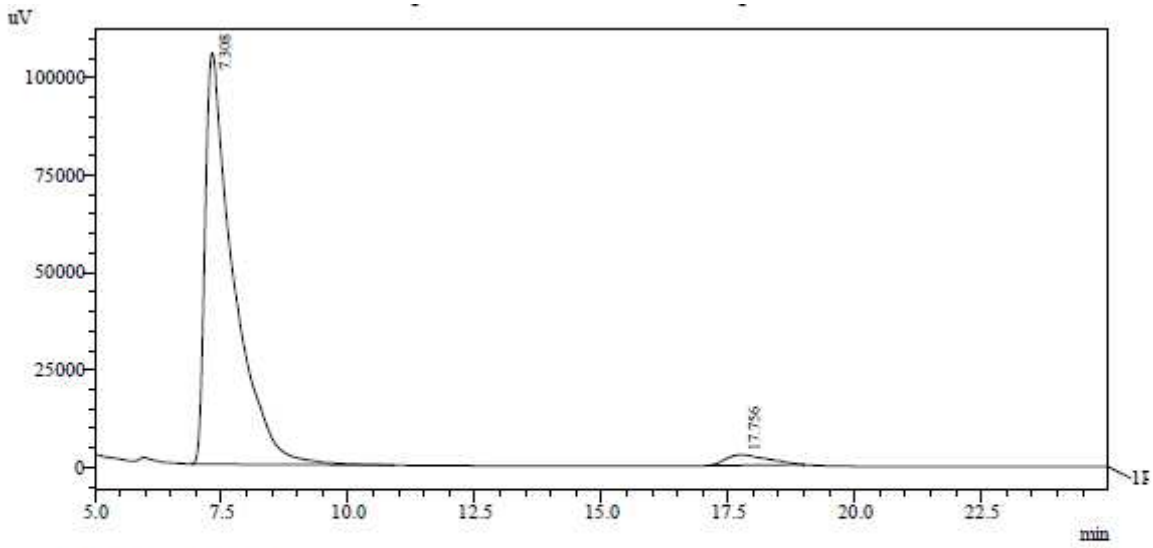


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.914	2446377	69787	50.450	65.522
2	15.341	2402698	36722	49.550	34.478
Total		4849076	106509	100.000	100.000

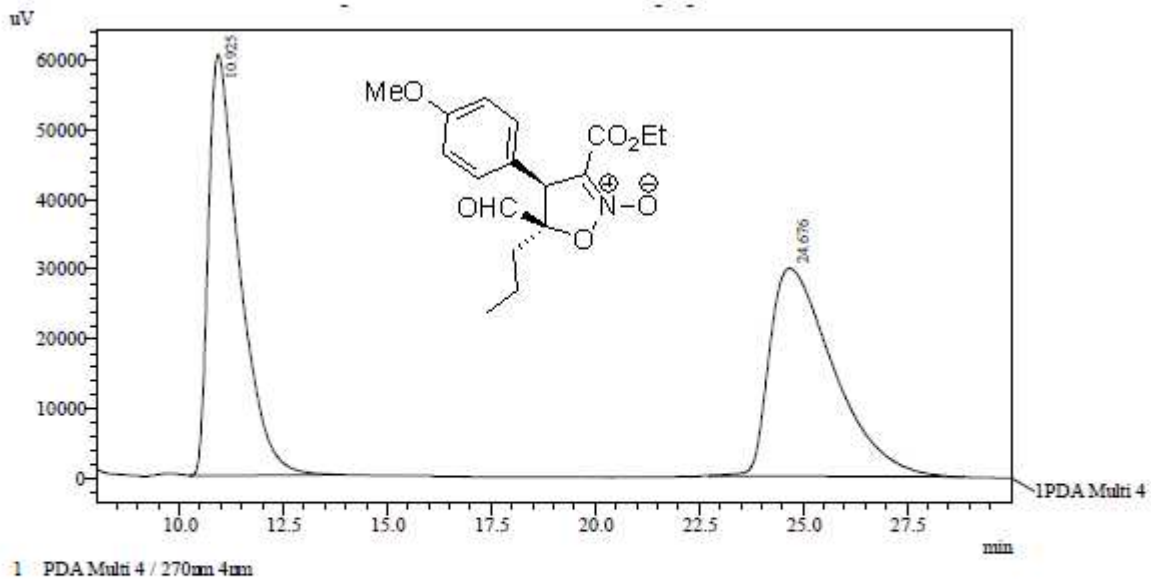


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.308	4113747	105702	96.326	97.516
2	17.756	156898	2693	3.674	2.484
Total		4270645	108395	100.000	100.000

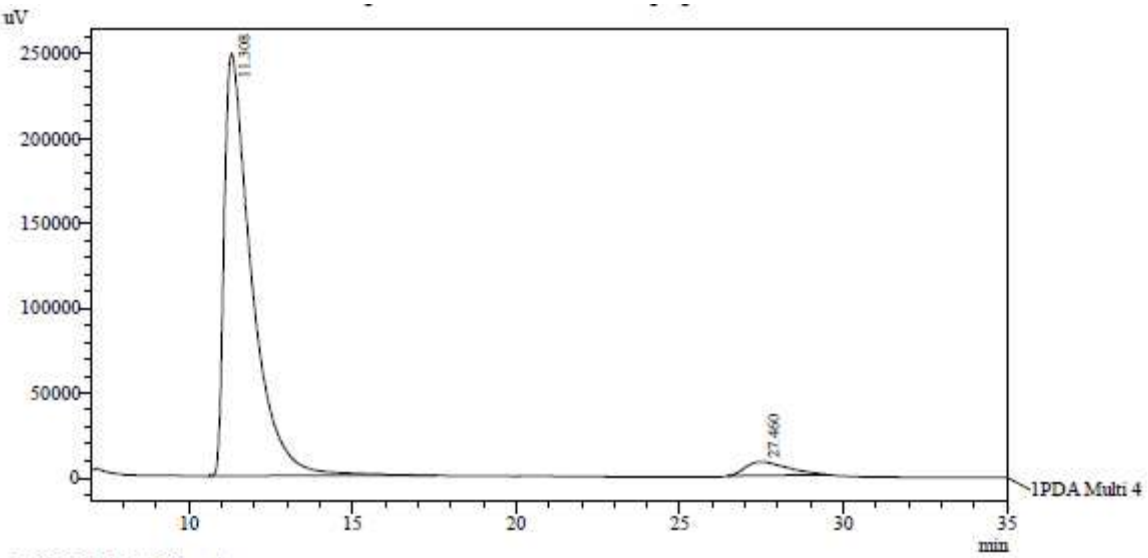


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.925	3132057	60205	49.536	66.932
2	24.676	3190774	29745	50.464	33.068
Total		6322831	89951	100.000	100.000

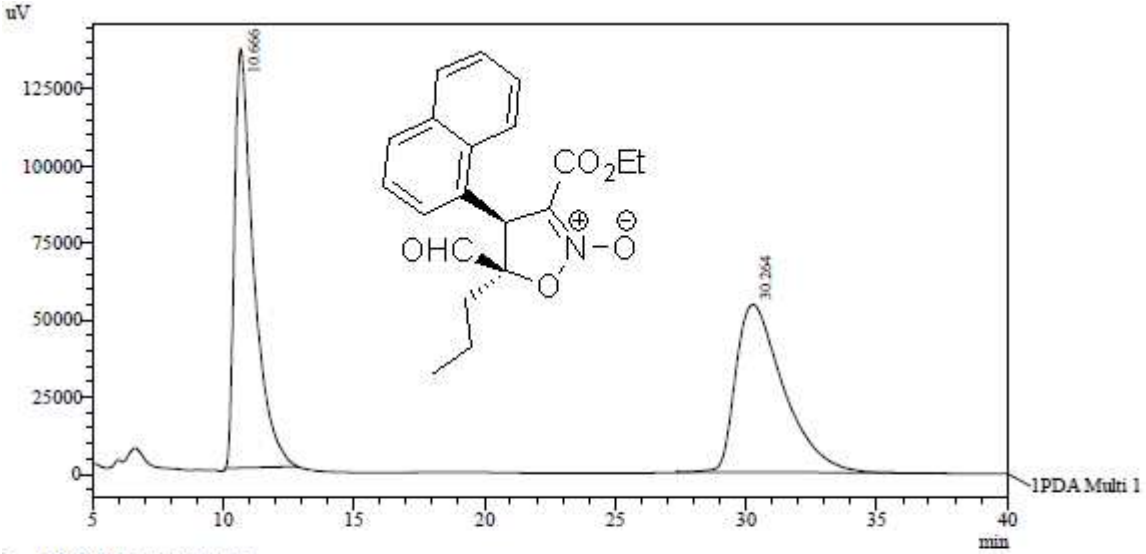


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.308	14485550	248884	95.361	96.884
2	27.460	704617	8004	4.639	3.116
Total		15190167	256888	100.000	100.000

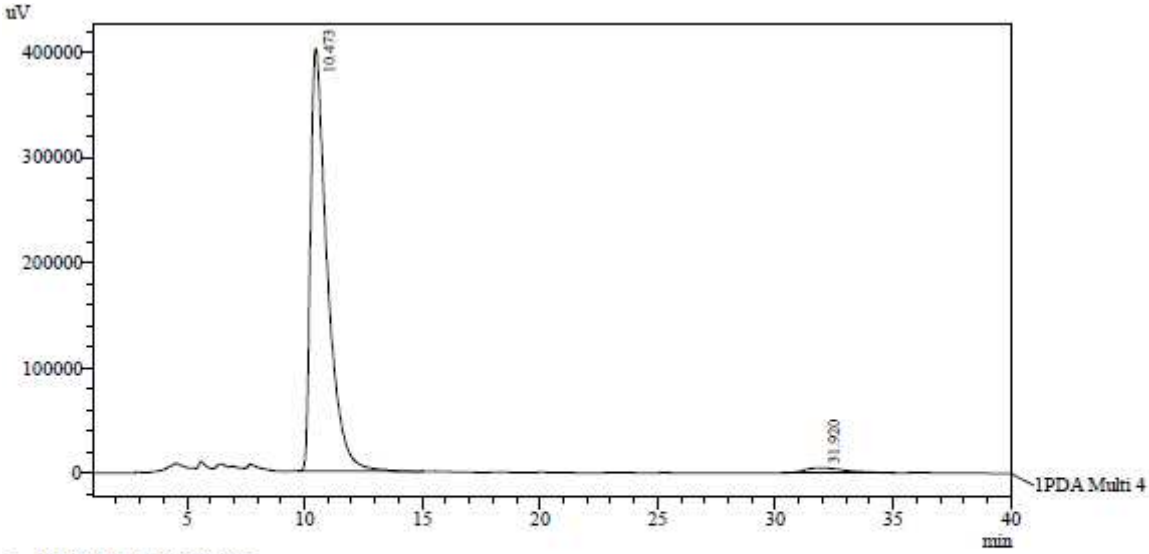


1 PDA Multi 1 / 220nm 4nm

PeakTable

PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.666	6944427	136031	49.868	71.384
2	30.264	6981322	54531	50.132	28.616
Total		13925749	190562	100.000	100.000

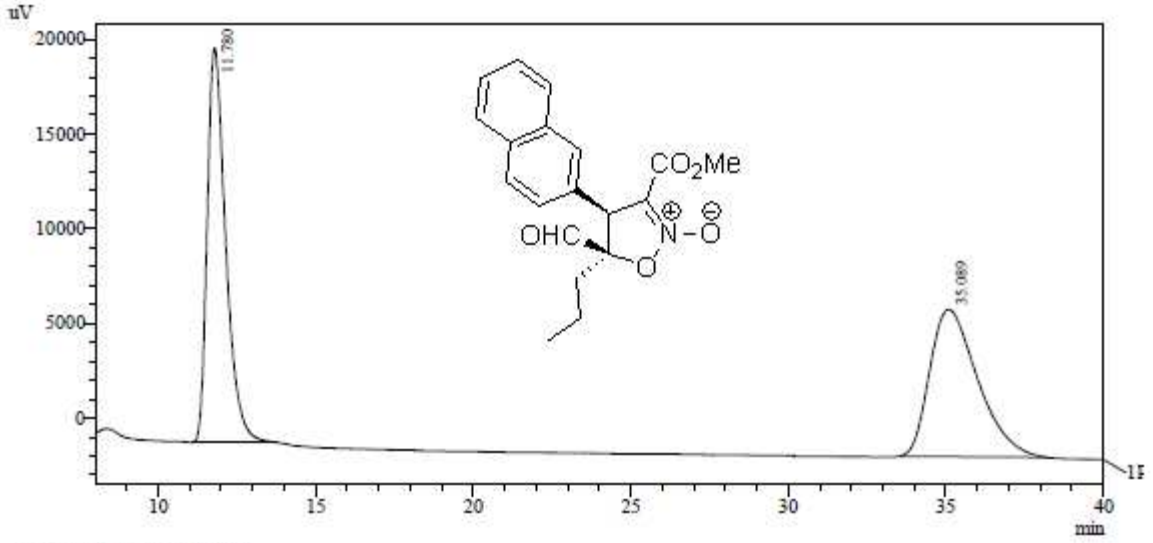


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.473	19916113	401637	97.151	98.807
2	31.920	584043	4847	2.849	1.193
Total		20500156	406484	100.000	100.000

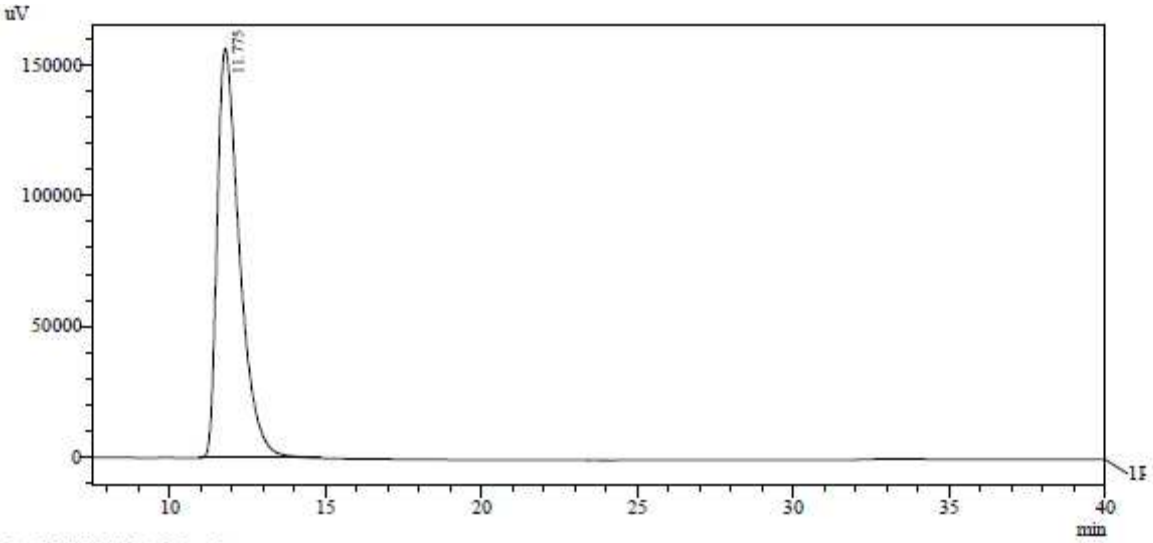


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.780	851525	20845	50.819	72.837
2	35.089	824070	7774	49.181	27.163
Total		1675595	28619	100.000	100.000

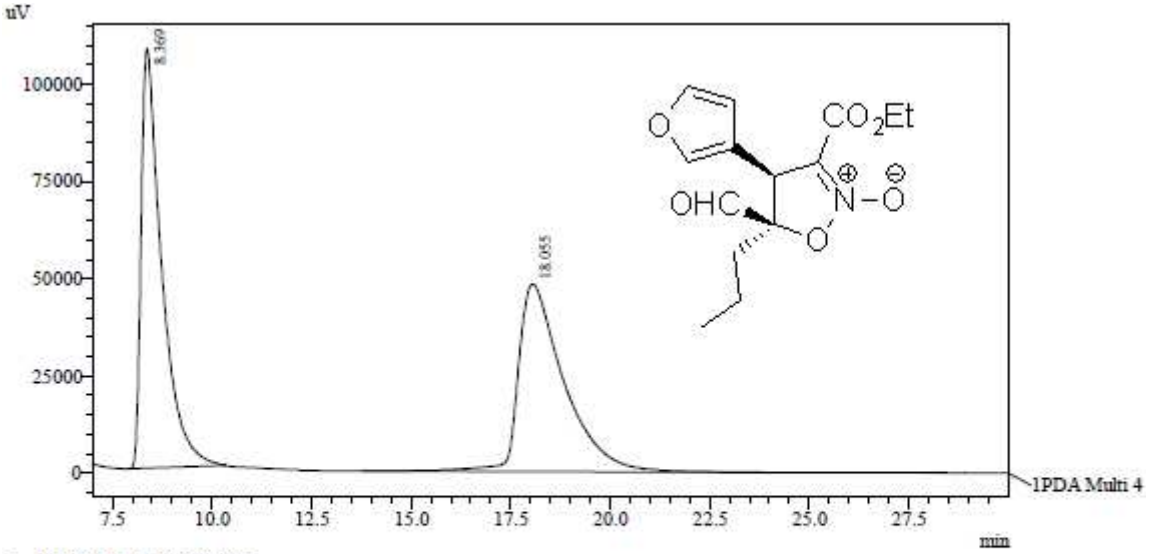


1 PDA Multi 1 / 220nm 4nm

PeakTable

PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.775	7793408	156328	100.000	100.000
Total		7793408	156328	100.000	100.000

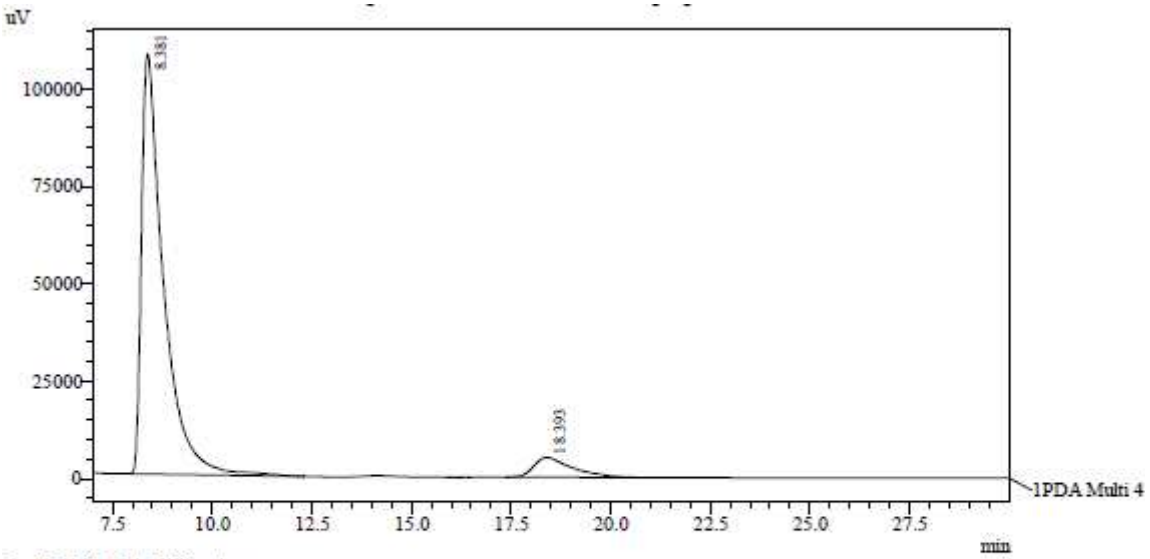


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.369	3878591	107790	50.231	69.120
2	18.055	3842860	48156	49.769	30.880
Total		7721451	155946	100.000	100.000

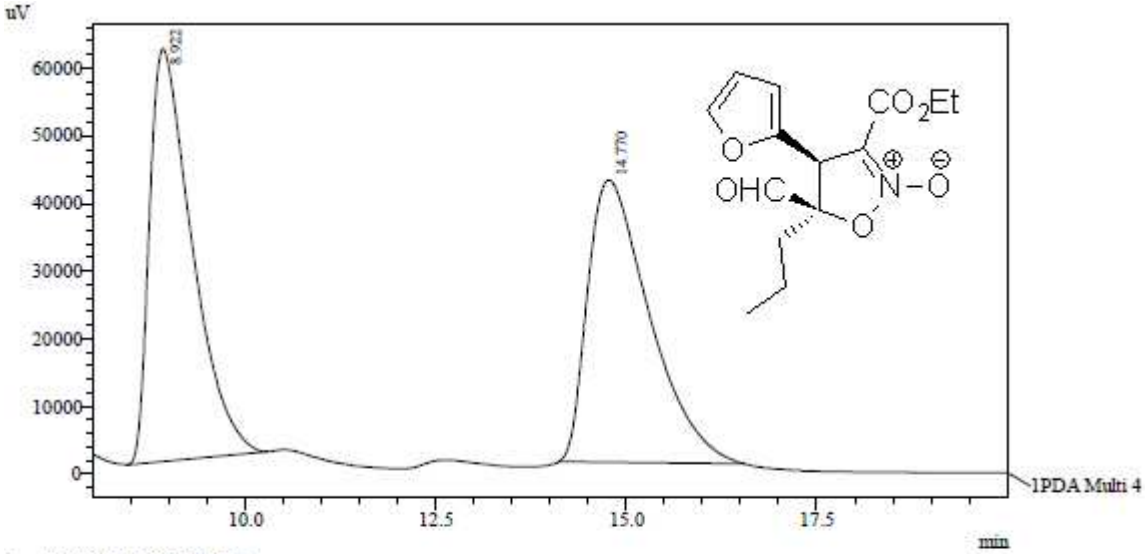


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.381	4136044	107864	92.533	95.573
2	18.393	333747	4997	7.467	4.427
Total		4469791	112860	100.000	100.000

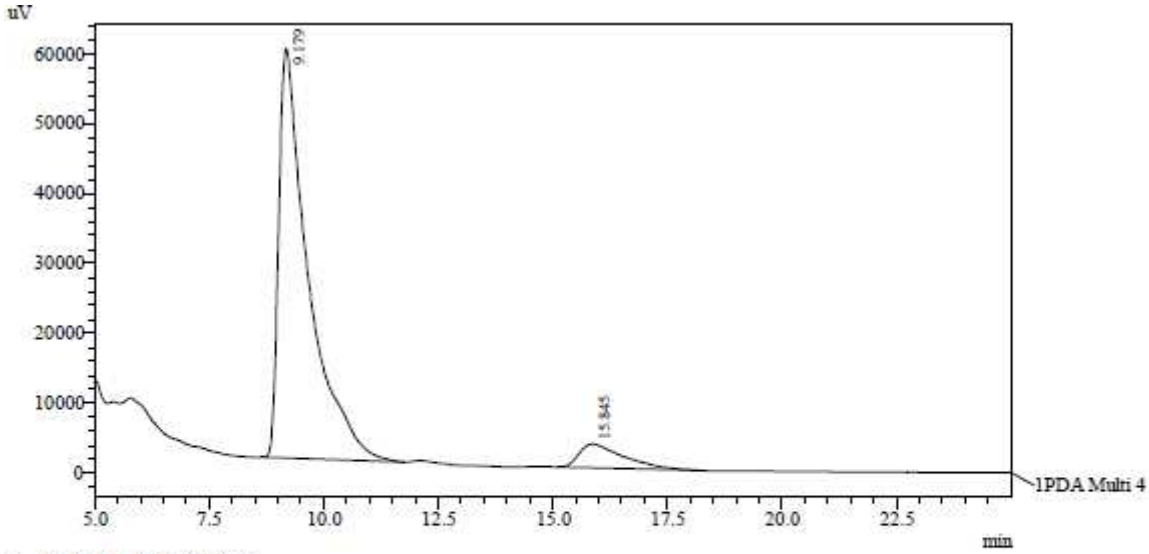


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.922	2368896	61022	50.056	59.395
2	14.770	2363586	41717	49.944	40.605
Total		4732482	102739	100.000	100.000

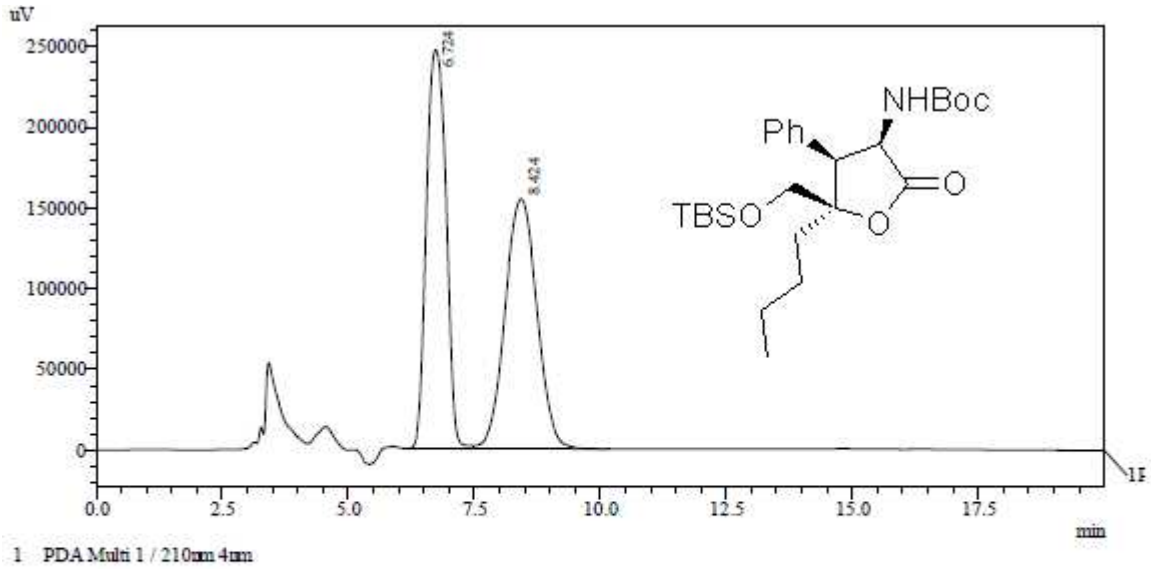


1 PDA Multi 4 / 270nm 4nm

PeakTable

PDA Ch4 270nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.179	2616504	58486	92.011	94.538
2	15.845	227185	3379	7.989	5.462
Total		2843690	61865	100.000	100.000

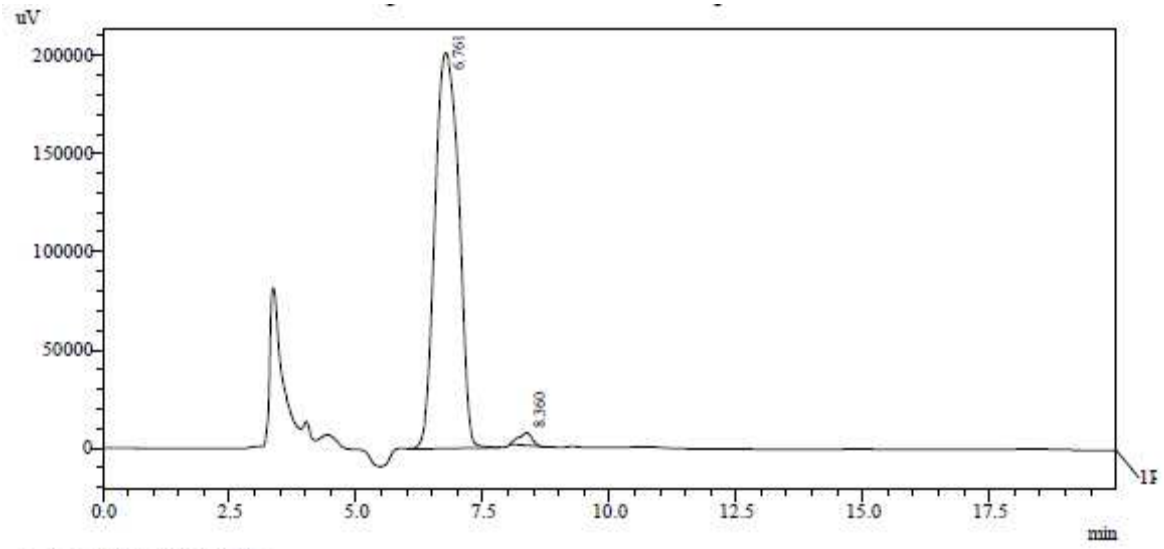


1 PDA Multi 1 / 210nm 4nm

PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.724	6725223	247303	49.598	61.457
2	8.424	6834115	155099	50.402	38.543
Total		13559337	402402	100.000	100.000



1 PDA Multi 1 / 210nm 4nm

PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.761	6584451	201458	98.214	96.905
2	8.360	119717	6434	1.786	3.095
Total		6704168	207892	100.000	100.000