Supporting Information

Diastereodivergent and Enantioselective Access to Spiroepoxides via Organocatalytic Epoxidation of Unsaturated Pyrazolones

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General Methods

All reactions requiring dry or inert conditions were conducted in flame-dried glassware under a positive pressure of nitrogen. THF and DCM were freshly distilled prior to use respectively over metallic Na and calcium hydride and stored under nitrogen, all other solvents were dried over molecular sieves. Molecular sieves (Aldrich Molecular Sieves, 4 Å, 1.6 mm pellets) were activated under vacuum at 200°C overnight.

Reactions were monitored by thin layer chromatography (TLC) on Macherey-Nagel pre-coated silica gel plates (0.25 mm) and visualized by UV light and, when necessary, by phosphomolybdic acid and ninhydrin staining solutions. Flash chromatography was performed on Merck silica gel (60, particle size: 0.040–0.063 mm). ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker Avance-400, Bruker Avance-300 or Bruker Avance-250 spectrometer in $CDCl_3$ or methanol-d_4 as solvent at room temperature. Chemical shifts for protons are reported using residual solvent protons (^{1}H NMR: δ = 7.26 ppm for $CDCl_3$, δ = 3.33 ppm for methanol-d_4) as internal standard. Carbon spectra were referenced to the shift of the ^{13}C signal of $CDCl_3$ (δ =77.0 ppm), CD_3OD (δ = 49.0 ppm). The following abbreviations are used to indicate the multiplicity in NMR spectra: s - singlet; d - doublet; t - triplet; q - quartet; dd - double doublet; m - multiplet; bs - broad signal; tt - triplet of triplets.

Optical rotation of compounds was performed on a Jasco P-2000 digital polarimeter using WI (Tungsten-Halogen) lamp (λ=589 nm). FTIR spectra were recorded as thin films on KBr plates using Bruker Tensor 27 spectrometer and absorption maxima are reported in wavenumber (cm^{-1}). High resolution mass spectra (HRMS) were acquired using a Bruker solariX XR Fourier transform ion cyclotron resonance mass spectrometer (Bruker Daltonik GmbH, Bremen, Germany) equipped with a 7 T refrigerated actively-shielded superconducting magnet. The samples were ionized in positive ion mode using the MALDI ion source. Melting points were measured with a Stuart Model SMP 30 melting point apparatus and are uncorrected.

Petrol ether (PE) refers to light petroleum ether (boiling point 40-60°C). Anhydrous toluene and α,α,α-trifluorotoluene, all starting materials (unless otherwise noted) were purchased from Aldrich and used as received.

Catalyst **4** was purchased from Aldrich and **5** from Strem Chemicals and used as received. Enantiomeric excess of epoxides **2/3** and **10a-b** was determined by HPLC (Waters-Breeze 2487, UV dual λ absorbance detector and 1525 Binary HPLC Pump) using Daicel chiral columns.

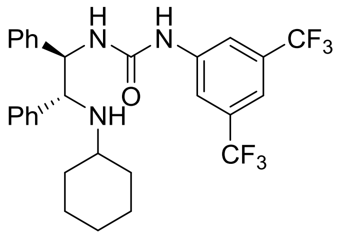
Experimental Procedures and Compounds Characterization

Cinchona alkaloids were purchased from Aldrich and used as received. Amine-thioureas **eQNT**, **eQDT**, **eCNT** were synthesized according to the literature.[1] Catalysts **eQNS**[2], **eHQNU**[3], **eQDU**,[4] **6**,[5] **8**,[6] are known and they were prepared according to the literature.

General procedure for the synthesis of catalyst 7

(1*R*,2*R*)-N[1]-cyclohexyl-1,2-diphenylethane-1,2-diamine[7] (90 mg, 0.30 mmol) was dissolved in anhydrous DCM (1.5 mL) in a flamed two necked round bottom flask under a positive pressure of nitrogen. The solution was cooled to 0 °C and 3,5-bis(trifluoromethyl)phenyl isocyanate (62 μL, 0.36 mmol) was added via syringe dropwised in 15 minutes. The reaction mixture was allowed to slowly warm up to room temperature under stirring, until the complete consumption of the starting material (14 h, TLC eluent: PE/ethyl acetate 8:2). After completion, monitored by TLC (eluent $CHCl_3$/ MeOH 98:2, visualized by UV light and by ninhydrin staining solution), the solvent was removed under reduced pressure and the crude product was purified by flash chromatography (PE/ ethyl ether 95:5 to 8:2, then $CHCl_3$) to give catalyst **7** (82 mg, 50%).

1-(3,5-bis(trifluoromethyl)phenyl)-3-((1*R*,2*R*)-2-(cyclohexylamino)-1,2-diphenylethyl)urea (7)



White solid, 82 mg, 50% yield. **mp** 198.3-200.6°C **$[\alpha]_D^{17}$** = -13.45 (*c* 0.56, $CHCl_3$). **FTIR** ν_{max} (KBr)/cm^{-1} 2931, 2855, 1662, 1575, 1505, 1475, 1388, 1278, 1172, 1132, 880, 758, 700, 682. **^{1}H NMR** (CD_3OD, 400 MHz): δ 7.91 (s, 2H), 7.45 (s, 1H), 7.28-7.16 (m, 10H), 4.93 (d, 1H, *J*= 6.4 Hz), 4.20 (d, 1H, *J*= 6.4 Hz), 2.27-2.18 (m, 1H), 1.91-1.83 (m, 1H), 1.74-1.67 (m, 1H), 1.63-1.45 (m, 3H), 1.15-0.85 (m, 5H). **^{13}C NMR** (CD_3OD, 100 MHz): δ 157.5, 143.8, 142.5, 142.3, 133.6

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[1] (a) Vakulya, B.; Varga S.; Csámpai, A.; Soós T. *Org. Lett.* **2005**, *7*, 1967-1969; (b) Yoneda, N.; Fukata, Y.; Asano, K.; Matsubara, S. *Angew. Chem. Int. Ed.* **2015**, *54*, 15497–15500.
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[3] Manna, M. S.; Mukherjee, S. *J. Am. Chem. Soc.* **2015**, *137*, 130-133.
[4] (a) Miyaji, R.; Asano K.; Matsubara, S. *Org. Lett.* **2013**, *15*, 3658-3661; (b) Amere, M.; Lasne, M.-C.; Rouden, J. *Org. Lett.* **2007**, *9*, 2621-2624; (c) Wu, W.; Min, L.; Zhu, L.; Lee, C.-S. *Adv. Synth. Catal.* **2011**, *353*, 1135-1145.
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[6] Meninno, S.; Overgaard, J.; Lattanzi, A. *Synthesis*, **2017**, *49*, 1509-1518.
[7] Wang, M.; Lin, L.; Shi, J.; Liu, X.; Kuang, Y.; Feng, X. *Chem. Eur. J.* **2011**, *17*, 2365.

($^{2}J_{CF}$= 33 Hz), 129.9, 129.75, 129.66, 128.9, 128.8, 128.5, 125.3 ($^{1}J_{CF}$= 272 Hz), 119.4, 116.0 ($^{3}J_{CF}$= 3.7 Hz), 65.8, 61.5, 54.9, 35.7, 33.4, 27.6, 26.6, 26.1. **HRMS** (MALDI-FT ICR) m/z [M+H]+ calcd for $C_{29}H_{30}F_6N_3O$: 550.2288; found: 550.2290.

General procedure for the synthesis of racemic epoxides 2/3 and 10

Alkenes **1**[8] and **9**[9] were prepared using general procedures reported in the literature.

In a sample vial containing a solution of alkene **1** or **9** (0.05 mmol) in anhydrous toluene (500 µL) 2-piperidinemethanol (1.2 mg, 0.01 mmol) followed by *tert*-butyl hydroperoxide (TBHP) (~5.5 M in decane, 11 µL, 0.06 mmol) were added. The reaction was stirred at room temperature for 10-20 minutes for epoxides **2**/**3**, and 4 hours for epoxides **10a** and **10b** monitored by TLC (eluent PE/ ethyl acetate 90/10, visualized by UV light and phosphomolybdic acid staining solution). After completion, the reaction mixture was filtered through a short plug of flash silica-gel (eluent $CHCl_3$) to remove 2-piperidinemethanol and isolate the mixture of two diastereomers **2**/**3** (90-98% yield) or by flash chromatography (eluting with PE/ ethyl acetate 100/0.5 to 98/2) to isolate the pure products **10a** and **10b** (90 and 98% yield, respectively).

General procedure for the asymmetric epoxidation of alkenes 1 with 8/TBHP system

A sample vial was charged with alkene **1** (0.10 mmol) and catalyst **8** **(**6.7 mg, 0.01 mmol) in anhydrous toluene (1 mL). The solution was cooled to -20°C and after about 5 minutes TBHP (~5.5 M in decane, 22 µL, 0.12 mmol) was added and the mixture was stirred at -20°C until completion, monitored by TLC (eluent PE/ ethyl acetate 9/1, visualized by UV light and by phosphomolybdic acid staining solution). After completion, the reaction mixture was filtered through a short plug of flash silica-gel (eluent PE/ ethyl acetate 8/2) to remove the catalyst and the diastereoisomeric ratio was determined by ^{1}H-NMR analysis of the crude reaction mixture. Purification of the crude mixture by flash chromatography (eluting with PE/ ethyl acetate 100/1) allows to separate the two diastereoisomers giving enantioenriched epoxides **2a-k, n**. The diastereomeric products **2l,m** (major) and **3l,m** (minor) were not separated by flash chromatography because they have the same Rf value. Absolute configuration of epoxides **2** was assumed to be (2*R*,3*S*) in analogy to that determined on compound **2f** by single-crystal X-ray analysis (see the X-ray analysis section).

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[8] (a) Chen, Q.; Liang, J.; Wang, S.; Wang, D.; Wang, R. *Chem. Commun*. **2013**, *49*, 1657; (b) Jia, Y.; Tang, X.; Cai, G.; Jia, R.; Wang, B.; Miao Z. *Eur. J. Org. Chem.* **2015**, 4720-4725; (c) Fioravanti, S.; Morreale, A.; Pellacani, L.; Tardella, P. A. *Synlett* **2004**, 1083; (d) Nahra, F.; Macé, Y.; Boreux, A.; Billard, F.; Riant, O. *Chem. Eur. J.* **2014**, *20*, 10970; (e) Sun, J.; Yan, C.-G.; Han Y. *Synth. Commun*. **2001**, *31*, 151.

[9] Rassu, G.; Zambrano, V.; Pinna, L; Curti, C.; Battistini, L.; Sartori, A.; Pelosi, G.; Casiraghi, G.; Zanardi, F. *Adv. Synth. Catal.* **2014**, *356*, 2330.

For the reaction carried out at 1 mmol scale: alkene **1a** (262.3 mg, 1 mmol), catalyst **8** (66.6 mg, 0.1 mmol), TBHP (~5.5 M in decane, 220 μL, 1.2 mmol) in anhydrous toluene (10 mL) at -20°C for 5 h isolating products **2a** (208 mg, 75% yield, 96% ee) and **3a** (61 mg, 22% yield, 63% ee).

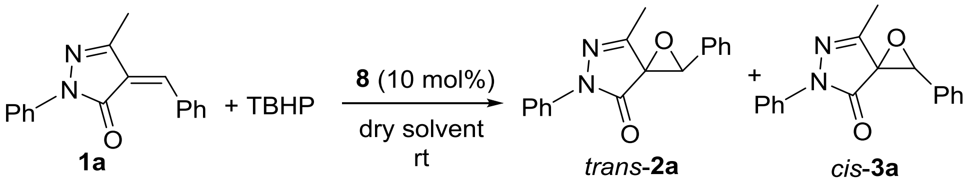
General procedure for the asymmetric epoxidation of alkenes 1 with eQDT/TBHP system

A sample vial was charged with alkene **1** (0.10 mmol) and catalyst **eQDT** (5.9 mg, 0.01 mmol) in anhydrous α,α,α-trifluorotoluene (1 mL). Then *tert*-butyl hydroperoxide (~5.5 M in decane, 22 μL, 0.12 mmol) was added and the mixture was stirred at room temperature until completion, monitored by TLC (eluent PE/ ethyl acetate 9/1, visualized by UV light and by phosphomolybdic acid staining solution). After completion, the reaction mixture was filtered through a short plug of flash silica-gel (eluent PE/ ethyl acetate 8/2) to remove the catalyst and the diastereoisomeric ratio was determined by ^{1}H-NMR analysis of the crude reaction mixture. Purification of the crude mixture by flash chromatography (eluting with PE/ ethyl acetate 100/1 to 98/2) allows to separate the two diastereoisomers giving enantioenriched epoxides **3a**, **3b**, **3f**, **3g**, **3i**, **3n**. Absolute configuration of epoxides **3** was assumed to be (2*S*,3*S*) in analogy to that determined on compound **3g** by single-crystal X-ray analysis (see the X-ray analysis section).

General procedure for the enantioselective epoxidation of alkenes 9 with eQDT/TBHP system

A sample vial was charged with alkene **9** (0.10 mmol) and catalyst **eQDT** (5.9 mg, 0.01 mmol) in anhydrous α,α,α-trifluorotoluene (1 mL). The solution was cooled to -20°C and after about 5 minutes *tert*-butyl hydroperoxide (~5.5 M in decane, 22 μL, 0.12 mmol) was added and the mixture was stirred at -20°C until completion, monitored by TLC (eluent PE/ ethyl acetate 9/1, visualized by UV light and by phosphomolybdic acid staining solution). After completion the crude product was purified by flash chromatography (eluting with PE/ ethyl acetate 100/0.5 to 98/2) to afford enantioenriched epoxide **10a** and **10b**.

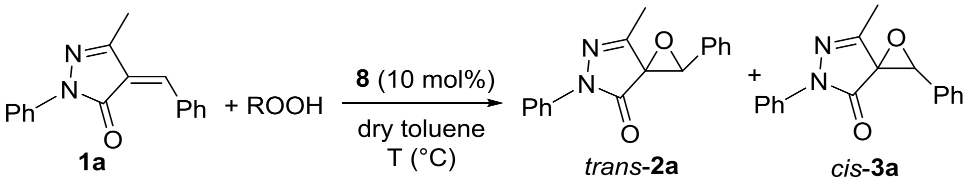
Table S1. Solvent screening with 8/TBHP system [a]



entry	solvent	t(h)	yield (%)[b]	**2a/3a**[c]	ee**2a**(%)[d]	ee**3a**(%)[d]
1	toluene	1	98	80:20	-96	-56
2	m-xylene	1.5	93	80:20	-96	-62
3	$CF_3C_6H_5$	1.5	96	75:25	-95	-70
4	*t*BuOMe	5	97	78:22	-96	-58
5	$CHCl_3$	5	83	80:20	-95	-29

[a]Reaction were performed at 0.08 mmol scale of **1a** (C 0.1 M) using TBHP (1.2 equiv). [b]Determined by ^{1}H NMR analysis with 1,3,5-$(MeO)_3C_6H_3$ as an internal standard. [c]Determined by ^{1}H NMR analysis of the crude reaction mixture. [d]Determined by chiral HPLC analysis.

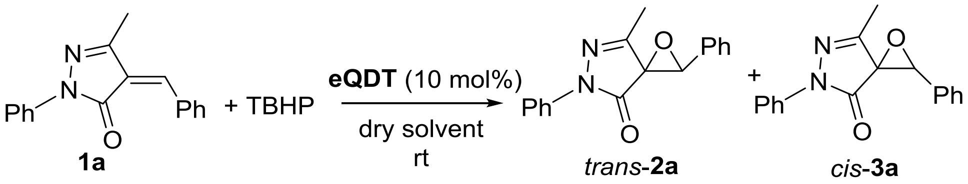
Table S2. Optimization of reaction parameters with catalyst 8 [a]



entry	R	T (°C)	t(h)	yield (%)[b]	**2a/3a**[c]	ee**2a**(%)[d]	ee**3a**(%)[d]
1	*t*Bu	rt	1	98	80:20	-96	-56
2[e]	H	rt	3.5	39	90:10	-29	-43
2	*t*Bu	0	1.5	98	81:19	-97	-62
3[f]	*t*Bu	0	21	56	79:21	-75	-9
3	$Ph(Me)_2C$	0	1.5	83	54:46	-98	-70
4	*t*Bu	-20	3	98	83:17	-97	-67
5	*t*Bu	-40	8	92	87:13	-94	-75

[a]Reaction were performed at 0.08 mmol scale of **1a** (C 0.1 M) using 1.2 equiv. of the oxidant. [b]Determined by ^{1}H NMR analysis with 1,3,5-$(MeO)_3C_6H_3$ as an internal standard. [c]Determined by ^{1}H NMR analysis of the crude reaction mixture. [d]Determined by chiral HPLC analysis. [e]50 wt.% H_2O_2 was used. [f]5 mol% of **8** was used.

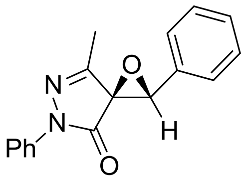
Table S3. Solvent screening with eQDT/TBHP system[a]



entry	solvent	t(h)	yield (%)[b]	**2a/3a**[c]	ee**2a**(%)[d]	ee**3a**(%)[d]
1	toluene	6	90	22:78	-29	+94
2	m-xylene	4	89	21:79	-23	+95
3	$CF_3C_6H_5$	2	97	17:83	-14	+96
4[e]	$CF_3C_6H_5$	2	91	12:88	+10	+90
5	ClC_6H_5	1.5	98	20:80	-13	+95
6	C_6F_6	21	53	75:25	-27	+57
7	*t*BuOMe	22	90	19:81	-18	+93
8[f]	$CHCl_3$	19	60	43:57	-22	+89
9	EtOAc	23	54	32:68	0	+88

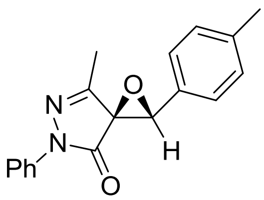
[a]Reaction were performed at 0.08 mmol scale of **1a** (C 0.1 M) using TBHP (1.2 equiv). [b]Determined by ^{1}H NMR analysis with 1,3,5-$(MeO)_3C_6H_3$ as an internal standard. [c]Determined by ^{1}H NMR analysis of the crude reaction mixture. [d]Determined by chiral HPLC analysis. [e]Cumene hydroperoxide (1.2 equiv.) was used. [f]After 4h additional 0.6 equiv. of TBHP was added.

(2*R*,3*S*)-7-methyl-2,5-diphenyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (2a)



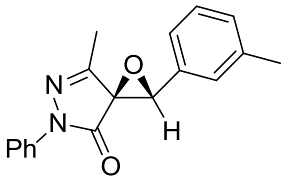
Light yellow solid, 20.8 mg, 75% yield. **mp** 75.6-78.7°C **[α]$_D$**^{17} = +296.2 (*c* 0.51, $CHCl_3$), 97% ee. **FTIR** ν_{max} (KBr)/cm^{-1} 1726, 1654, 1597, 1500, 1369, 1340, 1267, 888, 756, 702. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.95-7.91 (m, 2H), 7.49-7.40 (m, 7H), 7.25-7.19 (m, 1H), 4.79 (s, 1H), 1.54 (s, 3H). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 166.3, 155.5, 138.0, 132.0, 129.4, 129.0, 128.6, 126.5, 125.4, 118.4, 66.5, 63.7, 15.2. **HRMS** (MALDI-FT ICR) m/z [M+H]$^+$ calcd for $C_{17}H_{15}N_2O_2$: 279.1128; found: 279.1125. HPLC analysis with Chiralcel OD-H column, 9:1 *n*-hexane:2-propanol, 1 mL/min, 254 nm; minor enantiomer t_R = 7.7 min, major enantiomer t_R = 8.1 min.

(2*R*,3*S*)-7-methyl-5-phenyl-2-(p-tolyl)-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (2b)



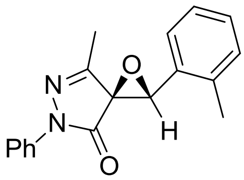
Yellow solid, 22.2 mg, 76% yield. **mp** 86.1-90.8°C **[α]$_D$**^{17} = +366.00 (*c* 0.57, $CHCl_3$), 97% ee. **FTIR** ν_{max} (KBr)/cm^{-1} 1726, 1598, 1501, 1369, 1339, 1162, 888, 815, 690, 607. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.94-7.91 (m, 2H), 7.45-7.40 (m, 2H), 7.35 (d, 2H, *J*= 7.8 Hz), 7.24-7.19 (m, 3H), 4.75 (s, 1H), 2.39 (s, 3H), 1.56 (s, 3H). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 166.4, 155.7, 139.4, 138.0, 129.3, 128.94, 128.87, 126.4, 125.4, 118.4, 66.7, 63.7, 21.3, 15.3. **HRMS** (MALDI-FT ICR) m/z $[M+H]^+$ calcd for $C_{18}H_{17}N_2O_2$: 293.1285; found: 293.1285. HPLC analysis with Chiralcel OD-H column, 98:2 *n*-hexane:2-propanol, 1 mL/min, 254 nm; minor enantiomer t_R = 11.7 min, major enantiomer t_R = 12.3 min.

(2*R*,3*S*)-7-methyl-5-phenyl-2-(m-tolyl)-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (2c)



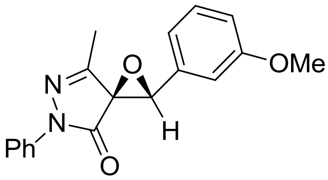
Pale yellow solid solid, 20.2 mg, 69% yield. **mp** 75.6-77.9°C **[α]$_D$**^{21} = +469.89 (*c* 0.56, $CHCl_3$), 96% ee. **FTIR** ν_{max} (KBr)/cm^{-1} 1728, 1598, 1501, 1369, 1338, 756, 705, 691. **^{1}H NMR** ($CDCl_3$, 250 MHz): δ 7.93-7.89 (m, 2H), 7.45-7.38 (m, 2H), 7.30-7.17 (m, 5H), 4.74 (s, 1H), 2.30 (s, 3H), 1.54 (s, 3H). **^{13}C NMR** ($CDCl_3$, 62.5 MHz): δ 166.4, 155.6, 138.5, 138.0, 131.8, 130.1, 129.0, 128.5, 127.1, 125.4, 123.5, 118.4, 66.6, 63.6, 21.4, 15.3. **HRMS** (MALDI-FT ICR) m/z $[M+H]^+$ calcd for $C_{18}H_{17}N_2O_2$: 293.1284; found: 293.1282. HPLC analysis with Chiralpak IC column, 9:1 *n*-hexane:2-propanol, 1 mL/min, 254 nm; minor enantiomer t_R = 13.9 min, major enantiomer t_R = 11.1 min.

(2*R*,3*S*)-7-methyl-5-phenyl-2-(o-tolyl)-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (2d)



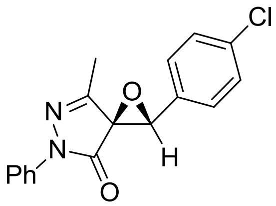
Pale yellow oil, 24.6 mg, 84% yield. **[α]$_D$**^{21} = +280.27 (*c* 0.66, $CHCl_3$), 77% ee. **FTIR** ν_{max} (KBr)/cm^{-1} 1743, 1590, 1488, 1322, 1264, 1077, 790, 698. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ 7.96-7.93 (m, 2H), 7.52-7.49 (m, 1H), 7.46-7.40 (m, 2H), 7.33-7.26 (m, 2H), 7.25-7.18 (m, 2H), 4.71 (s, 1H), 2.21 (s, 3H), 1.42 (s, 3H). **^{13}C NMR** ($CDCl_3$, 75 MHz): δ 166.4, 155.8, 138.1, 135.9, 130.8, 130.0, 129.3, 129.0, 126.4, 126.0, 125.4, 118.4, 65.9, 63.2, 18.6, 14.7. **HRMS** (MALDI-FT ICR) m/z $[M+H]^+$ calcd for $C_{18}H_{17}N_2O_2$: 293.1284; found: 293.1285. HPLC analysis with Chiralpak IC column, 9:1 *n*-hexane:2-propanol, 1 mL/min, 254 nm; minor enantiomer t_R = 11.1 min, major enantiomer t_R = 8.3 min.

(2*R*,3*S*)-2-(3-methoxyphenyl)-7-methyl-5-phenyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (2e)



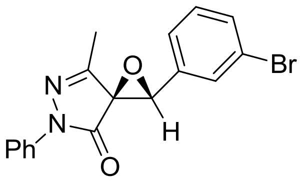
Light yellow solid, 23.3 mg, 76% yield. **mp** 74.5-78.2°C $[\alpha]_D^{21}$ = +324.8 (*c* 0.75, $CHCl_3$), 95% ee. **FTIR** ν_{max} (KBr)/cm^{-1}1725, 1597, 1501, 1458, 1434, 1407, 1370, 1338, 1270, 1149, 1044, 758, 691, 703. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.94-7.91 (m, 2H), 7.45-7.41 (m, 2H), 7.33 (t, 1H, *J*= 7.9 Hz), 7.22 (t, 1H, *J*= 7.4 Hz), 7.04 (d, 1H, *J*= 7.6 Hz), 6.99 (s, 1H), 6.94 (dd, 1H, *J*= 8.3, 2.2 Hz), 4.75 (s, 1H), 3.83 (s, 3H), 1.59 (s, 3H). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 166.3, 159.8, 155.5, 138.0, 133.4, 129.8, 129.0, 125.4, 118.7, 118.4, 115.1, 111.9, 66.4, 63.6, 55.4, 15.3. **HRMS** (MALDI-FT ICR) m/z $[M+H]^+$ calcd for $C_{18}H_{17}N_2O_3$: 309.1234; found: 309.1230. HPLC analysis with Chiralpak IC column, 9:1 *n*-hexane:2-propanol, 1 mL/min, 254 nm; minor enantiomer t_R = 16.8 min, major enantiomer t_R = 14.6 min.

(2*R*,3*S*)-2-(4-chlorophenyl)-7-methyl-5-phenyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (2f)



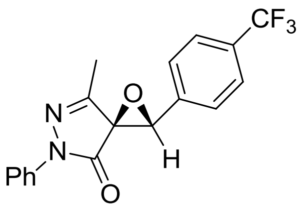
Light yellow solid, 24.4 mg, 78% yield. **mp** 112.1-114.5°C $[\alpha]_D^{19}$ = +393.62 (*c* 0.57, $CHCl_3$), 95% ee. **FTIR** ν_{max} (KBr)/cm^{-1} 1726, 1598, 1501, 1370, 1338, 1163, 1092, 1016, 829, 756, 691, 667, 551. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.93-7.89 (m, 2H), 7.45-7.39 (m, 6H), 7.25-7.20 (m, 1H), 4.74 (s, 1H), 1.58 (s, 3H). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 166.0, 155.0, 137.9, 135.5, 130.5, 129.0, 128.0, 125.6, 118.4, 65.8, 63.7, 15.4. **HRMS** (MALDI-FT ICR) m/z $[M+Na]^+$ calcd for $C_{17}H_{13}ClN_2NaO_2$: 335.0558; found: 335.0553. HPLC analysis with Chiralpak IC column, 9:1 *n*-hexane:2-propanol, 1 mL/min, 254 nm; minor enantiomer t_R = 12.0 min, major enantiomer t_R = 11.4 min.

(2*R*,3*S*)-2-(3-bromophenyl)-7-methyl-5-phenyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (2g)



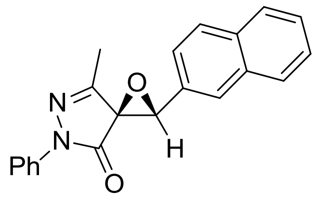
White solid, 24.9 mg, 70% yield. **mp** 44.1-46.7°C $[\alpha]_D^{17}$ = +361.07 (*c* 0.67, $CHCl_3$), 96% ee. **FTIR** ν_{max} (KBr)/cm^{-1} 1734, 1597, 1500, 1369, 1165, 1094, 755, 739, 699. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.93-7.89 (m, 2H), 7.64 (s, 1H), 7.57-7.54 (m, 1H), 7.46-7.40 (m, 3H), 7.34-7.28 (m, 1H), 7.24-7.21 (m, 1H), 4.73 (s, 1H), 1.59 (s, 3H). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 165.8, 154.9, 137.9, 134.2, 132.6, 130.3, 129.6, 129.0, 125.5, 125.2, 122.8, 118.4, 65.3, 63.6, 15.4. **HRMS** (MALDI-FT ICR) m/z $[M+H]^+$ calcd for $C_{17}H_{14}BrN_2O_2$: 357.0233; found: 357.0229. HPLC analysis with Chiralpak IC column, 9:1 *n*-hexane:2-propanol, 1 mL/min, 254 nm; minor enantiomer t_R = 13.1 min, major enantiomer t_R = 12.3 min.

(2*R*,3*S*)-7-methyl-5-phenyl-2-(4-(trifluoromethyl)phenyl)-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (2h)



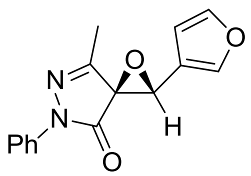
White solid, 22.5 mg, 65% yield. **mp** 107.6-11.7°C $[\alpha]_D^{21}$ = +232.88 (*c* 0.61, $CHCl_3$), 96% ee. **FTIR** ν_{max} (KBr)/cm^{-1} 1731, 1713, 1502, 1372, 1346, 1328, 1167, 1127, 1068, 1109, 756, 692, 663. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.93-7.89 (m, 2H), 7.72 (d, 2H, *J*= 8.0 Hz), 7.62 (d, 2H, *J*= 8.0 Hz), 7.46-7.40 (m, 2H), 7.26-7.21 (m, 1H), 4.80 (s, 1H), 1.55 (s, 3H). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 165.7, 154.6, 137.9, 135.9, 131.6 (q, $^2J_{CF}$= 33 Hz), 129.0, 127.1, 125.7 (q, $^3J_{CF}$= 3.7 Hz), 125.6, 123.7 (q, $^1J_{CF}$= 272 Hz), 118.4, 65.5, 63.6, 15.3. **HRMS** (MALDI-FT ICR) m/z $[M+H]^+$ calcd for $C_{18}H_{14}F_3N_2O_2$: 347.1002; found: 347.1002. HPLC analysis with Chiralpak IC column, 98:2 *n*-hexane:2-propanol, 1 mL/min, 254 nm; minor enantiomer t_R = 20.5 min, major enantiomer t_R = 18.2 min.

(2*R*,3*S*)-7-methyl-2-(naphthalen-2-yl)-5-phenyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (2i)



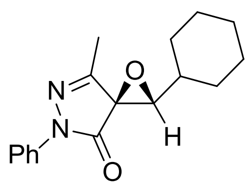
Pale yellow solid, 21.3 mg, 65% yield. **mp** 115.2-118.1°C **[α]$_D$**^{22} = +535.30 (*c* 0.77, $CHCl_3$), 95% ee. **FTIR** ν_{max} (KBr)/cm^{-1} 1724, 1598, 1501, 1408, 1369, 1354, 1327, 1276, 821, 751, 691. **^{1}H NMR** ($CDCl_3$, 250 MHz): δ 7.99-7.86 (m, 6H), 7.58-7.51 (m, 3H), 7.47-7.41 (m, 2H), 7.26-7.20 (m, 1H), 4.95 (s, 1H), 1.53 (3, 3H). **^{13}C NMR** ($CDCl_3$, 62.5 MHz): δ 166.3, 155.5, 138.0, 133.5, 132.7, 129.3, 129.0, 128.6, 128.1, 127.9, 127.0, 126.9, 126.1, 125.4, 123.5, 118.4, 66.7, 63.9, 15.4. **HRMS** (MALDI-FT ICR) m/z [M+H]$^+$ calcd for $C_{21}H_{17}N_2O_2$: 329.1285; found: 329.1285. HPLC analysis with Chiralcel ODH column, 98:2 *n*-hexane:2-propanol, 1 mL/min, 254 nm; minor enantiomer t_R = 24.2 min, major enantiomer t_R = 27.7 min.

(2*R*,3*S*)-2-(furan-3-yl)-7-methyl-5-phenyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (2j)



Yellow solid, 17.6 mg, 66% yield. **mp** 60.6-63.4°C **[α]$_D$**^{18} = +195.78 (*c* 0.67, $CHCl_3$), 96% ee. **FTIR** ν_{max} (KBr)/cm^{-1} 1726, 1591, 1501, 1368, 1277, 1163, 875, 756, 690. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.93-7.89 (m, 2H), 7.61-7.59 (m, 1H), 7.48 (t, 1H, *J*= 1.7 Hz), 7.46-7.39 (m, 2H), 7.22 (tt, 1H, *J*= 7.4, 1.1 Hz), 6.50-6.49 (m, 1H), 4.58 (s, 1H), 1.81 (s, 3H). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 166.2, 155.4, 143.9, 141.6, 138.0, 129.0, 125.5, 118.4, 118.1, 109.1, 63.4, 61.1, 15.2. **HRMS** (MALDI-FT ICR) m/z [M+H]$^+$ calcd for $C_{15}H_{13}N_2O_3$: 269.0921; found:269.0923. HPLC analysis with Chiralpak IC column, 90:10 *n*-hexane:2-propanol, 1 mL/min, 254 nm; minor enantiomer t_R = 14.6 min, major enantiomer t_R = 13.9 min.

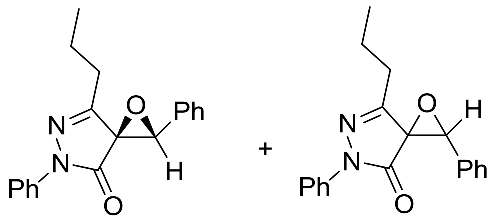
(2*R*,3*S*)-2-cyclohexyl-7-methyl-5-phenyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (2k)



Light yellow solid, 19.9 mg, 70% yield. **mp** 87.9-90.9°C **[α]$_D$**^{17} = +149.43 (*c* 0.82, $CHCl_3$), 96% ee. **FTIR** ν_{max} (KBr)/cm^{-1} 1730, 1599, 1498, 1443, 1367, 1342, 1118, 759. **^{1}H NMR** ($CDCl_3$, 250

MHz): δ 7.93-7.88 (m, 2H), 7.45-7.38 (m, 2H), 7.24-7.17 (m, 1H), 3.41 (d, 1H, *J*= 9.0 Hz), 2.19 (s, 3H), 2.15-2.07 (m, 1H), 1.89-1.45 (m, 5H), 1.37-1.16 (m, 5H). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 167.4, 155.4, 138.0, 128.9, 125.3, 118.4, 72.1, 62.0, 38.2, 30.9, 28.8, 25.8, 25.3, 25.1, 15.5. **HRMS** (MALDI-FT ICR) m/z $[M+Na]^+$ calcd for $C_{17}H_{20}N_2NaO_2$: 307.1417; found: 307.1417. HPLC analysis with Chiralpak IC column, 90:10 *n*-hexane:2-propanol, 1 mL/min, 220 nm; minor enantiomer t_R = 11.8 min, major enantiomer t_R = 9.0 min.

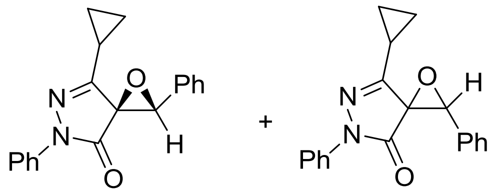
2,5-diphenyl-7-propyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (2l)



2l **3l**

The diastereomeric products **2l** (major) and **3l** (minor) were not separated by flash chromatography because they have the same Rf value. Orange liquid, 30.0 mg, 98% yield. **FTIR** ν_{max} (KBr)/cm^{-1} 1727, 1598, 1501, 1456, 1404, 1357, 1154, 898, 755, 729, 691. **^{1}H NMR** ($CDCl_3$, 250 MHz): δ 7.95 (d, 2H, *J*= 7.6 Hz) [7.83 (d, 2H, *J*= 7.9 Hz)]$_{minor}$, 7.54-7.36 (m, 8H), 4.77 (s, 1H) [4.68 (s, 1H), 2.44 (t, 2H, *J*= 7.7 Hz)]$_{minor}$, 1.76-1.31 (m, 4H), 0.78 (t, 3H, *J*= 7.3 Hz) [1.09 (t, 3H, *J*= 7.4 Hz]$_{minor}$. **^{13}C NMR** ($CDCl_3$, 62.5 MHz): δ 166.4, 158.1 [158.4]$_{minor}$, 138.1, 132.0 [129.4, 128.7, 127.8, 127.6]$_{minor}$, 129.3, 128.9, 128.6, 126.4, 125.3 [125.1]$_{minor}$, 118.3, 66.7 [65.2]$_{minor}$, 63.6, 30.8 [28.5, 19.1, 13.9]$_{minor}$, 18.7, 13.6. **HRMS** (MALDI-FT ICR) m/z $[M+H]^+$ calcd for $C_{19}H_{19}N_2O_2$: 307.1441; found: 307.1443. HPLC analysis with Chiralpak IC column, 90:10 *n*-hexane:2-propanol, 1 mL/min, 254 nm; minor enantiomer t_R = 14.0 min, major enantiomer t_R = 13.1 min.

7-cyclopropyl-2,5-diphenyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (2m)

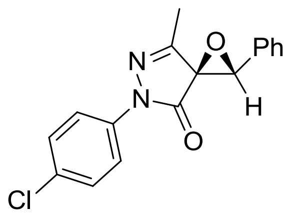


2m **3m**

The diastereomeric products **2m** (major) and **3m** (minor) were not separated by flash chromatography because they have the same Rf value. Orange wax, 29.8 mg, 98% yield. **FTIR** ν_{max} (KBr)/cm^{-1} 1725, 1597, 1501, 1455, 1407, 1358, 1277, 1154, 1133, 1055, 1028, 906, 884, 756, 729, 706, 692. **^{1}H NMR** ($CDCl_3$, 250 MHz): δ 7.92 (d, 2H, *J*= 8.0 Hz), [7.78 (d, 2H, *J*= 8.3 Hz), 7.65-

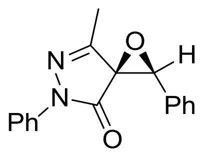
7.60 (m, 2H)]$_{minor}$, 7.55-7.48 (m, 2H), 7.46-7.36 (m, 5H), 7.23-7.17 (m, 1H), 4.81 (s, 1H) overlapped with [4.81 (s, 1H)]$_{minor}$, [1.69-1.54 (m, 1H)]$_{minor}$, 1.17-1.05 (m, 1H), 0.95-0.85 (m, 1H), 0.81-0.70 (m, 1H), 0.51-0.40 (m, 1H), 0.19-0.08 (m, 1H). **^{13}C NMR** ($CDCl_3$, 62.5 MHz): δ 166.5, 159.8, 138.2, 132.3, 129.1, 128.9, 128.5, 126.7, 125.3, 118.3, 66.7, 63.9, 9.5, 9.2, 7.4. **HRMS** (MALDI-FT ICR) m/z $[M+H]^+$ calcd for $C_{19}H_{17}N_2O_2$: 305.1284; found: 305.1284. HPLC analysis with Chiralpak IC column, 90:10 *n*-hexane:2-propanol, 1 mL/min, 254 nm; minor enantiomer t_R = 13.6 min, major enantiomer t_R = 12.2 min.

(2*R*,3*S*)-5-(4-chlorophenyl)-7-methyl-2-phenyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (2n)



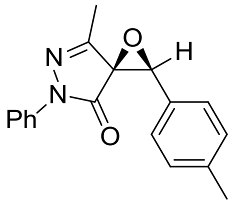
White solid, 18.0 mg, 58% yield. **mp** 135.6-137.9°C $[\alpha]_D^{22}$ = +438.27 (*c* 0.90, $CHCl_3$), 95% ee. **FTIR** ν_{max} (KBr)/cm^{-1} 1731, 1638, 1495, 1415, 1367, 1351, 1271, 1161, 1093, 879, 821, 763, 736, 701, 683, 648, 556. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.90 (d, 2H, *J*= 9.1 Hz), 7.48-7.41 (m, 5H), 7.39 (d, 2H, *J*= 9.1 Hz), 4.78 (s, 1H), 1.54 (s, 3H). **^{13}C NMR** ($CDCl_3$, 62.5 MHz): δ 166.3, 155.9, 136.6, 131.8, 130.5, 129.5, 129.0, 128.7, 126.5, 119.4, 66.6, 63.6, 15.3. **HRMS** (MALDI-FT ICR) m/z $[M+H]^+$ calcd for $C_{17}H_{14}ClN_2O_2$: 313.0738; found: 313.0725. HPLC analysis with Chiralpak IC column, 90:10 *n*-hexane:2-propanol, 1 mL/min, 254 nm; minor enantiomer t_R = 9.7 min, major enantiomer t_R = 8.8 min.

(2*S*,3*S*)-7-methyl-2,5-diphenyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (3a)



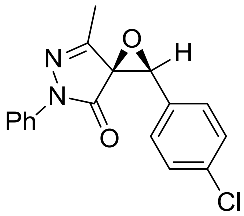
Yellow solid, 23.4 mg, 84% yield. **mp** 64.4-67.3°C $[\alpha]_D^{22}$ = -25.54 (*c* 0.73, $CHCl_3$), 97% ee. **FTIR** ν_{max} (KBr)/cm^{-1} 1728, 1597, 1500, 1368, 1302, 1158, 991, 756, 691, 648. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ 7.83-7.79 (m, 2H), 7.62-7.58 (m, 2H), 7.46-7.38 (m, 3H), 7.37-7.31 (m, 2H), 7.18-7.12 (m, 1H), 4.67 (s, 1H), 2.20 (s, 3H). **^{13}C NMR** ($CDCl_3$, 75 MHz): δ 164.5, 155.8, 138.1, 129.5, 128.8, 127.9, 127.6, 125.2, 118.4, 65.1, 63.2, 12.4. **HRMS** (MALDI-FT ICR) m/z $[M+H]^+$ calcd for $C_{17}H_{15}N_2O_2$: 279.1134; found: 279.1129. HPLC analysis with Chiralcel OD-H column, 90:10 *n*-hexane:2-propanol, 1 mL/min, 254 nm; minor enantiomer t_R = 12.6 min, major enantiomer t_R = 16.7 min.

(2*S*,3*S*)-7-methyl-5-phenyl-2-(p-tolyl)-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (3b)



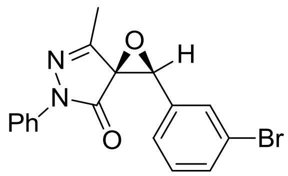
Yellow wax, 16.9 mg, 58% yield. **[α]$_{D}$**^{22} = -21.86 (*c* 0.67, $CHCl_3$), 97% ee. **FTIR** ν_{max} (KBr)/cm^{-1} 1726, 1685, 1654, 1597, 1560, 1500, 1366, 756, 691. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.82-7.79 (m, 2H), 7.49 (d, 2H, *J*= 8.0 Hz), 7.35-7.31 (m, 2H), 7.22 (d, 2H, *J*= 8.0 Hz), 7.17-7.12 (m, 1H), 4.64 (s, 1H), 2.37 (s, 3H), 2.19 (s, 3H). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 164.7, 155.8, 139.5, 138.2, 128.7, 128.6, 127.6, 126.5, 125.1, 118.5, 65.3, 63.3, 21.4, 12.4. **HRMS** (MALDI-FT ICR) m/z $[M+H]^+$ calcd for $C_{18}H_{17}N_2O_2$: 293.1285; found: 293.1285. HPLC analysis with Chiralcel OD-H column, 98:2 *n*-hexane:2-propanol, 1 mL/min, 254 nm; minor enantiomer t_R = 14.4 min, major enantiomer t_R = 17.8 min.

(2*S*,3*S*)-2-(4-chlorophenyl)-7-methyl-5-phenyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (3f)



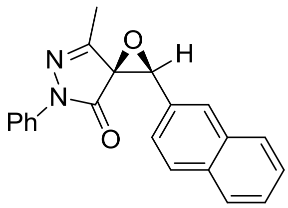
Light yellow solid, 24.4 mg, 78% yield. **mp** 107.4-110.6°C **[α]$_{D}$**^{19} = -64.69 (*c* 0.72, $CHCl_3$), 96% ee. **FTIR** ν_{max} (KBr)/cm^{-1} 1725, 1598, 1501, 1368, 1337, 1160, 1092, 1016, 829, 756, 691, 667. **^{1}H NMR** ($CDCl_3$, 400 MHz): δ 7.79 (d, 2H, *J*= 7.6 Hz), 7.55 (d, 2H, *J*= 8.4 Hz), 7.39 (d, 2H, *J*= 8.4 Hz), 7.35 (t, 2H, *J*= 7.6 Hz), 7.16 (t, 1H, *J*= 7.5 Hz), 4.63 (s, 1H), 2.19 (s, 3H). **^{13}C NMR** ($CDCl_3$, 75 MHz): δ 164.4, 155.5, 138.1, 135.6, 129.0, 128.8, 128.2, 128.0, 125.3, 118.5, 64.4, 63.1, 12.3. **HRMS** (MALDI-FT ICR) m/z $[M+Na]^+$ calcd for $C_{17}H_{13}ClN_2NaO_2$: 335.0558; found: 335.0554. HPLC analysis with Chiralpak IC column, 90:10 *n*-hexane:2-propanol, 1 mL/min, 254 nm; minor enantiomer t_R = 7.5 min, major enantiomer t_R = 6.9 min.

(2*S*,3*S*)-2-(3-bromophenyl)-7-methyl-5-phenyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (3g)



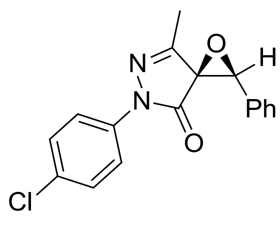
White solid, 31.8 mg, 89% yield. **mp** 106.6-111.0°C **[α]$_D$**^{18} = -35.57 (*c* 0.87, $CHCl_3$), 96% ee. **FTIR** ν_{max} (KBr)/cm^{-1} 1728, 1597, 1500, 1369, 1337, 1162, 893, 765, 690. **^{1}H NMR** ($CDCl_3$, 250 MHz): δ 7.80 (d, 2H, *J*= 7.8 Hz), 7.73 (bs, 1H), 7.58-7.50 (m, 2H), 7.39-7.35 (m, 2H), 7.32-7.29 (m, 1H), 7.19-7.13 (m, 1H), 4.61 (s, 1H), 2.19 (s, 3H). **^{13}C NMR** ($CDCl_3$, 62.5 MHz): δ 164.1, 155.4, 138.0, 132.5, 131.8, 130.6, 129.4, 128.8, 126.3, 125.3, 121.9, 118.5, 64.0, 62.9, 12.3. **HRMS** (MALDI-FT ICR) m/z [M+Na]$^+$ calcd for $C_{17}H_{13}BrN_2NaO_2$: 379.0053; found: 378.9844. HPLC analysis with Chiralcel OD-H column, 90:10 n-hexane:2-propanol, 1 mL/min, 254 nm; minor enantiomer t_R = 9.8 min, major enantiomer t_R = 12.0 min.

(2*S*,3*S*)-7-methyl-2-(naphthalen-2-yl)-5-phenyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (3i)



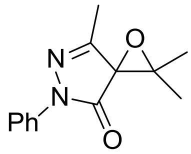
Yellow wax, 29.6 mg, 90% yield. **[α]$_D$**^{23} = -87.25 (*c* 0.64, $CHCl_3$), 98% ee. **FTIR** ν_{max} (KBr)/cm^{-1} 1724, 1596, 1500, 1366, 1220, 772. **^{1}H NMR** ($CDCl_3$, 250 MHz): δ 8.10 (s, 1H), 7.91-7.76 (m, 5H), 7.71 (dd, 1H, *J*= 8.6, 1.6 Hz), 7.54-7.47 (m, 2H), 7.36-7.29 (m, 2H), 7.17-7.10 (m, 1H), 4.84 (s, 1H), 2.24 (s, 3H). **^{13}C NMR** ($CDCl_3$, 62.5 MHz): δ 164.5, 155.7, 138.1, 133.8, 132.5, 128.7, 128.2, 127.8, 127.7, 127.6, 127.0, 126.8, 126.4, 125.2, 124.4, 118.5, 65.4, 63.4, 12.4. **HRMS** (MALDI-FT ICR) m/z [M+H]$^+$ calcd for $C_{21}H_{17}N_2O_2$: 329.1284; found: 329.1287. HPLC analysis with Chiralcel OD-H column, 98:2 n-hexane:2-propanol, 1 mL/min, 254 nm; minor enantiomer t_R = 37.8 min, major enantiomer t_R = 30.1 min.

(2*S*,3*S*)-5-(4-chlorophenyl)-7-methyl-2-phenyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (3n)



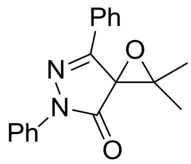
Pale yellow solid, 22.6 mg, 72% yield.**mp** 91.6-95.5 °C. **[α]$_D$**^{24} = -12.15 (*c* 0.89, $CHCl_3$), 99% ee. **FTIR** ν_{max} (KBr)/cm^{-1} 1727, 1636, 1493, 1367, 1338, 1302, 1156, 1122, 1092, 992, 880, 827, 722, 694, 544, 506. **^{1}H NMR** ($CDCl_3$, 250 MHz): δ 7.77 (d, 2H, *J*= 8.9 Hz), 7.61-7.54 (m, 2H), 7.45-7.36 (m, 3H), 7.28 (d, 2H, *J*= 8.9 Hz), 4.65 (s, 1H), 2.17 (s, 3H). **^{13}C NMR** ($CDCl_3$, 62.5 MHz): δ 164.5, 156.1, 136.7, 130.2, 129.6, 129.4, 128.8, 127.9, 127.6, 119.5, 65.3, 63.1, 12.4. **HRMS** (MALDI-FT ICR) m/z [M+H]$^+$ calcd for $C_{17}H_{14}ClN_2O_2$: 313.0738; found: 313.0738. HPLC analysis with Chiralpak IC column, 90:10 *n*-hexane:2-propanol, 1 mL/min, 254 nm; minor enantiomer t_R = 6.1 min, major enantiomer t_R = 7.5 min.

2,2,7-trimethyl-5-phenyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (10a)



White solid, 22.6 mg, 98% yield.**mp** 66.3-67.9 °C. **[α]$_D$**^{20} = -116.38 (*c* 0.86, $CHCl_3$), 50% ee. **FTIR** ν_{max} (KBr)/cm^{-1} 1722, 1598, 1436, 1366, 1303, 1126, 766, 691, 648. **^{1}H NMR** ($CDCl_3$, 300 MHz): δ 7.90-7.86 (m, 2H), 7.44-7.37 (m, 2H), 7.23-7.17 (m, 1H), 2.21 (s, 3H), 1.76 (s, 3H), 1.69 (s, 3H). **^{13}C NMR** ($CDCl_3$, 75 MHz): δ 167.6, 156.3, 138.1, 128.9, 125.3, 118.7, 69.4, 65.7, 22.4, 18.3, 16.7. **HRMS** (MALDI-FT ICR) m/z [M+Na]$^+$ calcd for $C_{13}H_{14}N_2NaO_2$: 253.0947; found: 253.0949. HPLC analysis with Chiralcel OD-H column, 90:10 n-hexane:2-propanol, 1 mL/min, 254 nm; minor enantiomer t_R = 5.7 min, major enantiomer t_R = 6.6 min.

2,2-dimethyl-5,7-diphenyl-1-oxa-5,6-diazaspiro[2.4]hept-6-en-4-one (10b)



Light yellow wax, 23.4 mg, 80% yield. **[α]$_D$**^{24} = -46.16 (*c* 0.87, $CHCl_3$), 59% ee. **FTIR** ν_{max} (KBr)/cm^{-1} 1724, 1598, 1492, 1388, 1377, 1321, 1309, 1148, 1101, 929, 759, 691, 642. **^{1}H NMR** ($CDCl_3$, 250 MHz): δ 7.97 (d, 2H, *J*= 8.2 Hz), 7.84-7.78 (m, 2H), 7.48-7.39 (m, 5H), 7.26-7.20 (m, 1H), 1.75 (s, 3H), 1.33 (s, 3H). **^{13}C NMR** ($CDCl_3$, 62.5 MHz): δ 167.8, 155.2, 138.3, 132.2, 130.4, 128.9, 128.7, 127.4, 125.5, 119.0, 70.2, 66.7, 20.9, 18.6. **HRMS** (MALDI-FT ICR) m/z [M+H]$^+$ calcd for $C_{18}H_{17}N_2O_2$: 293.1285; found: 293.1284. HPLC analysis with Chiralcel OD-H column, 90:10 n-hexane:2-propanol, 1 mL/min, 254 nm; minor enantiomer t_R = 5.4 min, major enantiomer t_R = 6.1 min.

X-Ray data for the absolute configuration assignment of compounds 2f and 3g

Single crystals of epoxide **2f** were obtained by slow evaporation of a solution of pentane and 2-propanol with a few drops of $CHCl_3$ at room temperature.

Single crystal diffraction data were collected on an Rigaku Oxford Diffraction Supernova CCD area detector diffractometer, using Mo Kα (λ = 0.71073 Å) radiation. Data reduction and absorption correction were performed using CrysalisPro. The structure was solved by direct methods using SHELXS[10] and refined by full-matrix least squares using SHELXL. [11] Hydrogen atoms were generated in calculated position. The absolute structure was determined with absolute confidence based on the value of the Flack[10] parameter = -0.00(3).

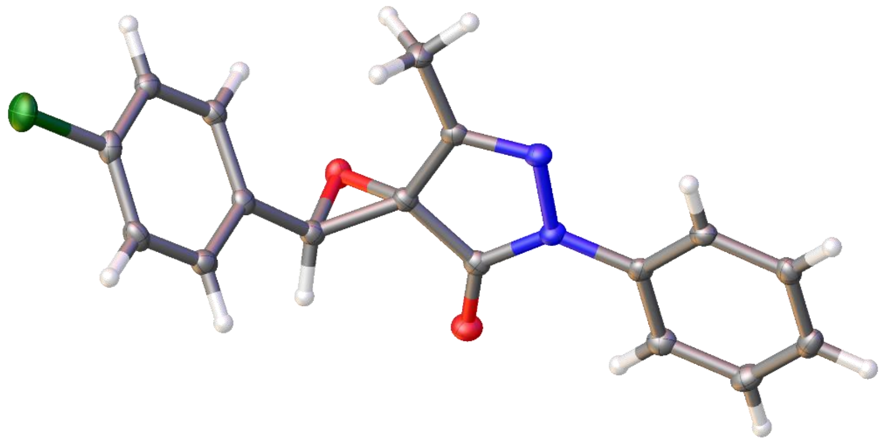


Figure S1. ORTEP drawing[12] of the molecular structure of **2f**, showing 50% probability ellipsoids.

[10] Sheldrick, G. M. *Acta Crystallogr. Sect. A* **2008**, *64*, 112-122.
[11] Parsons, S.; Flack, H. D.; Wagner, T. *Acta Crystallogr. Sect. B* **2013**, *69*, 249-259.
[12] Johnson C. K. in *ORTEP, Vol.* Oak Ridge National Laboratory, Tennessee, USA, **1965**.

Item	Value
Molecular formula	C17 H13 Cl N2 O2
Formula weight	312.74
Crystal system	orthorhombic
Space Group	P 21 21 21
a (Å)	8.3966
b (Å)	10.4923
c (Å)	16.3473
α (°)	90
β (°)	90
γ (°)	90
Volume (Å^3)	1440.19
Z	4
T (K)	100
ρ (g cm^{-1})	1.442
λ (Å)	0.71073
μ (mm^{-1})	0.274
# measured refl	15951
# unique refl	3613
R_{int}	0.0442
# parameters	200
R(F^2), all refl	0.0401
R_w(F^2), all refl	0.074
Goodness of fit	1.045

Single crystals of epoxide **3g** were obtained by slow evaporation of a solution of *n*-hexane/$CHCl_3$ at room temperature.

Single crystal diffraction data were collected on an Rigaku Oxford Diffraction Supernova CCD area detector diffractometer, using Mo Kα (λ = 0.71073 Å) radiation. Data reduction and absorption correction were performed using CrysalisPro. The structure was solved by direct methods using SHELXS[10] and refined by full-matrix least squares using SHELXL.[10] Hydrogen atoms were generated in calculated position. The Flack parameter[11] of -0.023(17) shows clearly that the absolute configuration has been correctly determined. The two independent molecules overlap almost quantitatively.

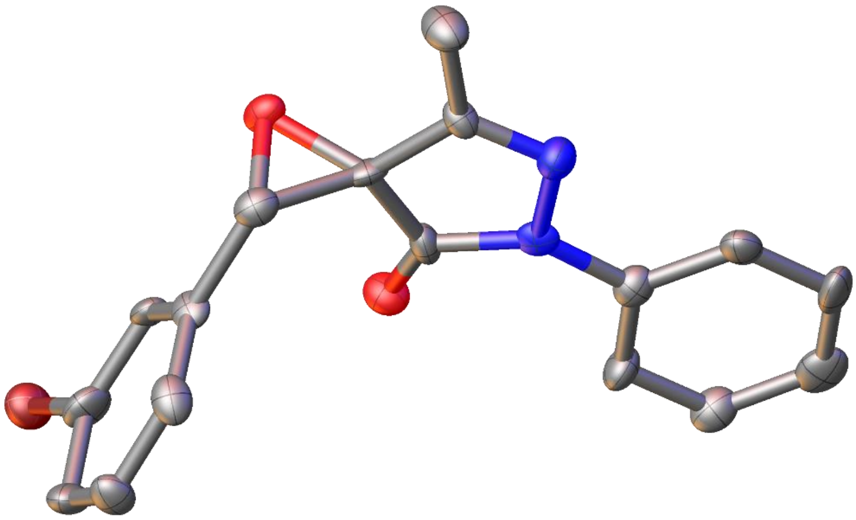
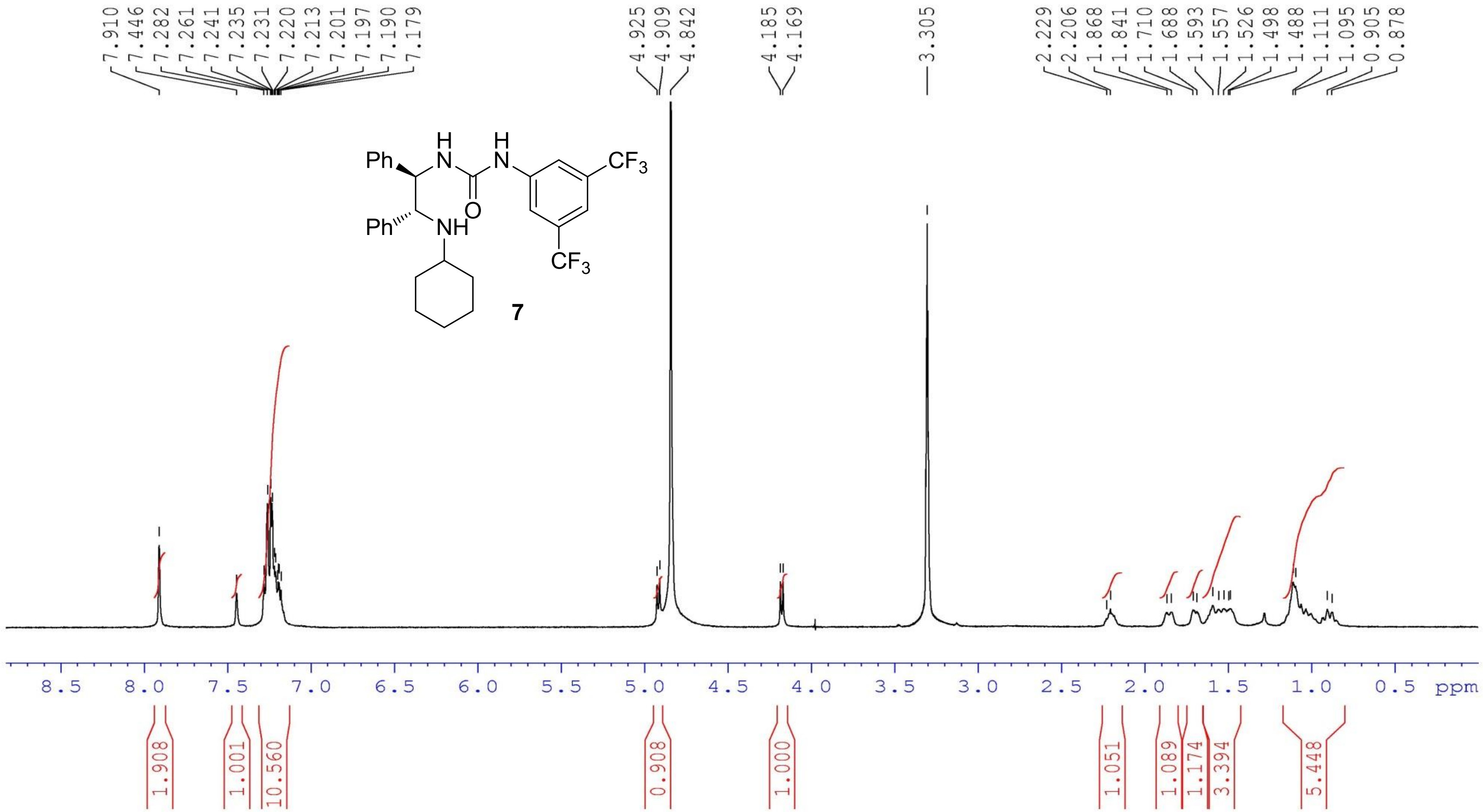


Figure S2. ORTEP-drawing[12] of one of the two independent molecules in **3g**. The figure shows 50% probability thermal ellipsoids.

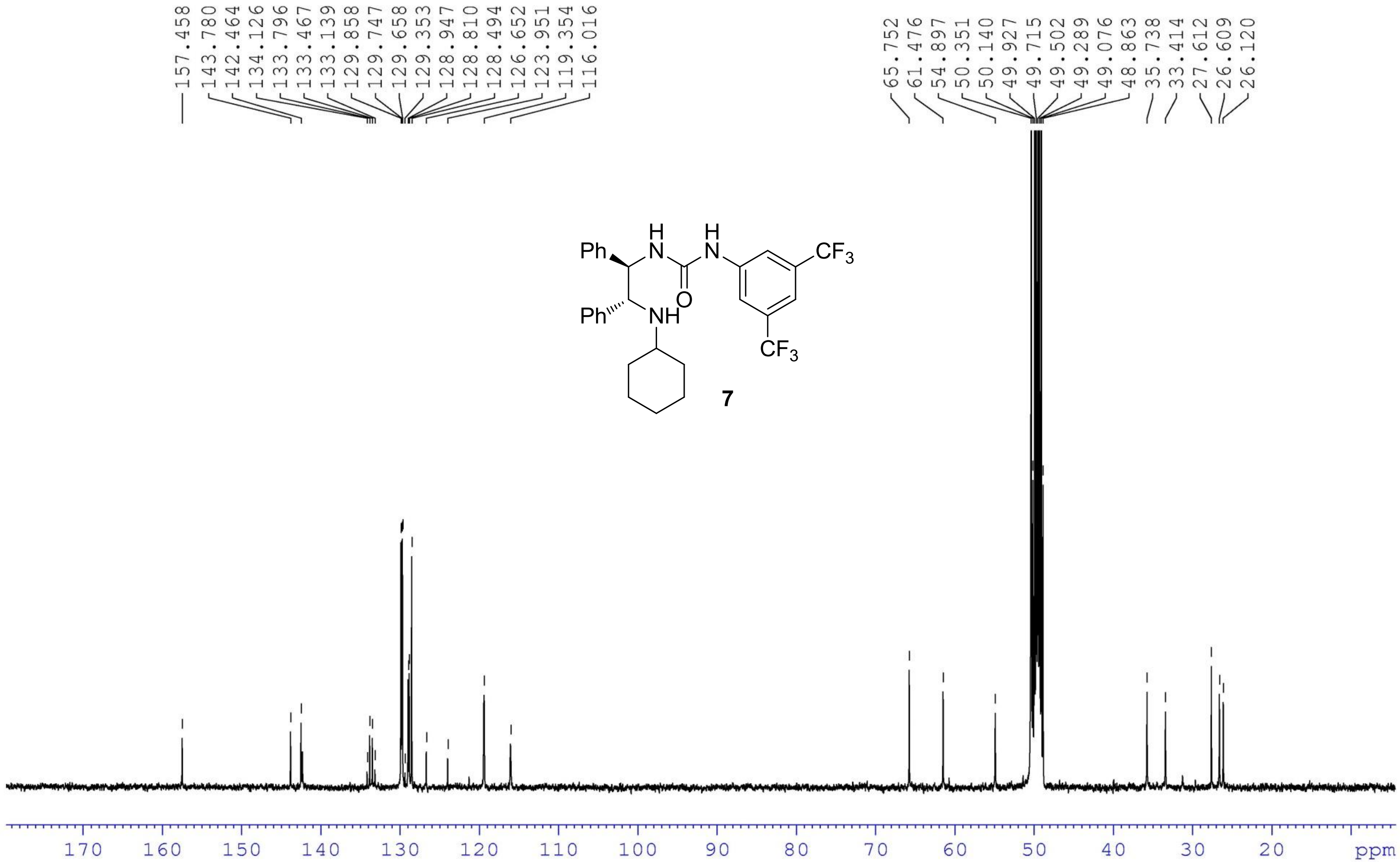
Item	Value
Molecular formula	C17 H13 Br N2 O2
Formula weight	357.2
Crystal system	tetragonal
Space Group	P 43
a (Å)	14.4914
b (Å)	14.4914
c (Å)	14.4935
α (°)	90
β (°)	90
γ (°)	90
Volume (Å^3)	3043.63
Z	8
T (K)	100
ρ (g cm^{-1})	1.559
λ (Å)	0.71073
μ (mm^{-1})	2.709
# measured refl	19151
# unique refl	5623
R_{int}	0.1103
# parameters	399
R(F^2), all refl	0.0841
R_w(F^2), all refl	0.1055
Goodness of fit	0.669

NMR Spectra

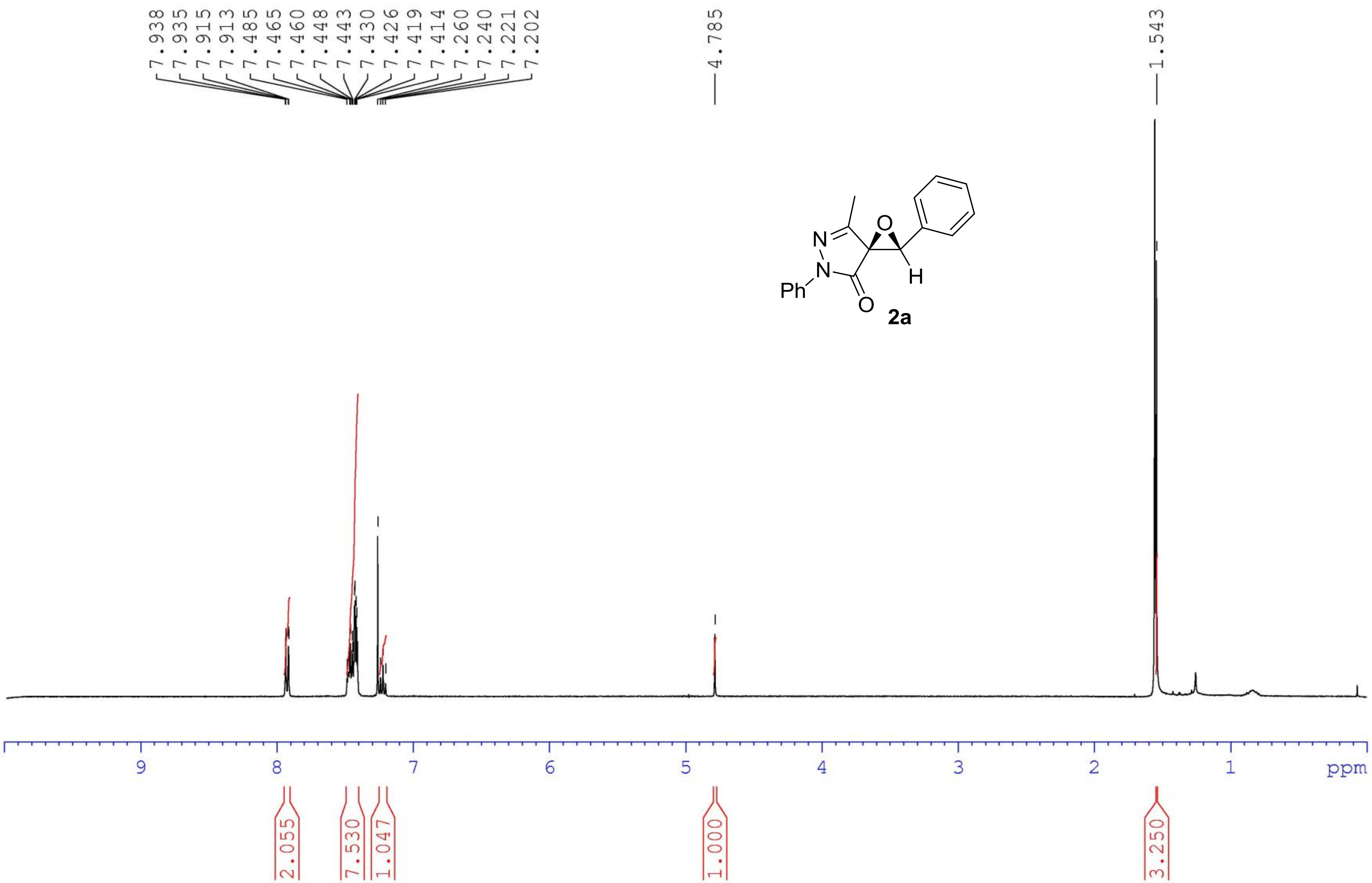
[1]H NMR in CD_3OD (400 MHz)



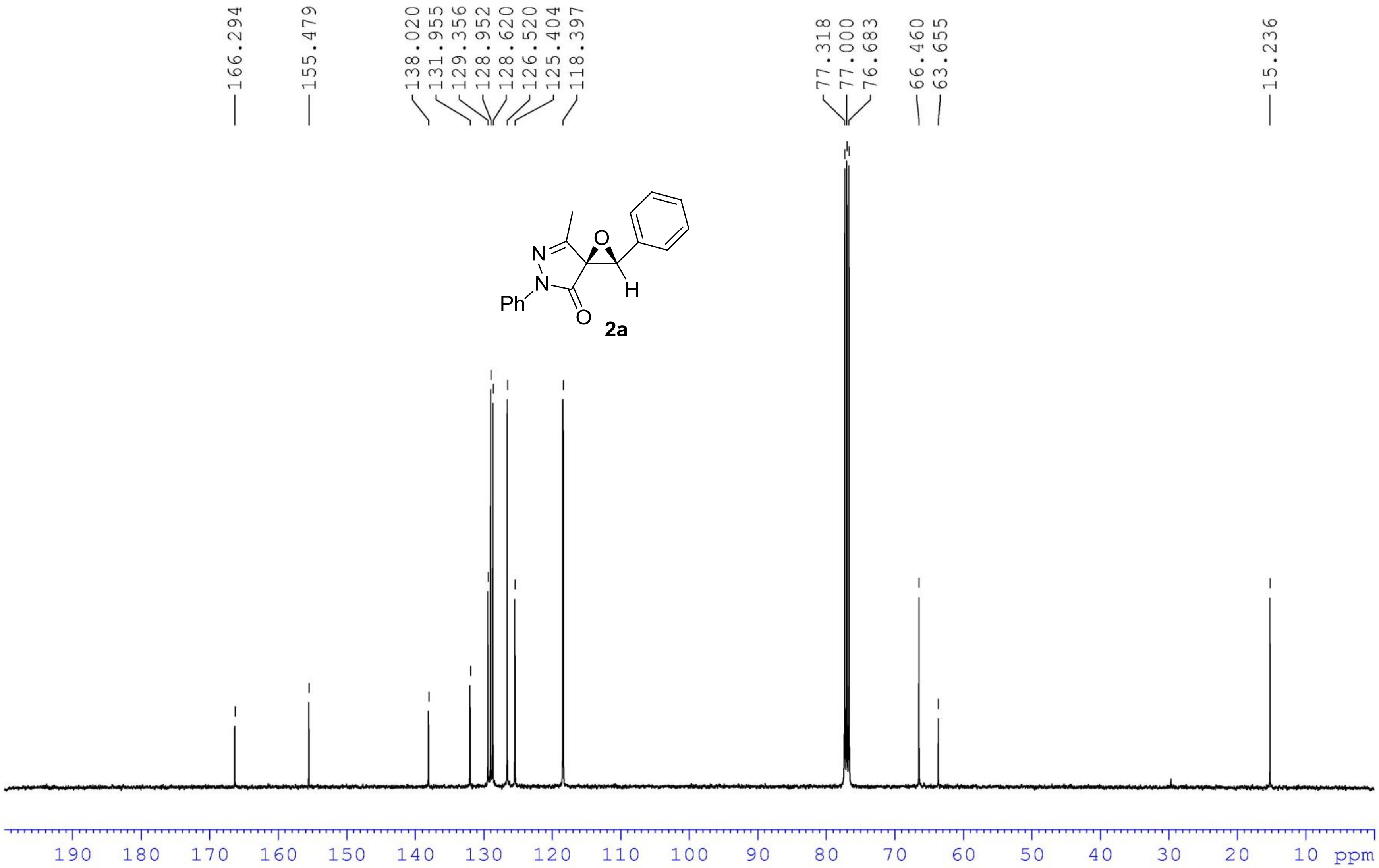
^{13}C NMR in CD_3OD (100 MHz)



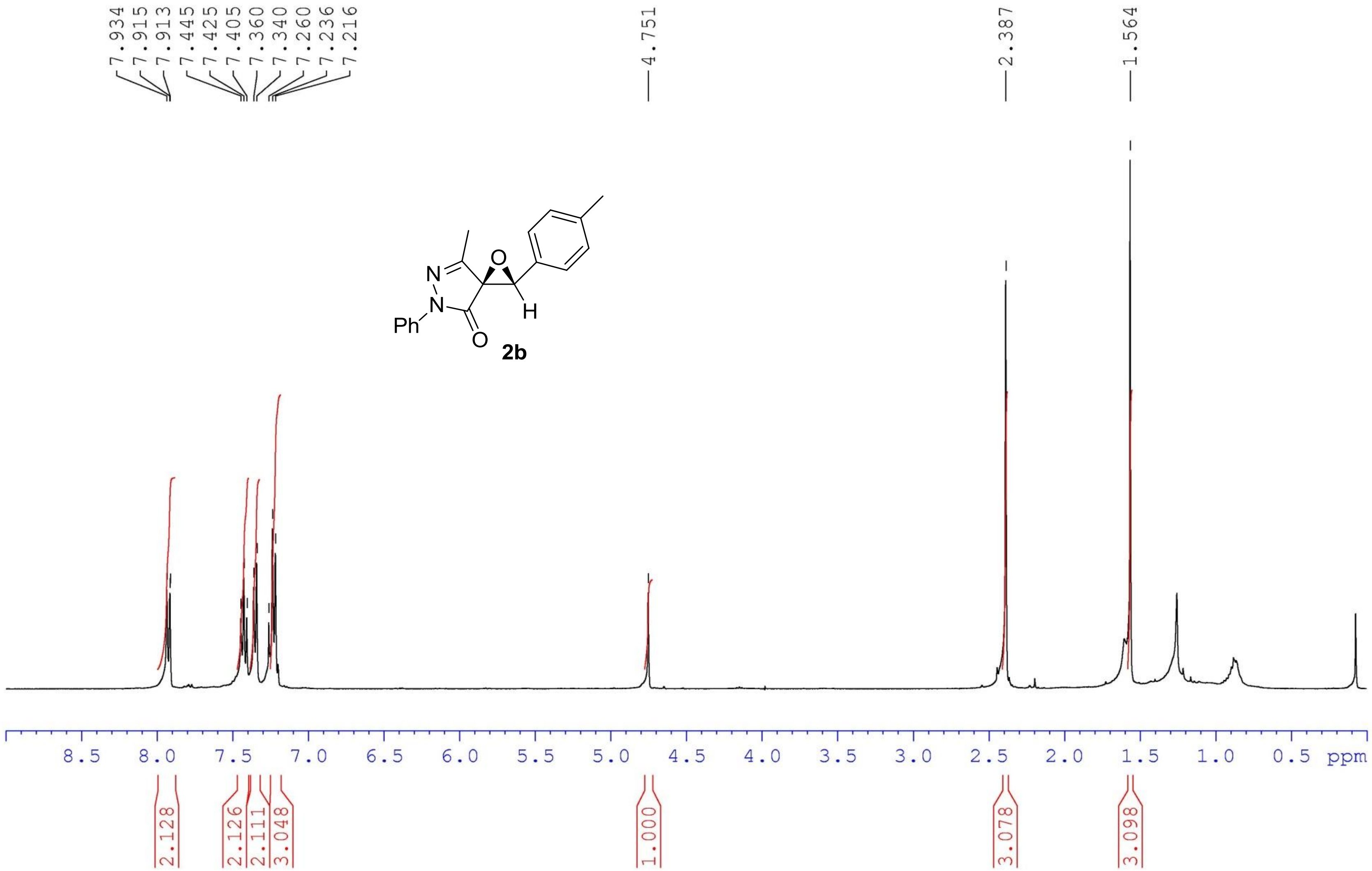
^{1}H NMR in $CDCl_3$ (400 MHz)



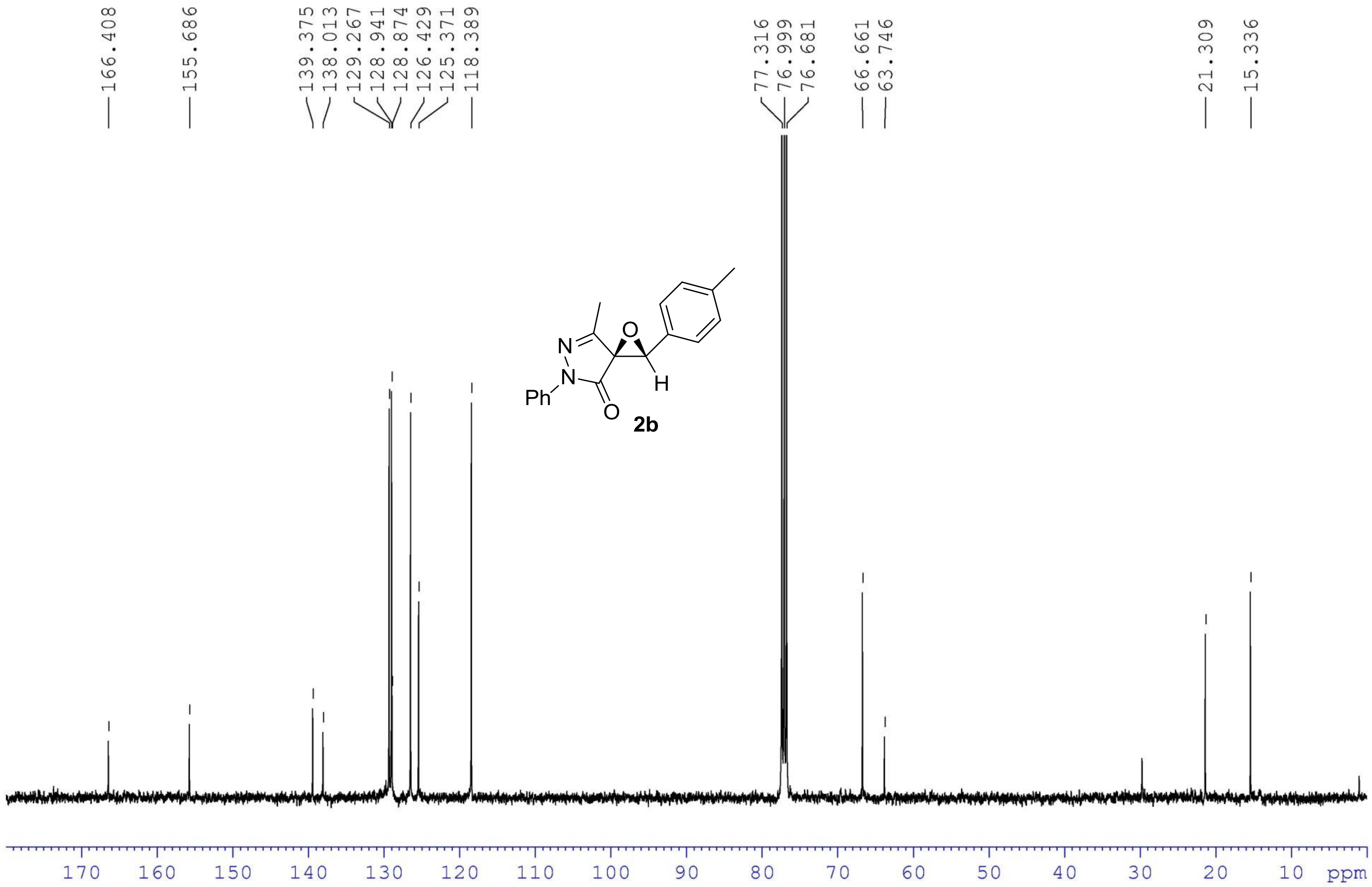
^{13}C NMR in $CDCl_3$ (100 MHz)



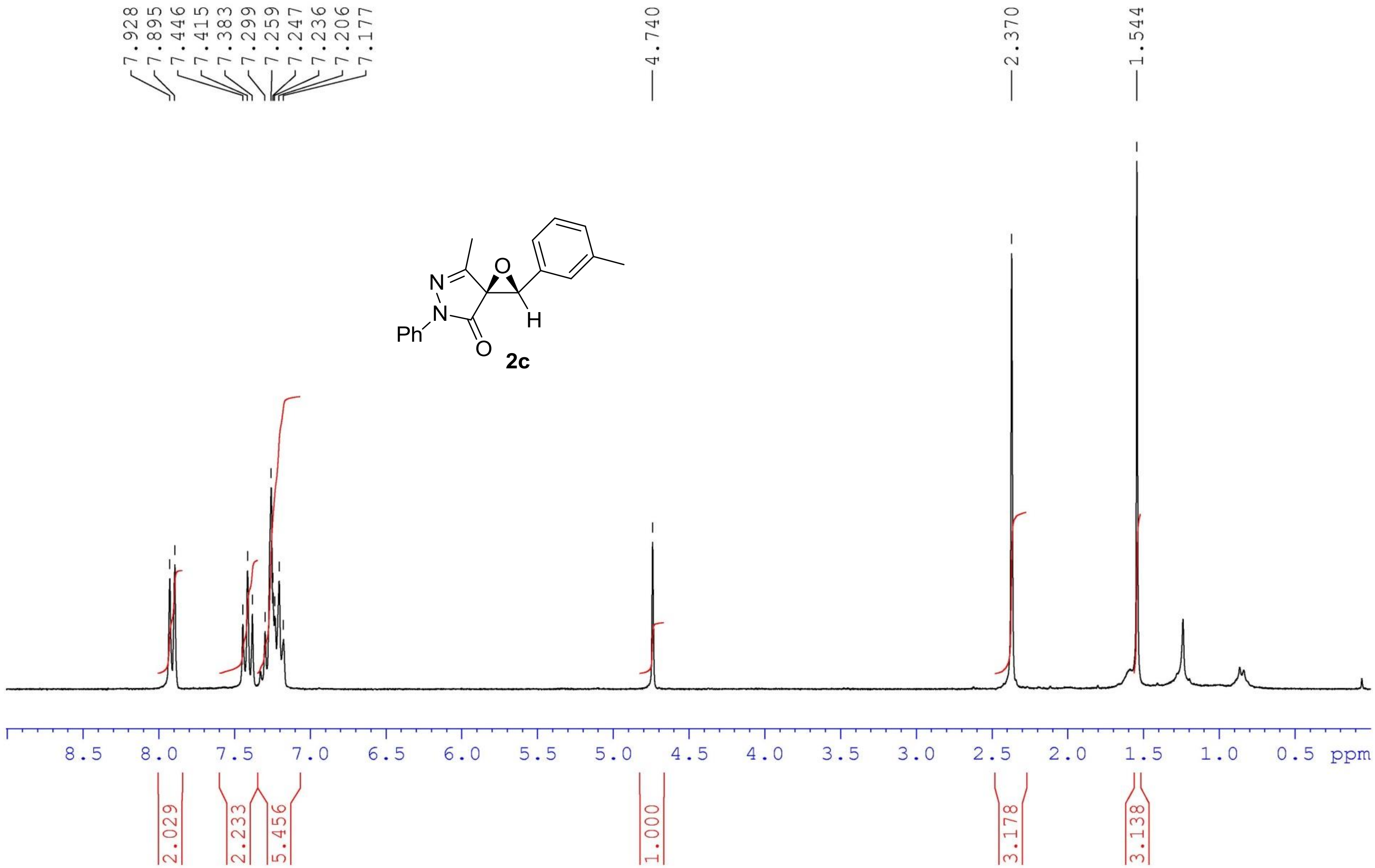
^{1}H NMR in $CDCl_3$ (400 MHz)



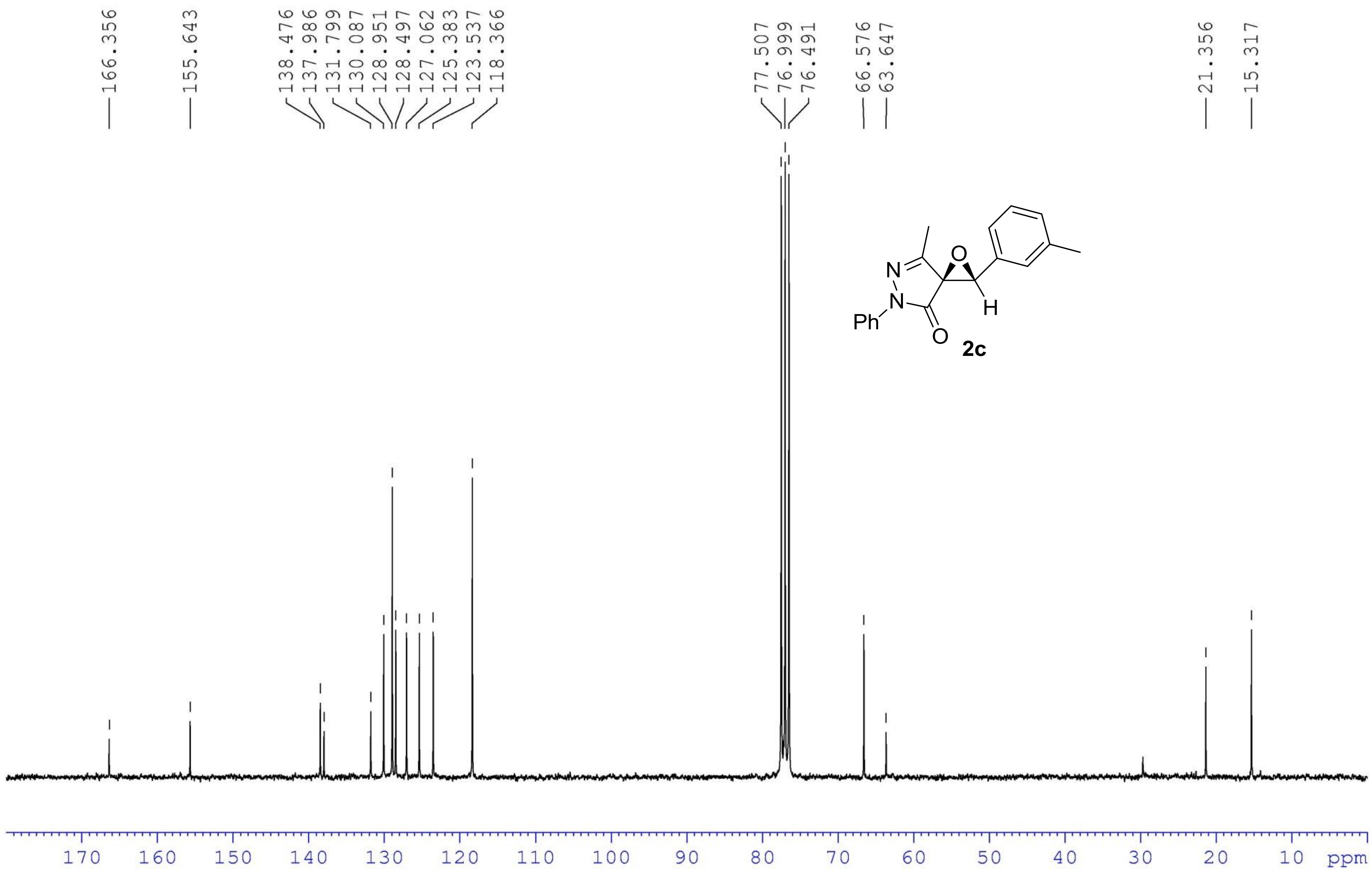
^{13}C NMR in $CDCl_3$ (100 MHz)



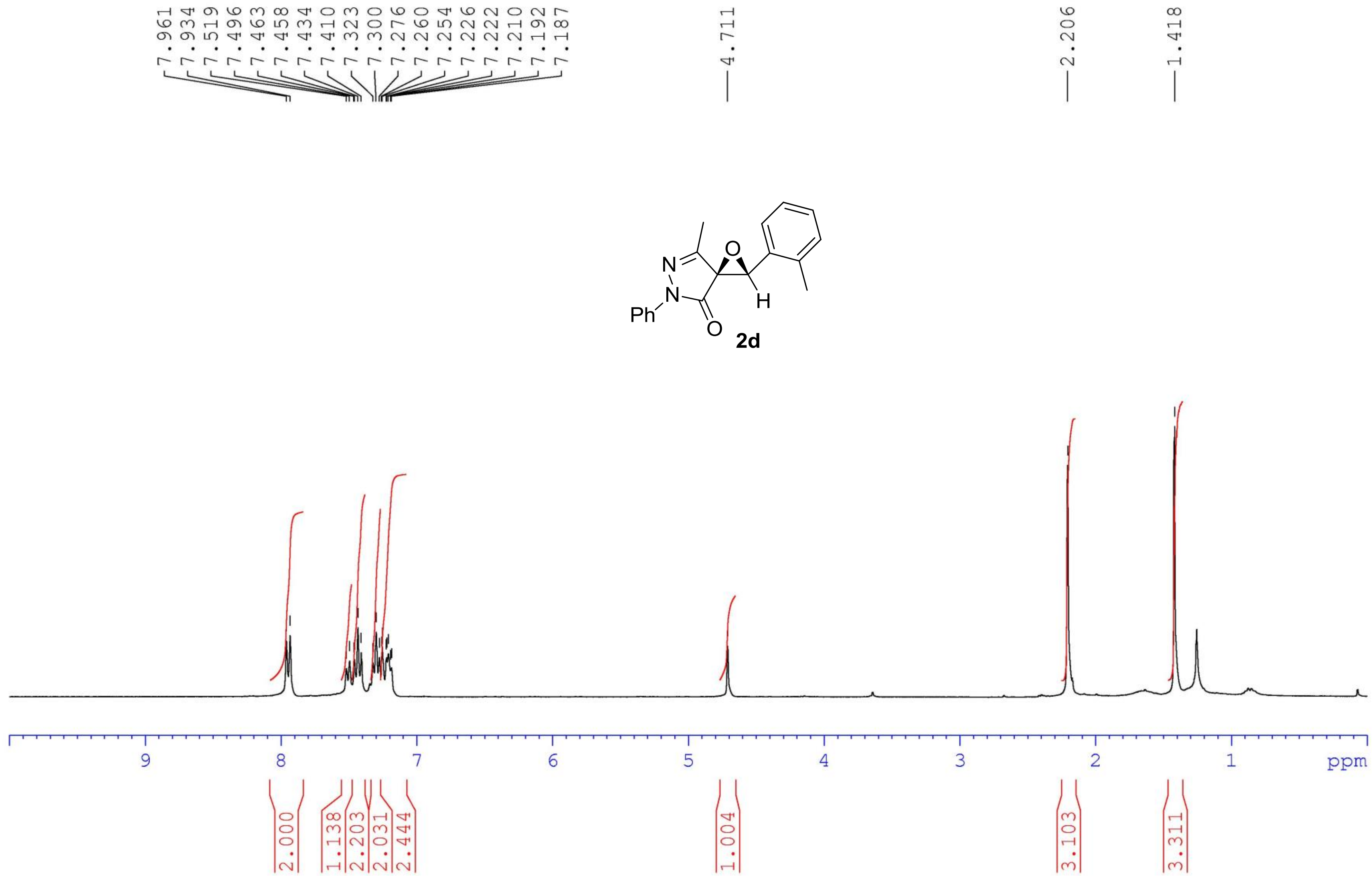
^{1}H NMR in $CDCl_3$ (250 MHz)



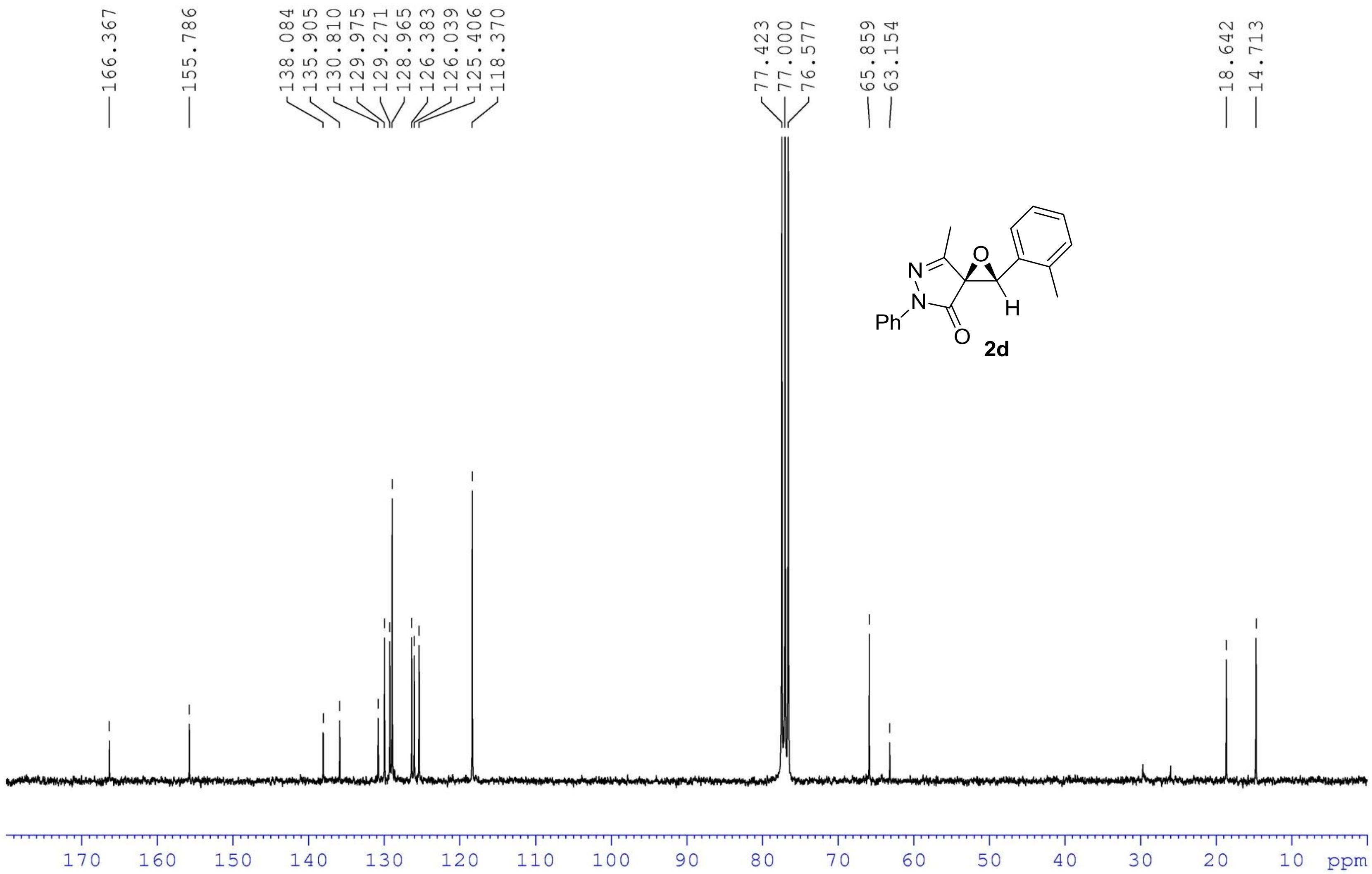
^{13}C NMR in $CDCl_3$ (62.5 MHz)



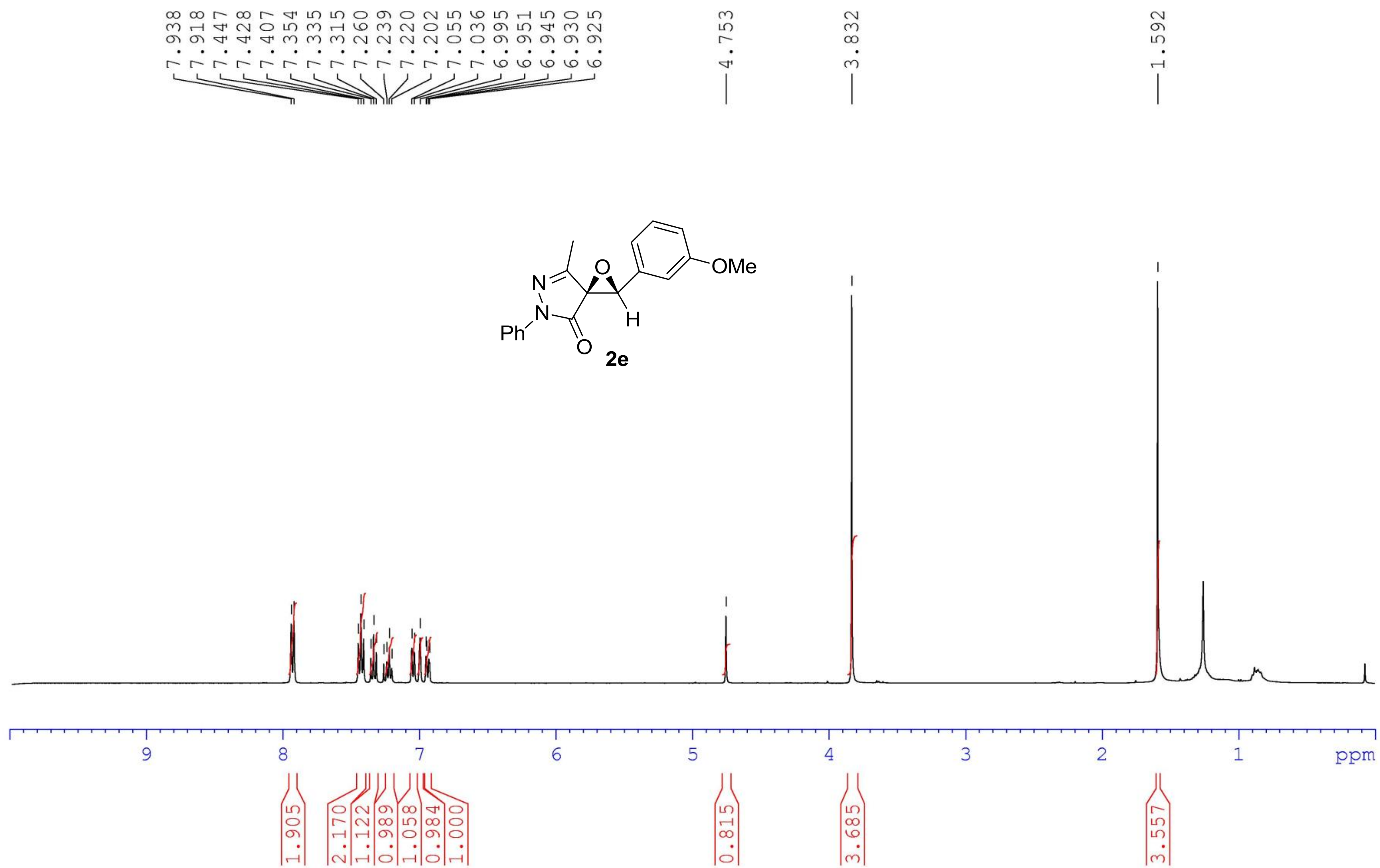
^{1}H NMR in $CDCl_3$ (300 MHz)



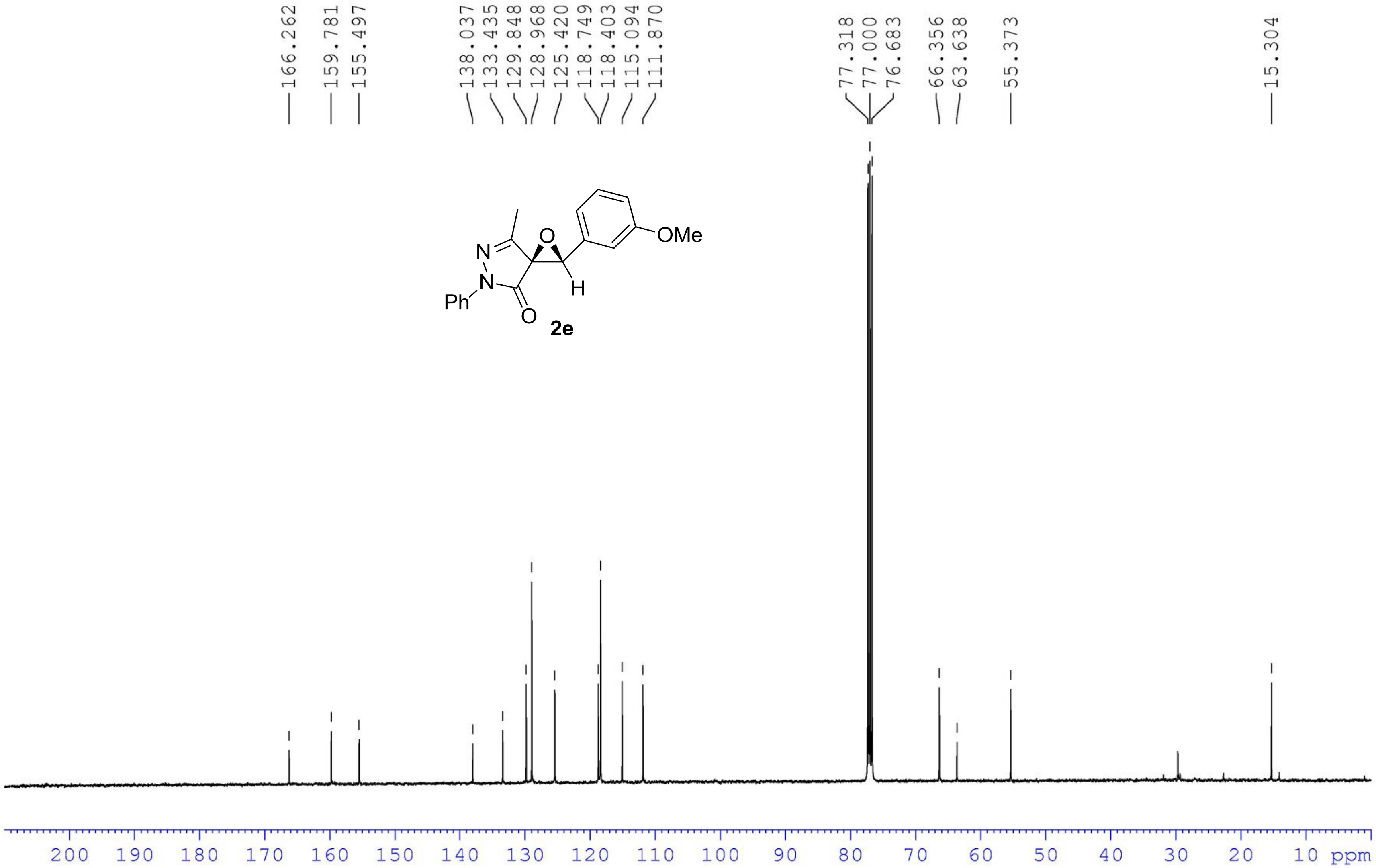
^{13}C NMR in $CDCl_3$ (75 MHz)



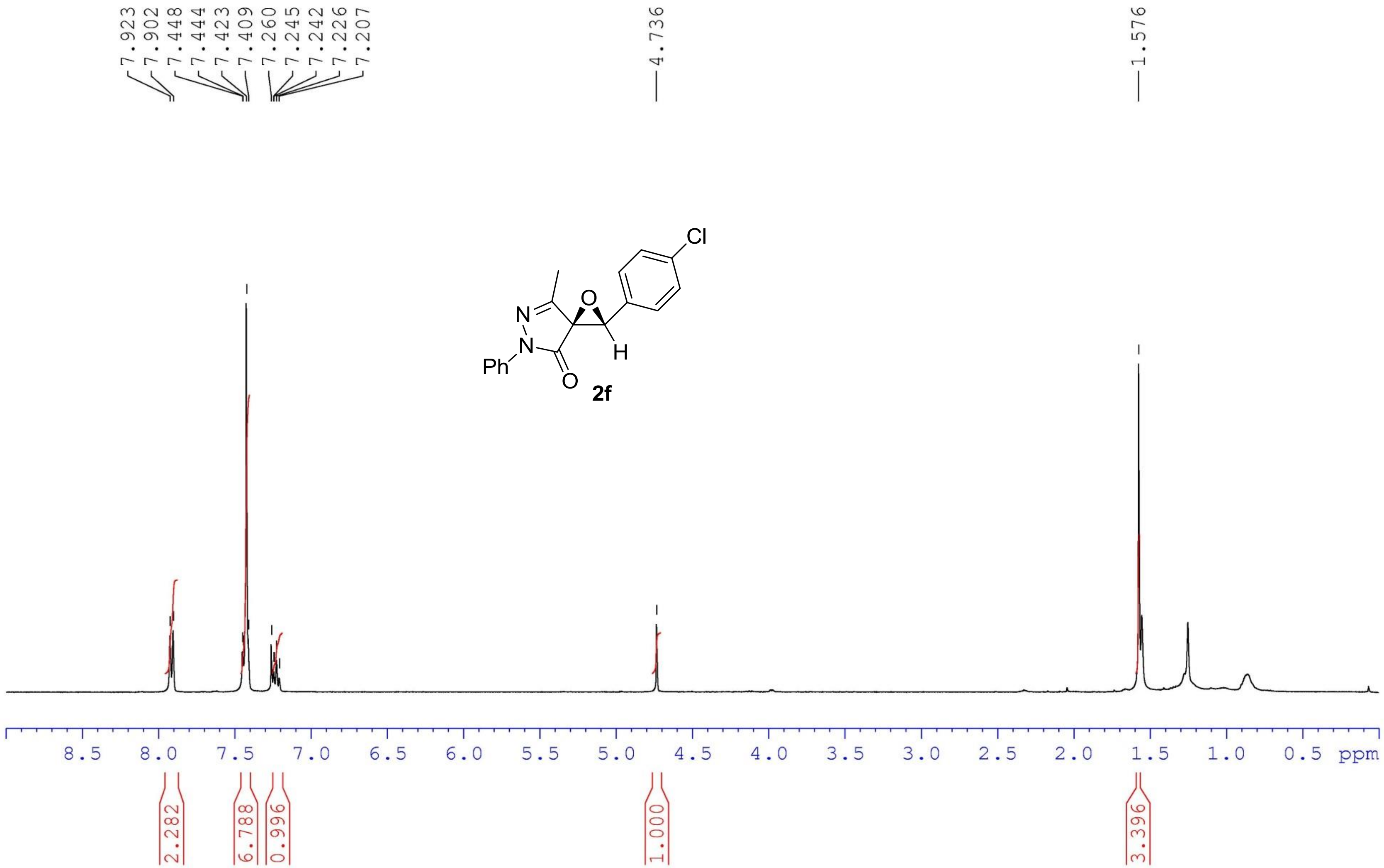
^{1}H NMR in $CDCl_3$ (400 MHz)



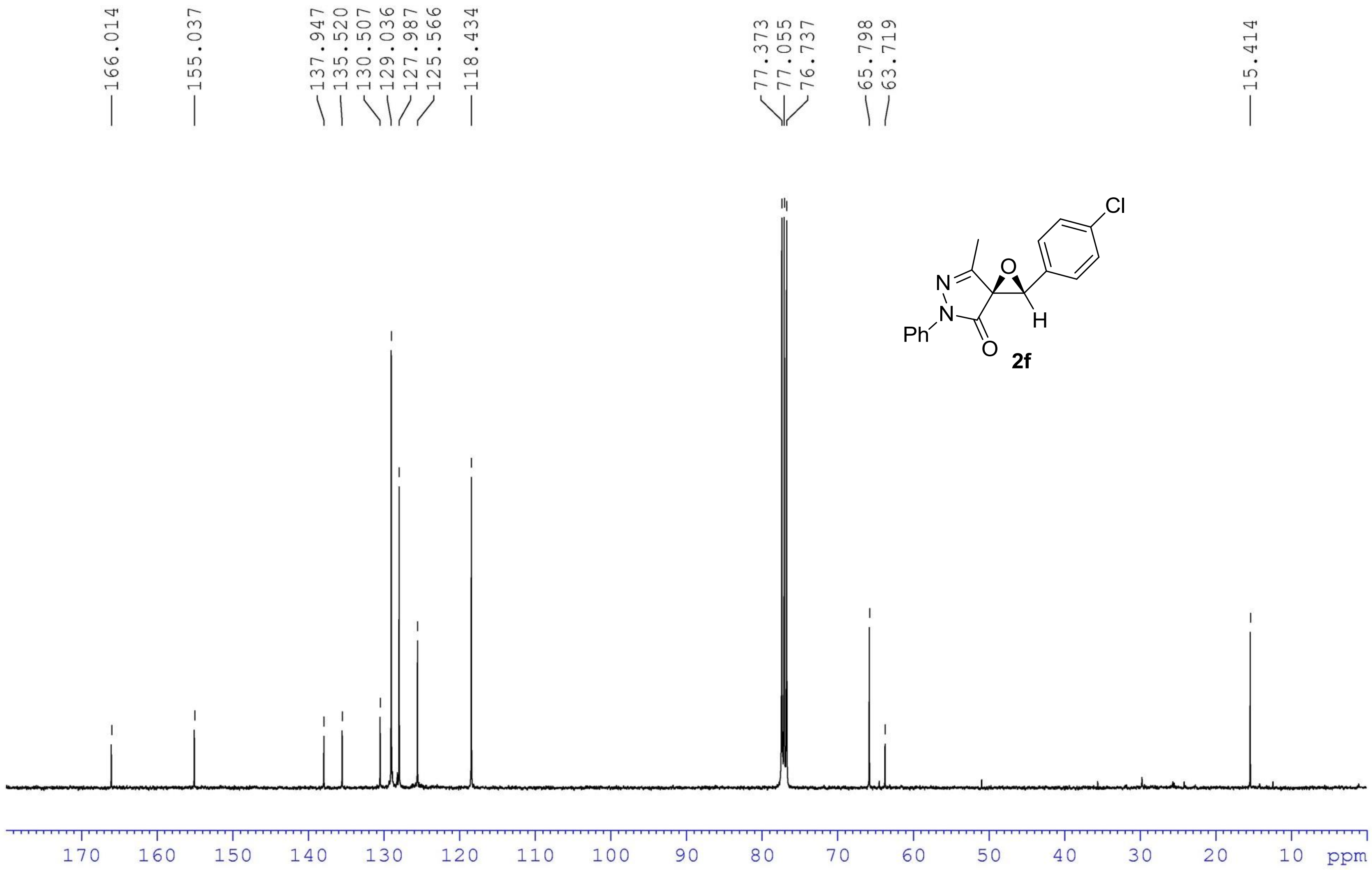
^{13}C NMR in $CDCl_3$ (100 MHz)



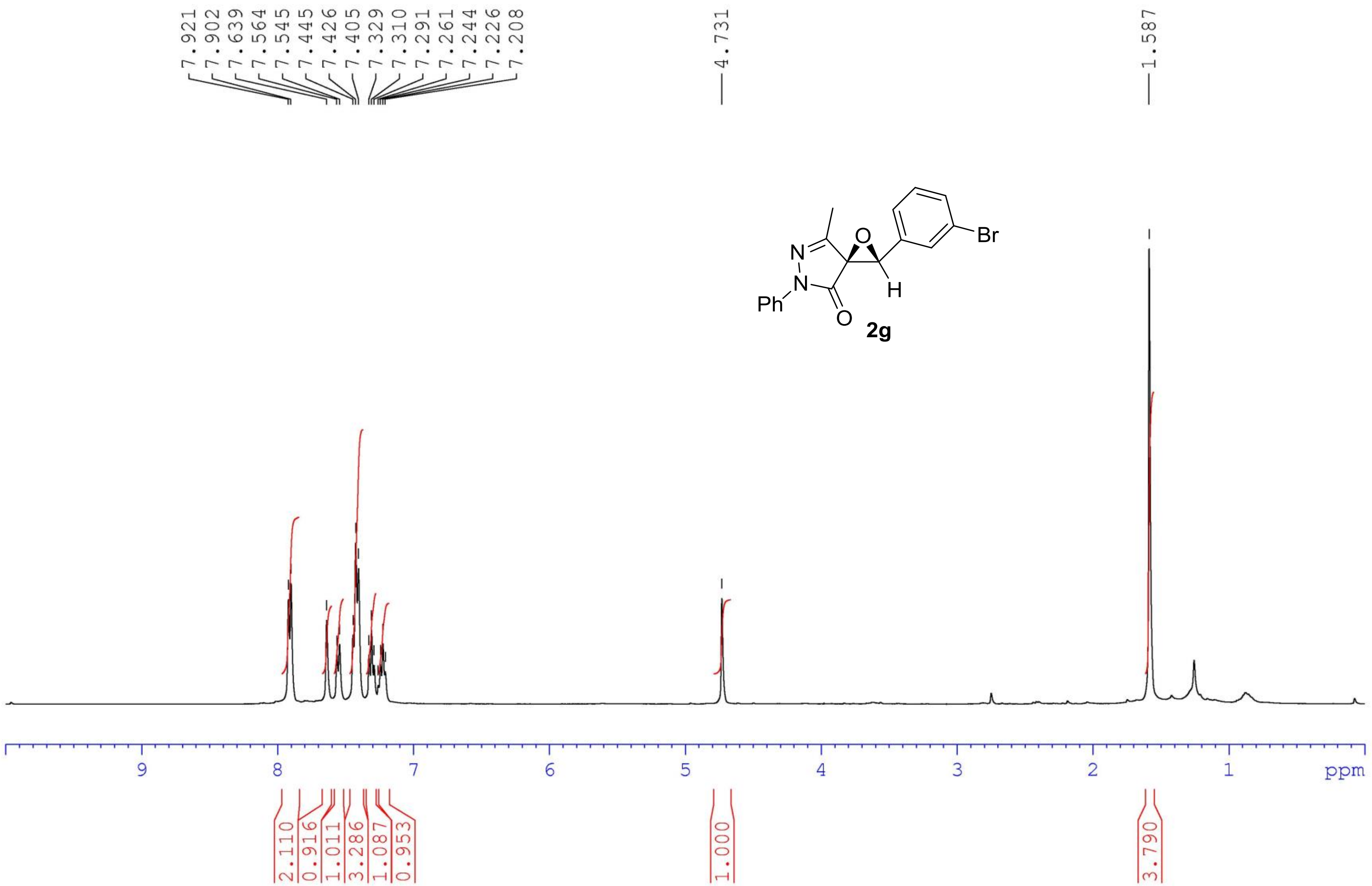
^1H NMR in $CDCl_3$ (400 MHz)



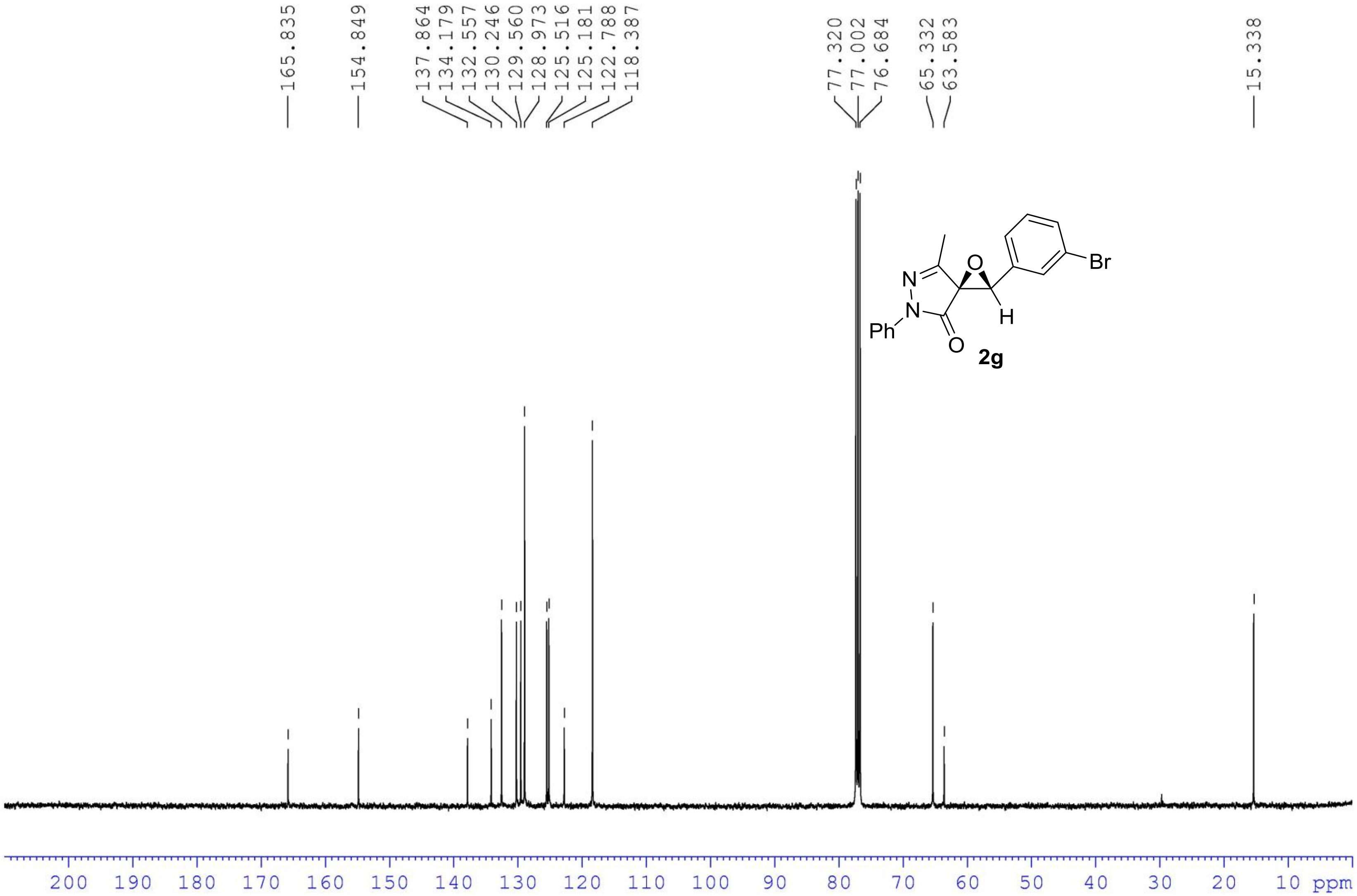
^{13}C NMR in $CDCl_3$ (100 MHz)



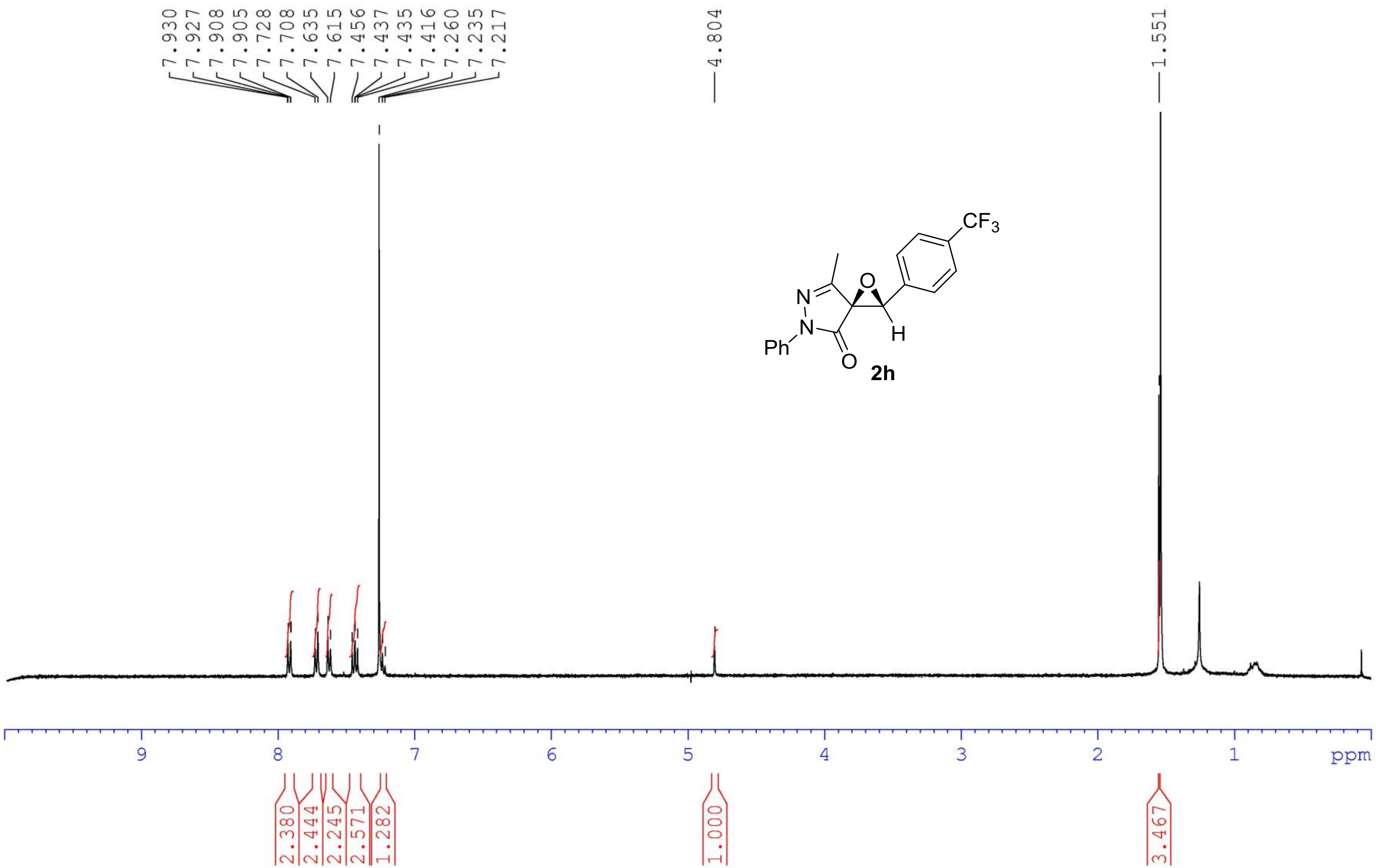
^{1}H NMR in $CDCl_3$ (400 MHz)



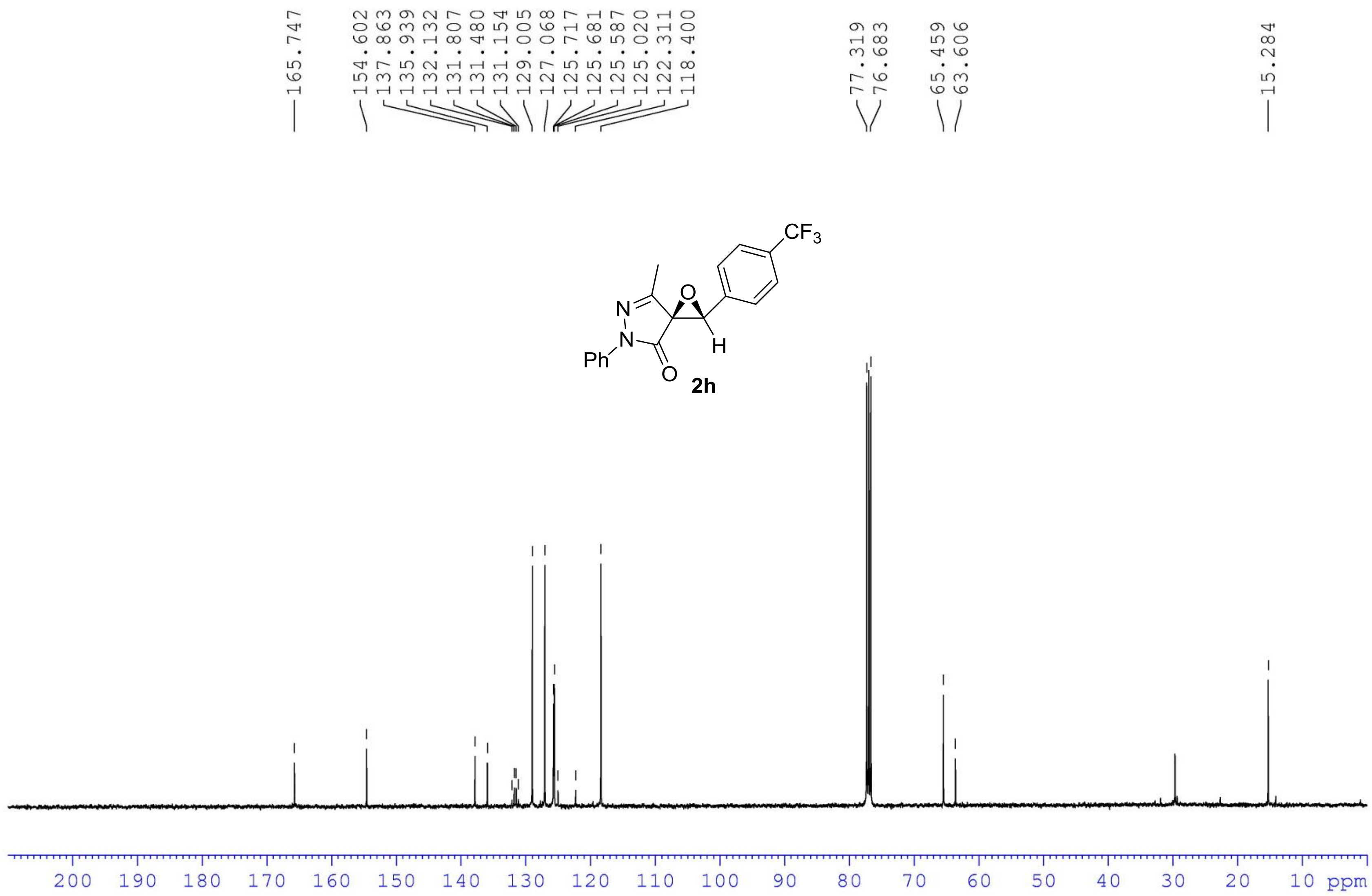
^{13}C NMR in $CDCl_3$ (100 MHz)



^{1}H NMR in $CDCl_3$ (400 MHz)

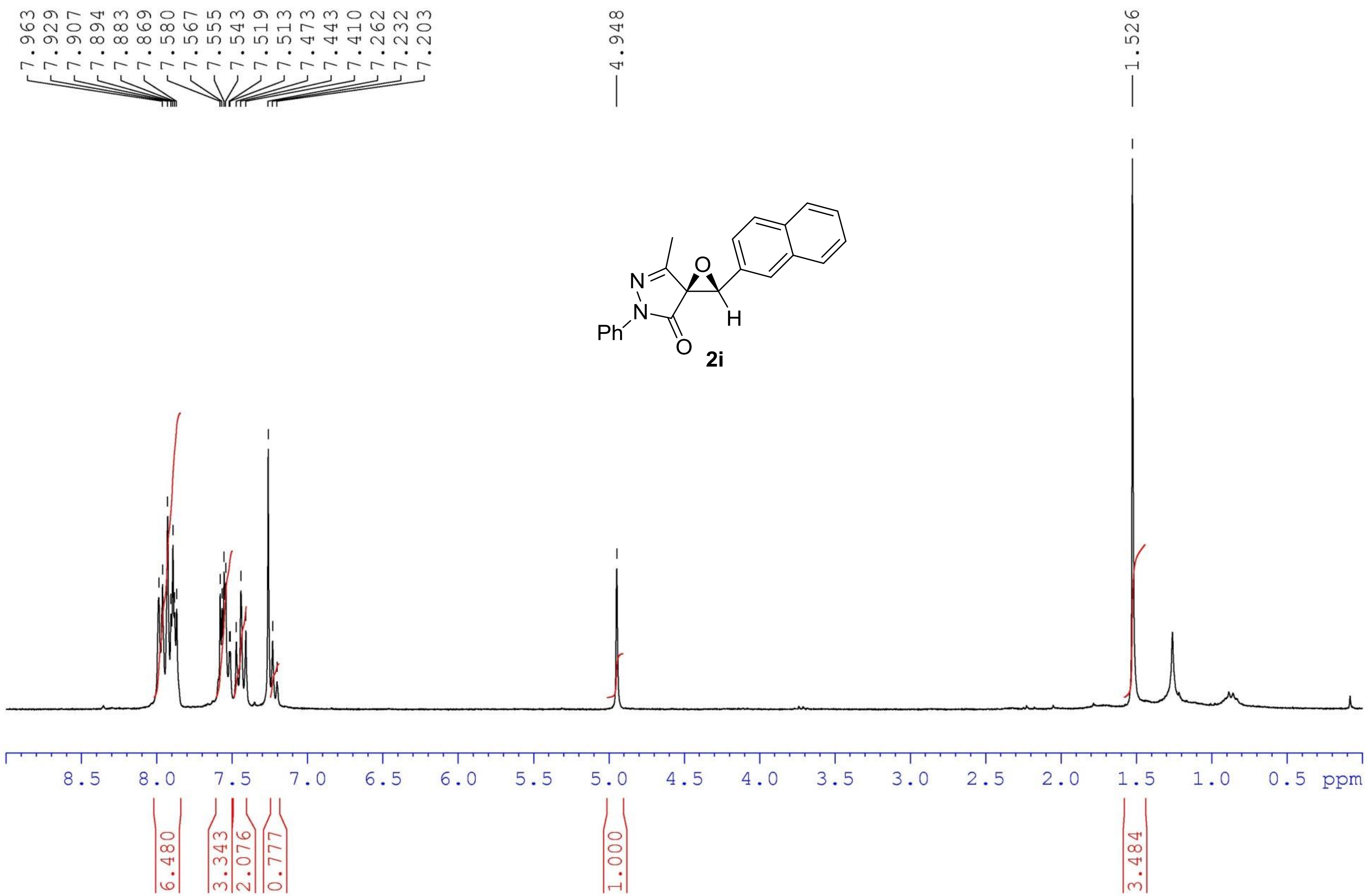


^{13}C NMR in $CDCl_3$ (100 MHz)

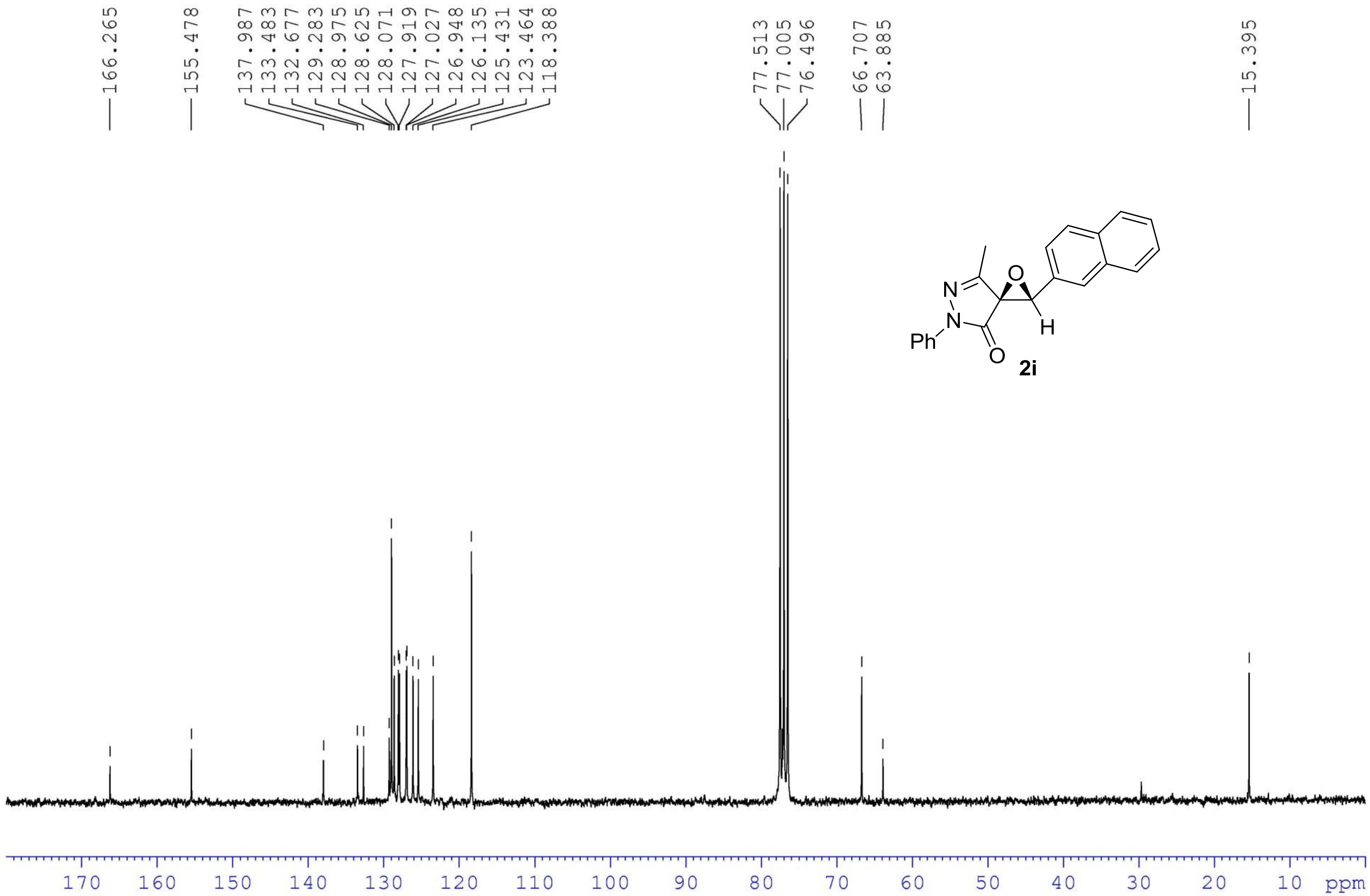


2h

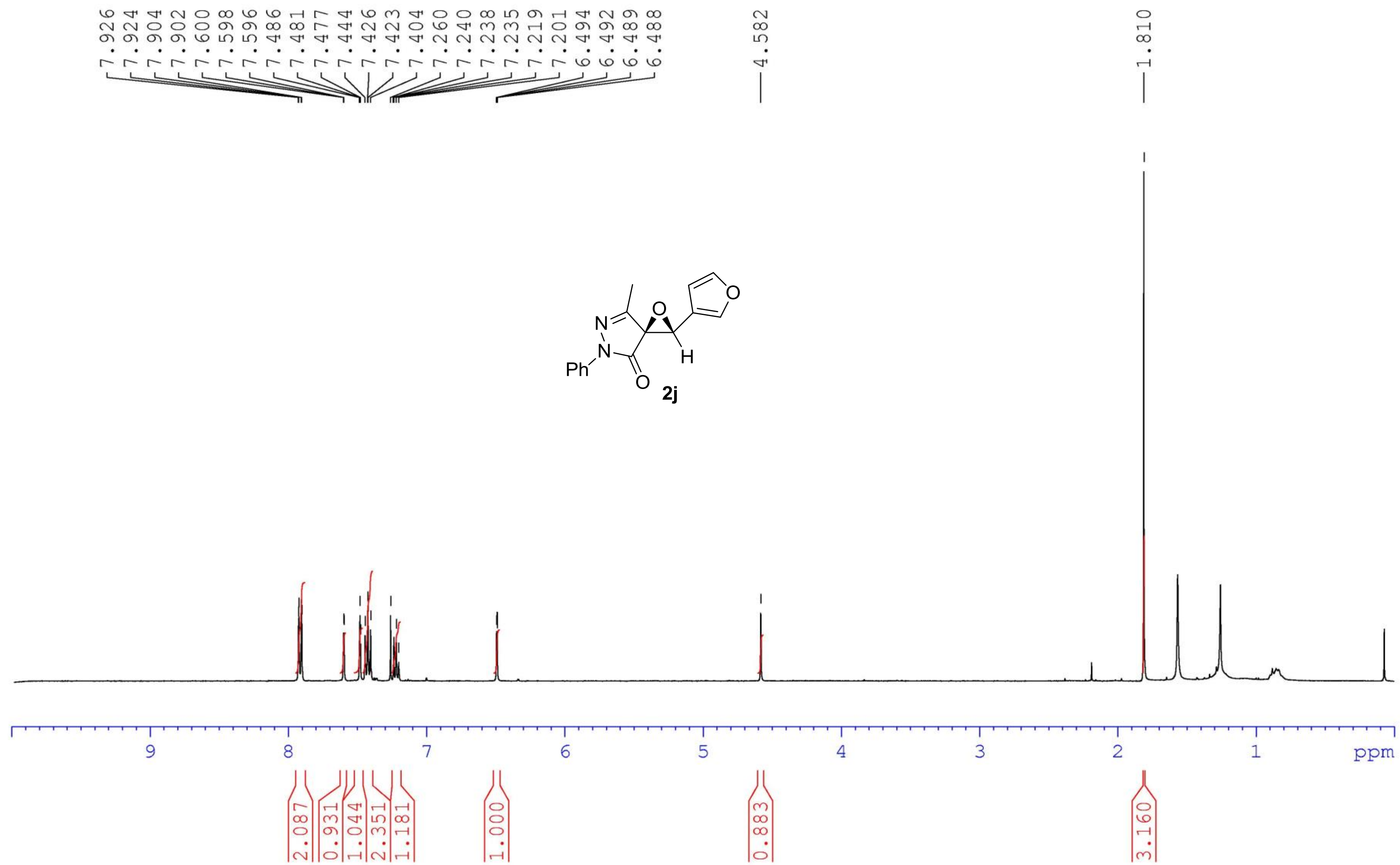
^{1}H NMR in $CDCl_3$ (250 MHz)



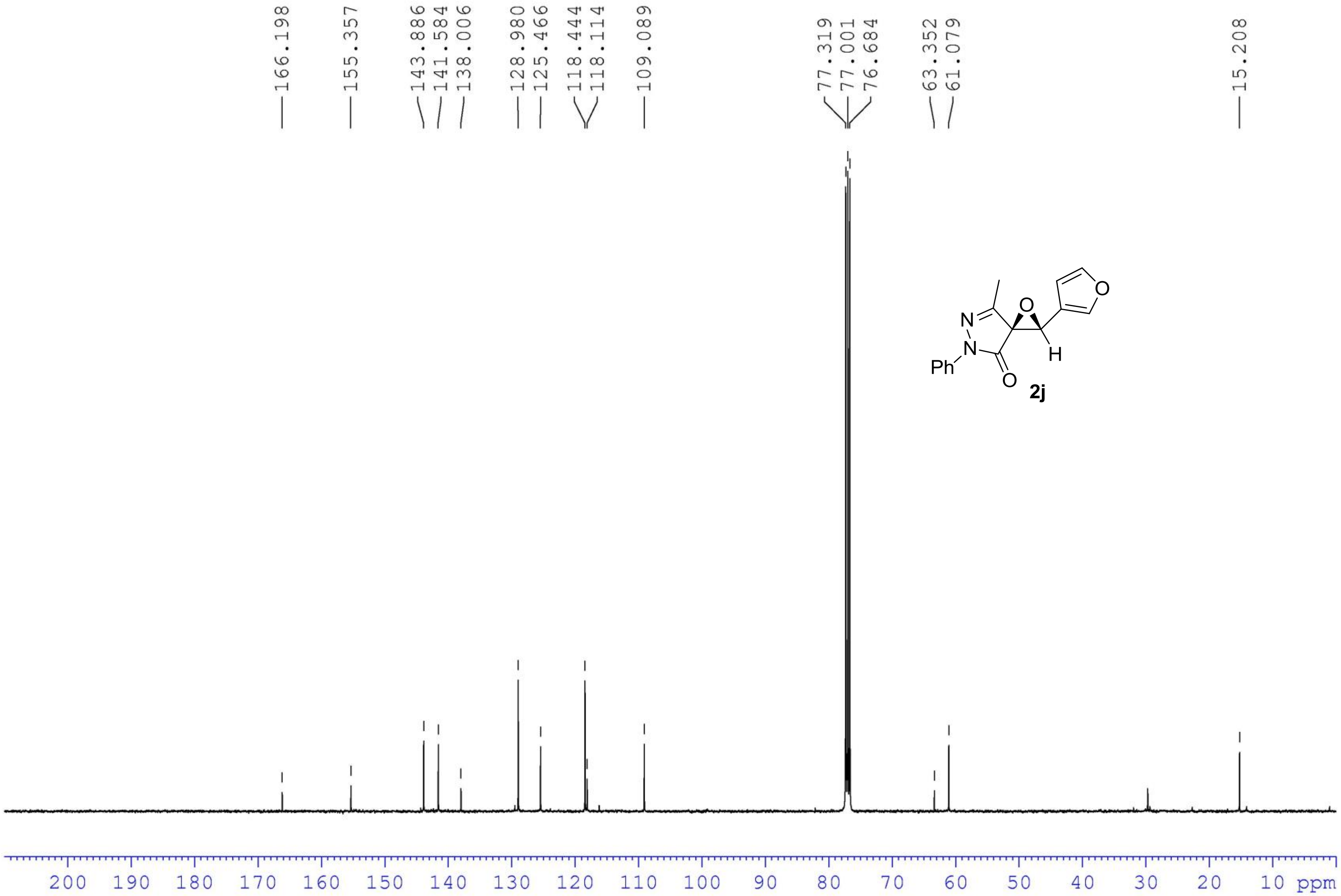
^{13}C NMR in $CDCl_3$ (62.5 MHz)



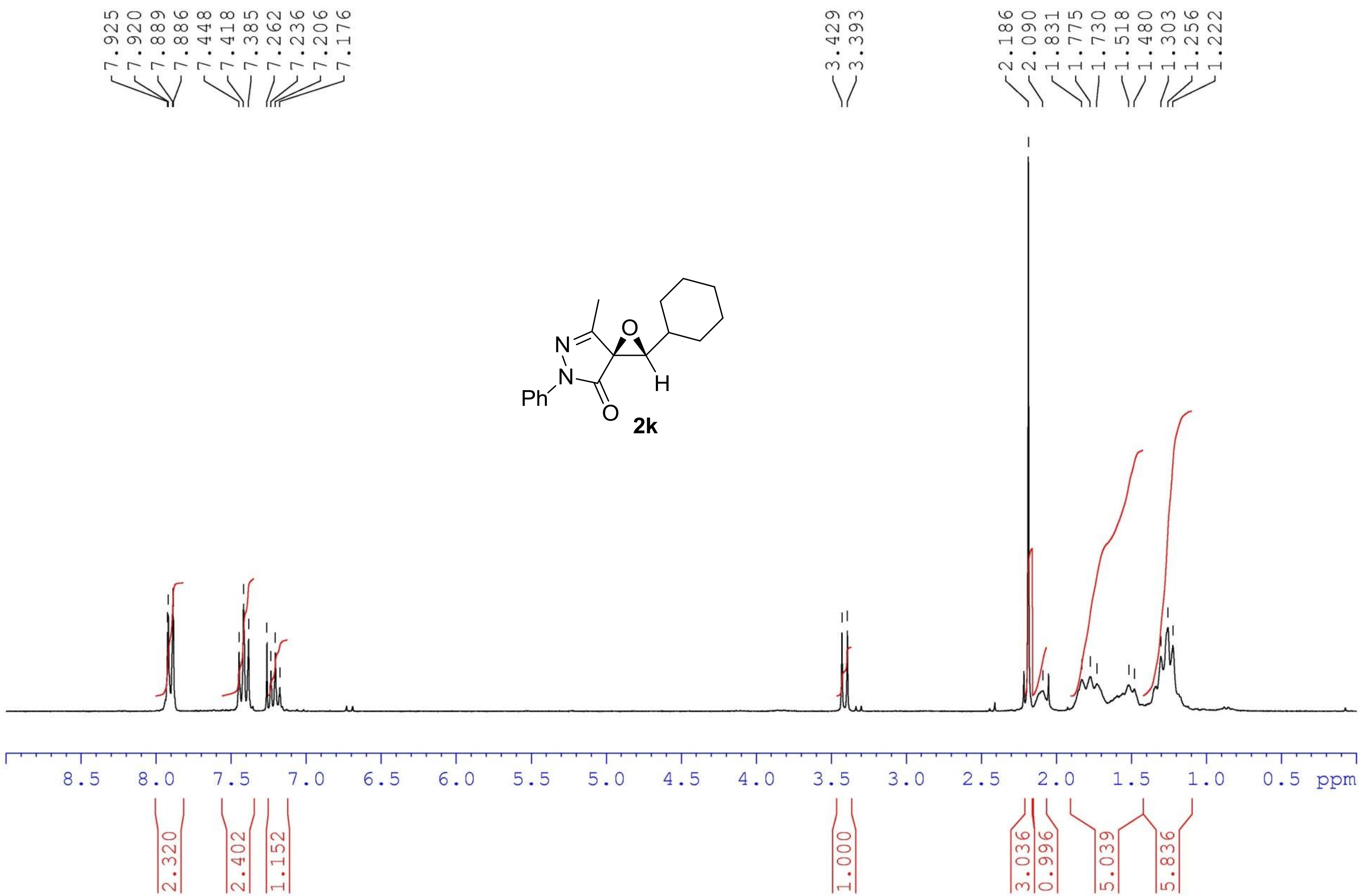
^{1}H NMR in $CDCl_3$ (400 MHz)



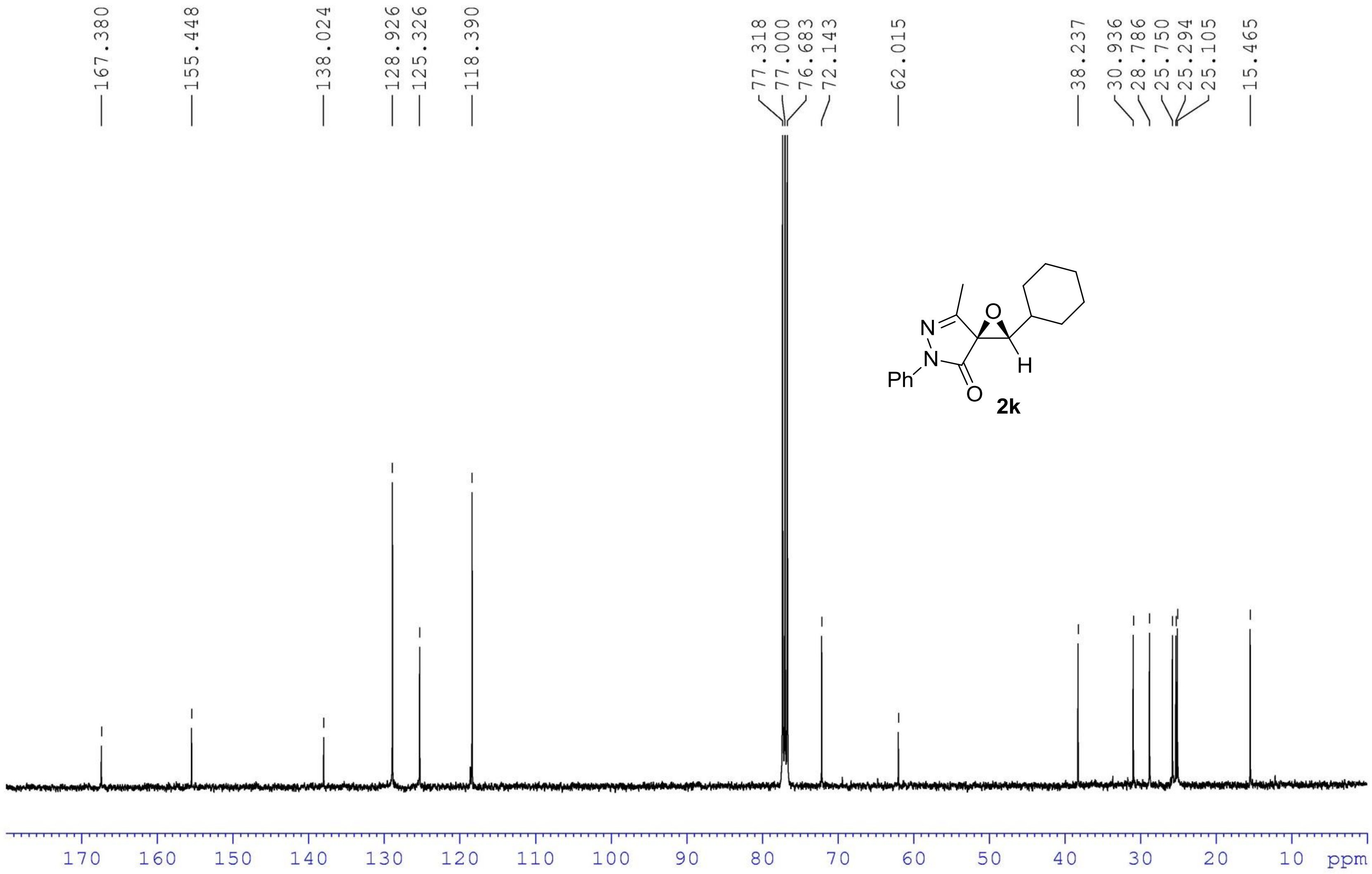
^{13}C NMR in $CDCl_3$ (100 MHz)



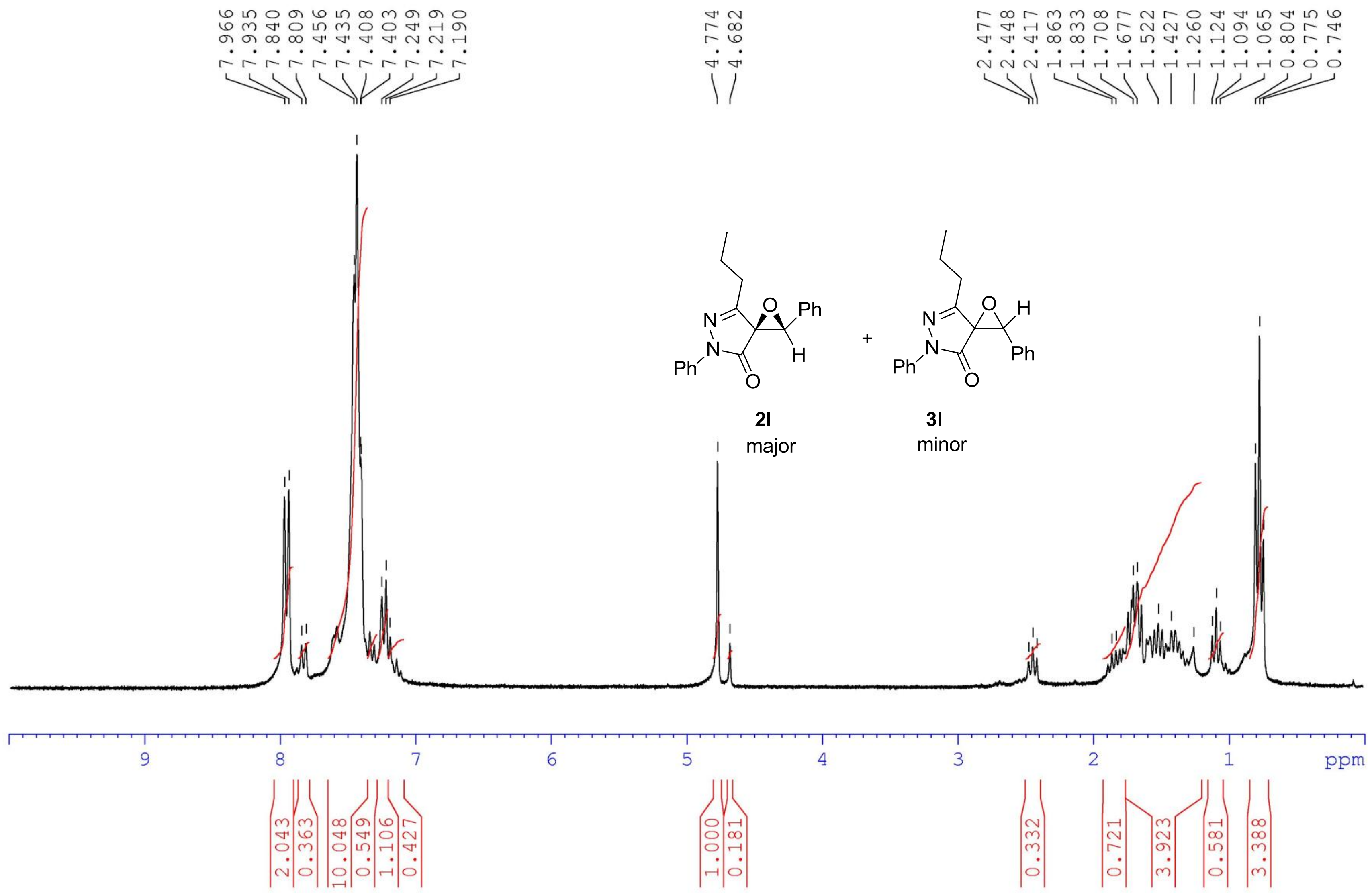
^{1}H NMR in $CDCl_3$ (250 MHz)



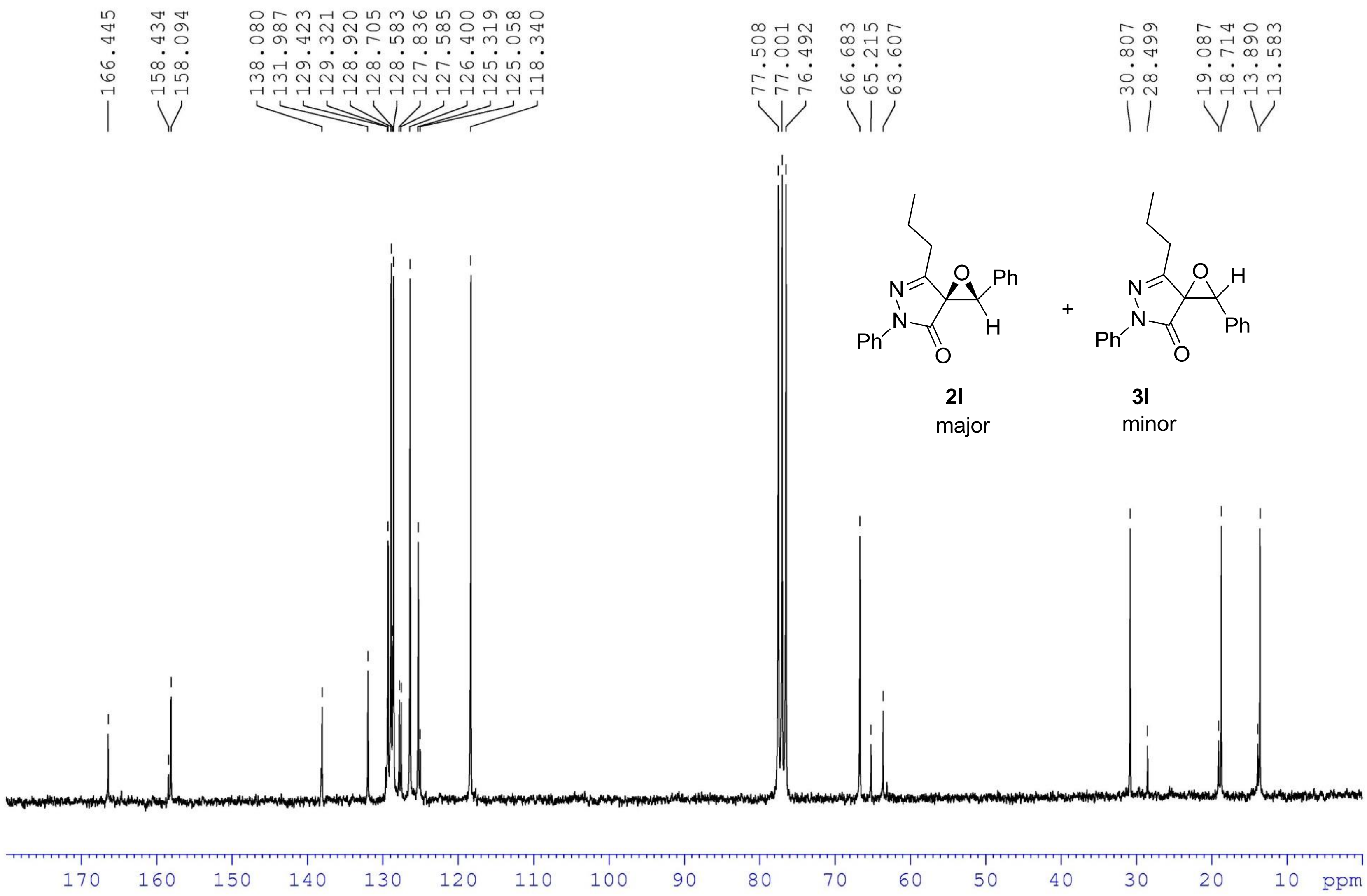
^{13}C NMR in $CDCl_3$ (100 MHz)



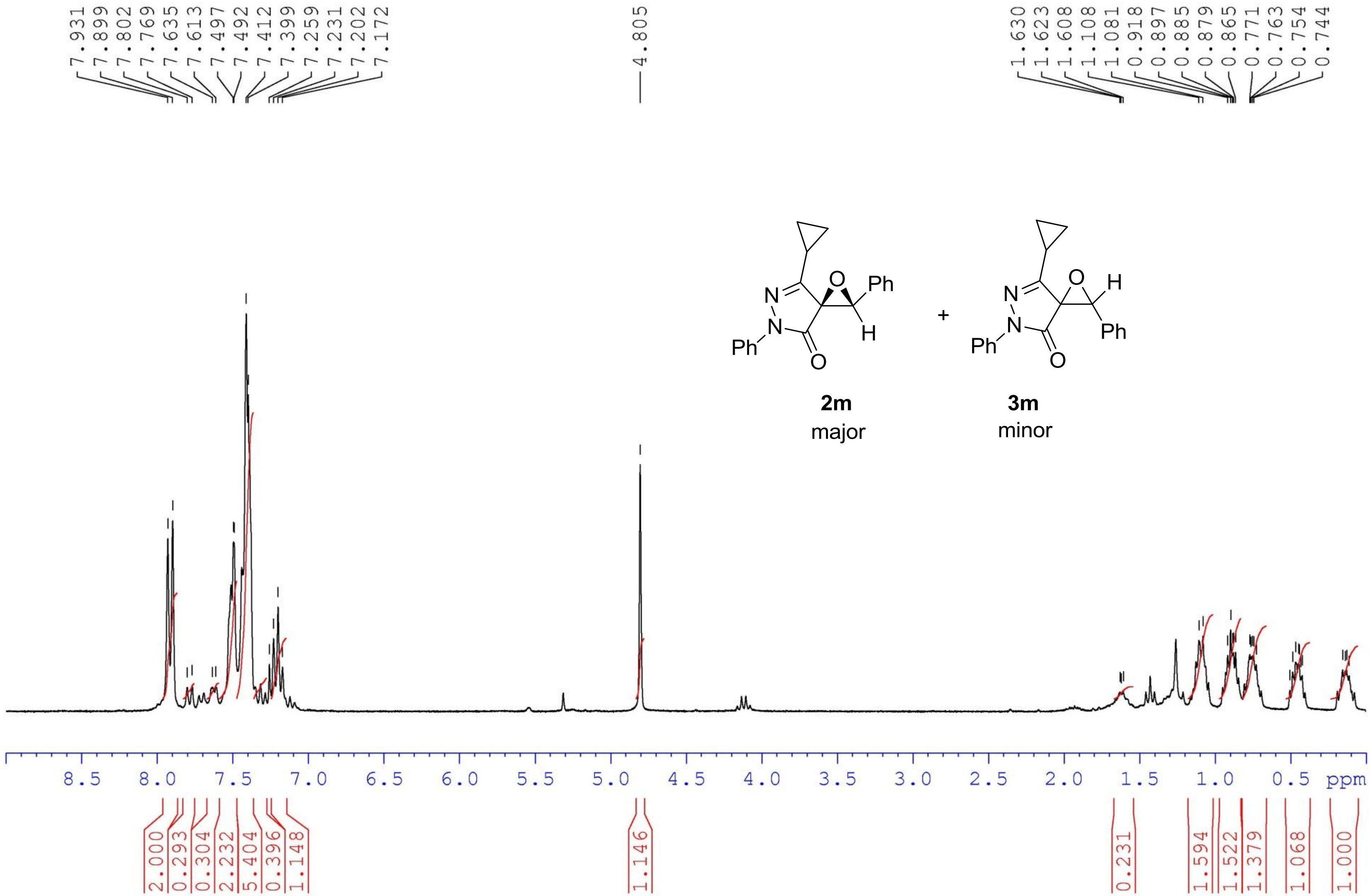
^{1}H NMR in $CDCl_3$ (250 MHz)



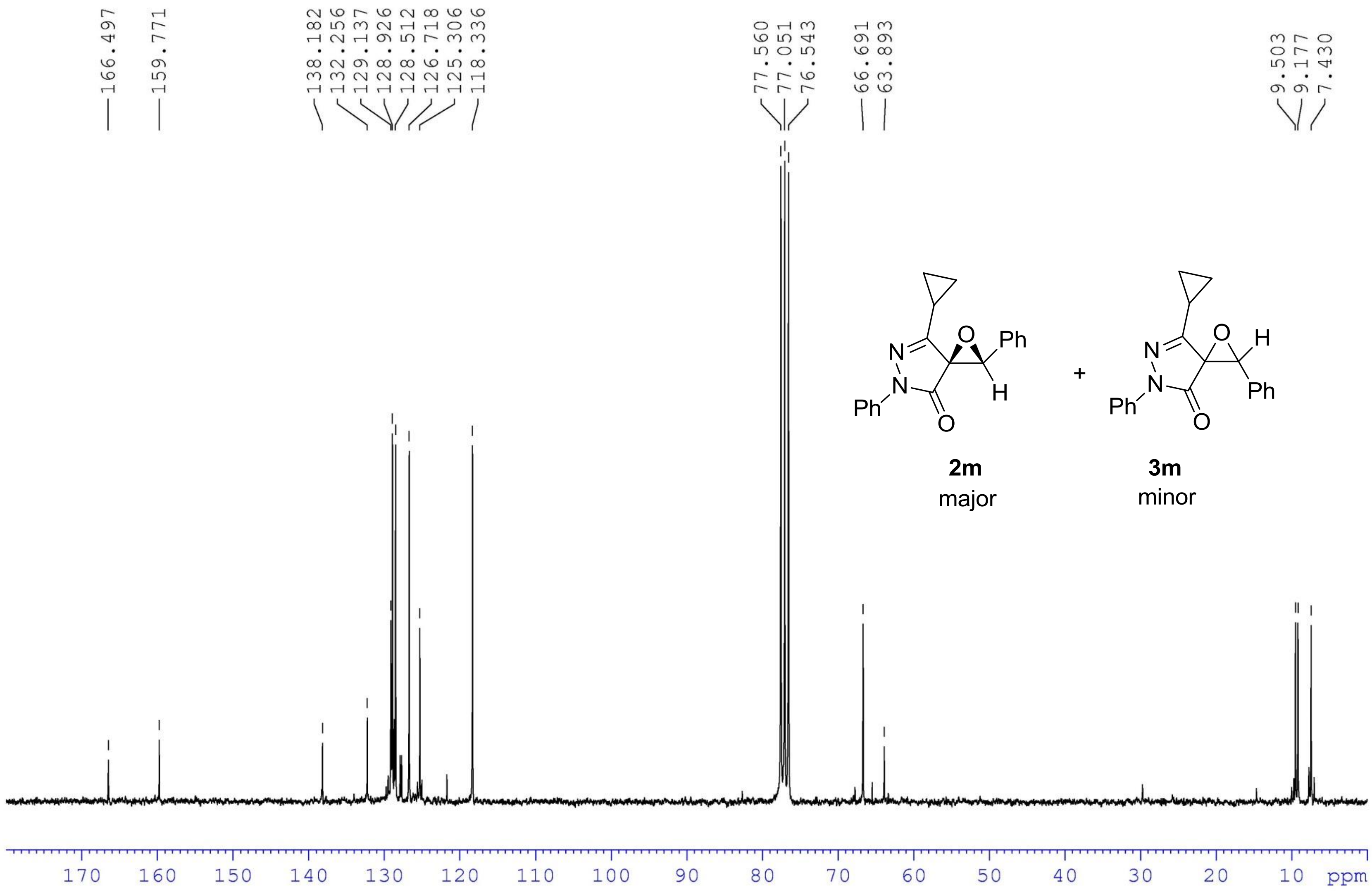
^{13}C NMR in $CDCl_3$ (62.5 MHz)



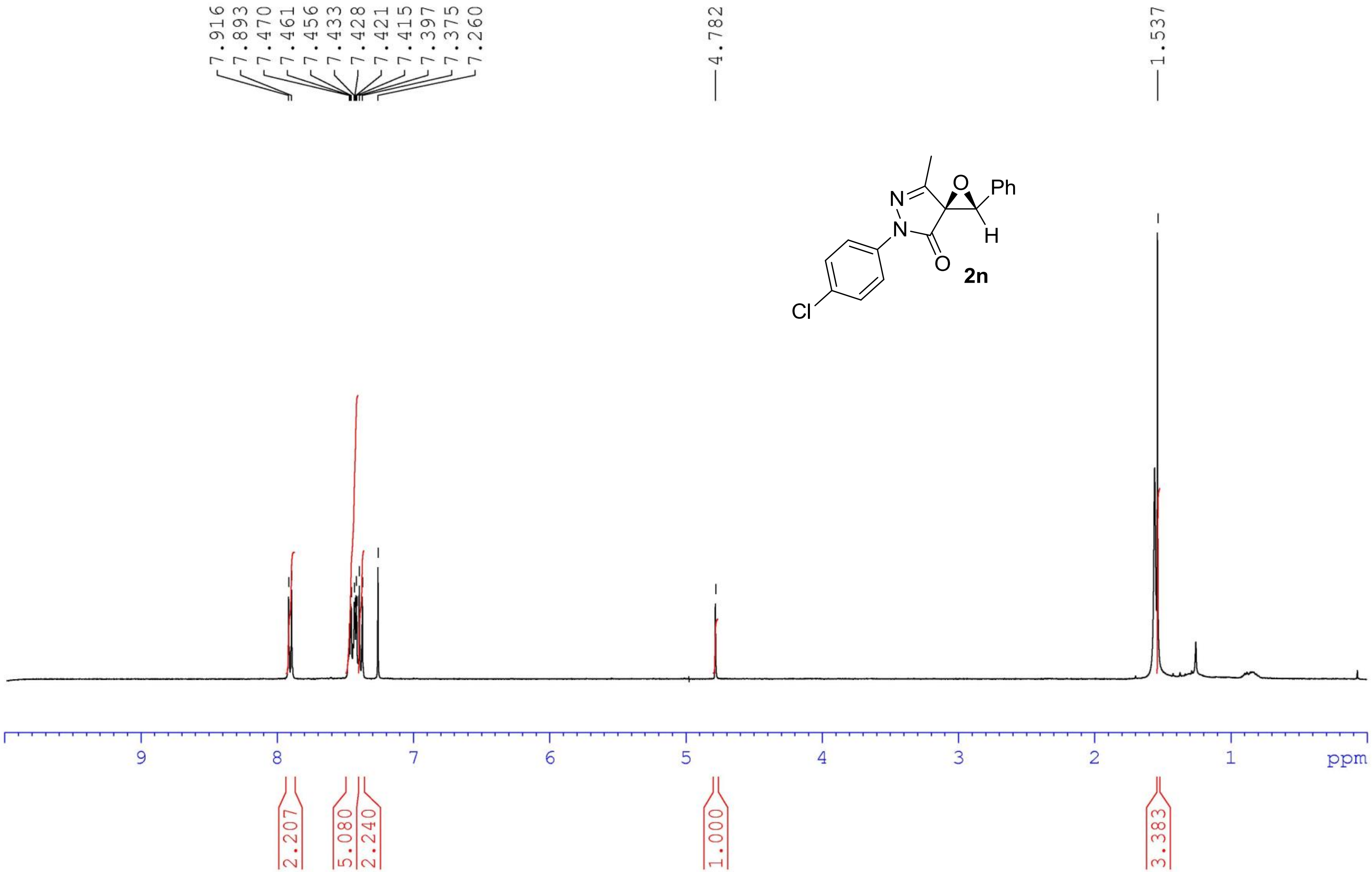
^{1}H NMR in $CDCl_3$ (250 MHz)



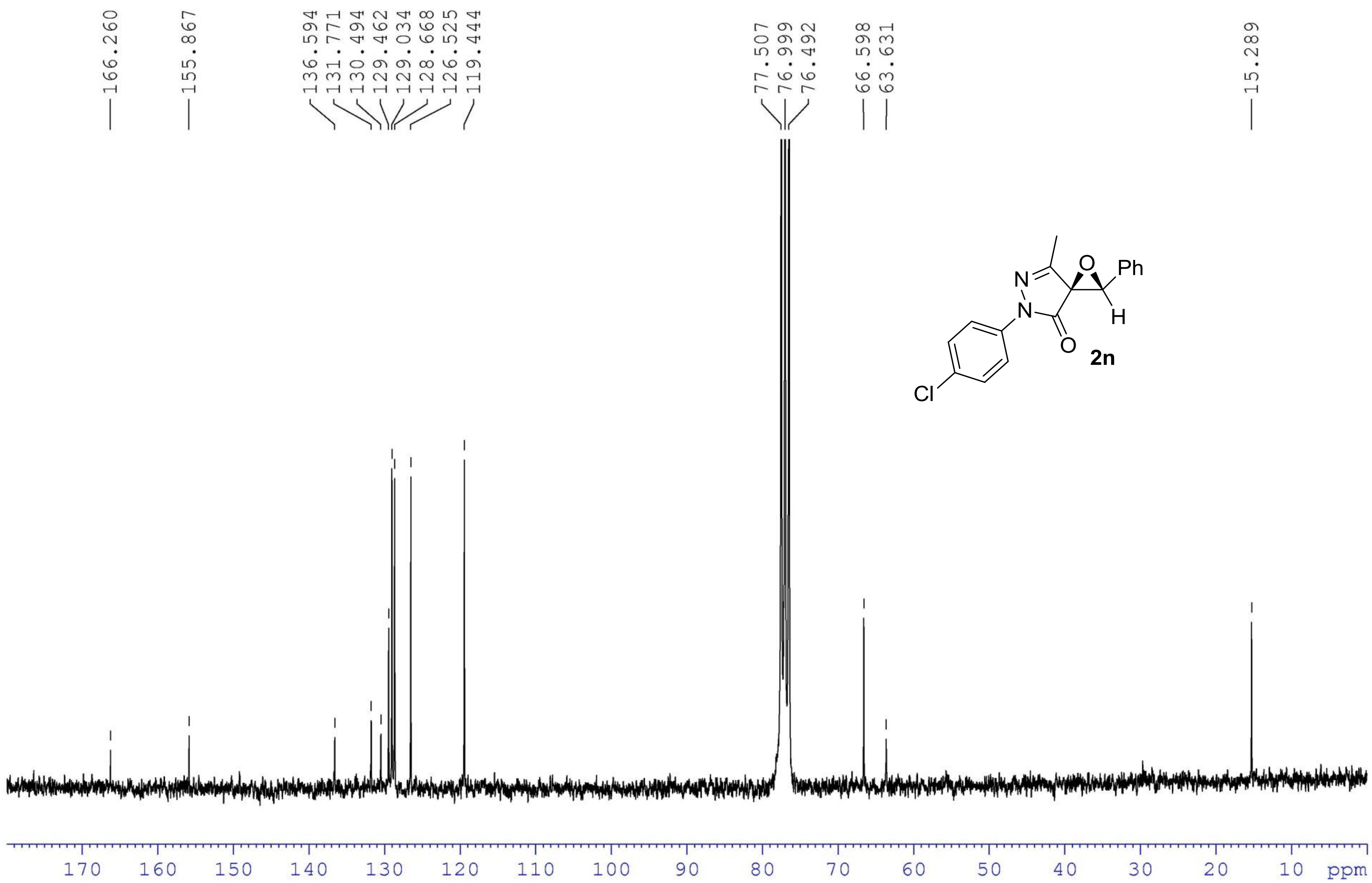
^{13}C NMR in $CDCl_3$ (62.5 MHz)



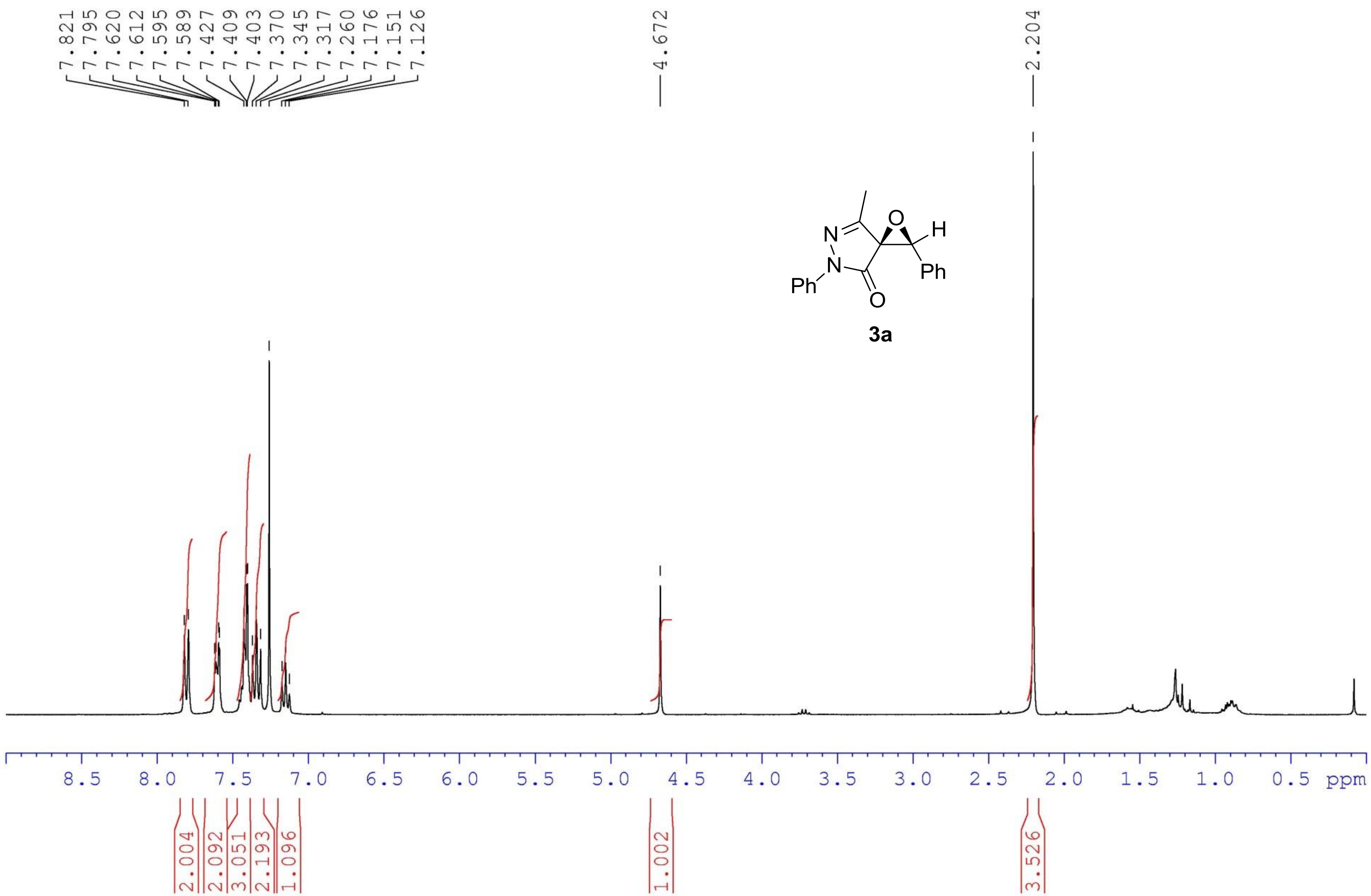
[1]H NMR in $CDCl_3$ (400 MHz)



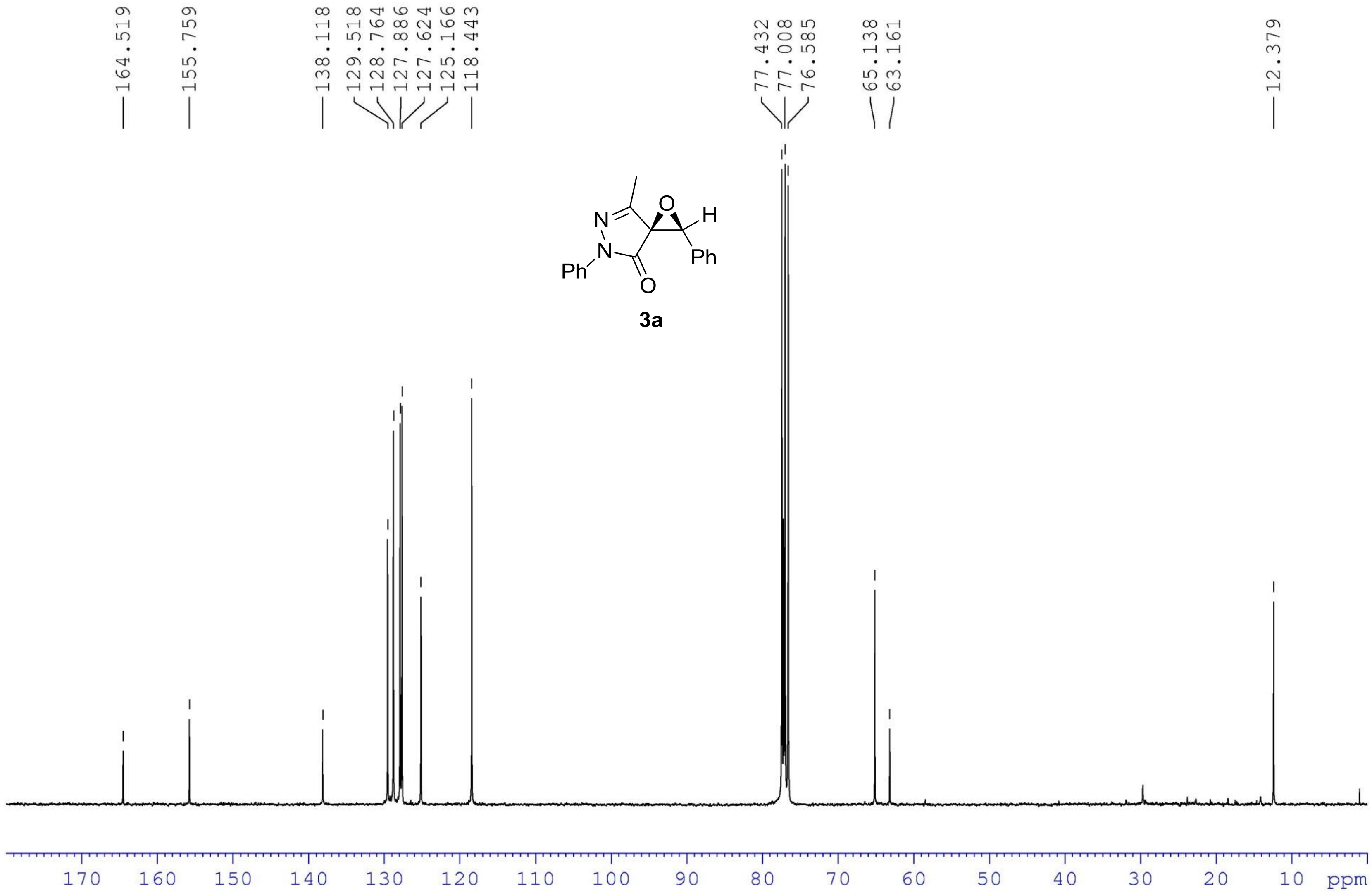
^{13}C NMR in $CDCl_3$ (62.5 MHz)



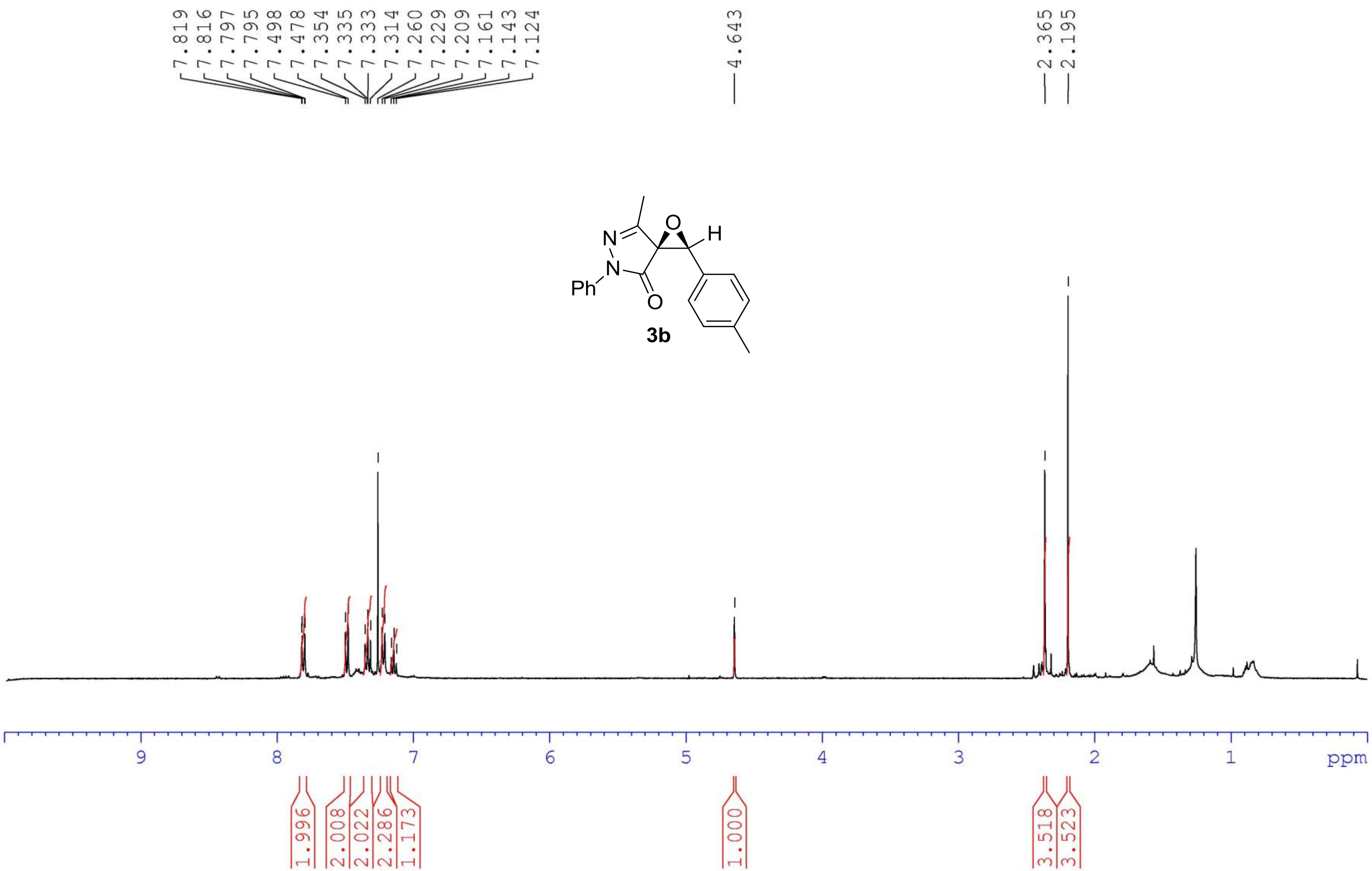
^{1}H NMR in $CDCl_3$ (300 MHz)



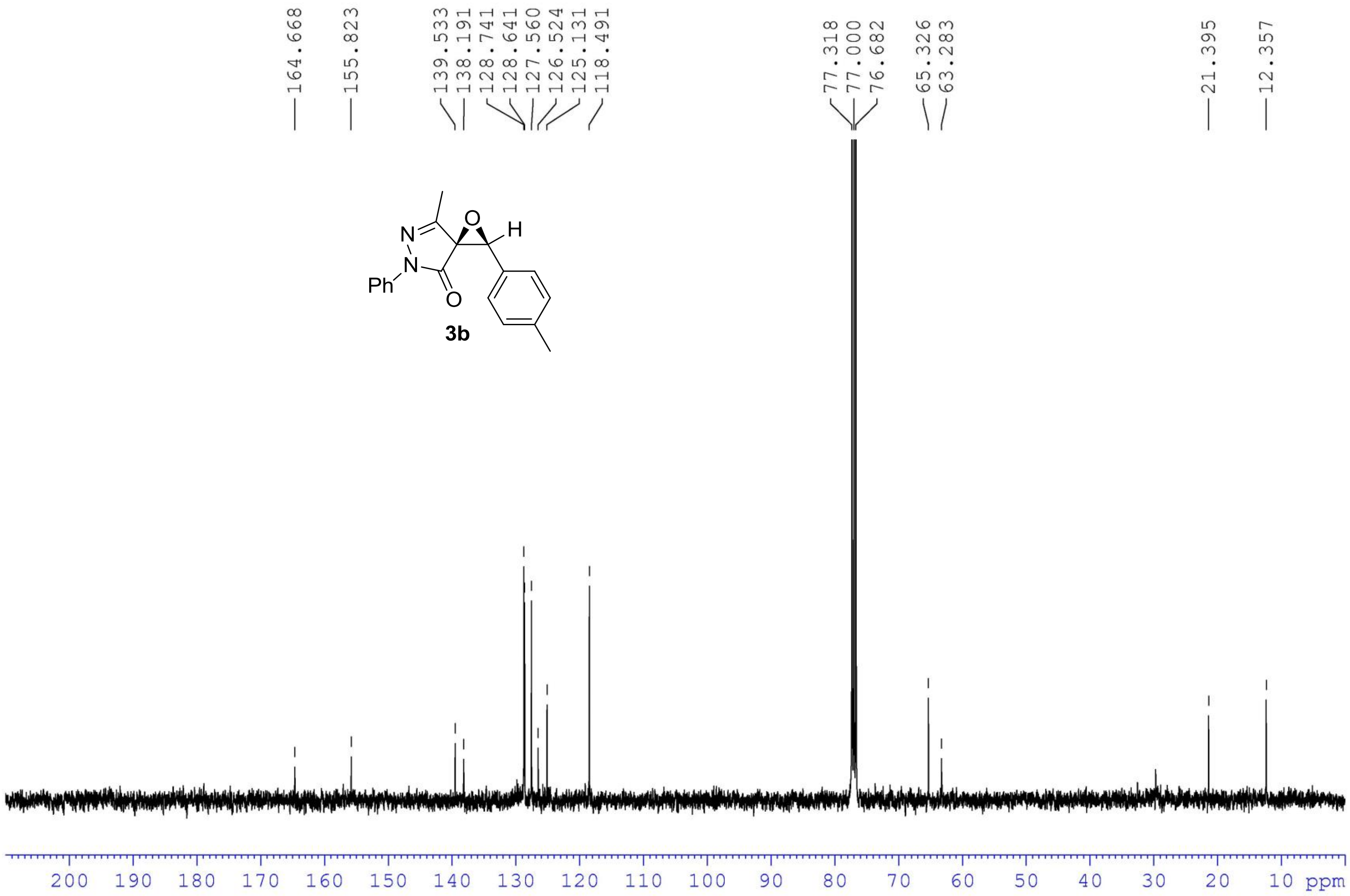
^{13}C NMR in $CDCl_3$ (75 MHz)



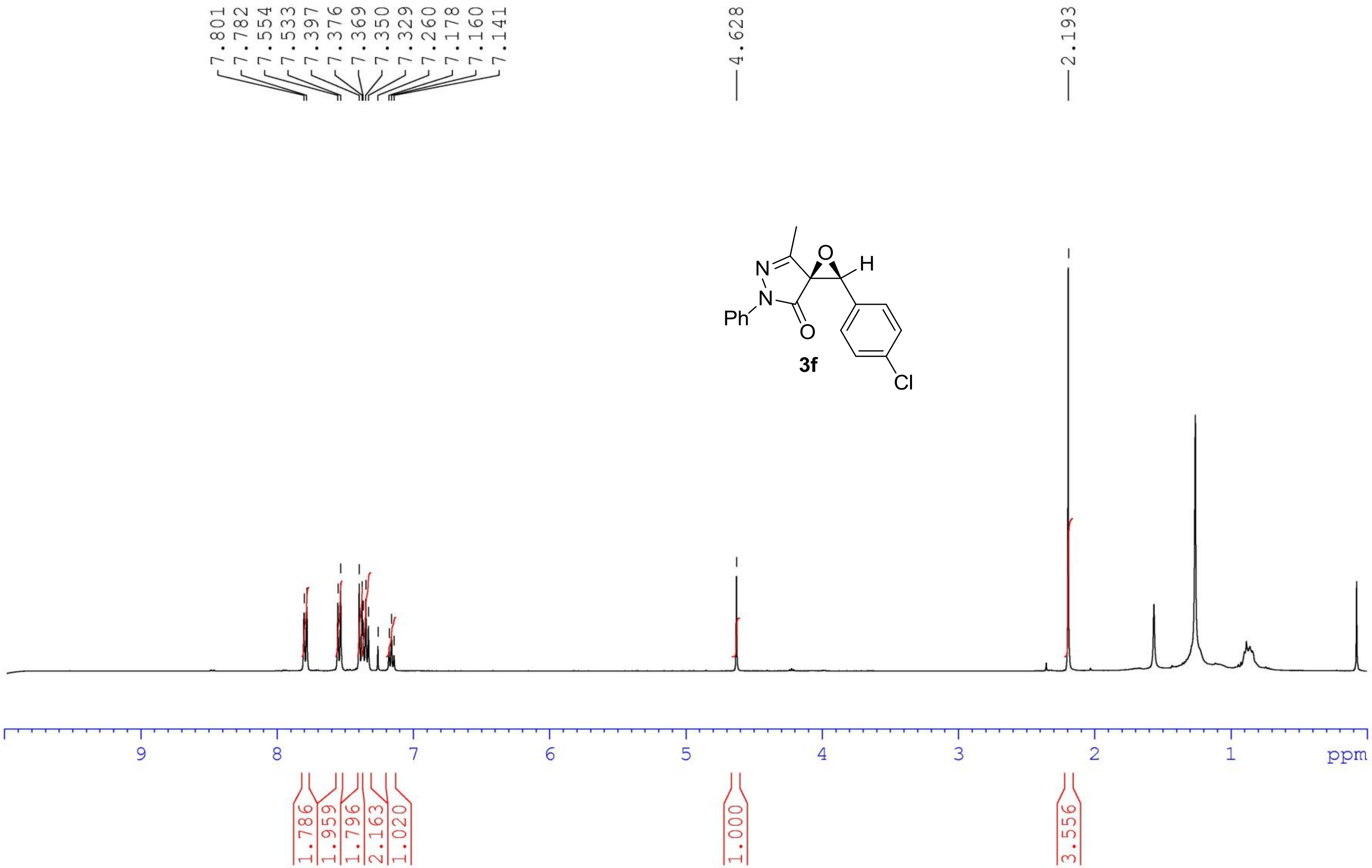
^1H NMR in $CDCl_3$ (400 MHz)



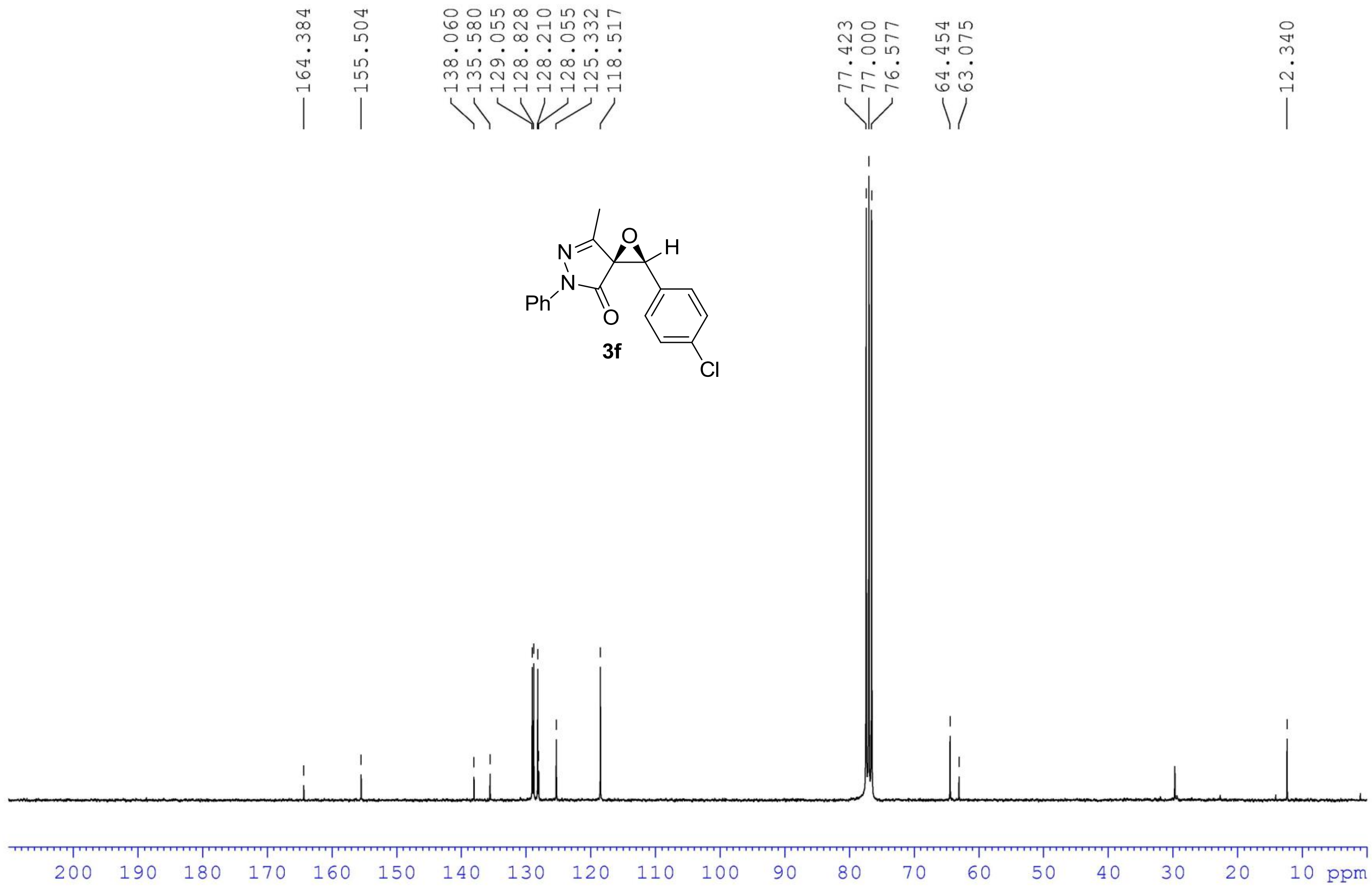
^{13}C NMR in $CDCl_3$ (100 MHz)



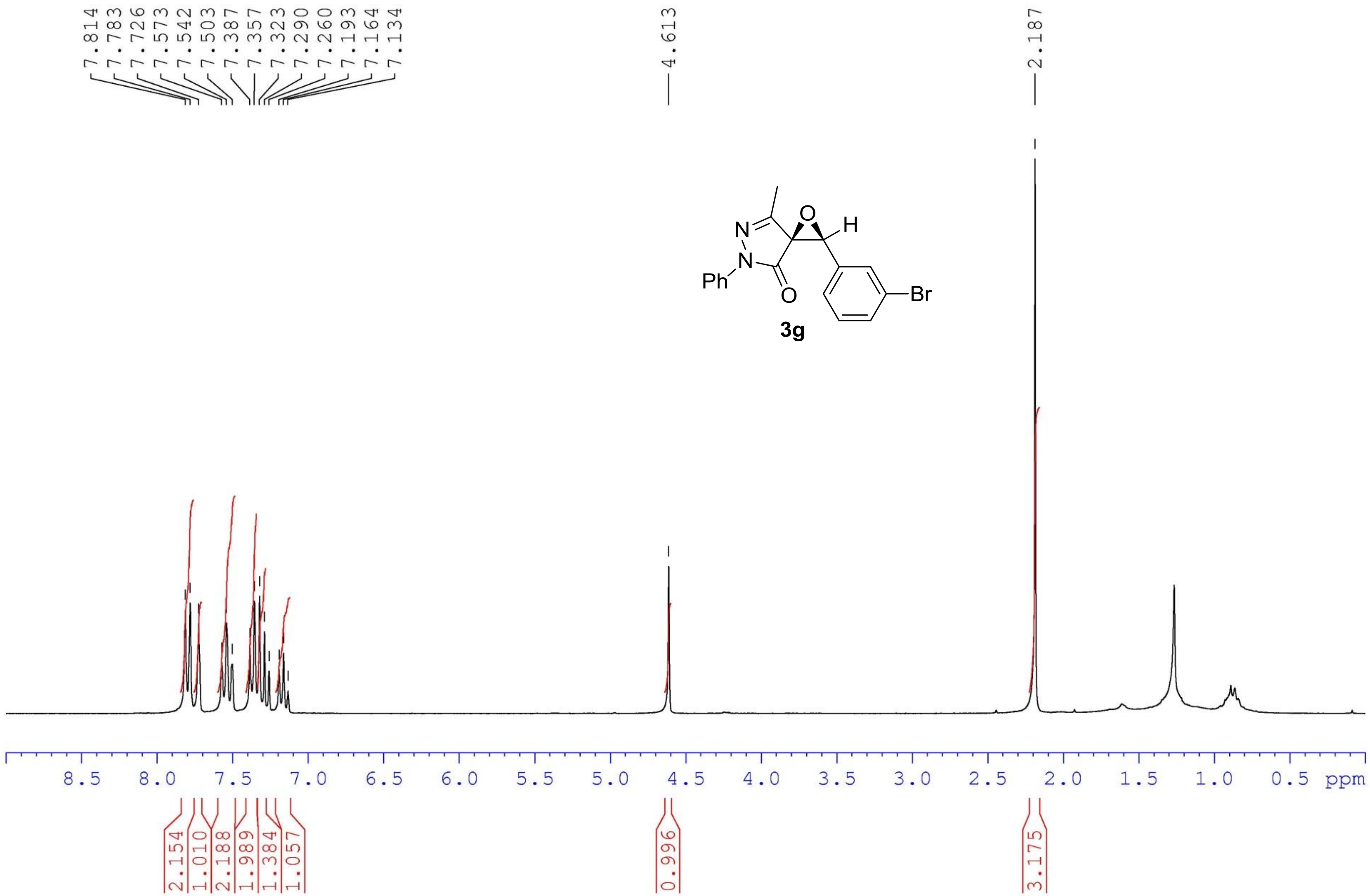
^{1}H NMR in $CDCl_3$ (400 MHz)



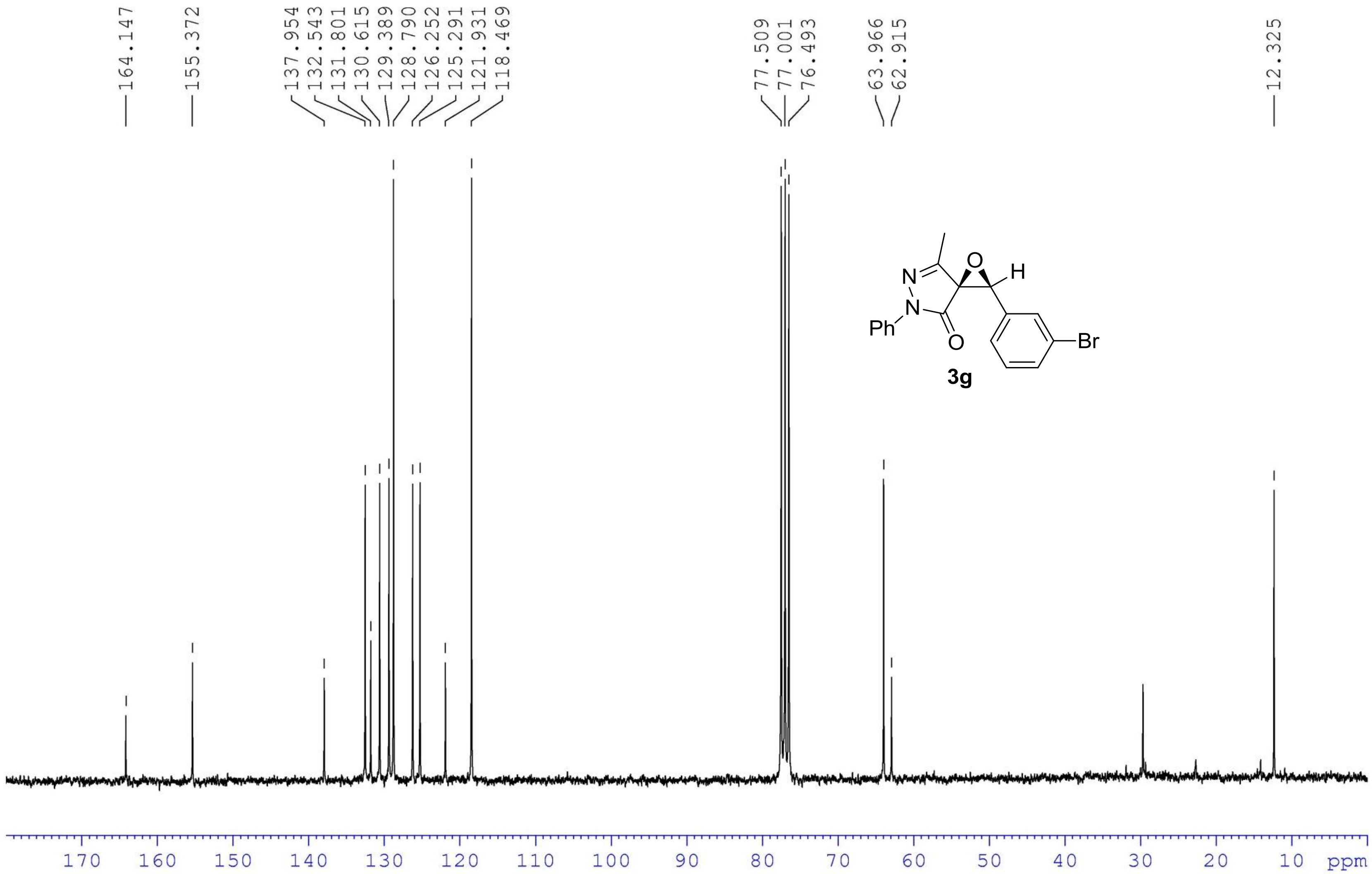
^{13}C NMR in $CDCl_3$ (75 MHz)



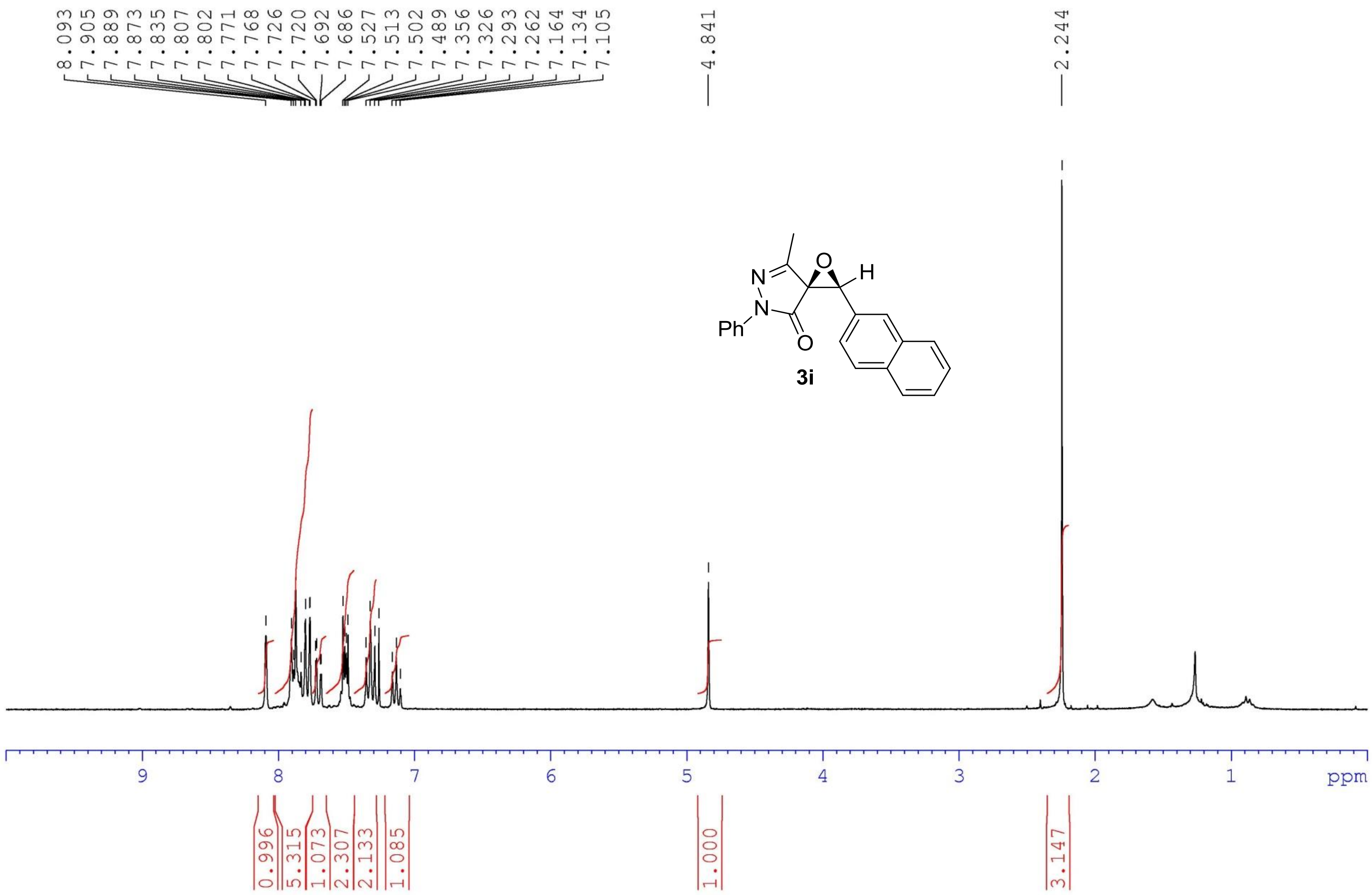
^{1}H NMR in $CDCl_3$ (250 MHz)



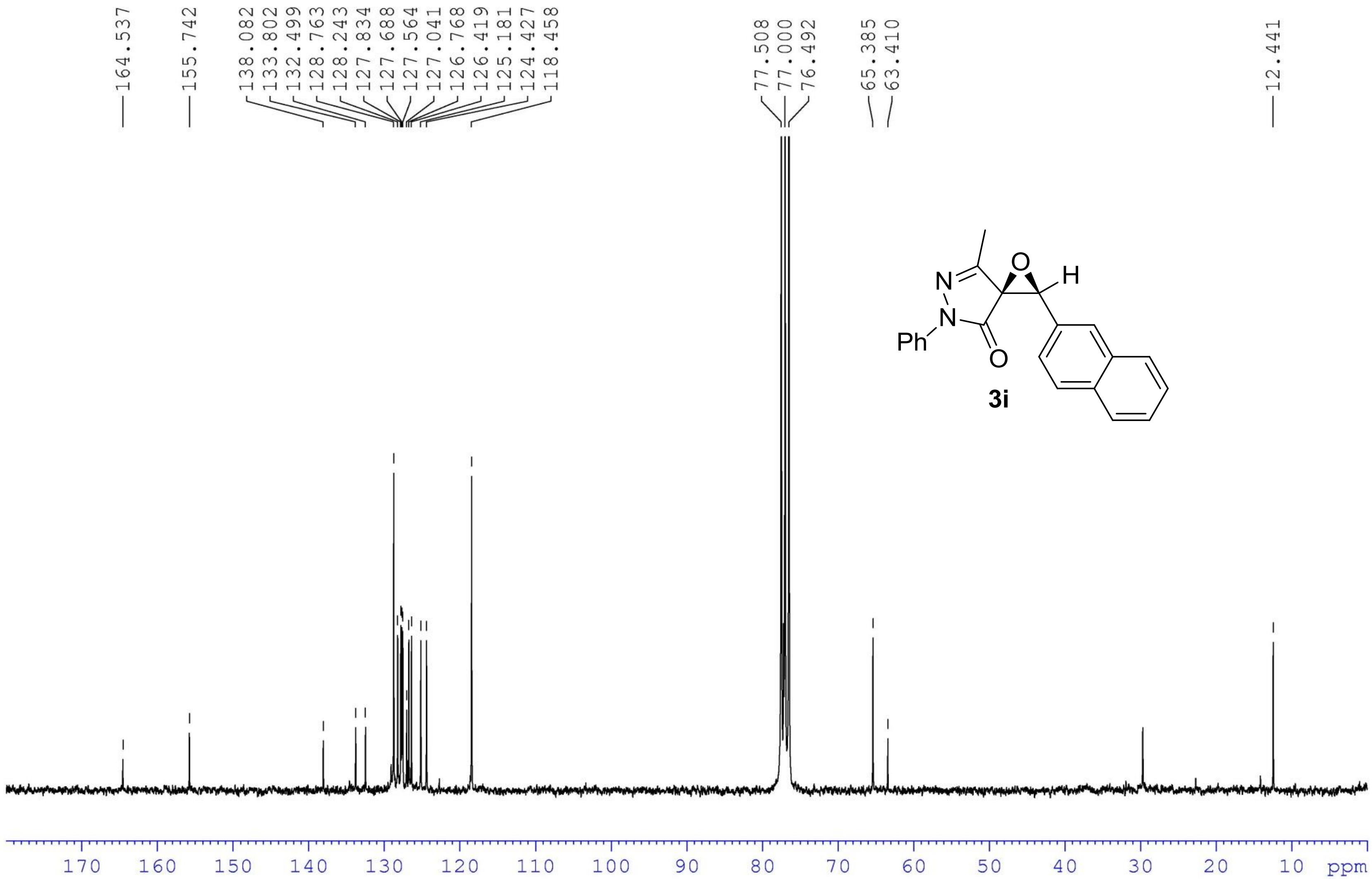
^{13}C NMR in $CDCl_3$ (62.5 MHz)



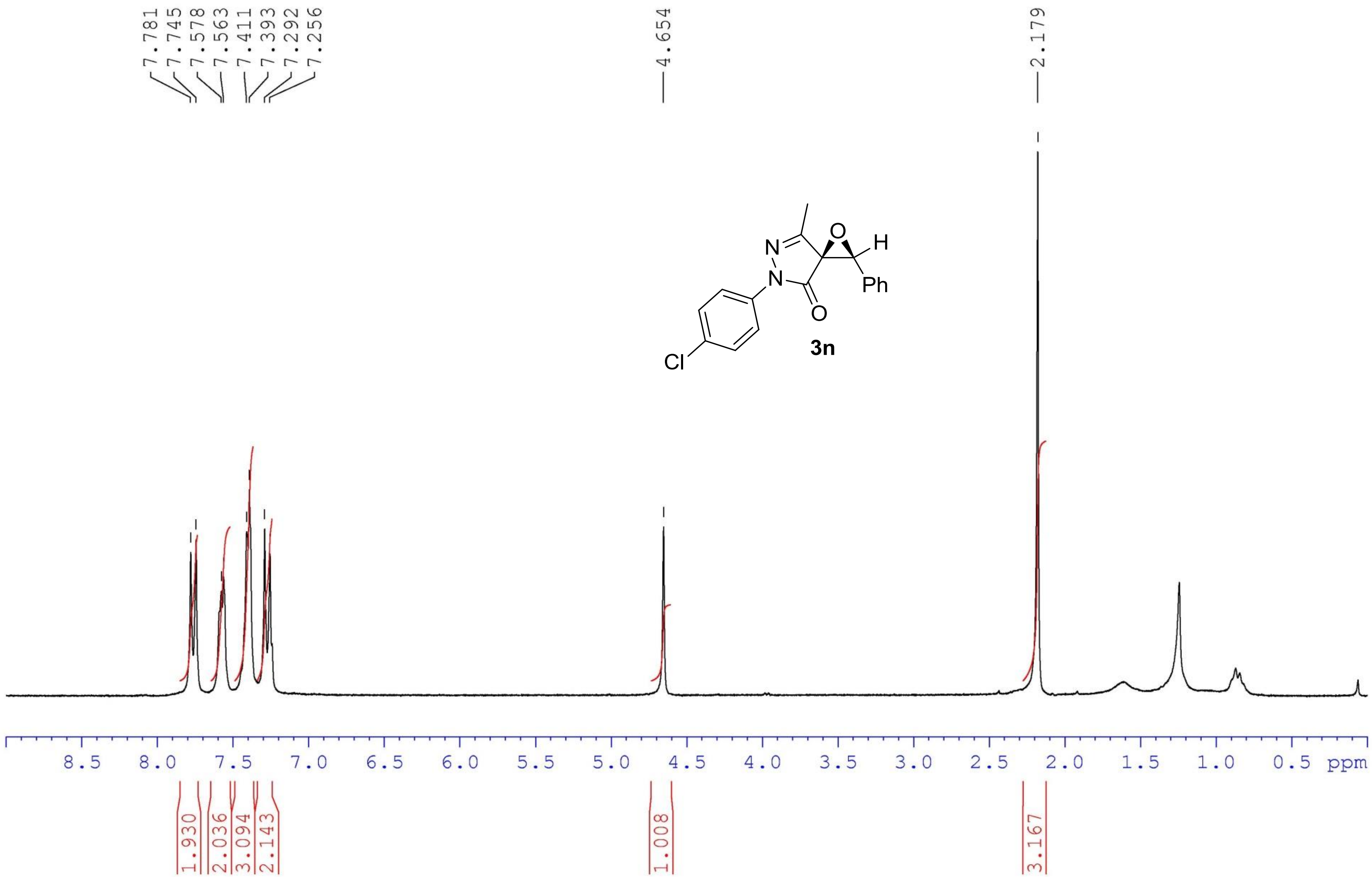
^{1}H NMR in $CDCl_3$ (250 MHz)



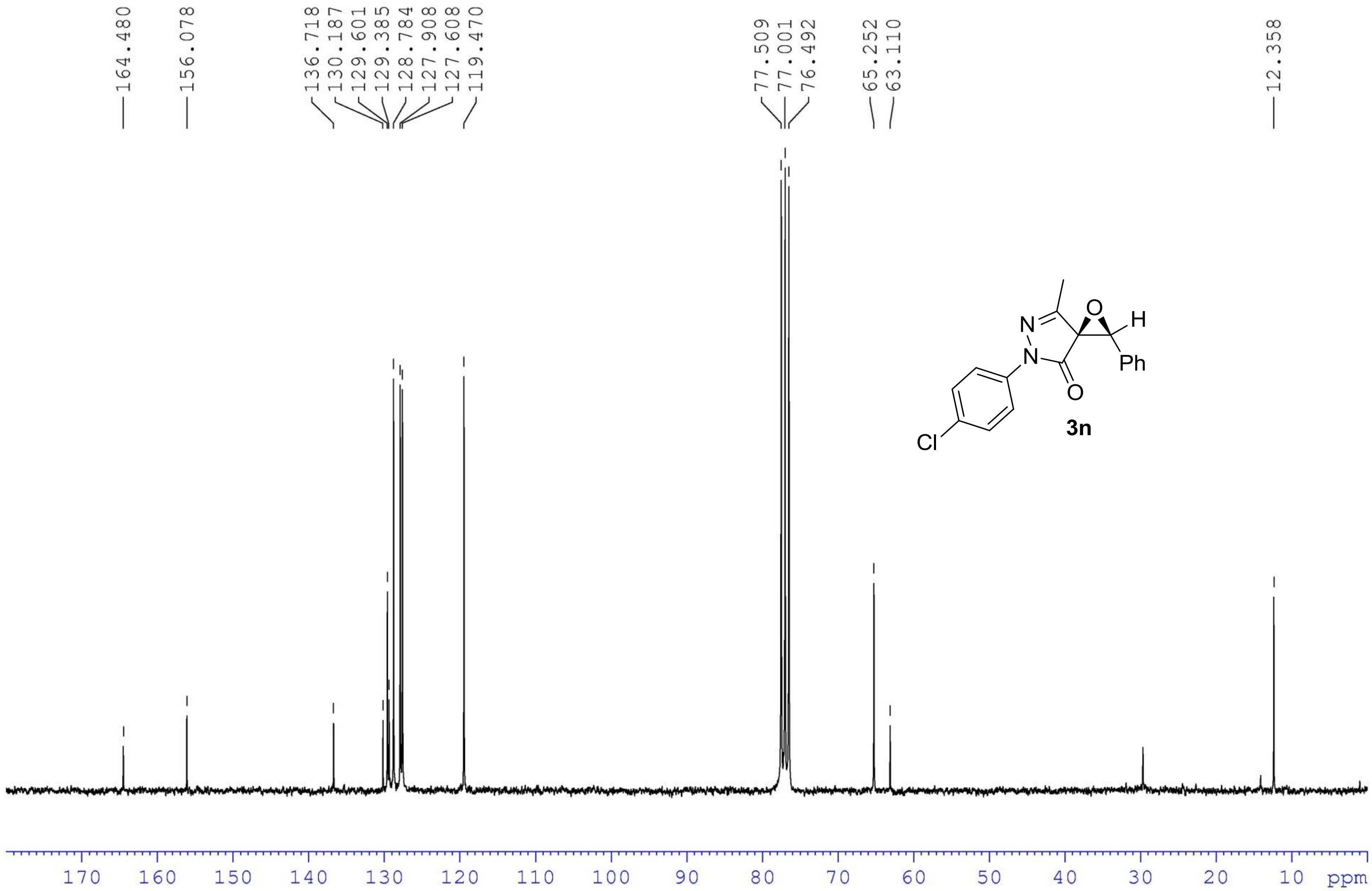
^{13}C NMR in $CDCl_3$ (62.5 MHz)



[1]H NMR in $CDCl_3$ (250 MHz)

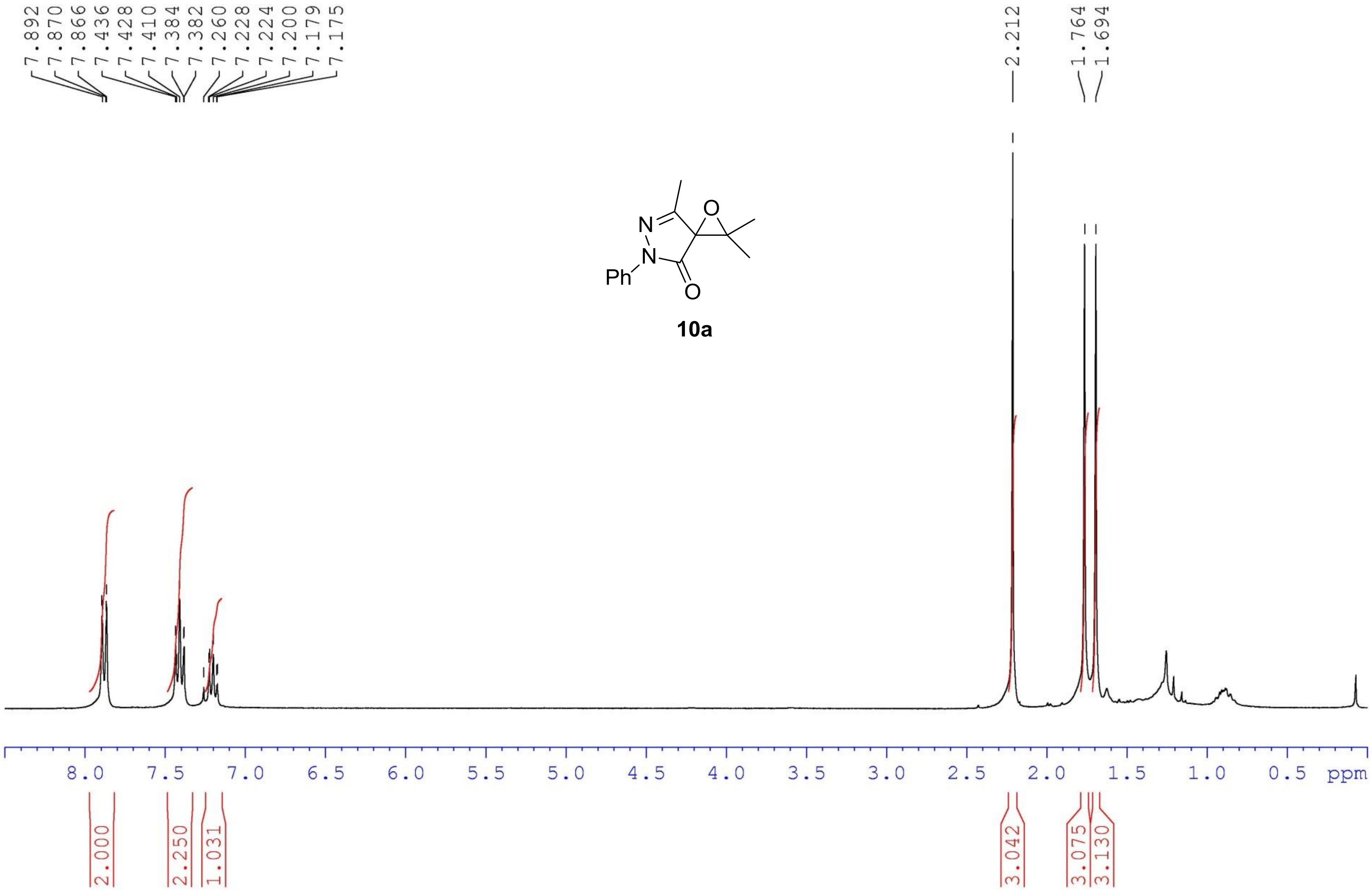


^{13}C NMR in $CDCl_3$ (62.5 MHz)

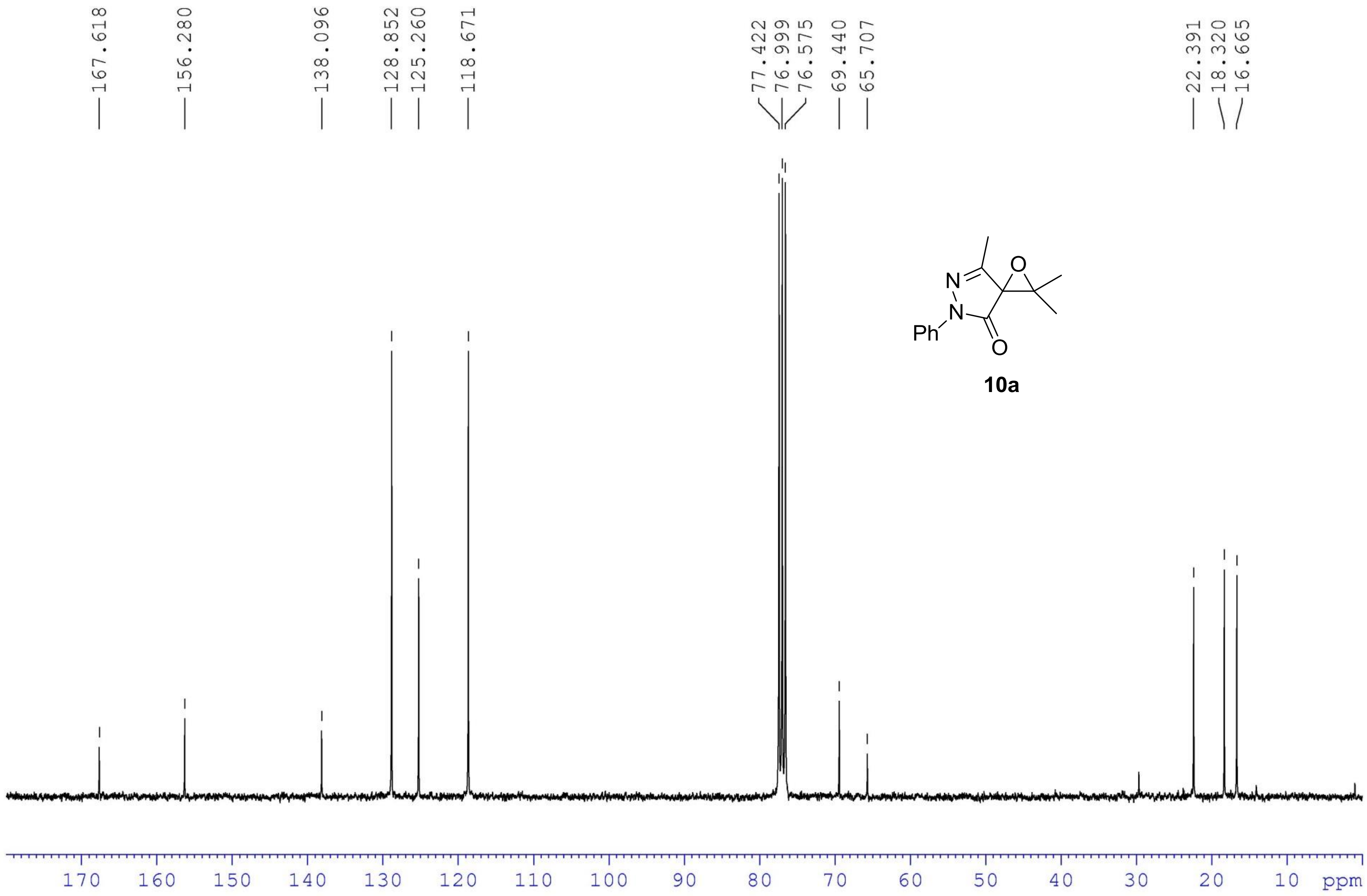


3n

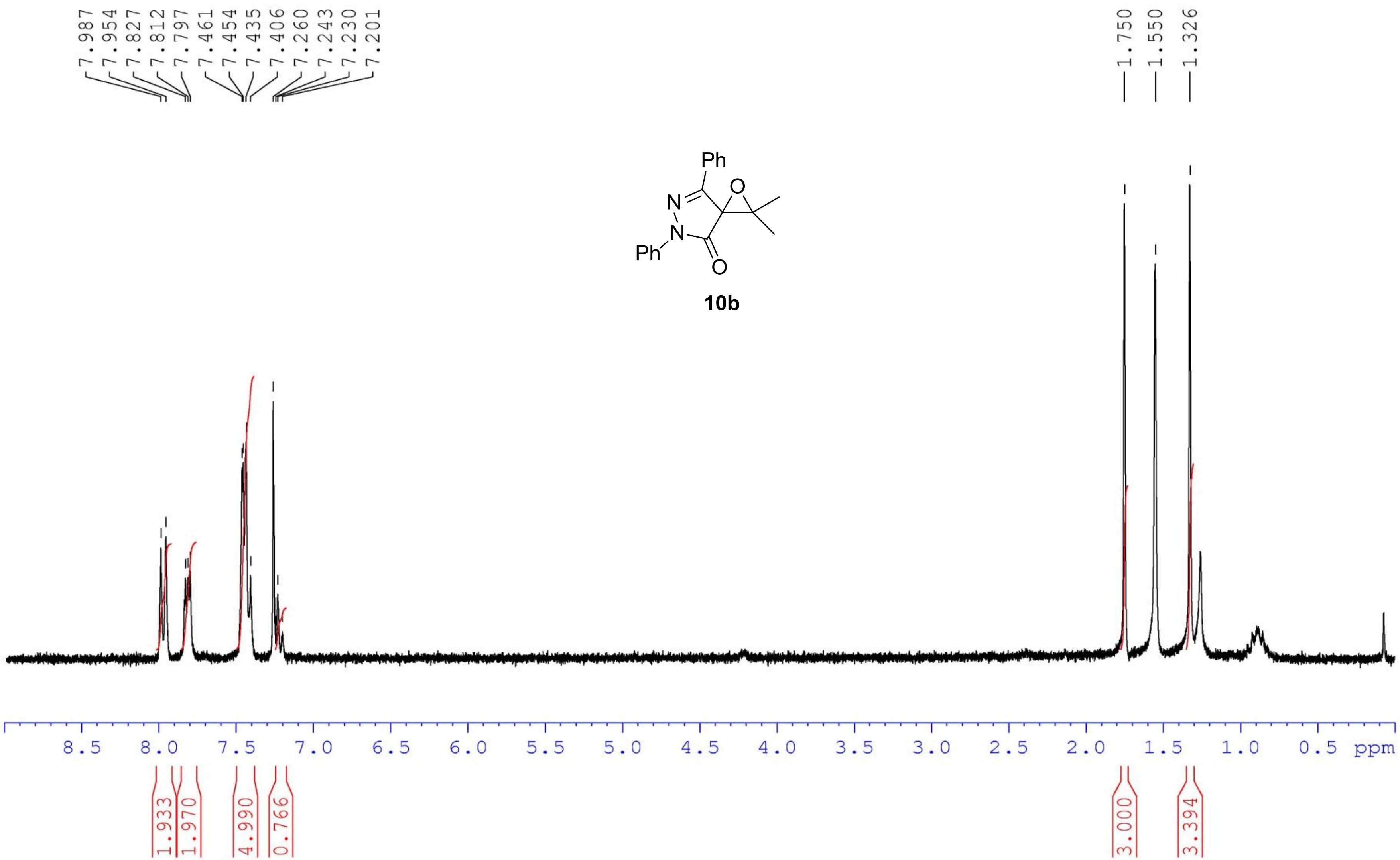
^{1}H NMR in $CDCl_3$ (300 MHz)



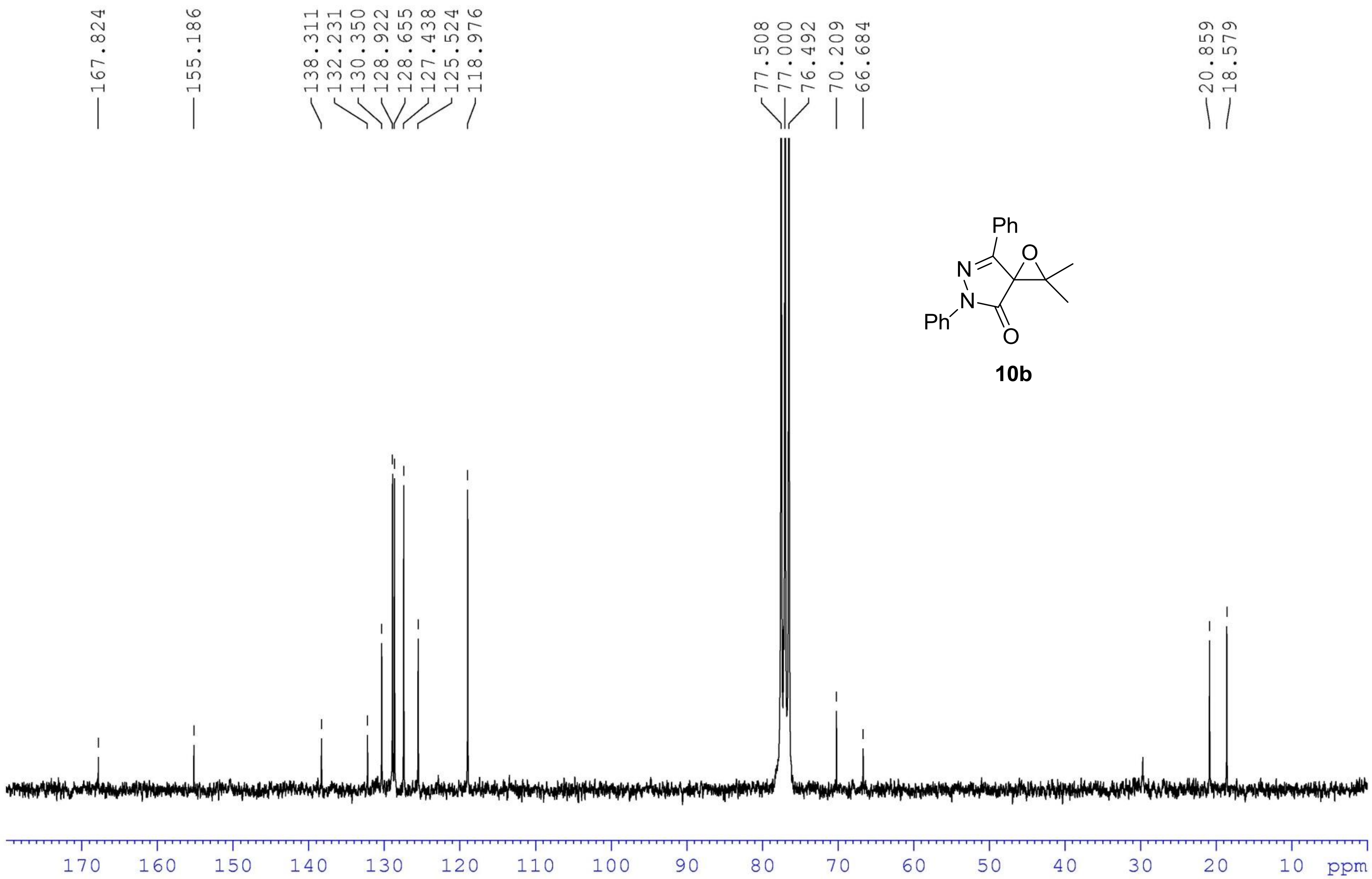
^{13}C NMR in $CDCl_3$ (75 MHz)



^{1}H NMR in $CDCl_3$ (250 MHz)

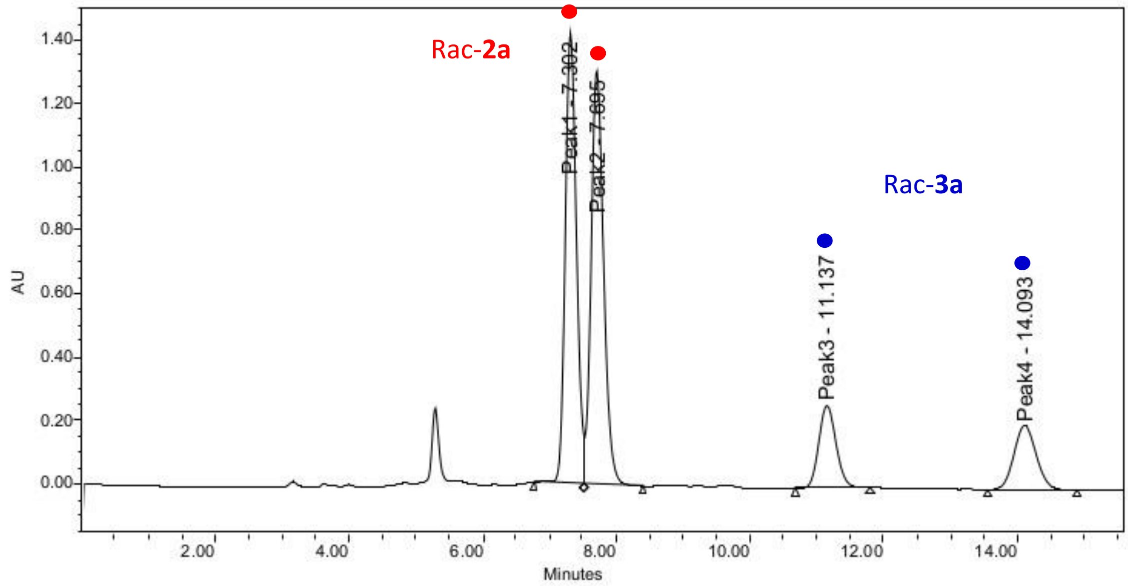


^{13}C NMR in $CDCl_3$ (62.5 MHz)

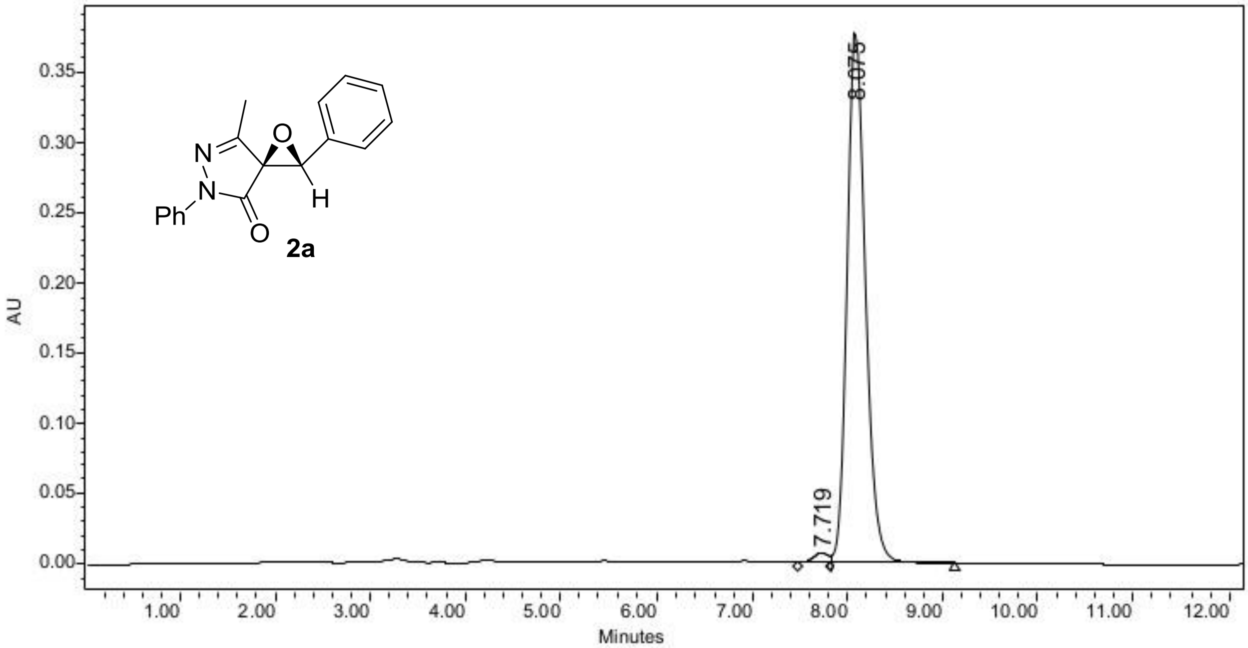


10b

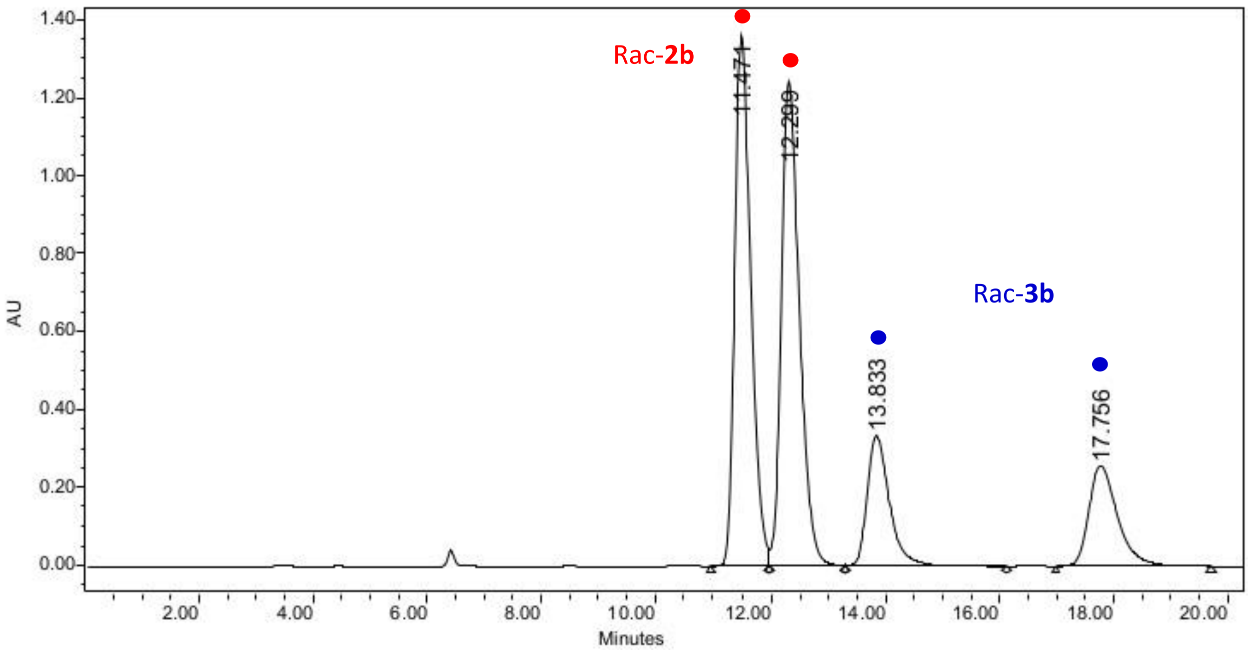
HPLC Chromatograms



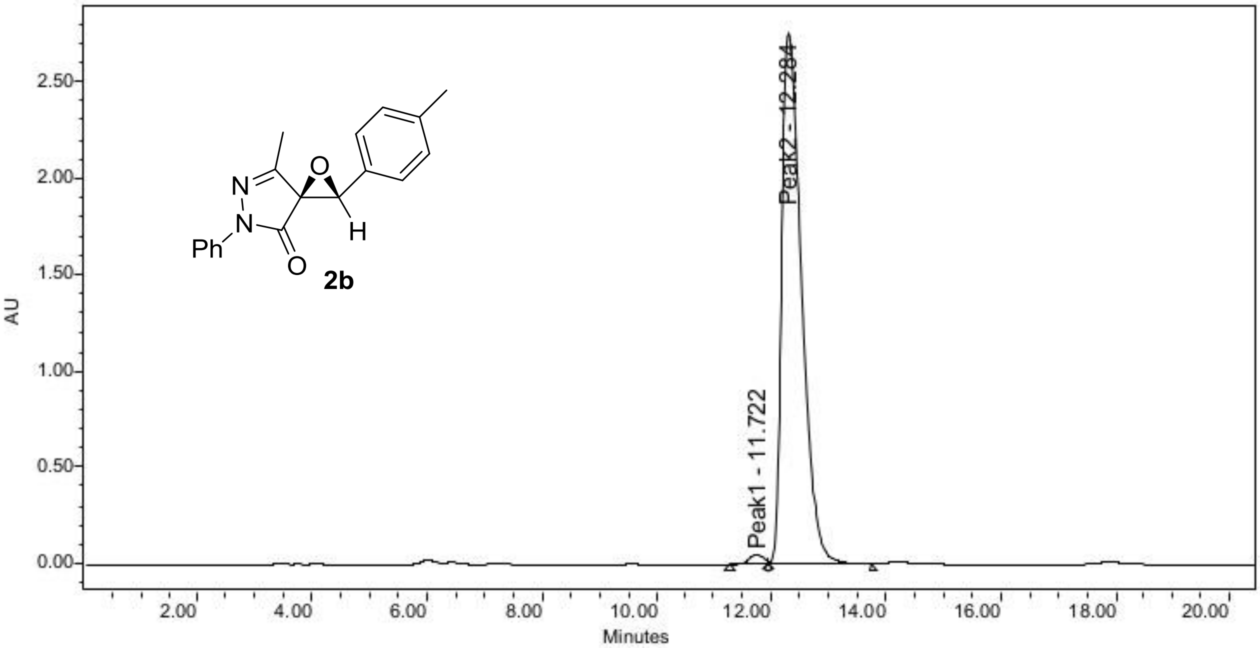
	Peak Name	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	Peak1	7.302	16549762	38.55	1421341	44.52
2	Peak2	7.695	16946283	39.47	1306925	40.93
3	Peak3	11.137	4724919	11.00	261807	8.20
4	Peak4	14.093	4713576	10.98	202864	6.35



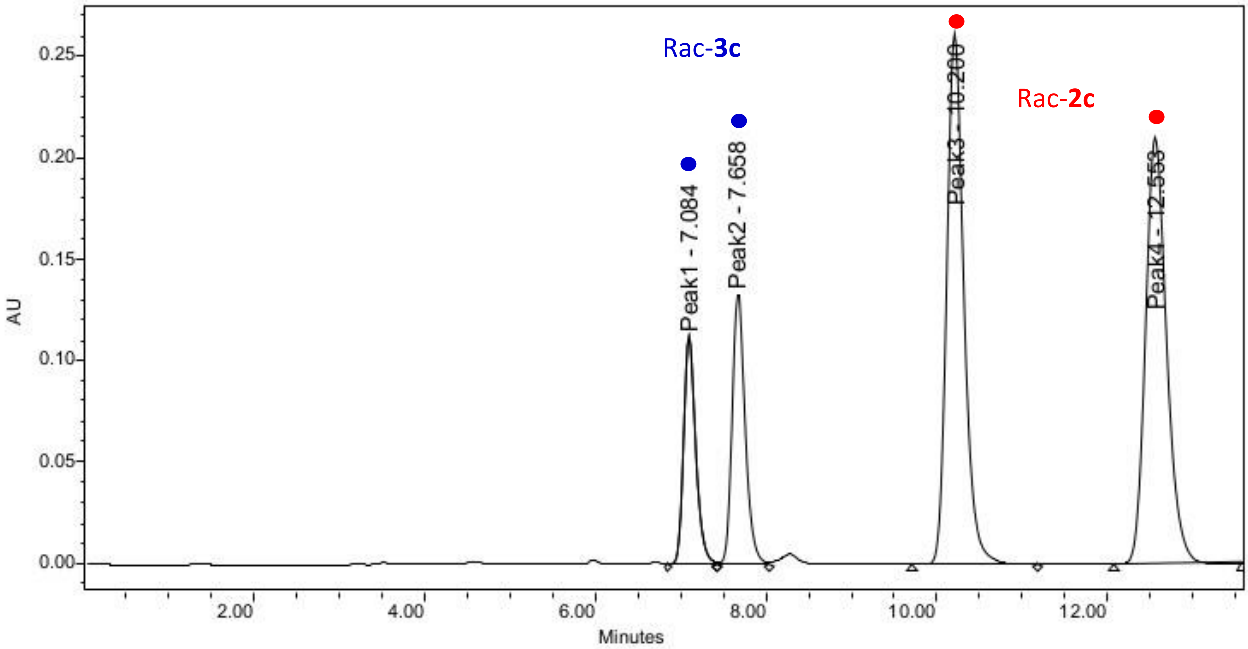
	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	7.719	79968	1.55	7053	1.83
2	8.075	5070906	98.45	378940	98.17



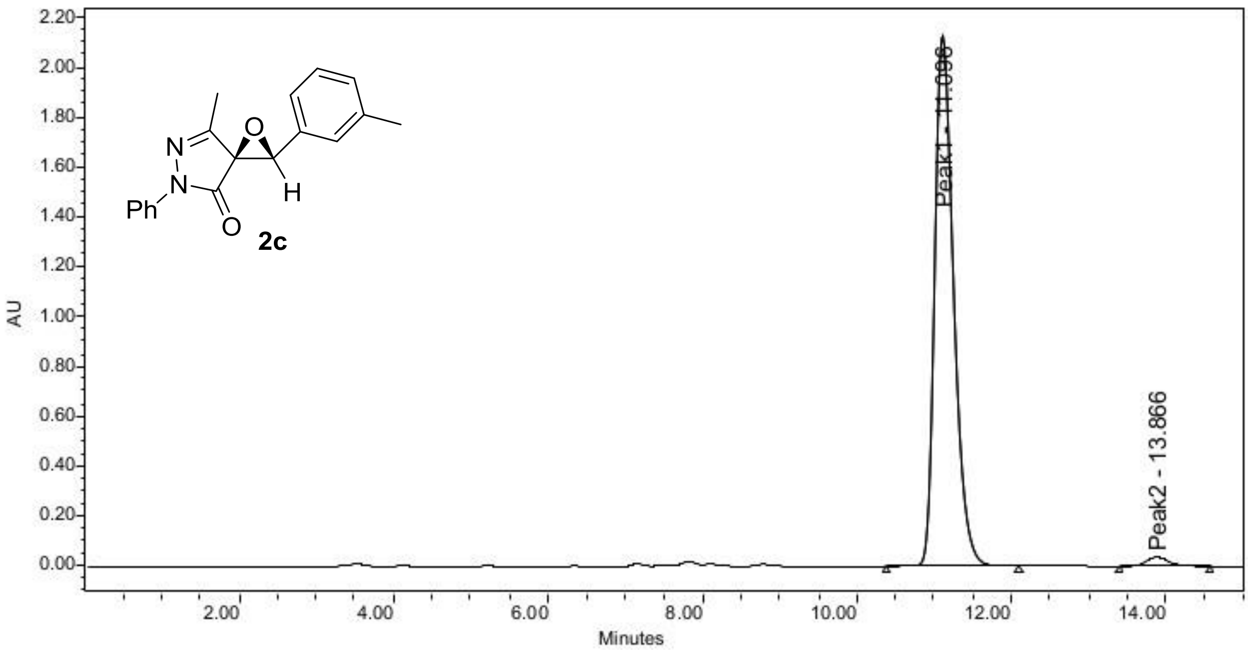
	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	11.471	26828956	37.08	1361565	42.56
2	12.299	27400463	37.87	1243207	38.86
3	13.833	9102459	12.58	335596	10.49
4	17.756	9012894	12.46	258734	8.09



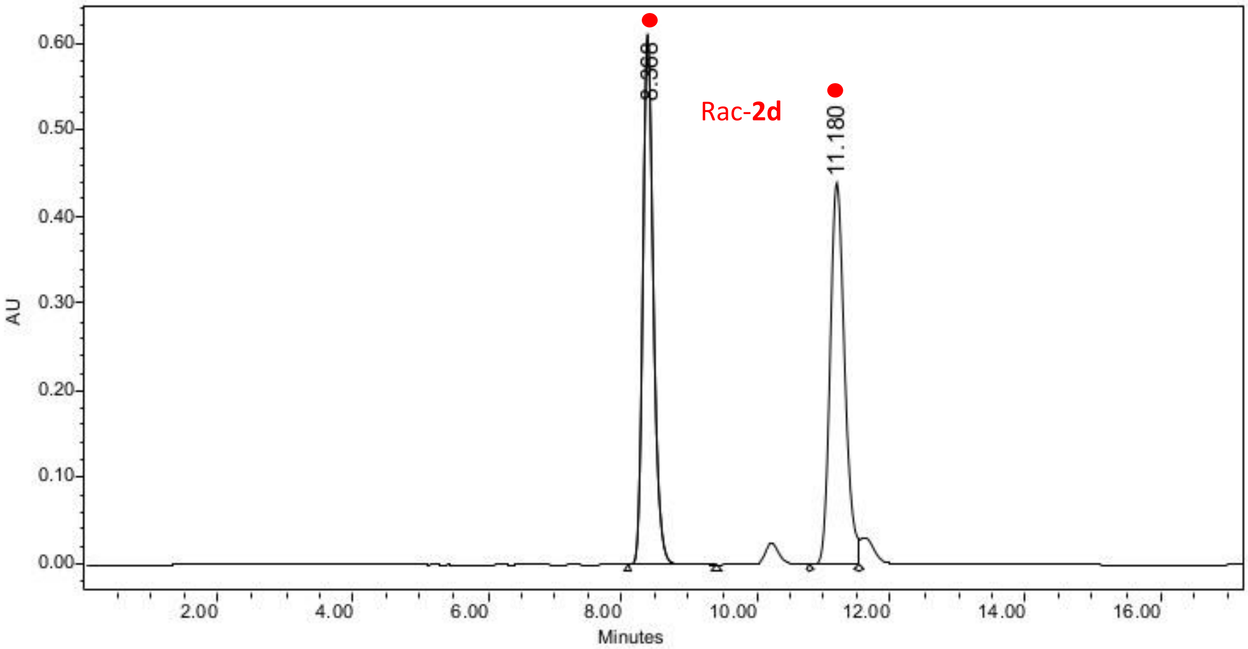
	Peak Name	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	Peak1	11.722	938274	1.40	52247	1.86
2	Peak2	12.284	66168690	98.60	2756033	98.14



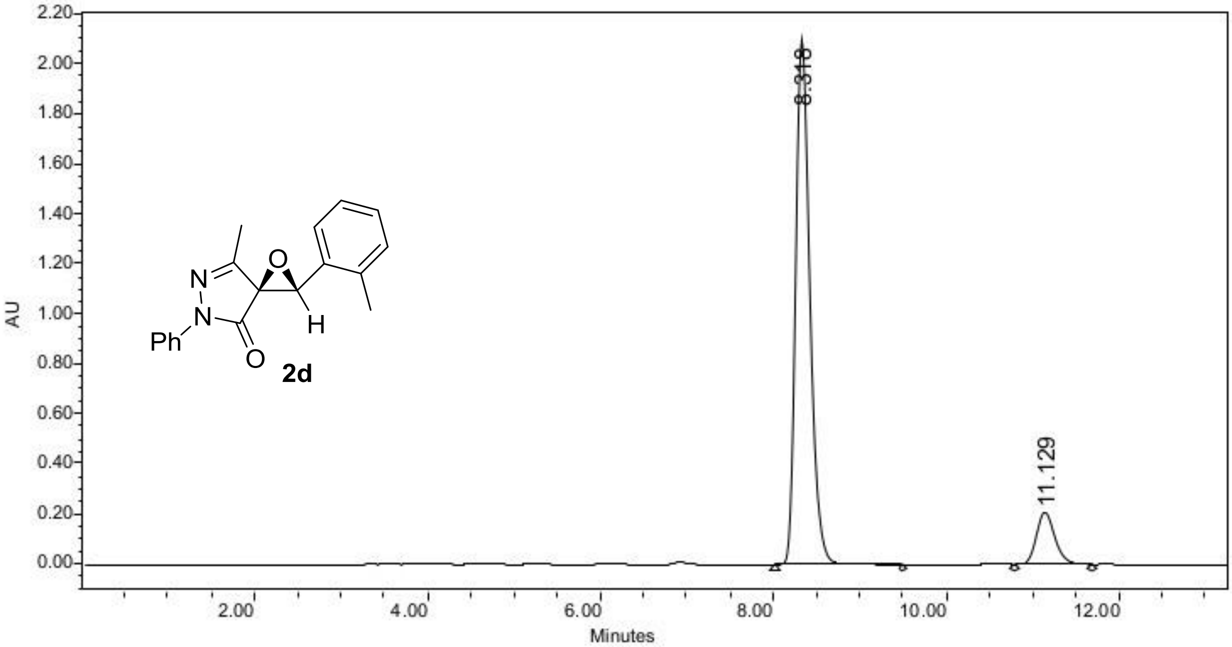
	Peak Name	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	Peak1	7.084	1113875	11.36	112403	15.64
2	Peak2	7.658	1416219	14.45	133964	18.64
3	Peak3	10.200	3652495	37.27	261642	36.41
4	Peak4	12.553	3618418	36.92	210660	29.31



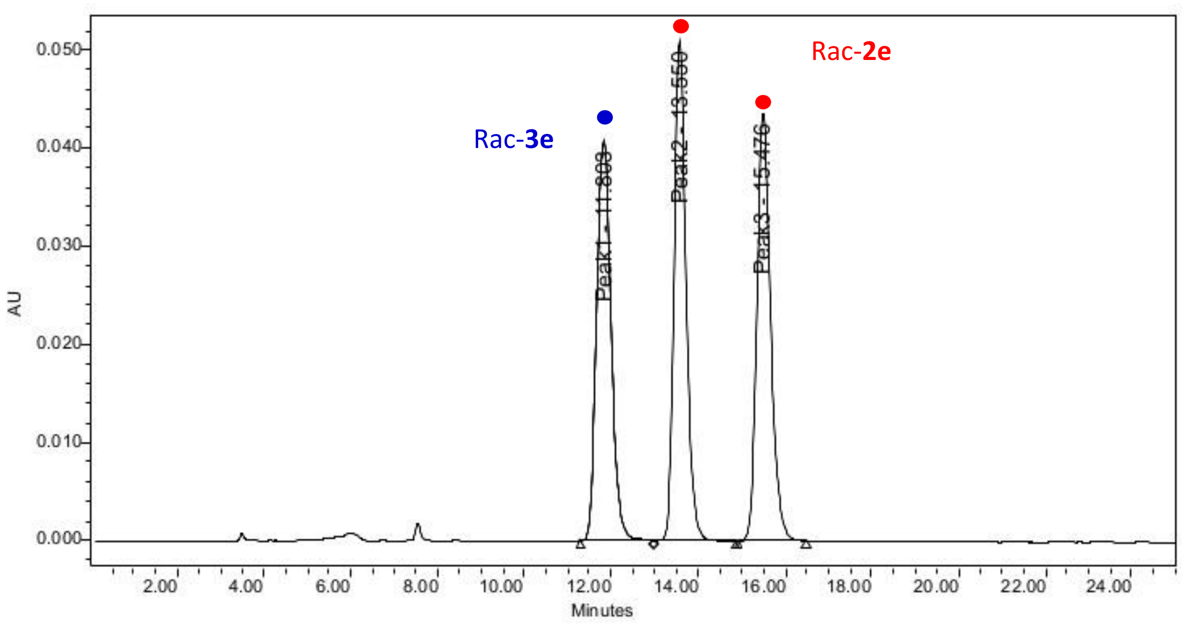
	Peak Name	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	Peak1	11.096	36121877	97.92	2126817	98.27
2	Peak2	13.866	766201	2.08	37506	1.73



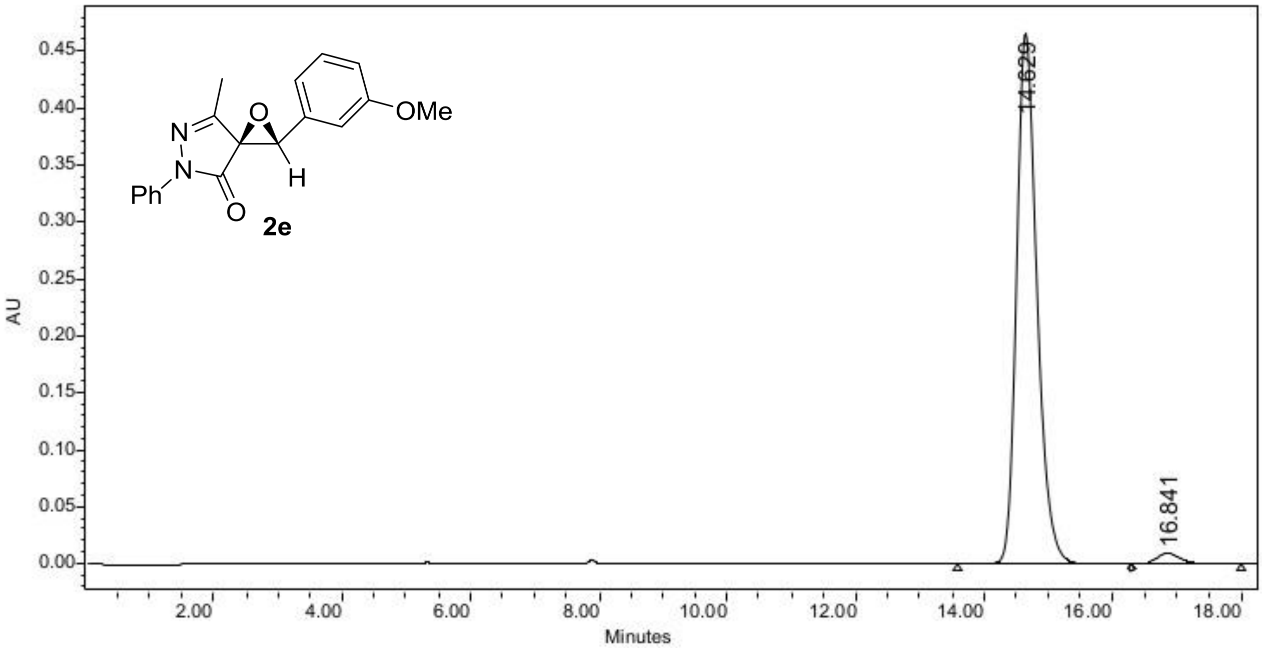
	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	8.368	6618573	49.80	611185	58.13
2	11.180	6670790	50.20	440284	41.87



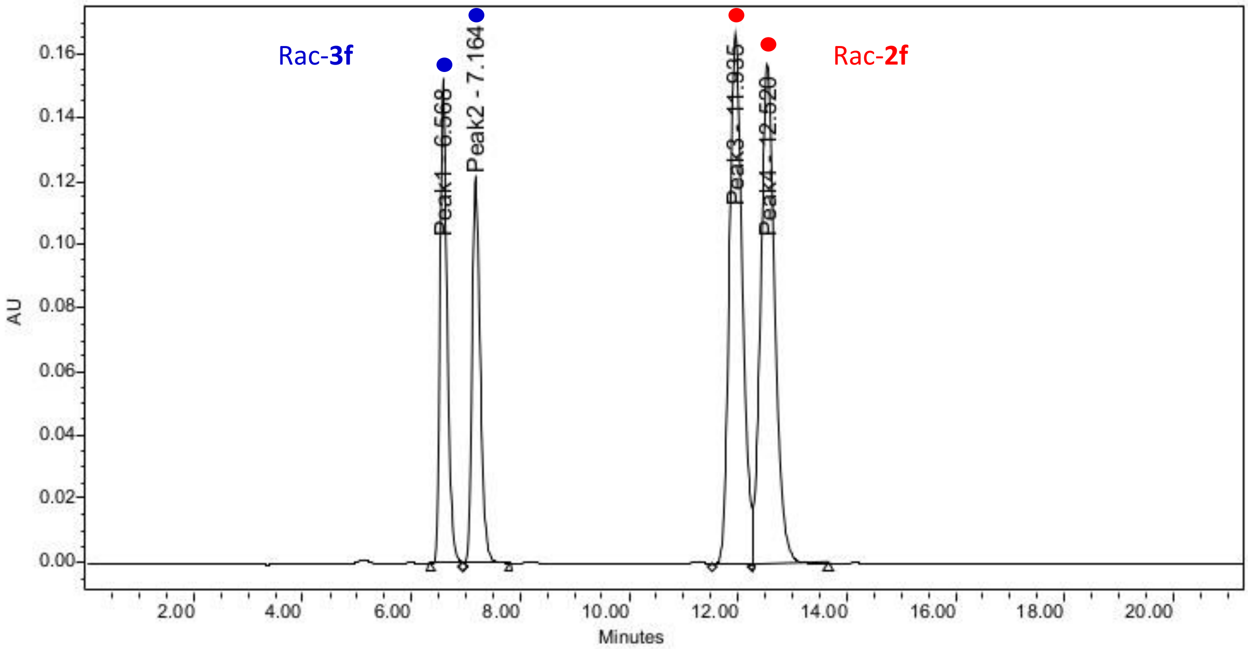
	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	8.318	24046882	88.44	2100775	90.89
2	11.129	3144507	11.56	210575	9.11



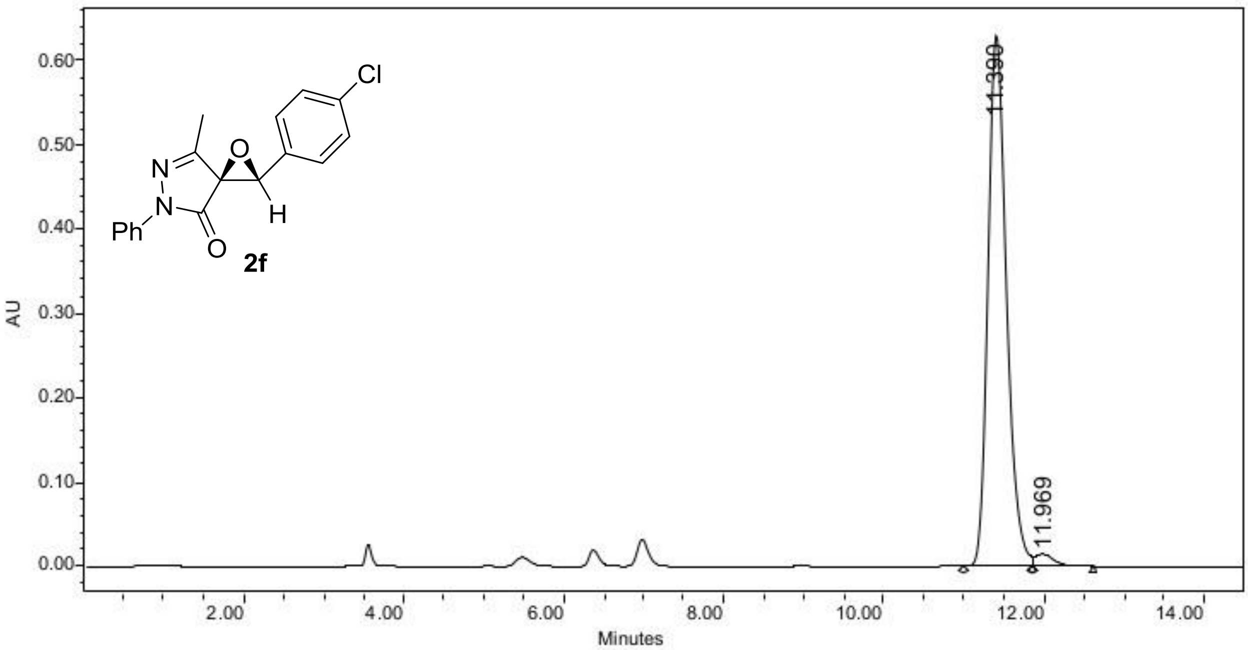
	Peak Name	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	Peak1	11.803	950416	32.88	40760	30.10
2	Peak2	13.550	973390	33.67	50952	37.62
3	Peak3	15.476	966870	33.45	43712	32.28



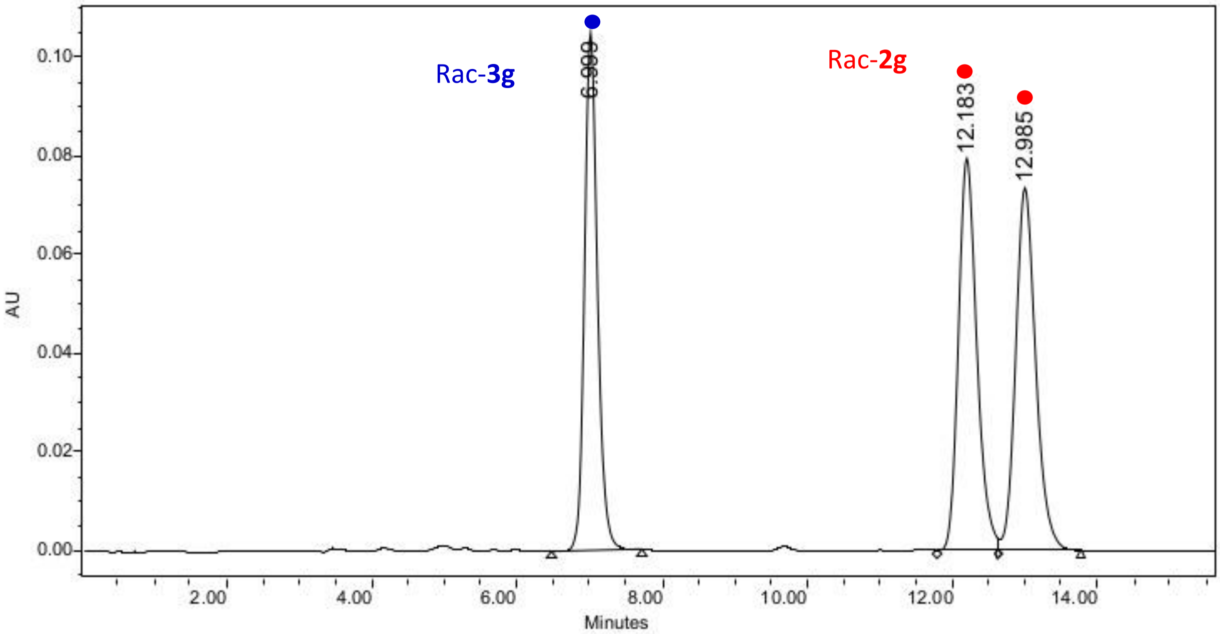
	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	14.629	10302783	97.55	466286	97.95
2	16.841	258672	2.45	9762	2.05



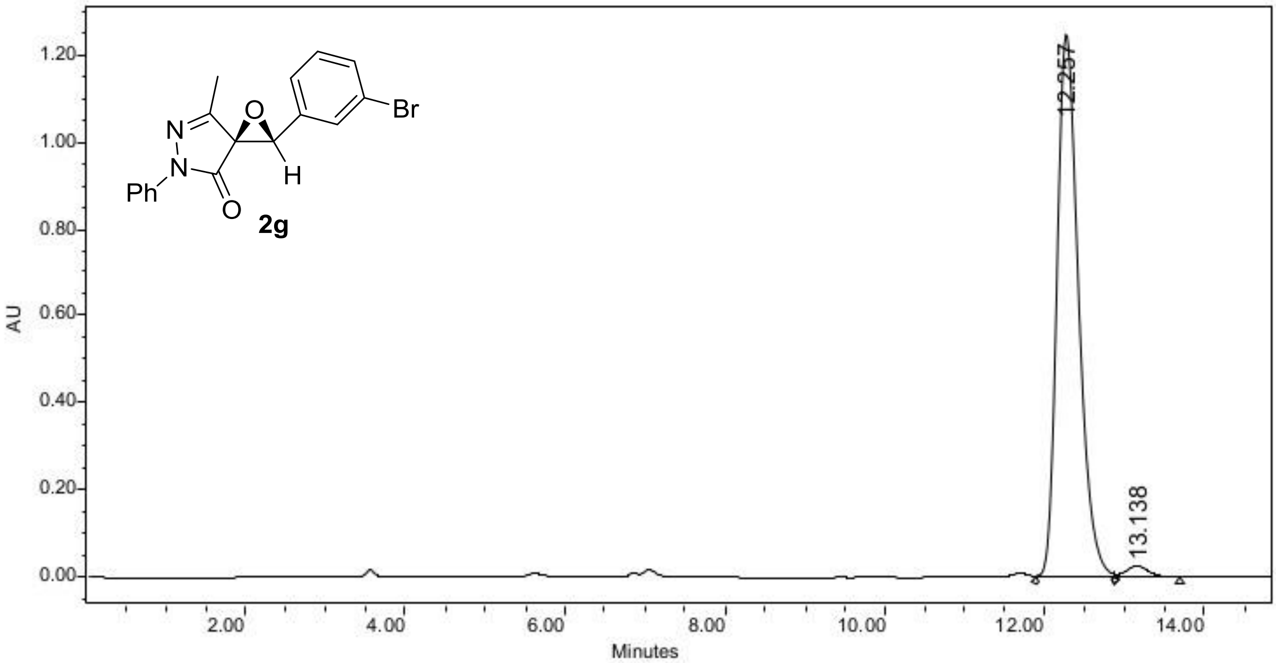
	Peak Name	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	Peak1	6.568	1385527	16.82	152344	25.48
2	Peak2	7.164	1247955	15.15	121716	20.36
3	Peak3	11.935	2758223	33.48	166733	27.89
4	Peak4	12.520	2847329	34.56	157090	26.27



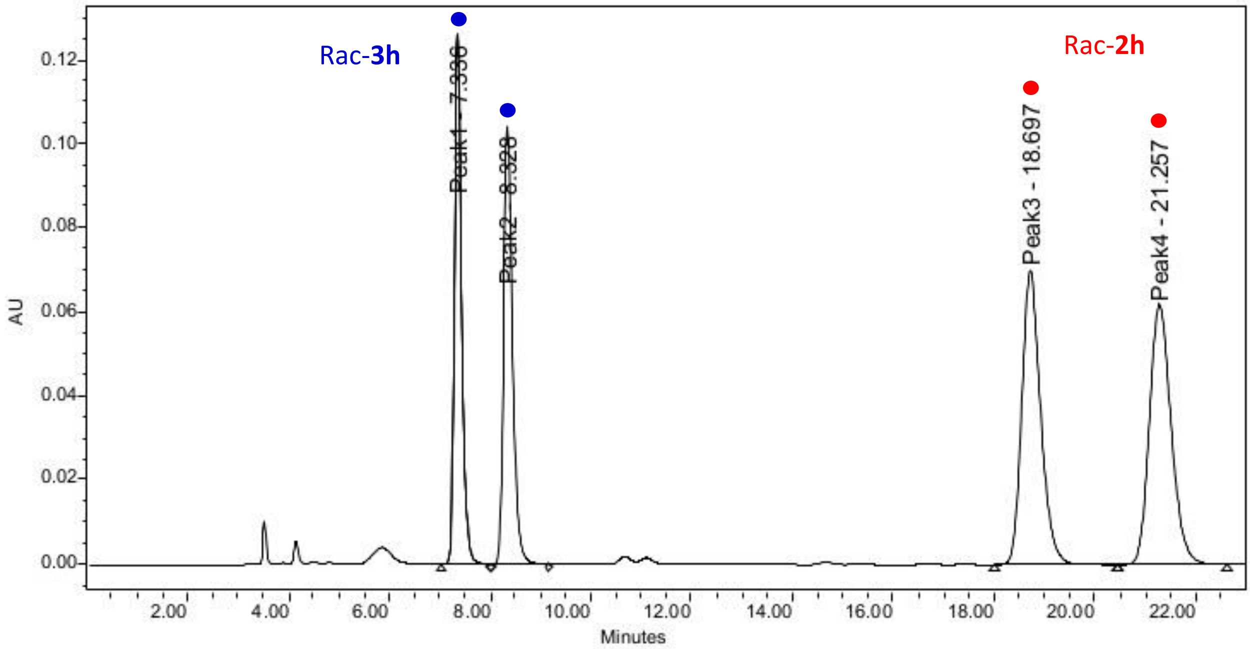
	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	11.390	10131895	97.72	632489	97.74
2	11.969	236563	2.28	14637	2.26



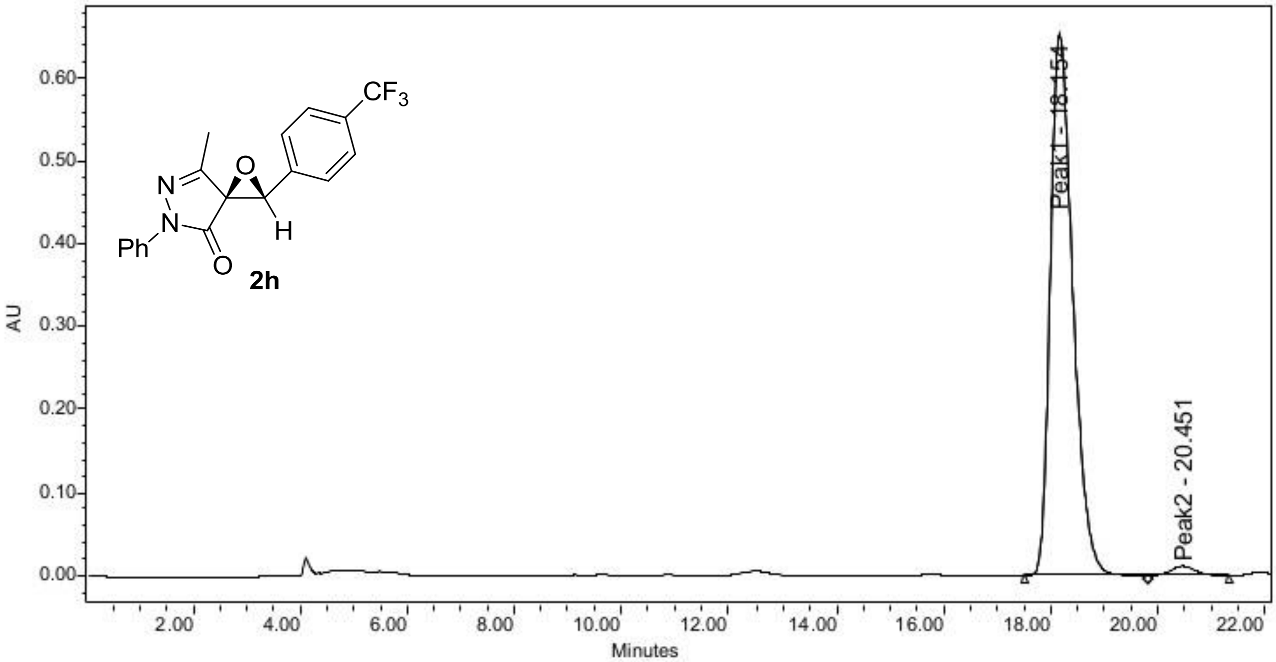
	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	6.999	1301229	31.54	104790	40.64
2	12.183	1406832	34.10	79522	30.84
3	12.985	1417408	34.36	73522	28.52



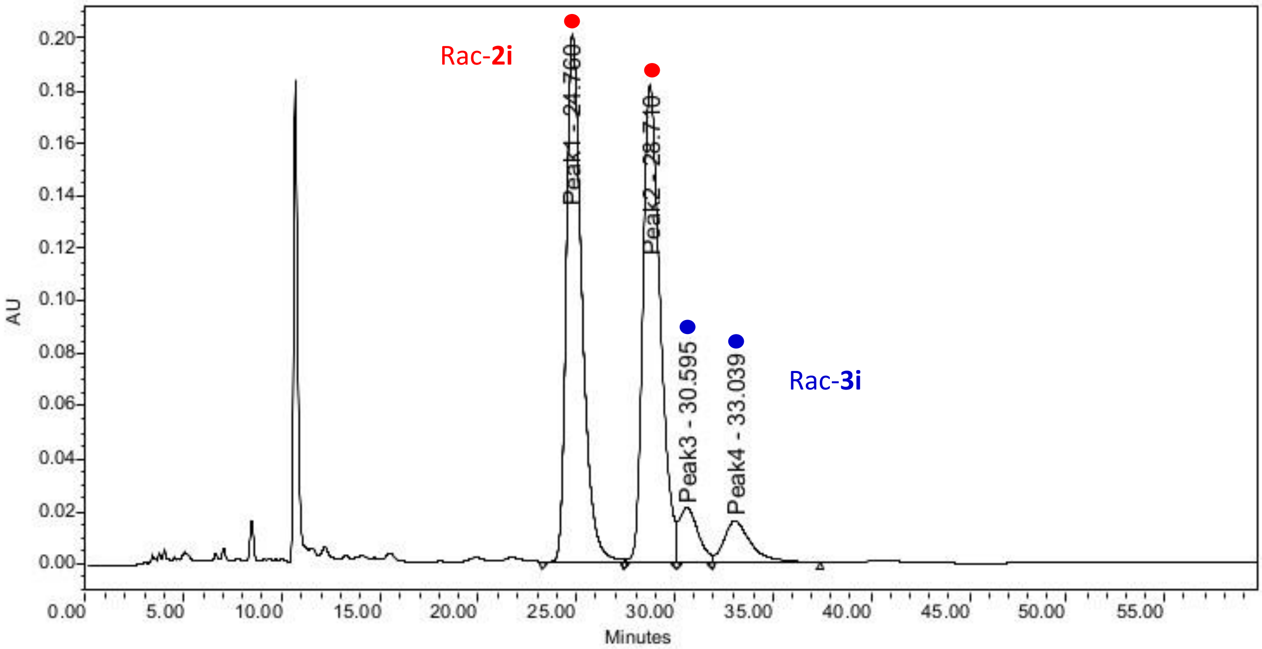
	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	12.257	23421931	97.85	1250633	97.99
2	13.138	515434	2.15	25702	2.01



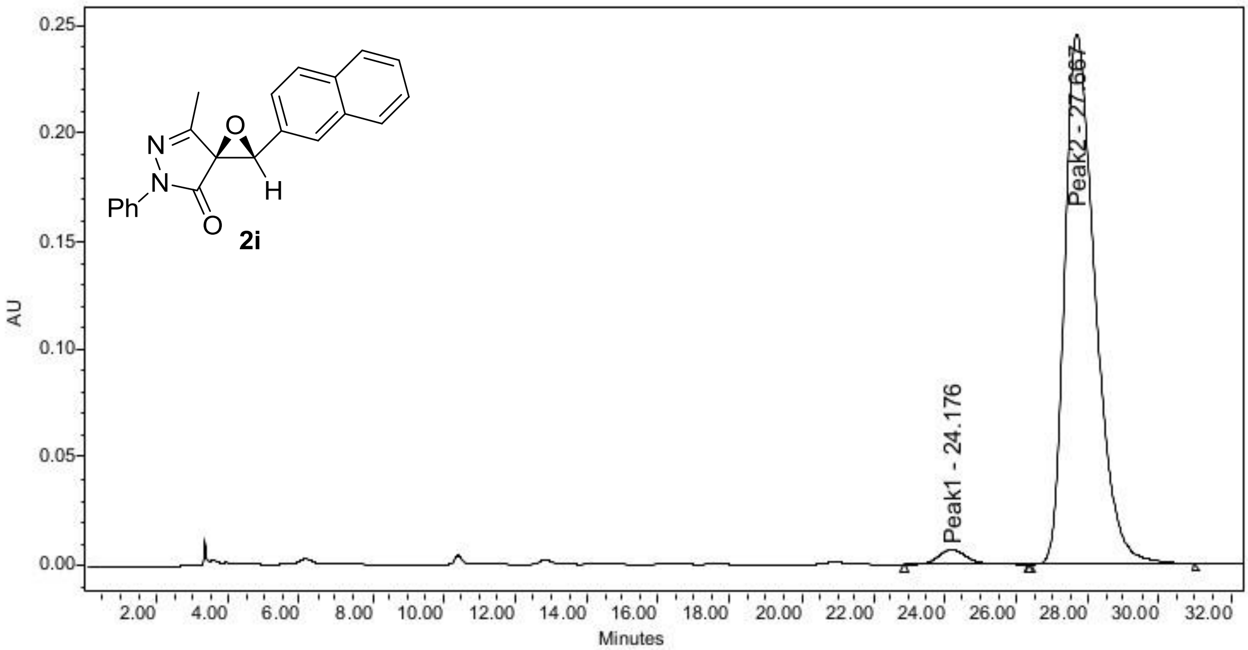
	Peak Name	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	Peak1	7.336	1311727	20.82	126187	34.82
2	Peak2	8.328	1303904	20.69	104365	28.80
3	Peak3	18.697	1838521	29.18	69954	19.30
4	Peak4	21.257	1846867	29.31	61909	17.08



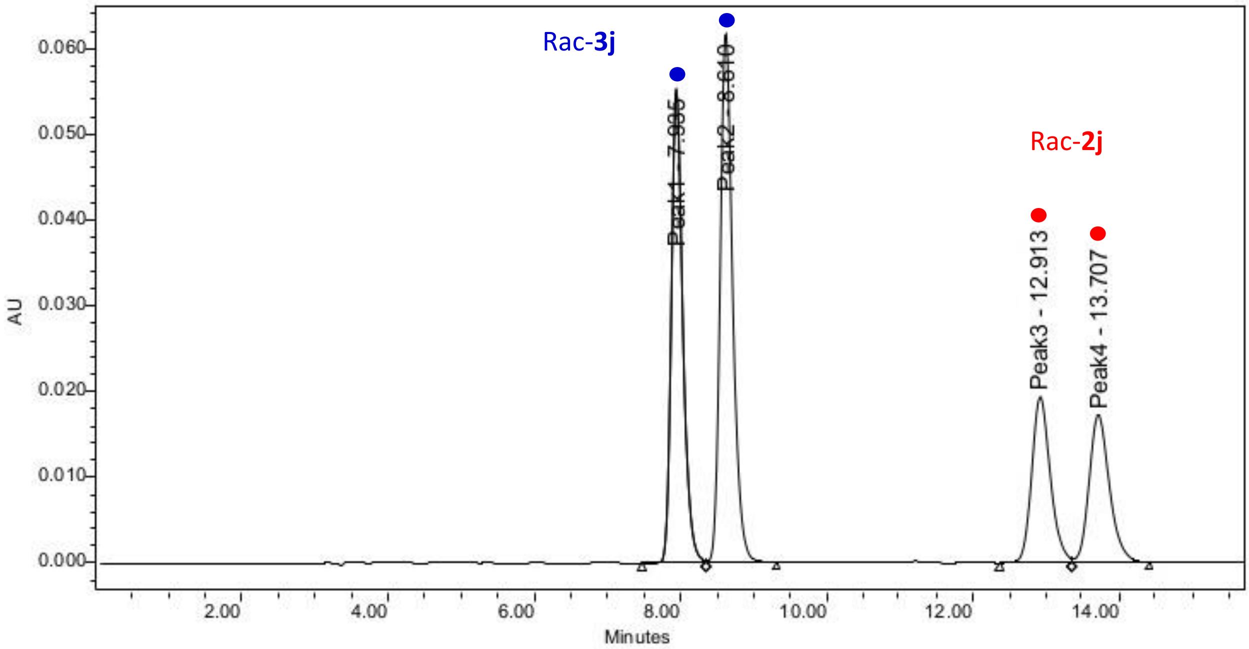
	Peak Name	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	Peak1	18.154	19289271	97.96	654147	98.22
2	Peak2	20.451	402089	2.04	11873	1.78



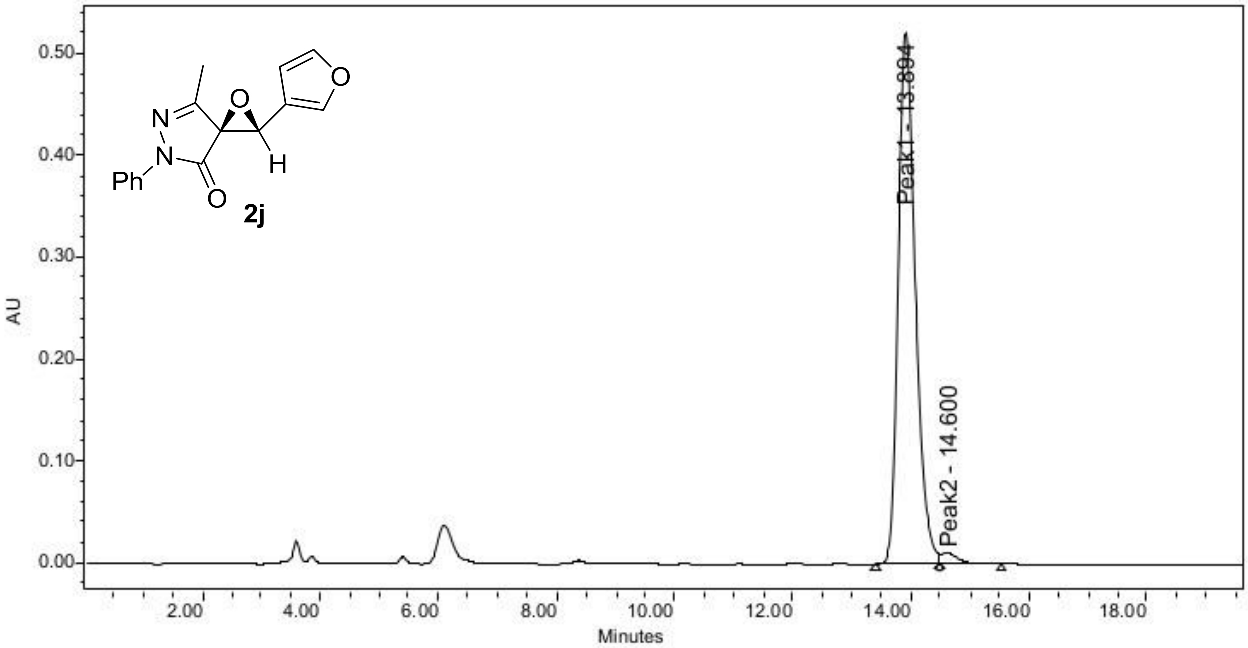
	Peak Name	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	Peak1	24.760	11112559	44.16	200853	47.96
2	Peak2	28.710	11163444	44.36	181361	43.31
3	Peak3	30.595	1387592	5.51	20789	4.96
4	Peak4	33.039	1502159	5.97	15789	3.77



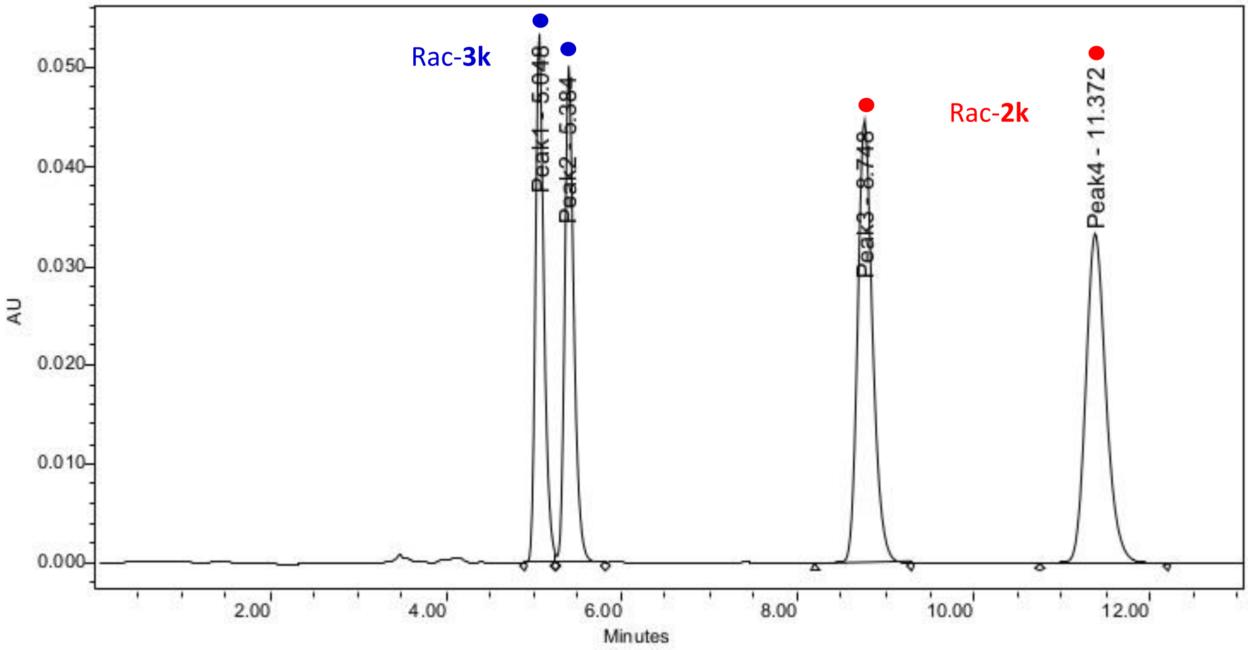
	Peak Name	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	Peak1	24.176	381241	2.56	6898	2.73
2	Peak2	27.667	14488747	97.44	245359	97.27



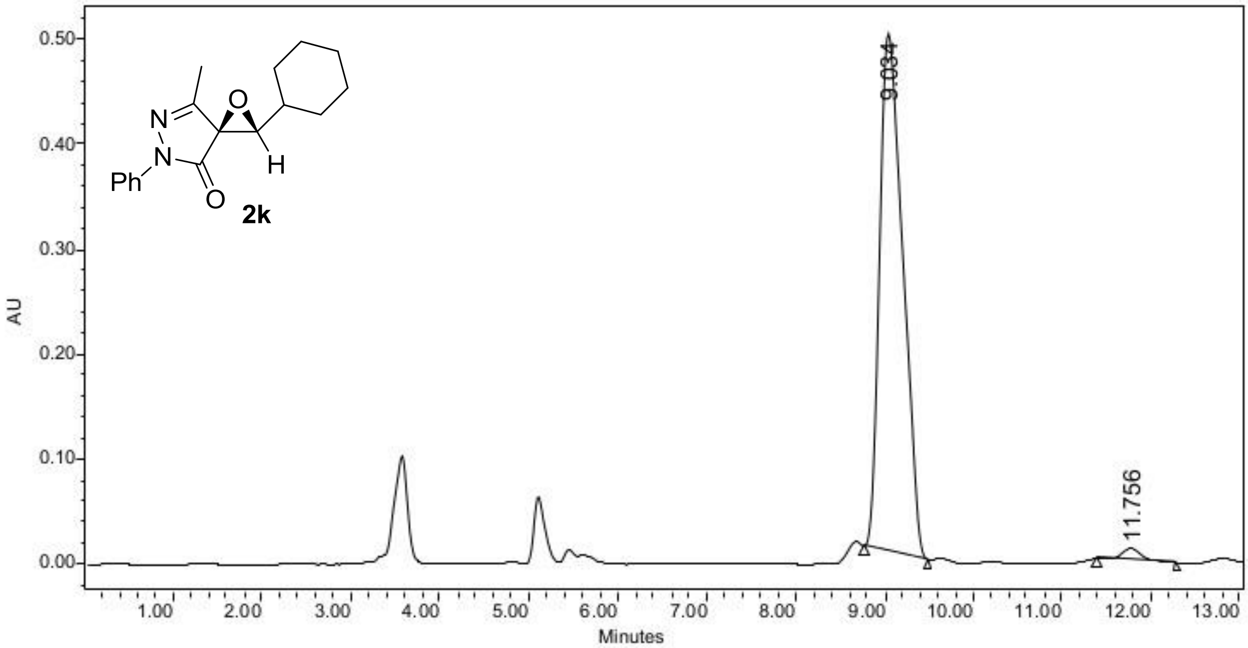
	Peak Name	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	Peak1	7.935	605582	29.95	55314	35.99
2	Peak2	8.610	738831	36.55	61844	40.24
3	Peak3	12.913	343872	17.01	19363	12.60
4	Peak4	13.707	333361	16.49	17177	11.18



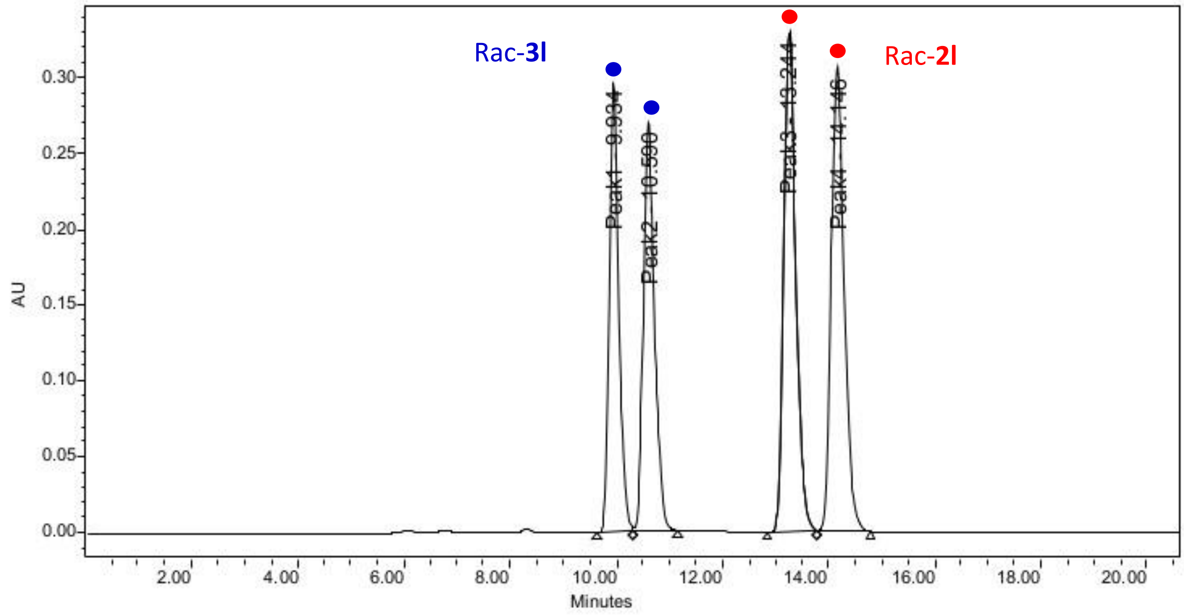
	Peak Name	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	Peak1	13.894	10453688	98.02	521382	97.97
2	Peak2	14.600	211288	1.98	10778	2.03



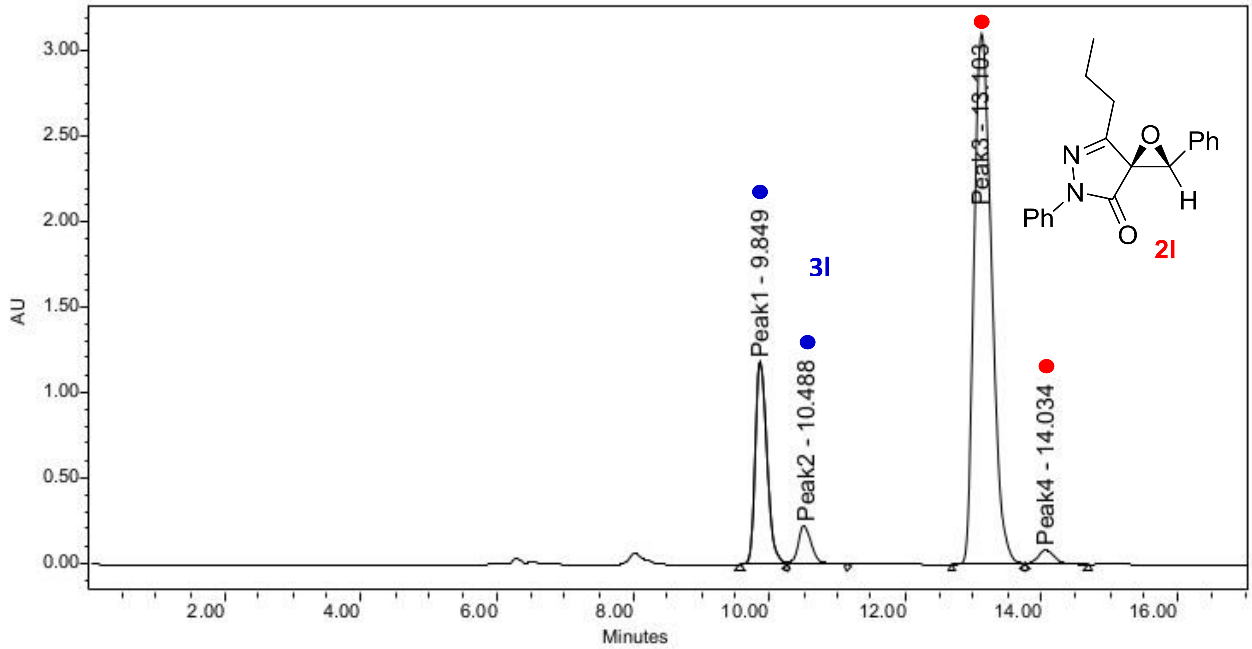
	Peak Name	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	Peak1	5.048	359435	20.07	53209	29.34
2	Peak2	5.384	363823	20.32	50017	27.58
3	Peak3	8.748	532032	29.71	44747	24.67
4	Peak4	11.372	535329	29.90	33380	18.41



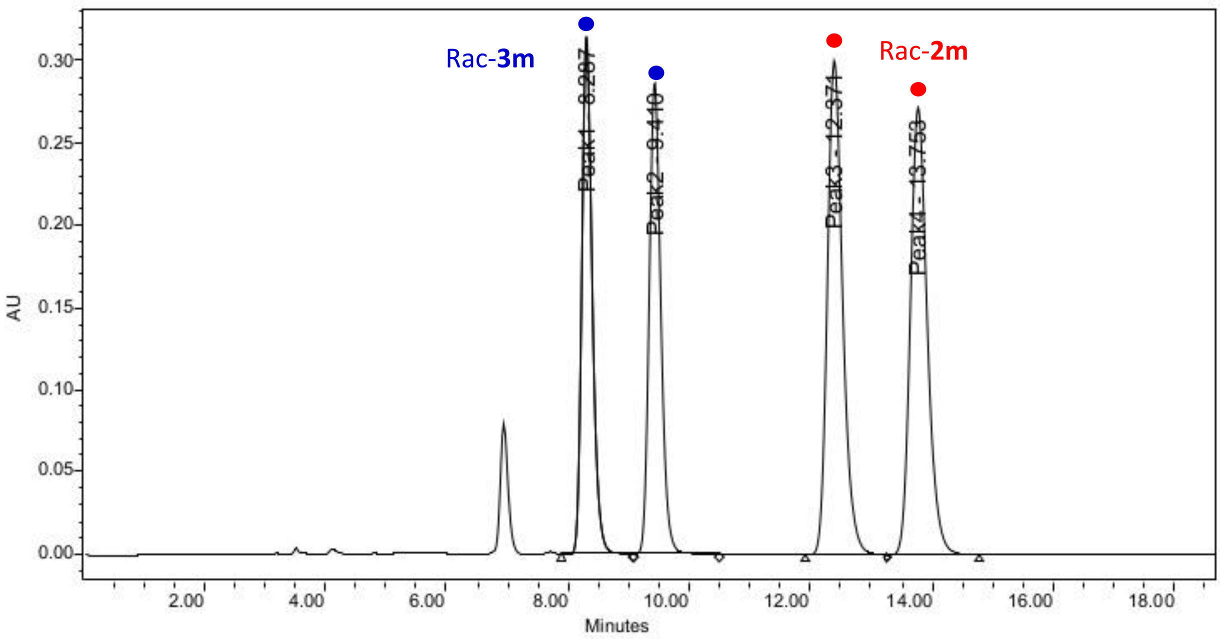
	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	9.034	8977543	98.09	494271	97.77
2	11.756	175067	1.91	11248	2.23



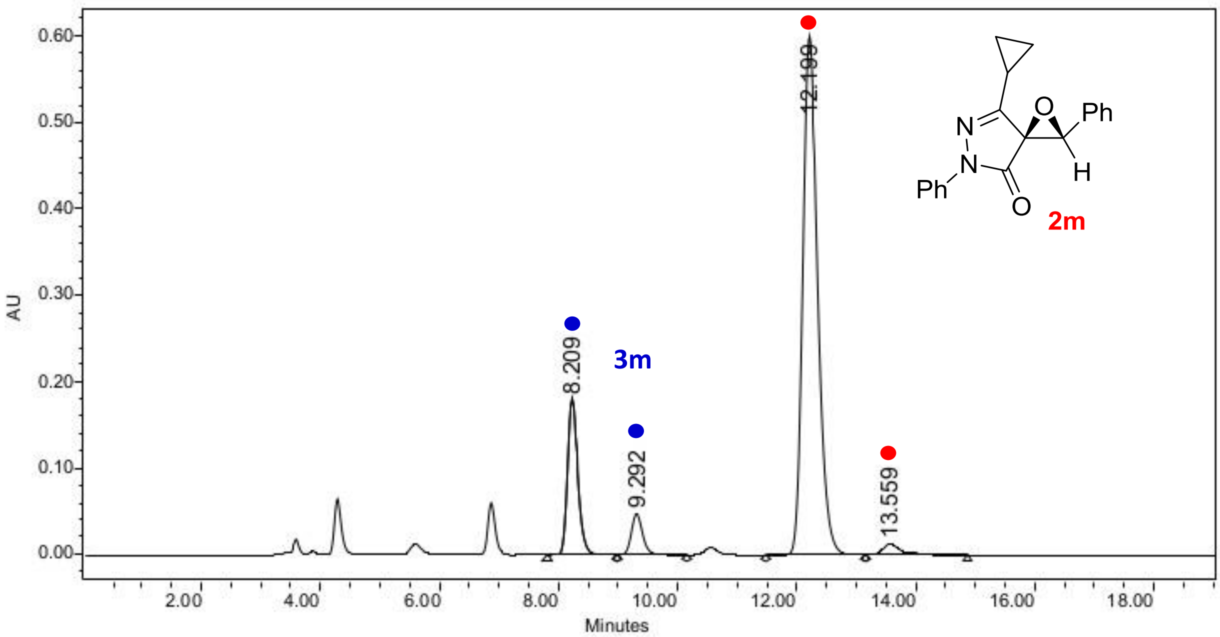
	Peak Name	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	Peak1	9.934	3659610	20.25	296836	24.65
2	Peak2	10.590	3944127	21.83	269964	22.42
3	Peak3	13.244	5250511	29.05	330405	27.44
4	Peak4	14.146	5217033	28.87	306820	25.48



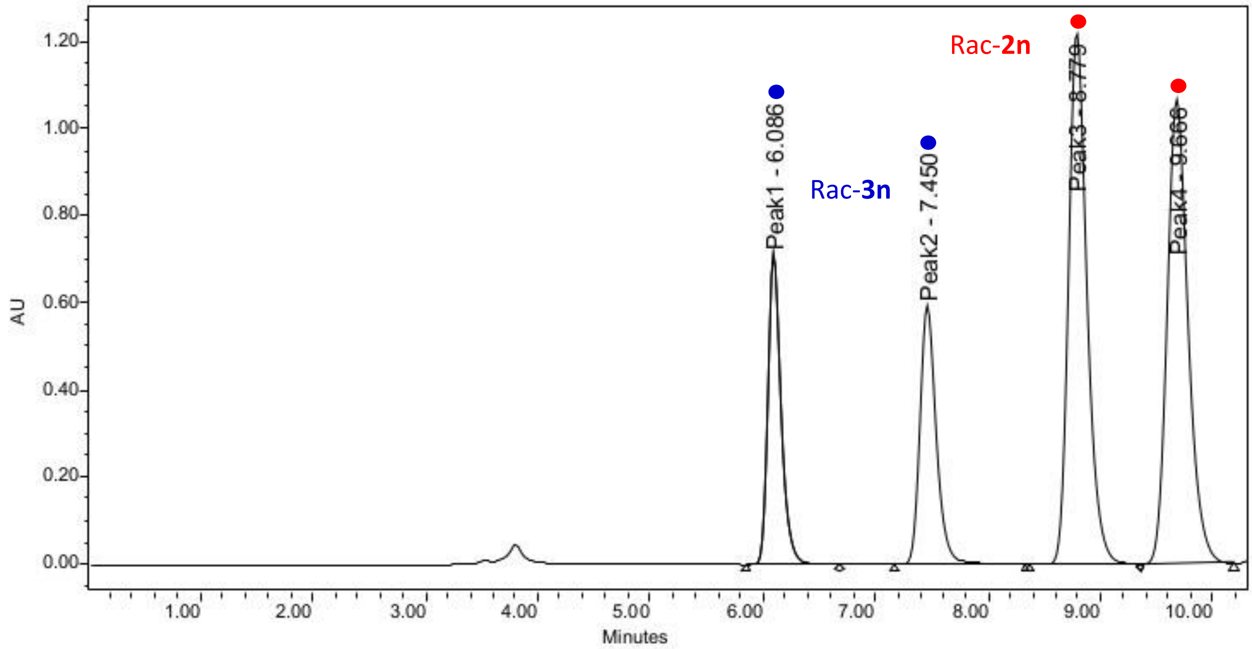
	Peak Name	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	Peak1	9.849	14285295	19.12	1186948	25.74
2	Peak2	10.488	3063350	4.10	227856	4.94
3	Peak3	13.103	55864903	74.79	3111056	67.47
4	Peak4	14.034	1486910	1.99	85488	1.85



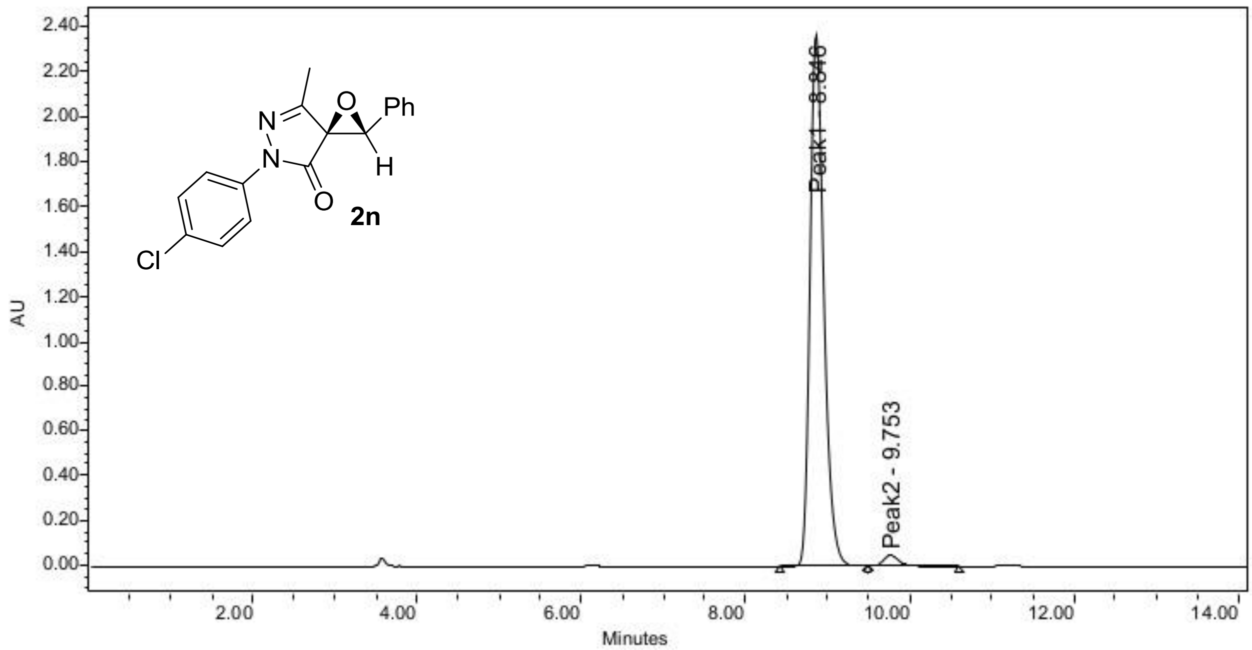
	Peak Name	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	Peak1	8.287	3750493	20.76	315532	26.83
2	Peak2	9.410	3827008	21.18	287454	24.45
3	Peak3	12.371	5252731	29.07	300716	25.57
4	Peak4	13.753	5239195	28.99	272144	23.14



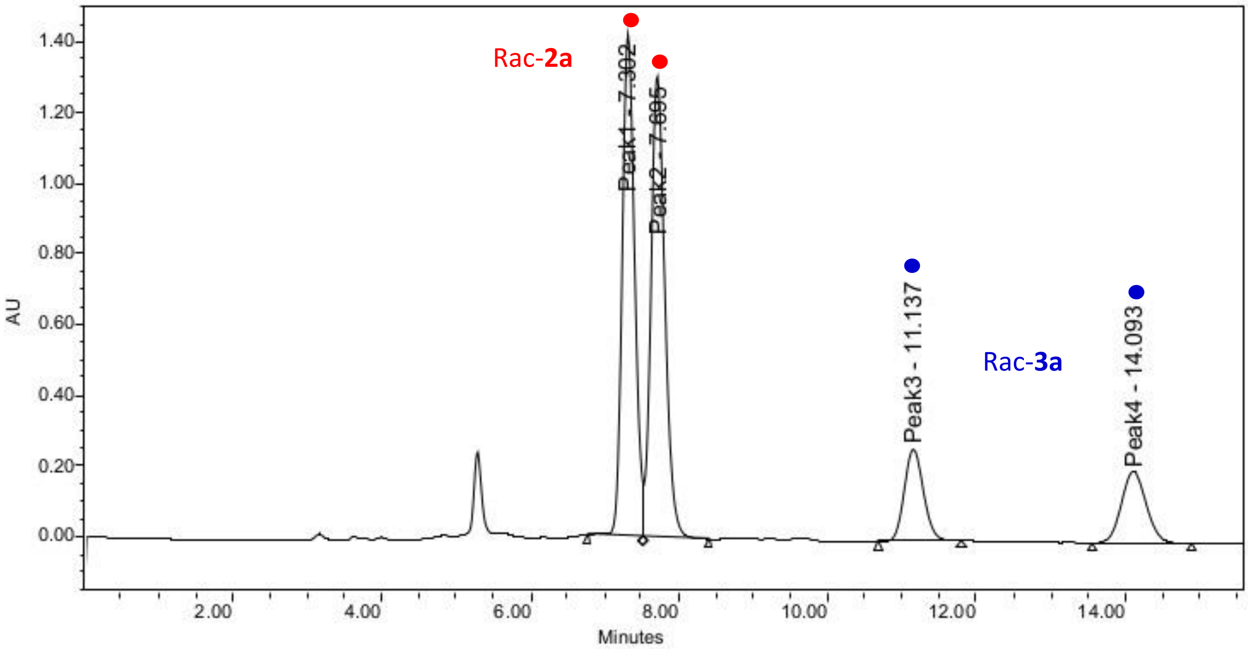
	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	8.209	2174635	16.10	182186	21.58
2	9.292	634575	4.70	47731	5.65
3	12.199	10410608	77.07	601595	71.27
4	13.559	288972	2.14	12617	1.49



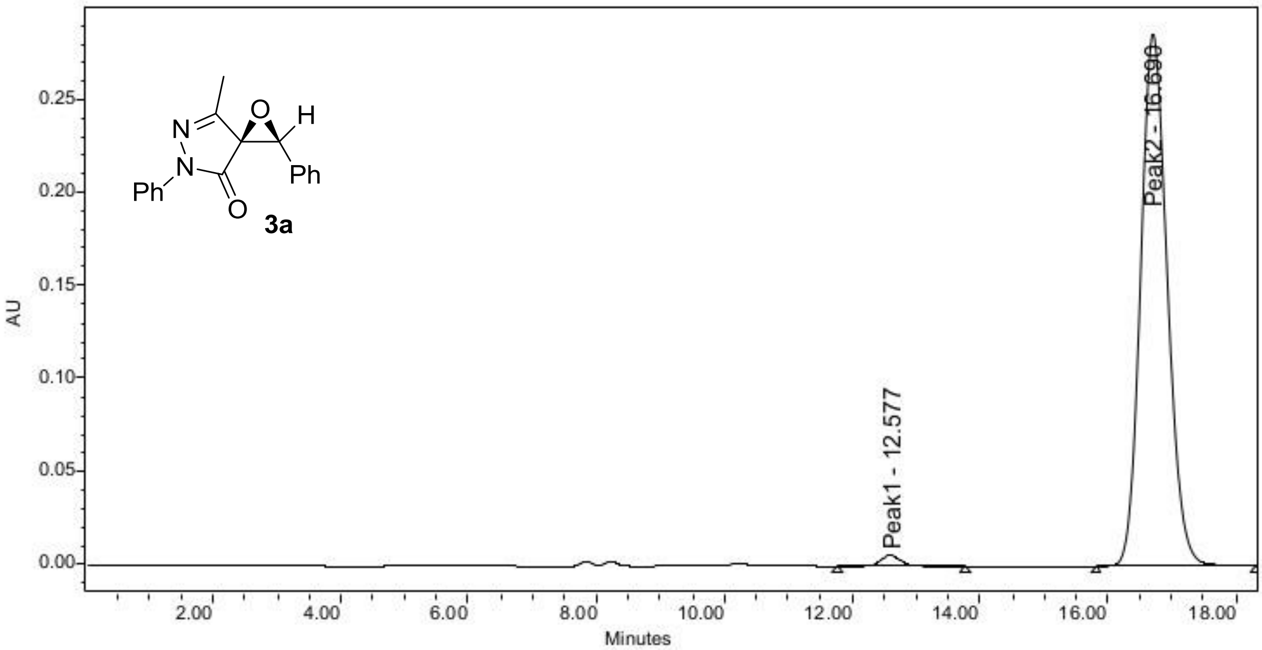
	Peak Name	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	Peak1	6.086	5842768	14.78	712353	19.83
2	Peak2	7.450	6000824	15.18	594069	16.53
3	Peak3	8.779	13860284	35.06	1219941	33.95
4	Peak4	9.666	13831890	34.99	1066613	29.69



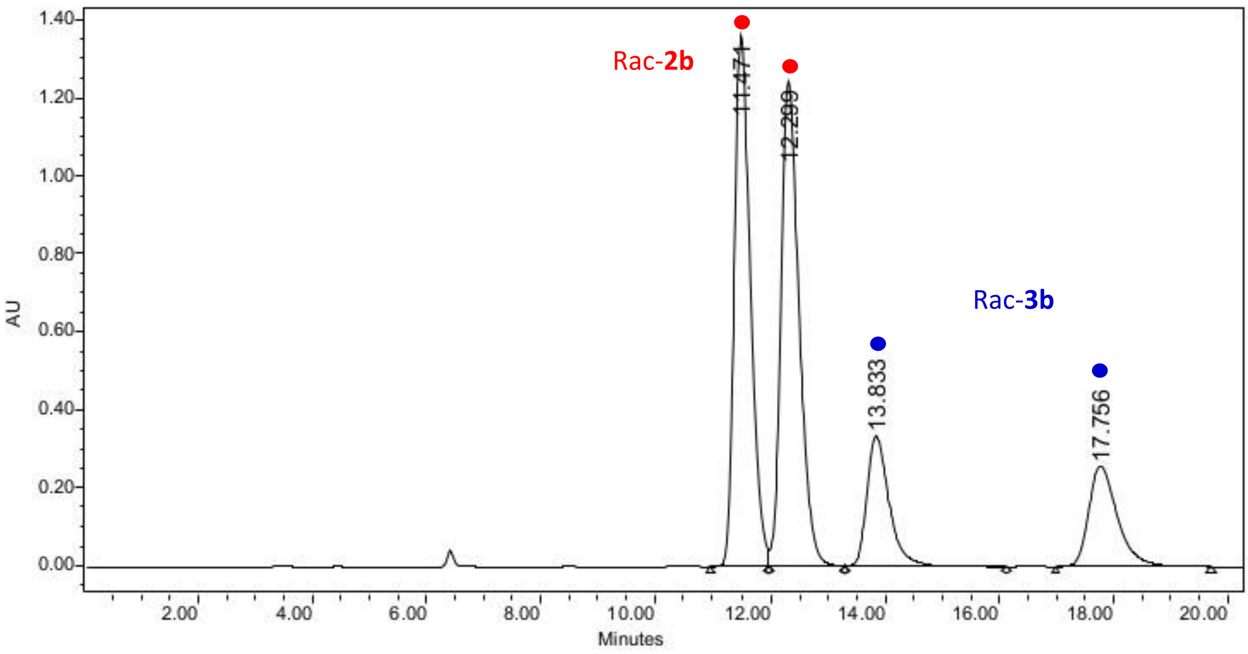
	Peak Name	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	Peak1	8.846	27763499	97.62	2372107	97.94
2	Peak2	9.753	676677	2.38	49869	2.06



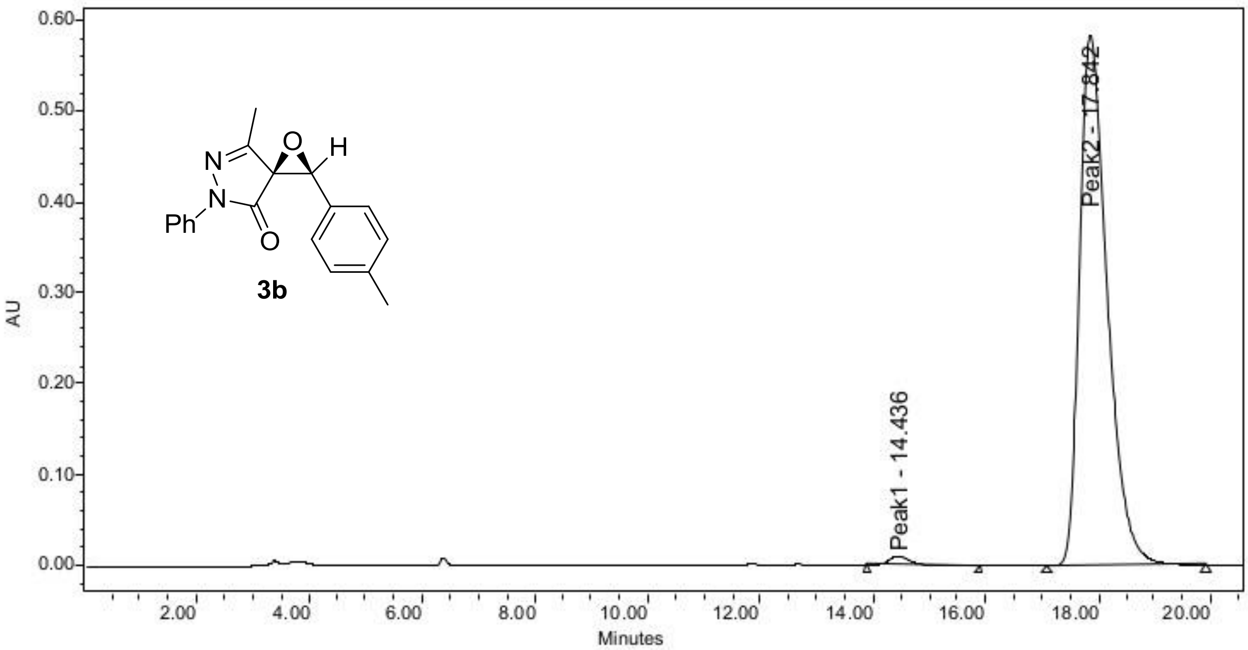
	Peak Name	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	Peak1	7.302	16549762	38.55	1421341	44.52
2	Peak2	7.695	16946283	39.47	1306925	40.93
3	Peak3	11.137	4724919	11.00	261807	8.20
4	Peak4	14.093	4713576	10.98	202864	6.35



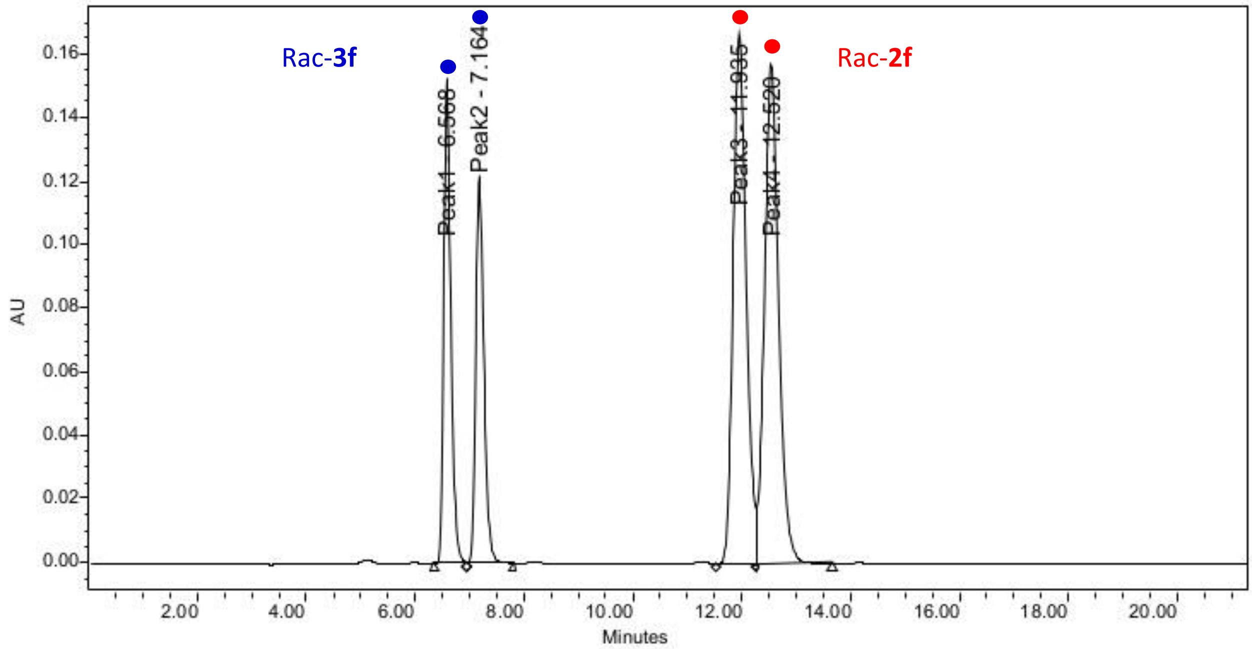
	Peak Name	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	Peak1	12.577	131246	1.56	5943	2.03
2	Peak2	16.690	8299157	98.44	286203	97.97



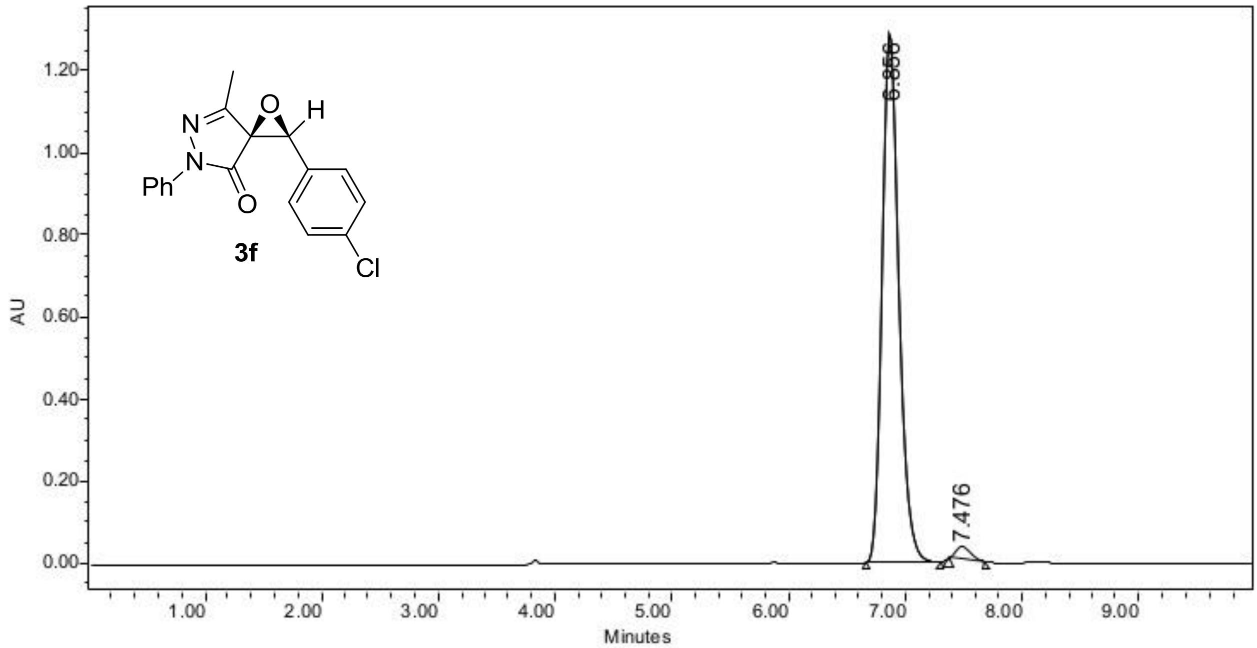
	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	11.471	26828956	37.08	1361565	42.56
2	12.299	27400463	37.87	1243207	38.86
3	13.833	9102459	12.58	335596	10.49
4	17.756	9012894	12.46	258734	8.09



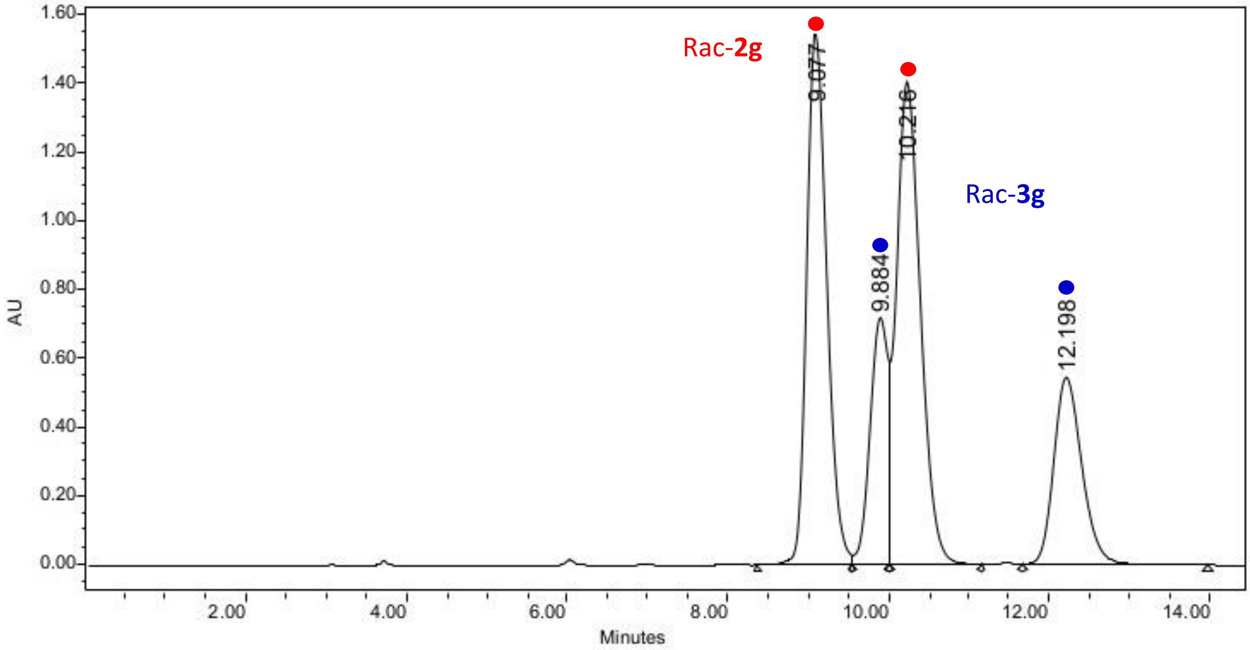
	Peak Name	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	Peak1	14.436	271129	1.34	10050	1.69
2	Peak2	17.842	19962335	98.66	583605	98.31



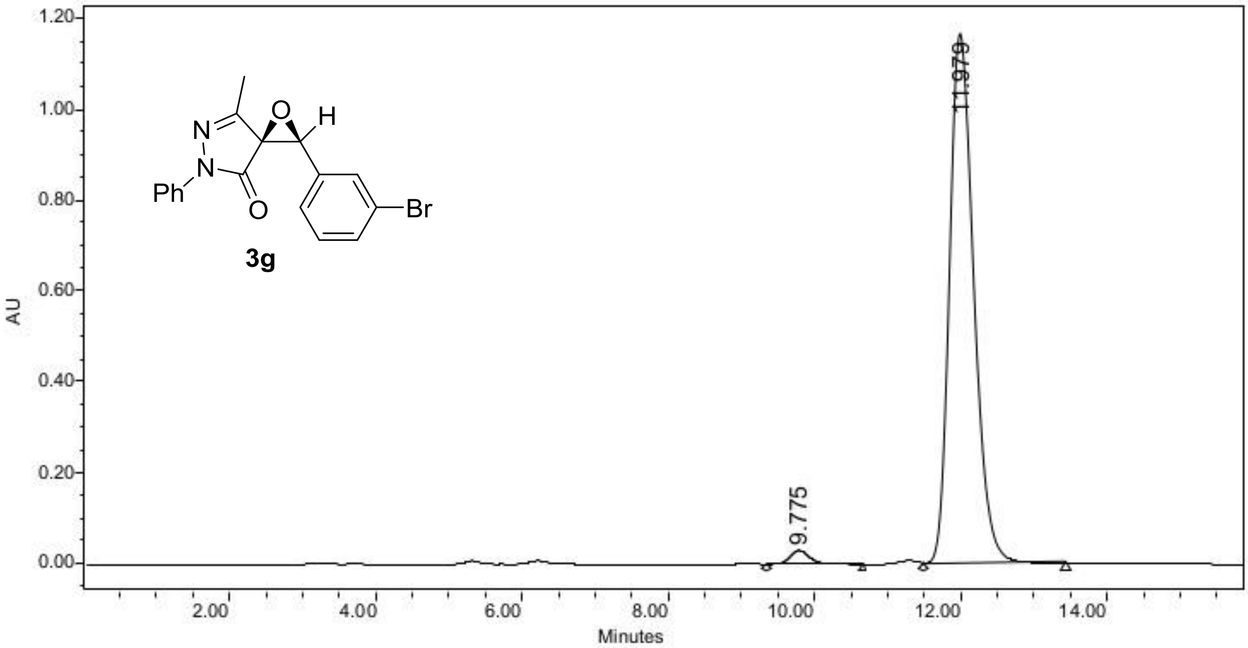
	Peak Name	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	Peak1	6.568	1385527	16.82	152344	25.48
2	Peak2	7.164	1247955	15.15	121716	20.36
3	Peak3	11.935	2758223	33.48	166733	27.89
4	Peak4	12.520	2847329	34.56	157090	26.27



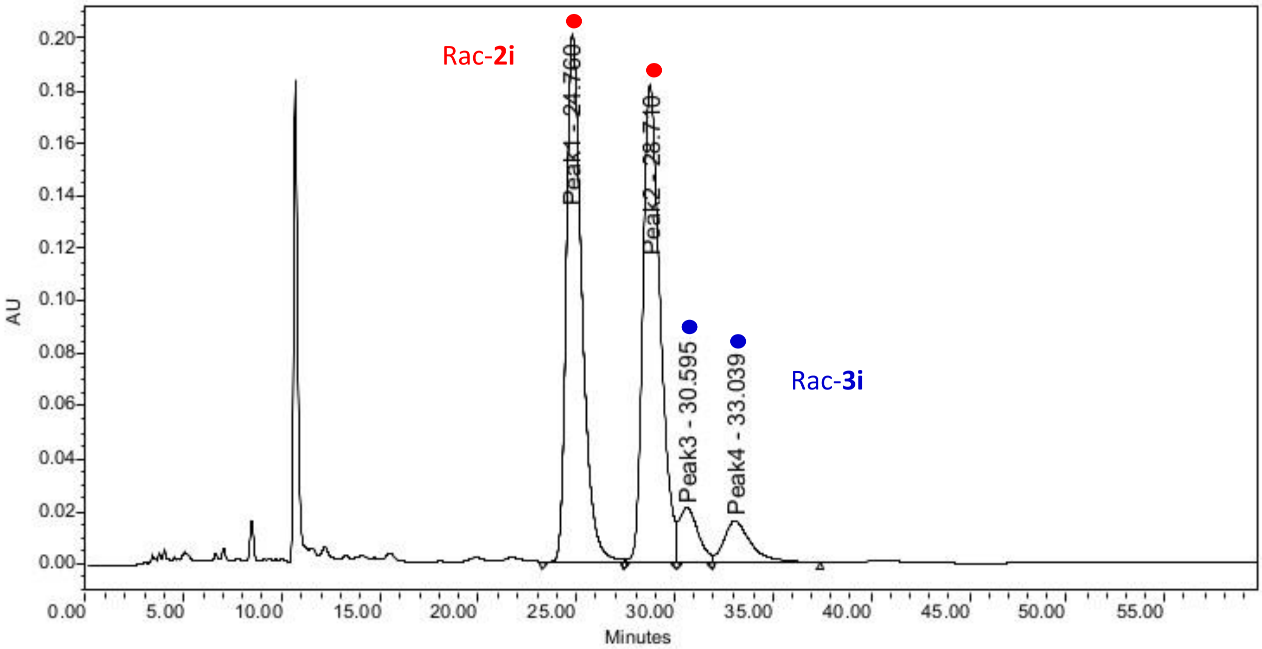
	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	6.856	12791637	97.84	1290605	97.65
2	7.476	282447	2.16	31090	2.35



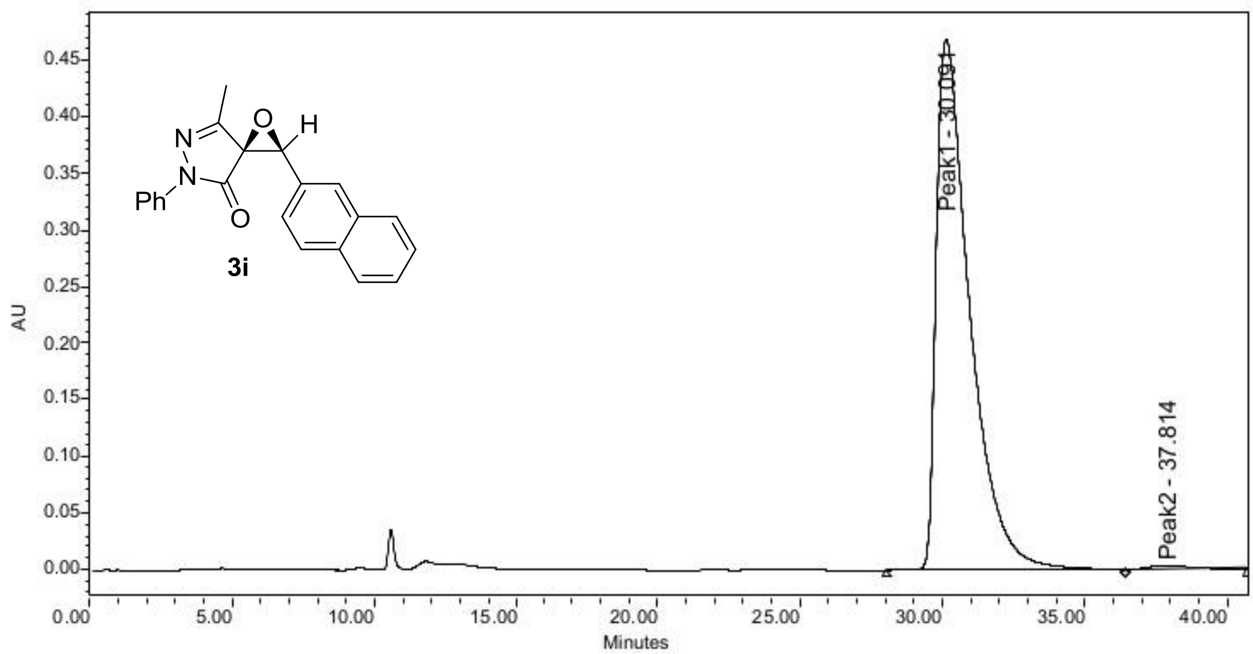
	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	9.077	26913968	33.34	1544182	36.63
2	9.884	10969349	13.59	719527	17.07
3	10.216	29446936	36.48	1405437	33.34
4	12.198	13386480	16.58	546142	12.96



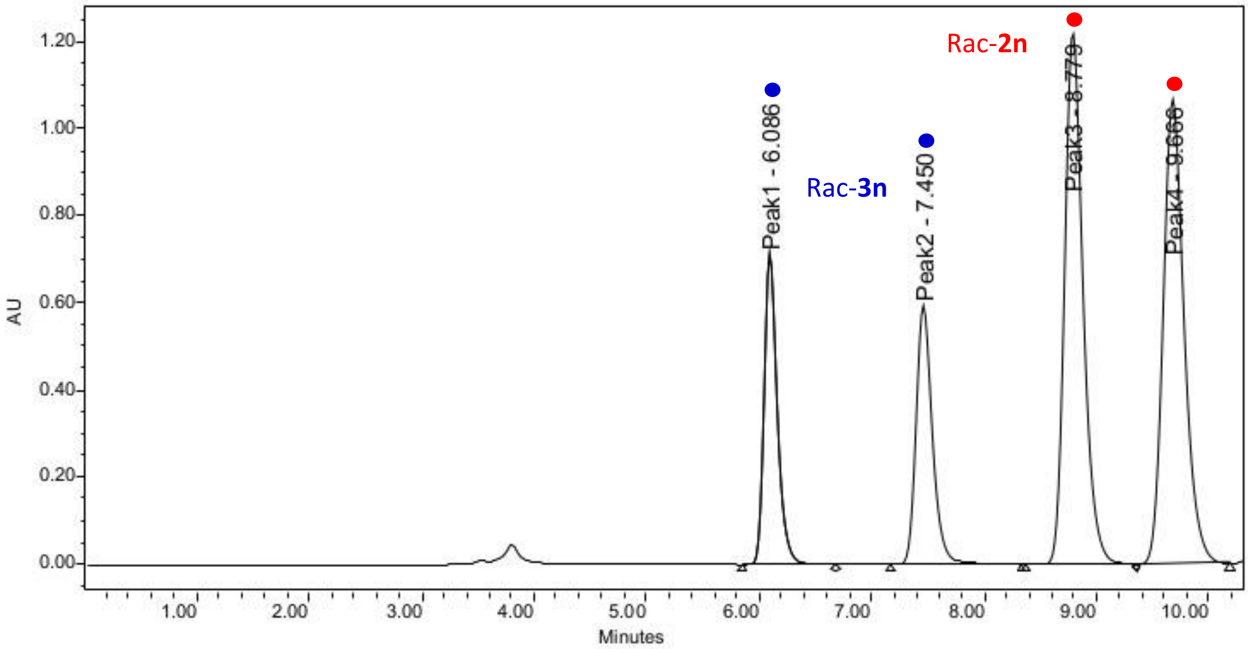
	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	9.775	588045	2.13	30572	2.55
2	11.979	26993190	97.87	1167362	97.45



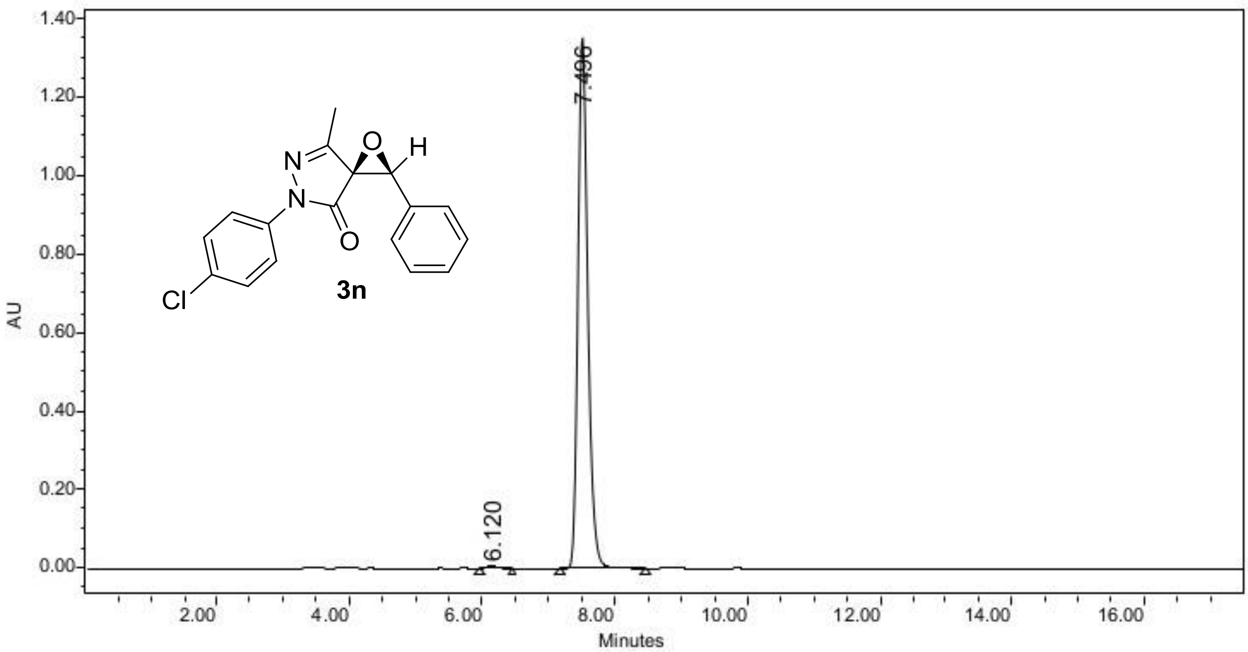
	Peak Name	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	Peak1	24.760	11112559	44.16	200853	47.96
2	Peak2	28.710	11163444	44.36	181361	43.31
3	Peak3	30.595	1387592	5.51	20789	4.96
4	Peak4	33.039	1502159	5.97	15789	3.77



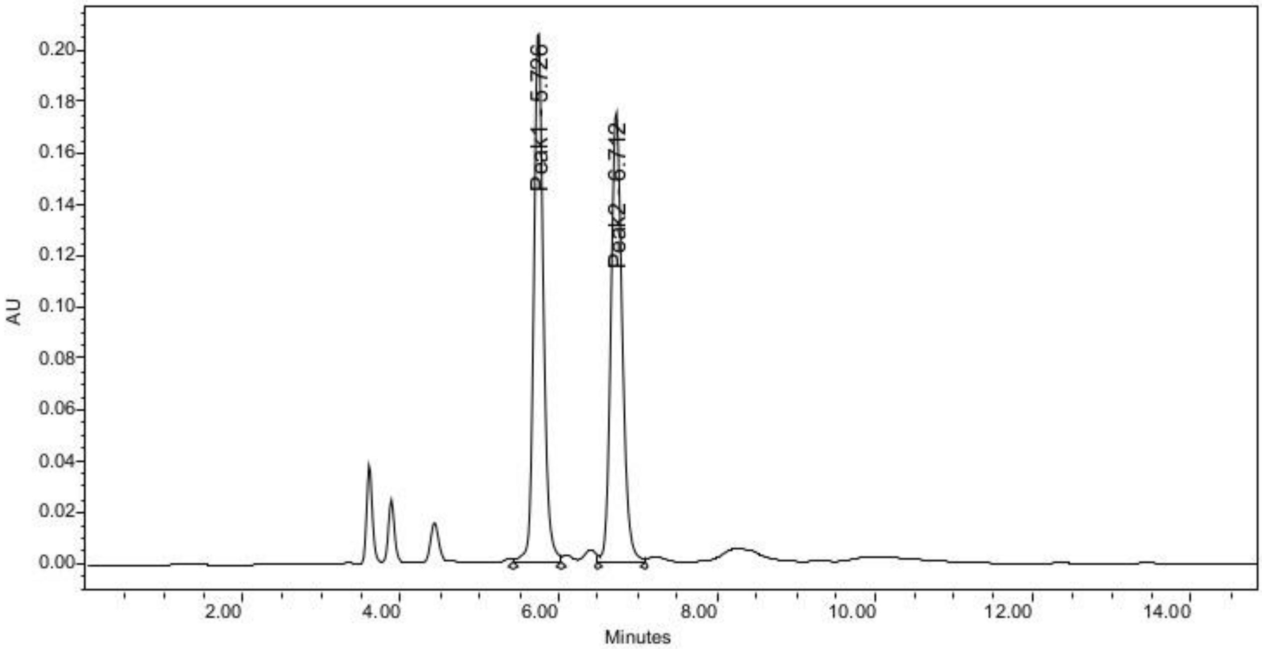
	Peak Name	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	Peak1	30.091	38615320	99.00	468516	99.24
2	Peak2	37.814	390183	1.00	3605	0.76



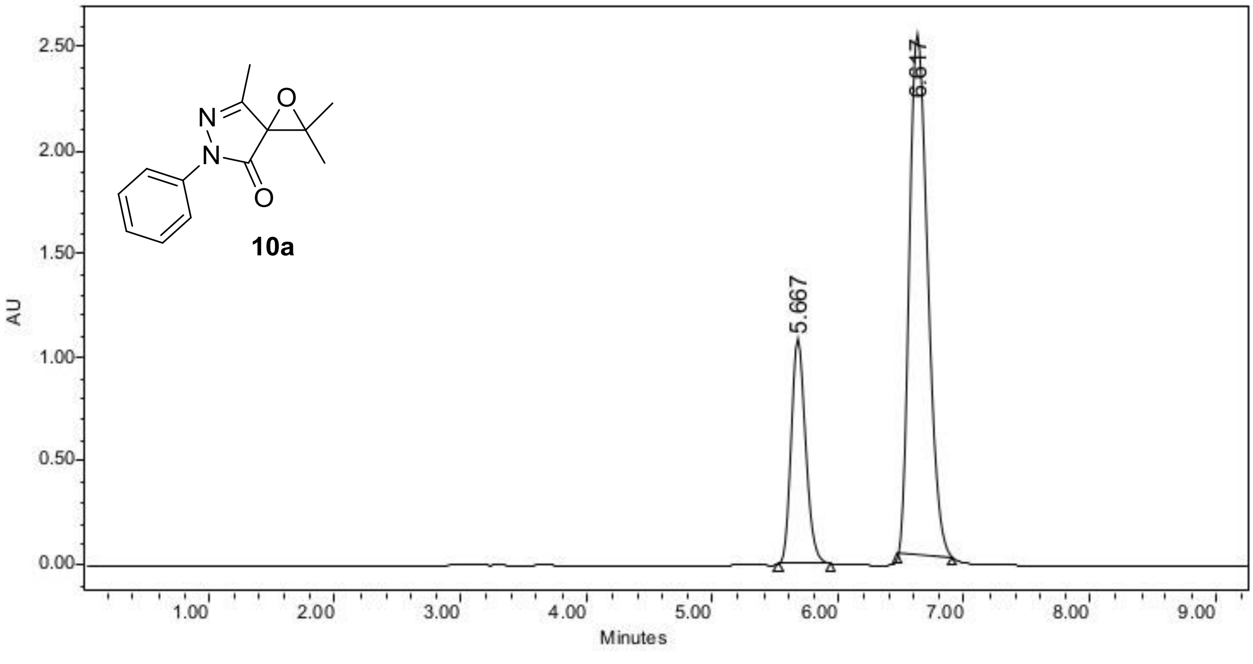
	Peak Name	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	Peak1	6.086	5842768	14.78	712353	19.83
2	Peak2	7.450	6000824	15.18	594069	16.53
3	Peak3	8.779	13860284	35.06	1219941	33.95
4	Peak4	9.666	13831890	34.99	1066613	29.69



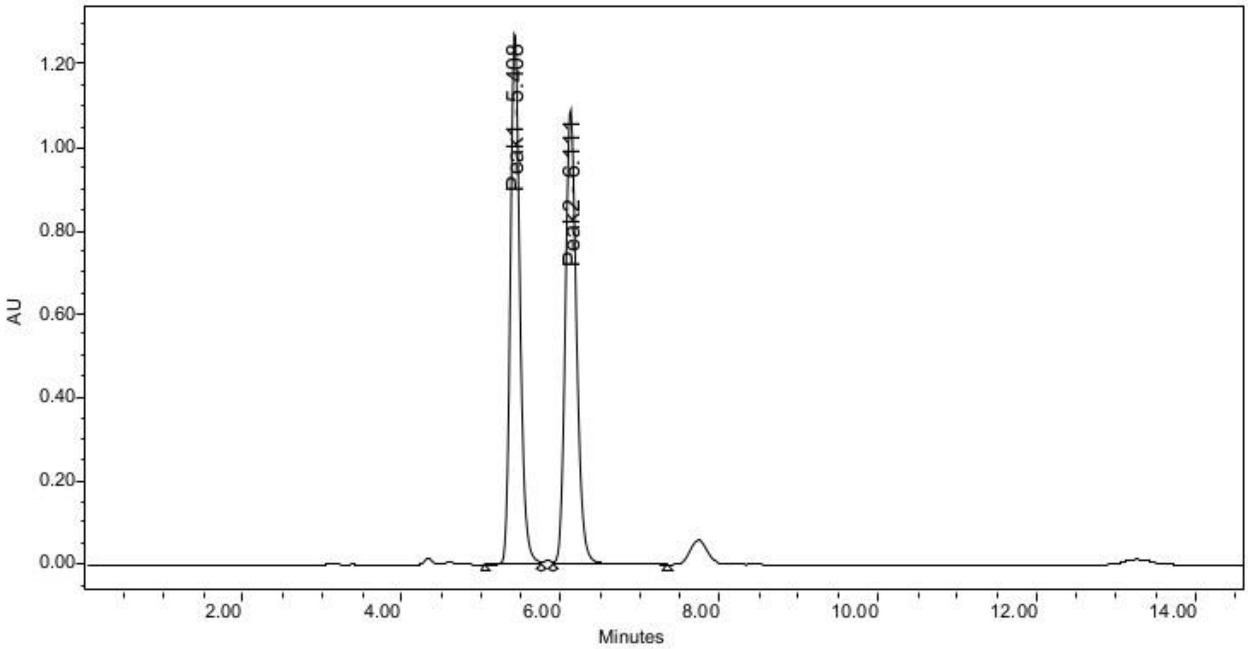
	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	6.120	65726	0.47	7795	0.57
2	7.496	13995756	99.53	1355475	99.43



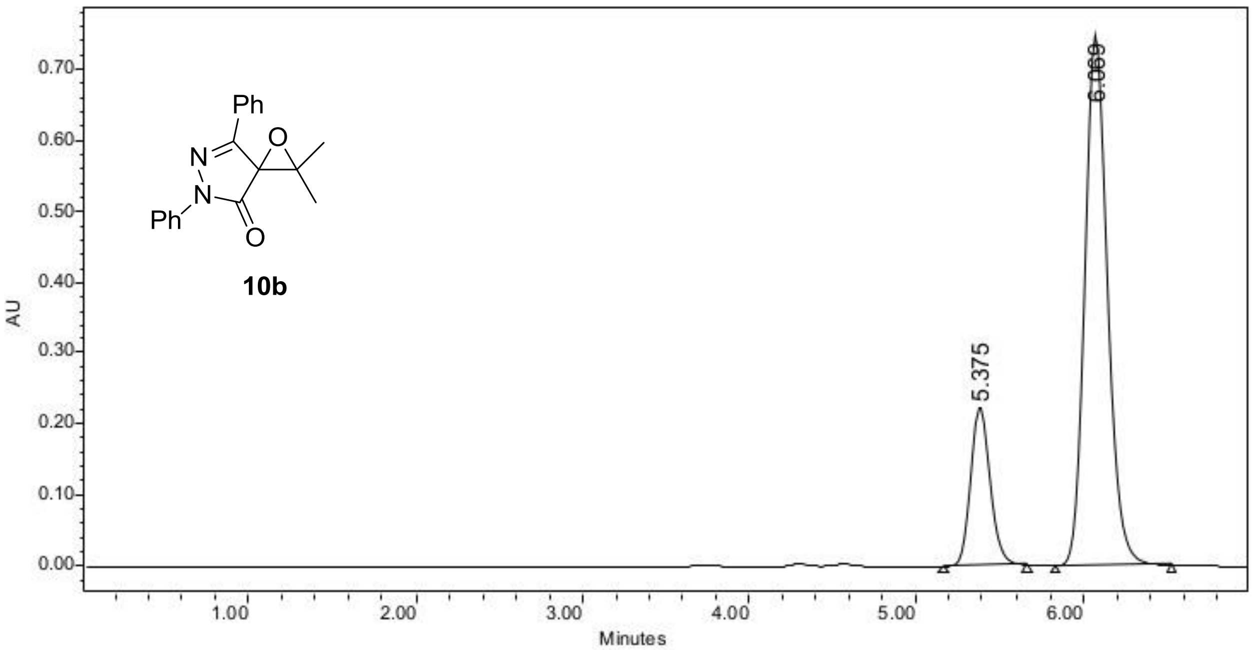
	Peak Name	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	Peak1	5.726	1751992	50.03	207168	54.11
2	Peak2	6.712	1749846	49.97	175673	45.89



	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	5.667	8675560	25.37	1087777	30.15
2	6.617	25525052	74.63	2519924	69.85



	Peak Name	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	Peak1	5.408	10692064	49.86	1284838	53.99
2	Peak2	6.111	10750887	50.14	1094946	46.01



	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	5.375	1840073	20.63	225937	23.18
2	6.069	7080594	79.37	748722	76.82

Optimized Geometries

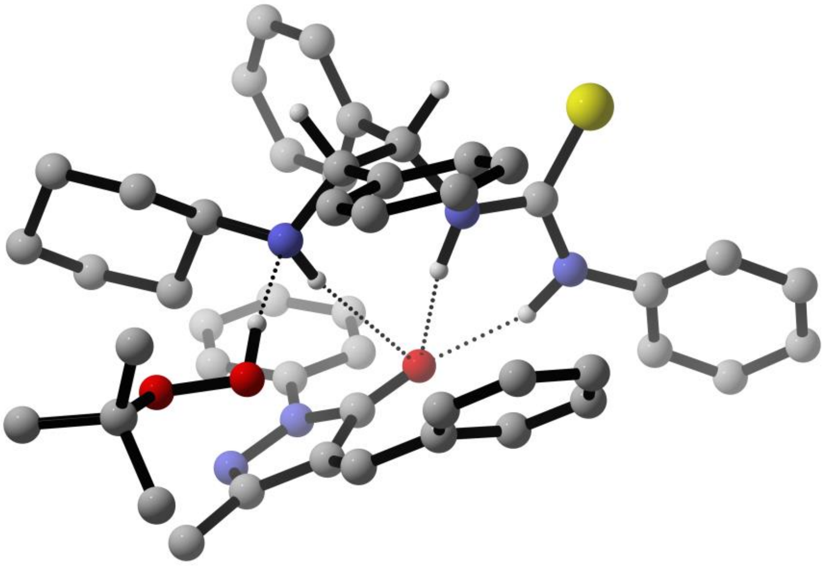


Figure S3. Optimized geometry of PRC-*R*, peripheral hydrogens have been omitted for clarity.

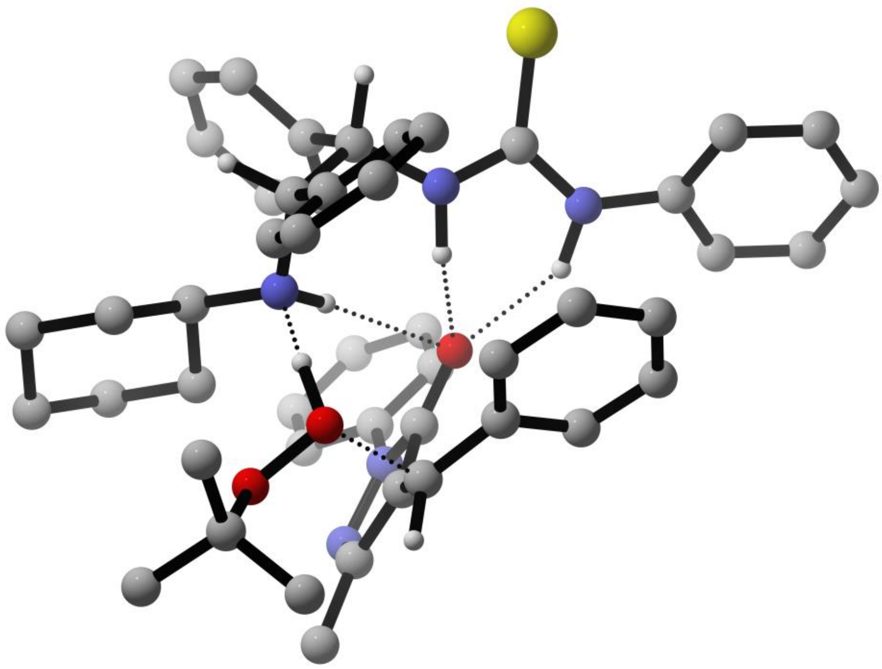


Figure S4. Optimized geometry of TS-*R*, peripheral hydrogens have been omitted for clarity.

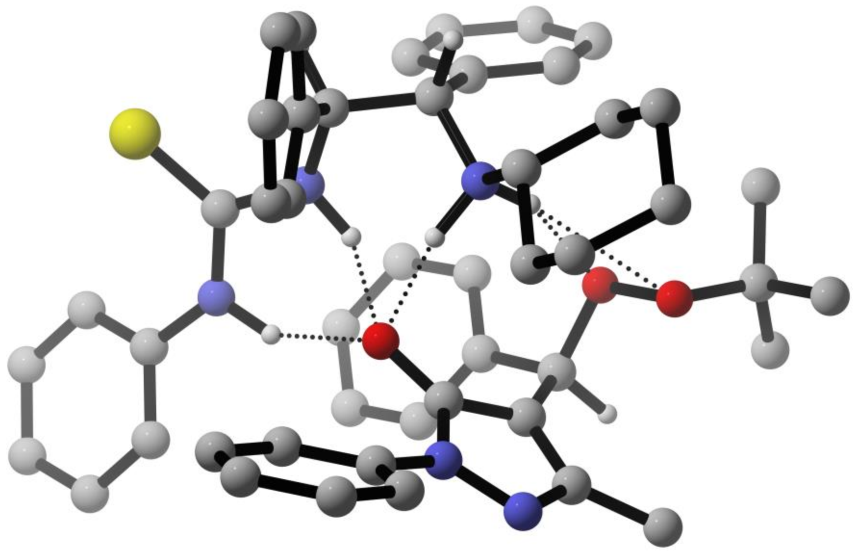


Figure S5. Optimized geometry of IC-*cis,* peripheral hydrogens have been omitted for clarity.

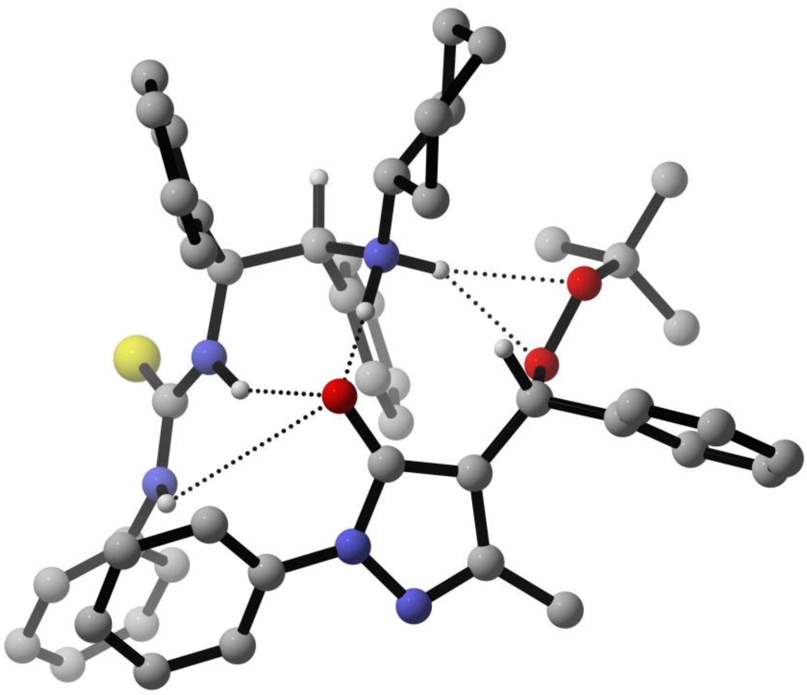


Figure S6. Optimized geometry of IC-*trans*, peripheral hydrogens have been omitted for clarity.

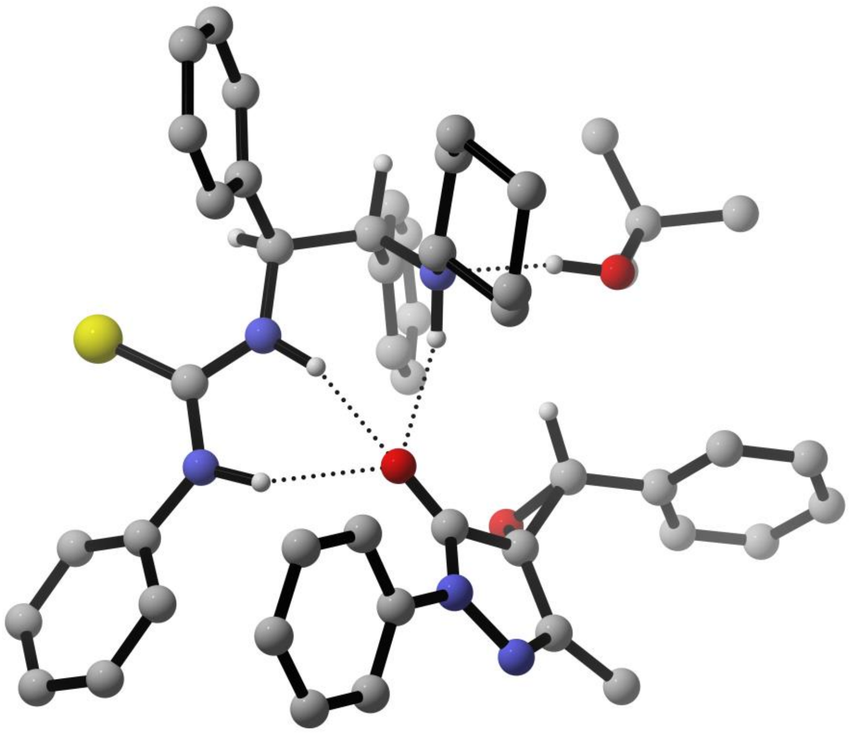


Figure S7. Optimized geometry of the product coordinated to the catalyst, peripheral hydrogens have been omitted for clarity.

Computational Details

Conformer search for the pre-reactive complexes was performed by using the MMFF force field and the Spartan software.[13] Geometry optimizations and computations of Hessian matrices needed to ascertain the nature of the located stationary points were carried out at the density functional level of theory (DFT) by using the M06-2X functional in conjunction with the 6-31G(d) basis set.[14] More accurate energies were obtained by single point computations employing the larger 6-311+G(2d,p) basis set. Solvent (toluene) effects were included in all computations by the polarizable continuum model.[15] All DFT calculations were carried out by using the Gaussian software.[16] Reported energies include zero point vibrational contributions evaluated at the (PCM)M06-2X/6-31G(d) level.

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[13] Spartan'04, Wavefunction, Inc. Irvine, CA, **2004**
[14] Zhao,Y.; Truhlar, D.G.; *Theor. Chem. Acc.* **2006**, *120*, 215-241.
[15] Miertuš, S.; Scrocco, E; Tomasi, J. *Chem. Phys.* **1981**, *55*, 117-129.
[16] Frisch, M. J. et al, Gaussian 09 Revision D.01, Gaussian Inc. Wallingford CT **2009**.