

## Supporting Information

### **Evaluation of Dual Potentiality of 2,4,5-Trisubstituted Oxazole Derivatives as Aquaporin-4 Inhibitors and anti-Inflammatory Agents in Lung Cells**

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## A. Copies of IR Spectra

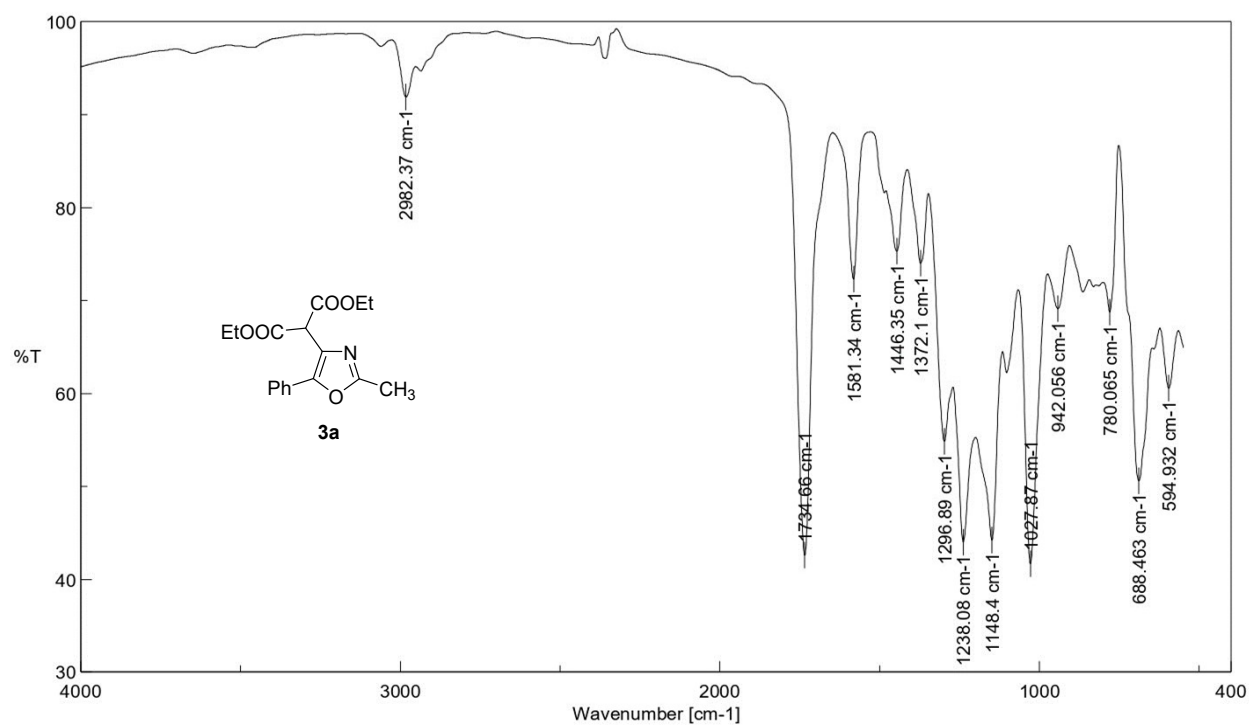
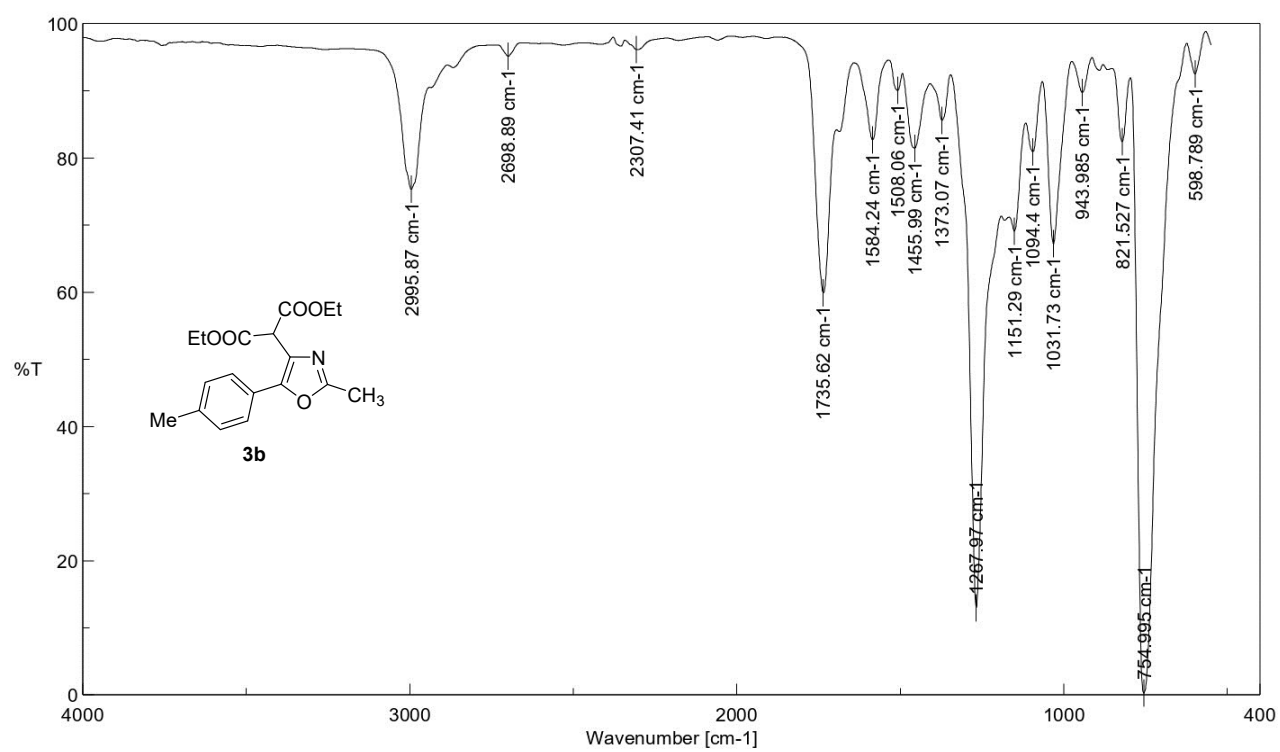
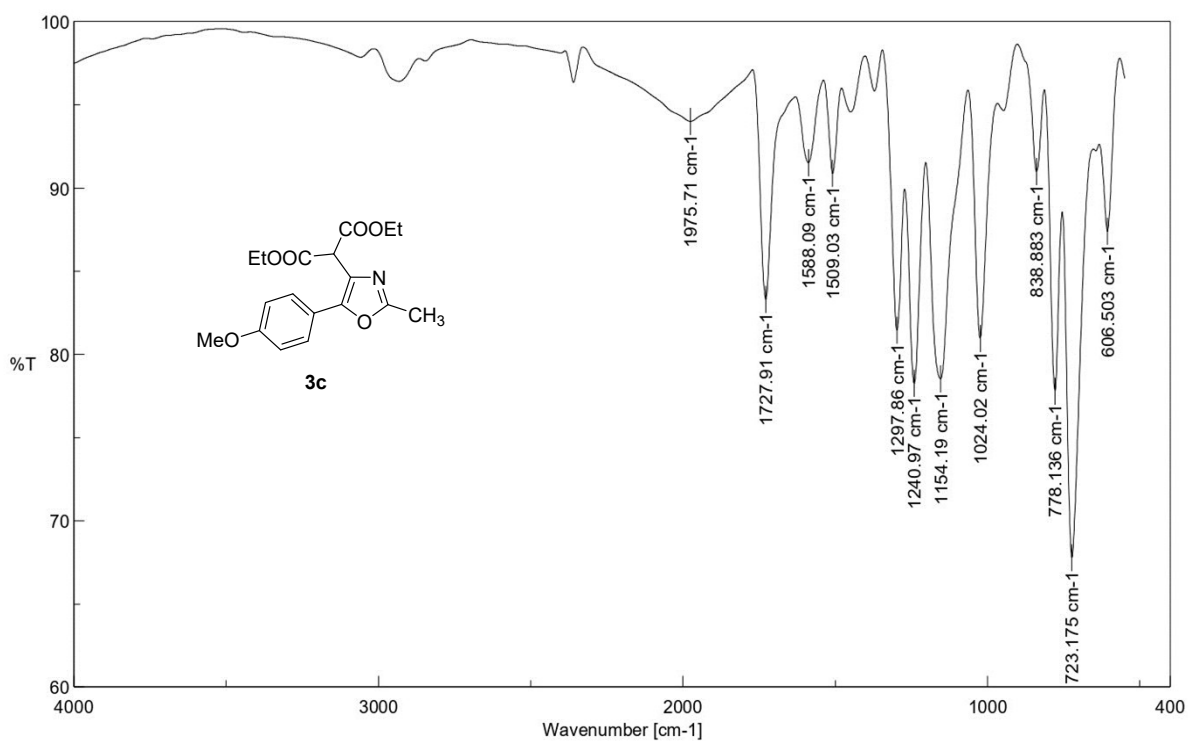


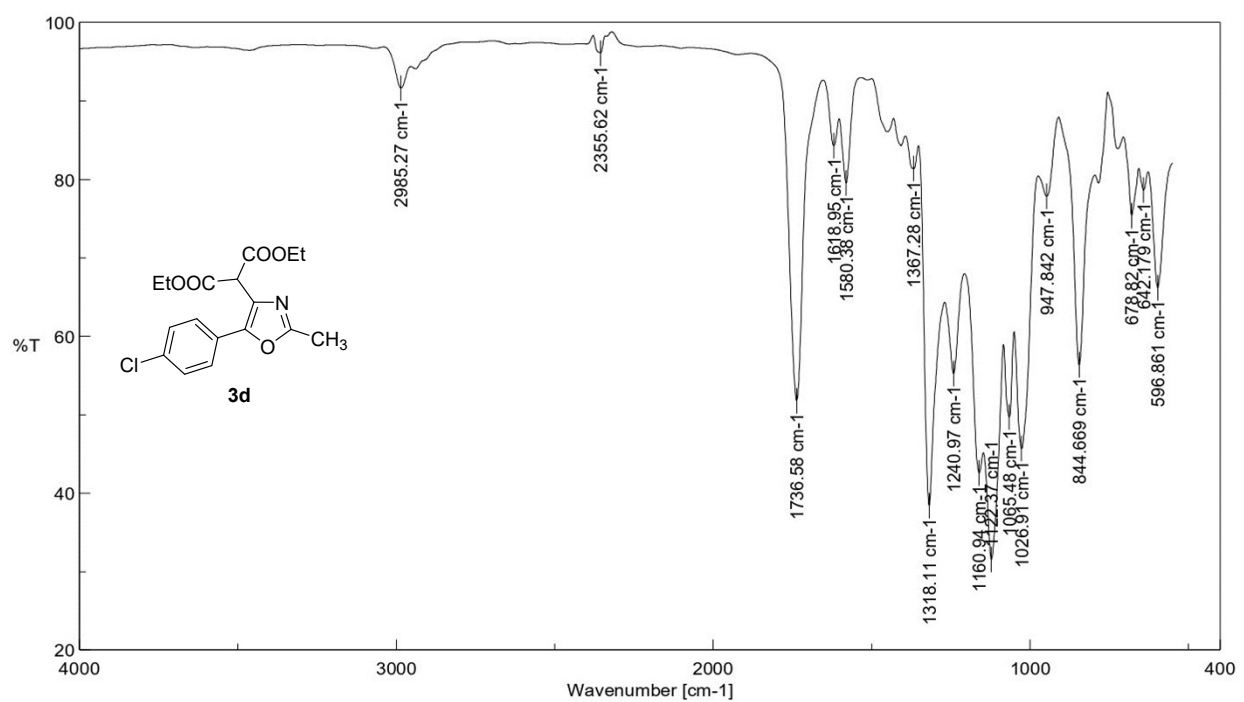
Figure S1. IR spectrum of **3a**



**Figure S2.** IR spectrum of **3b**



**Figure S3.** IR spectrum of **3c**



**Figure S4.** IR spectrum of **3d**

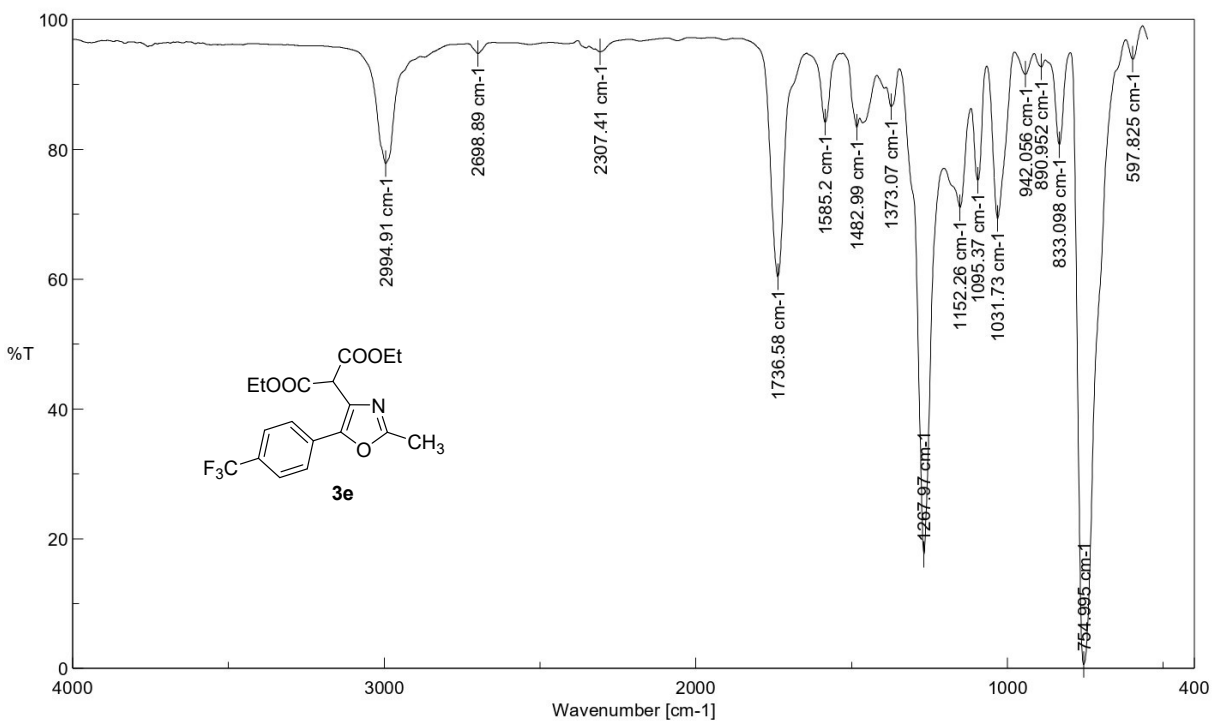
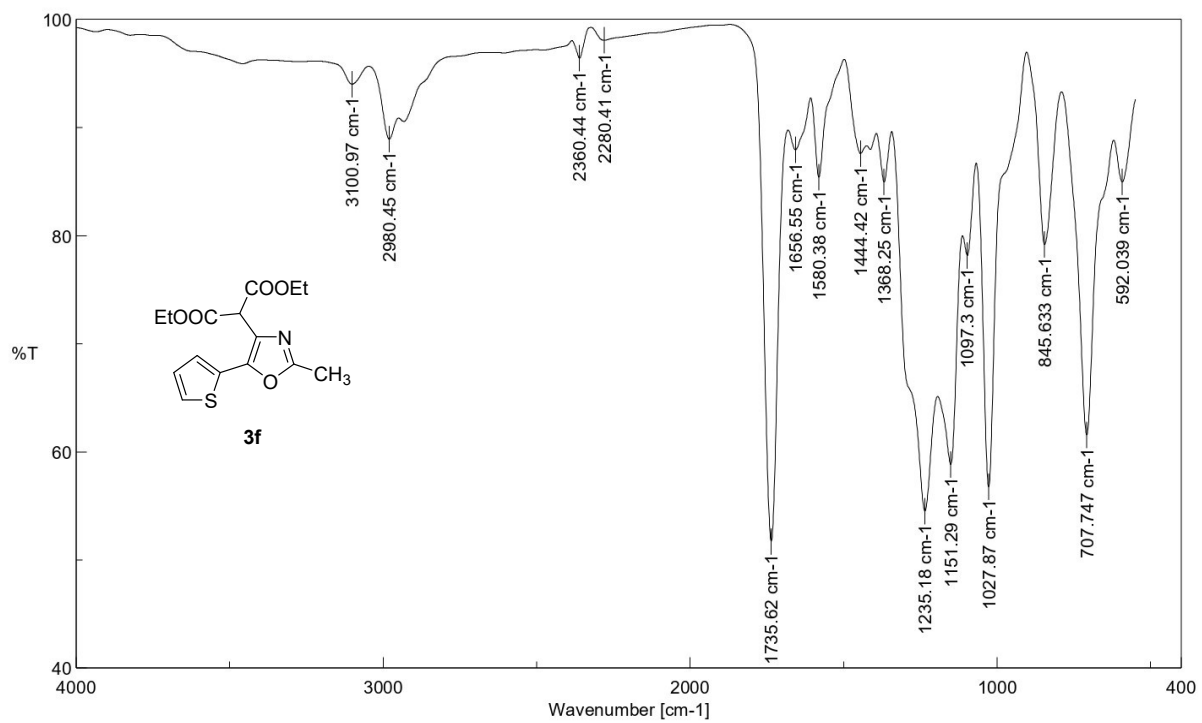
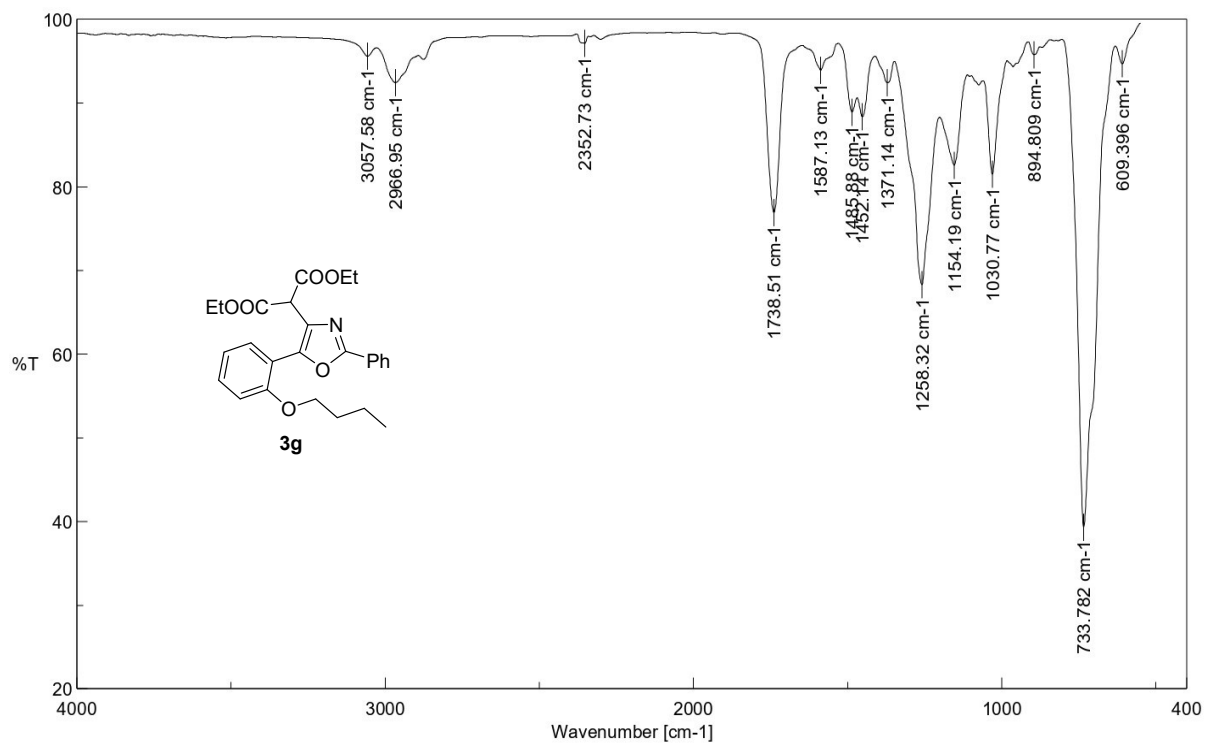


Figure S5. IR spectrum of **3e**

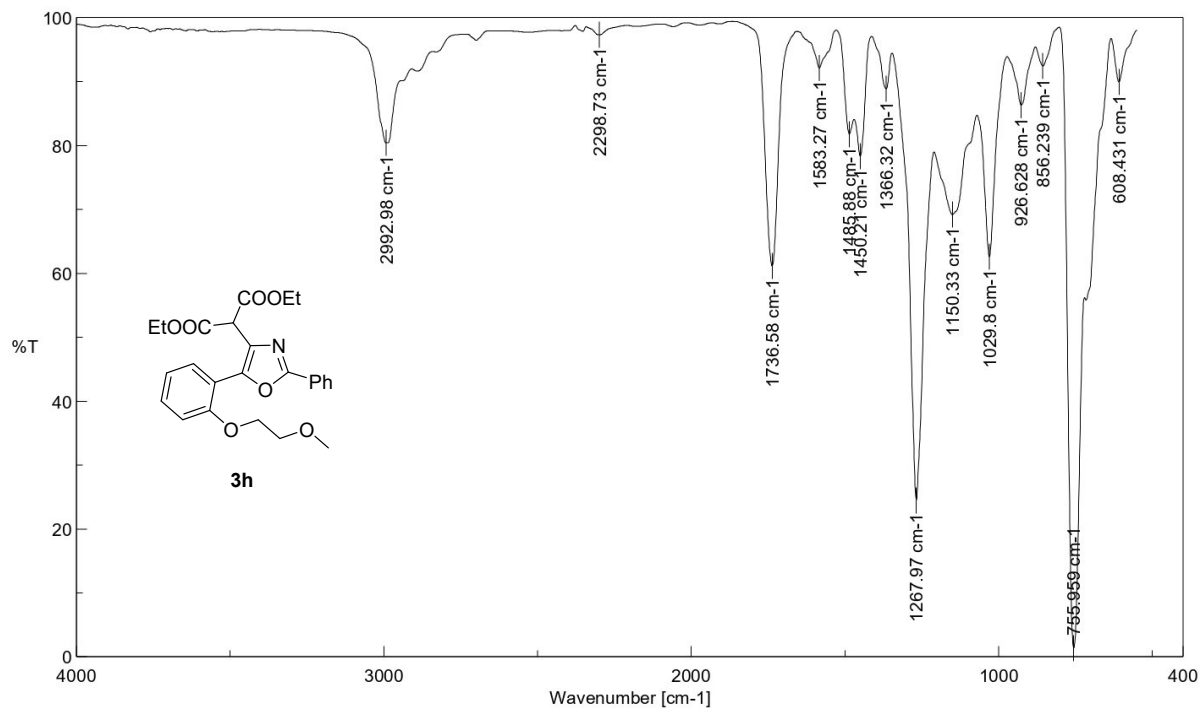


**Figure S6.** IR spectrum of **3f**

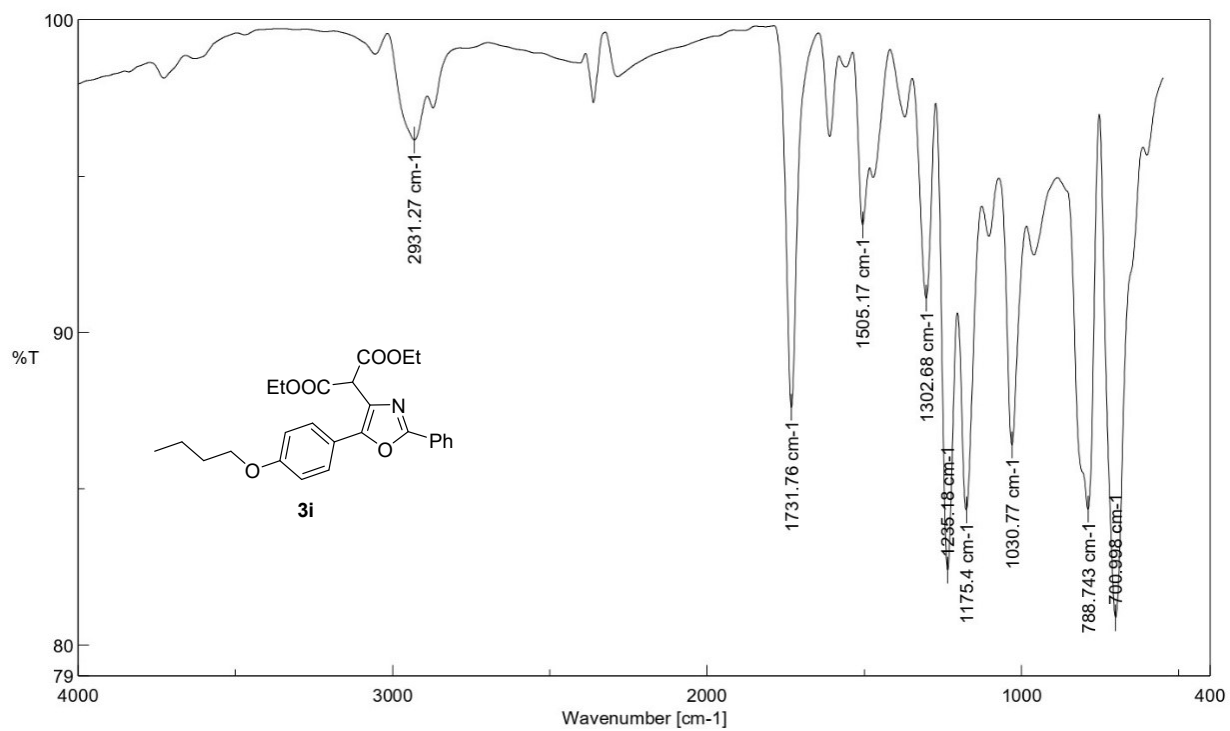


**Figure S7.** IR spectrum of **3g**

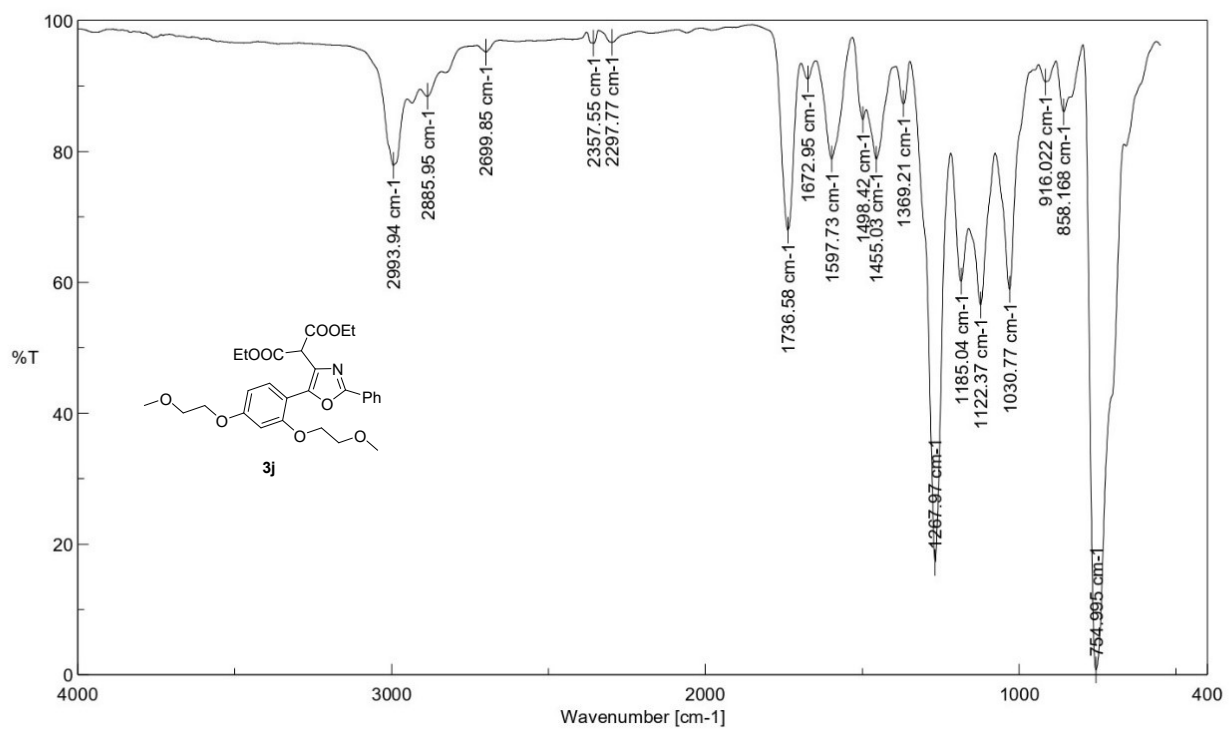




**Figure S8.** IR spectrum of **3h**



**Figure S9.** IR spectrum of **3i**



**Figure S10.** IR spectrum of **3j**

## B. Copies of $^1\text{H}$ NMR and $^{13}\text{C}$ NMR Spectra

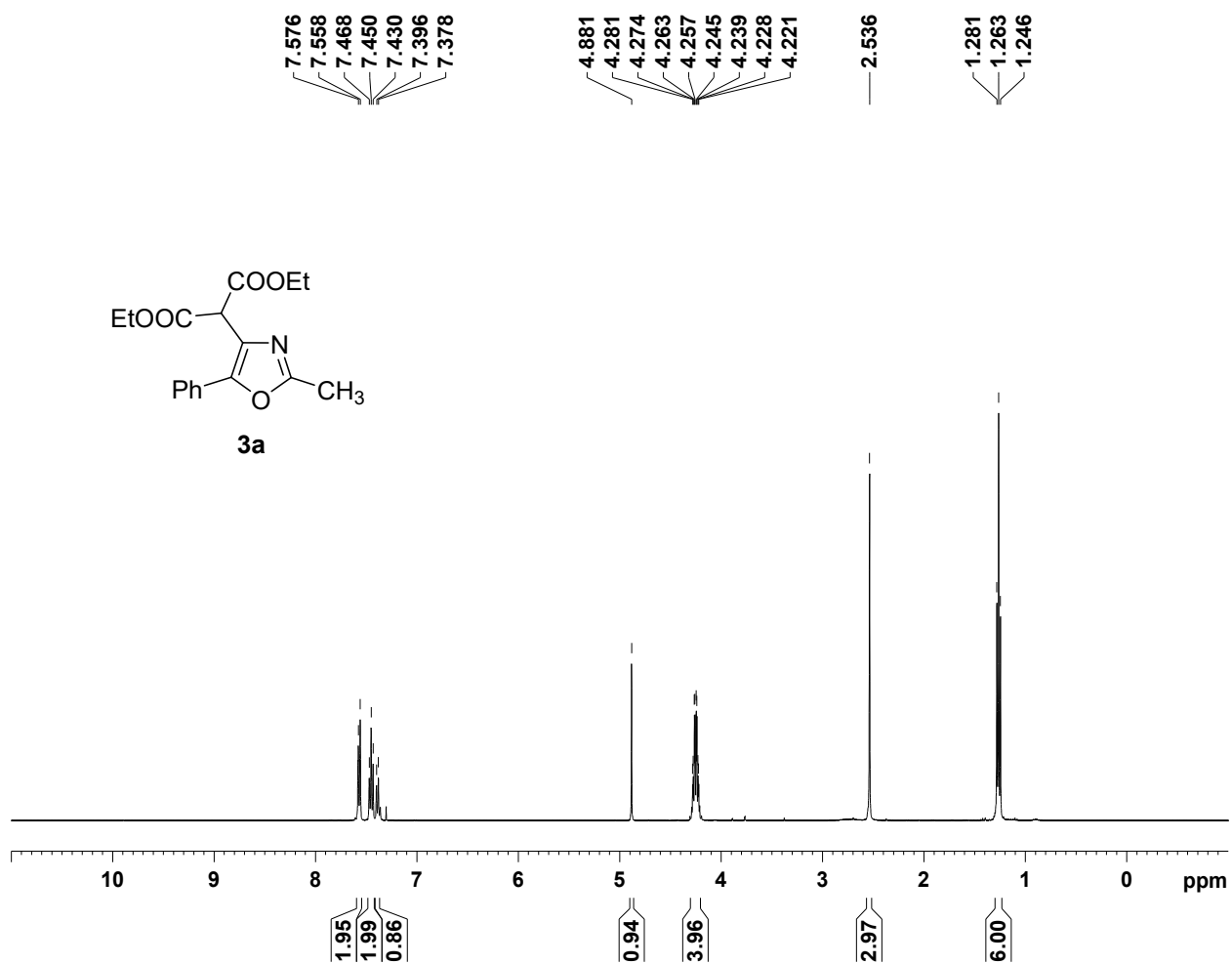


Figure S11.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) spectrum of **3a**

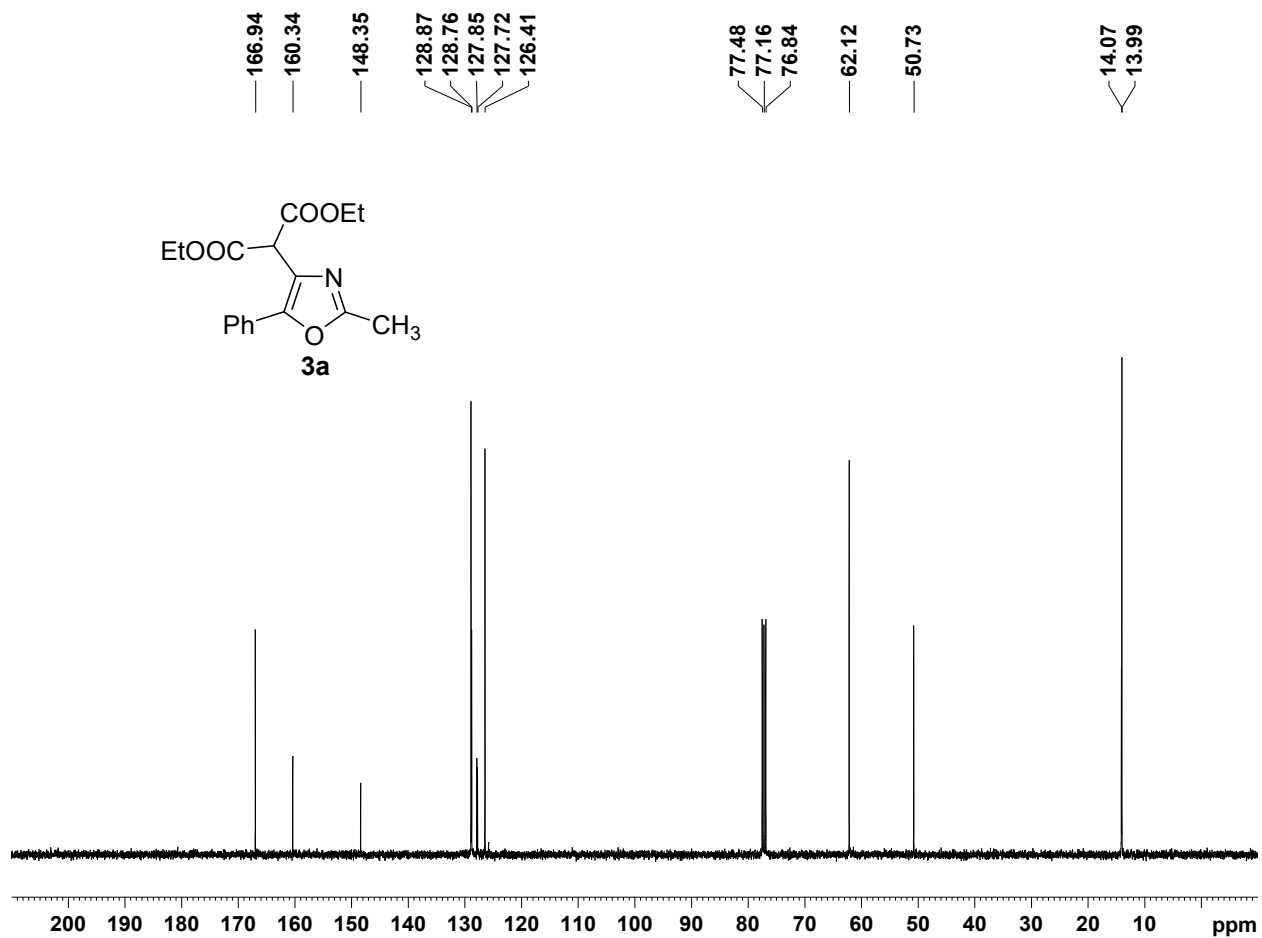


Figure S12.  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) spectrum of **3a**

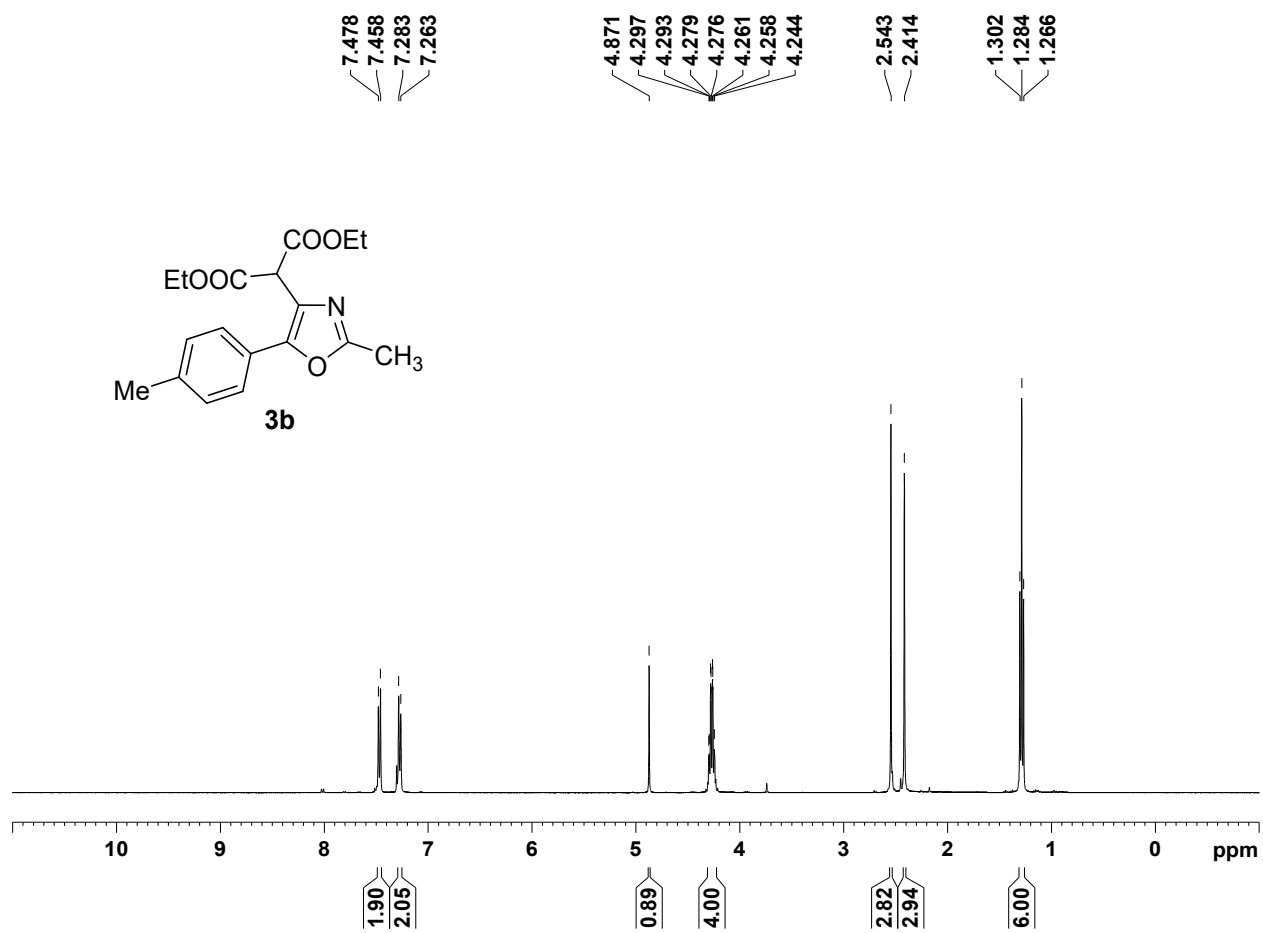


Figure S13. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of **3b**

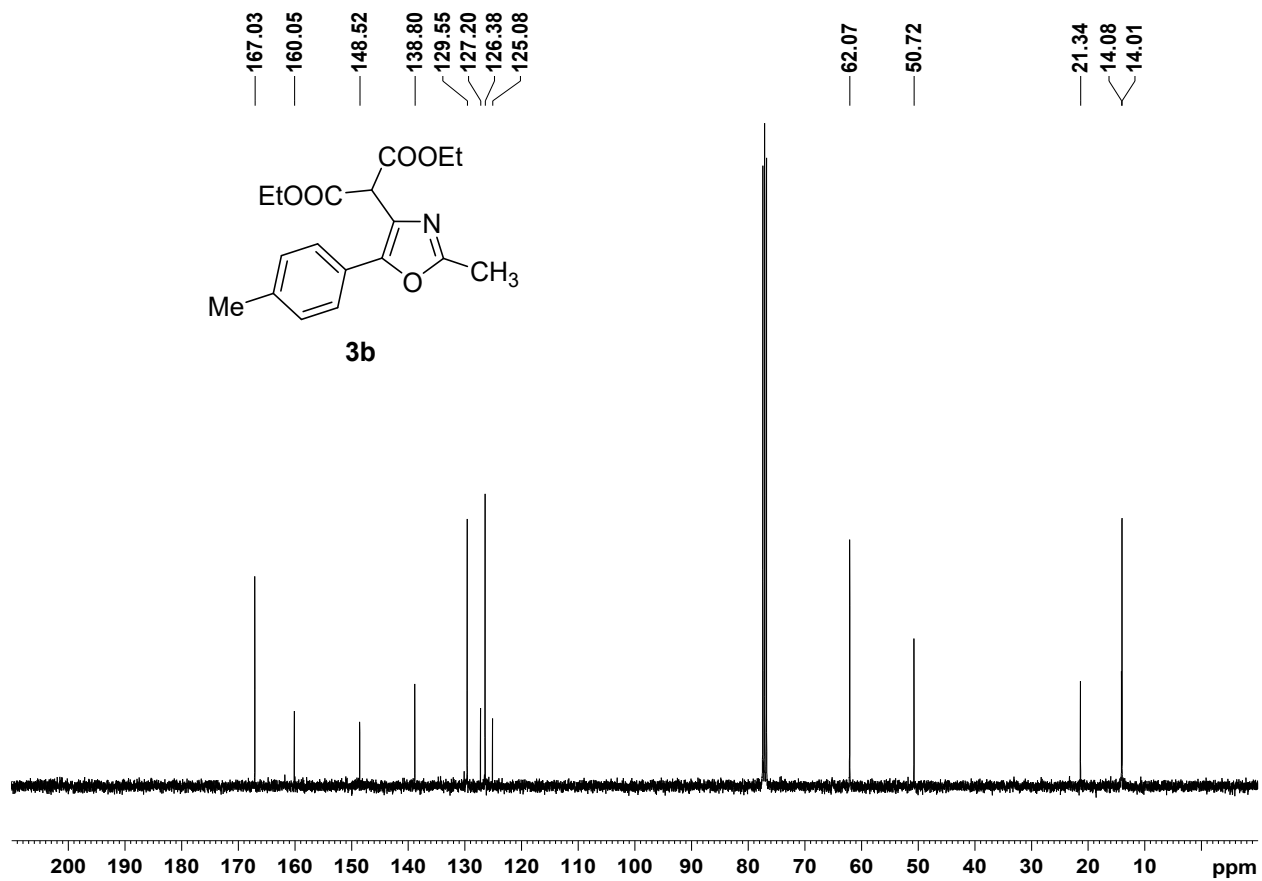


Figure S14. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of **3b**

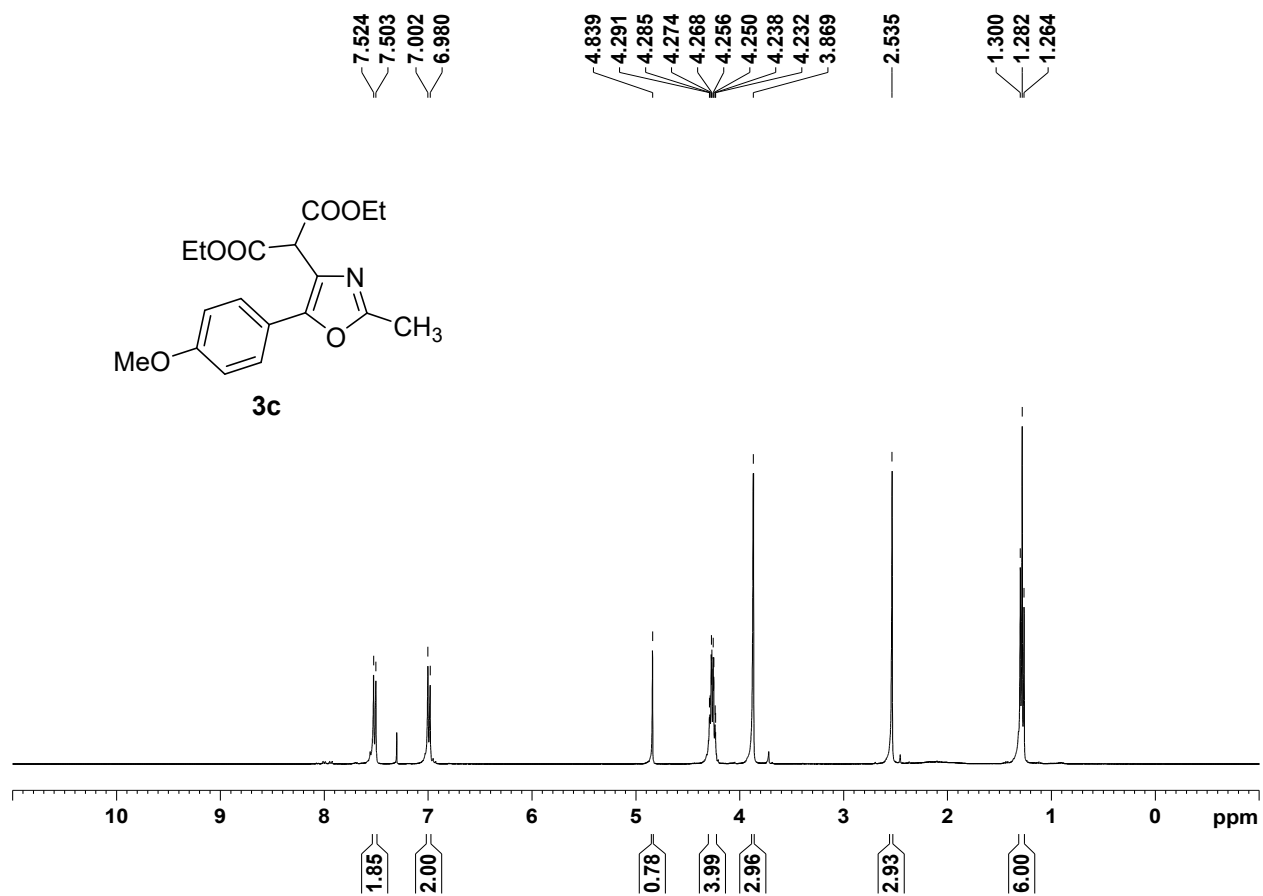


Figure S15. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of **3c**



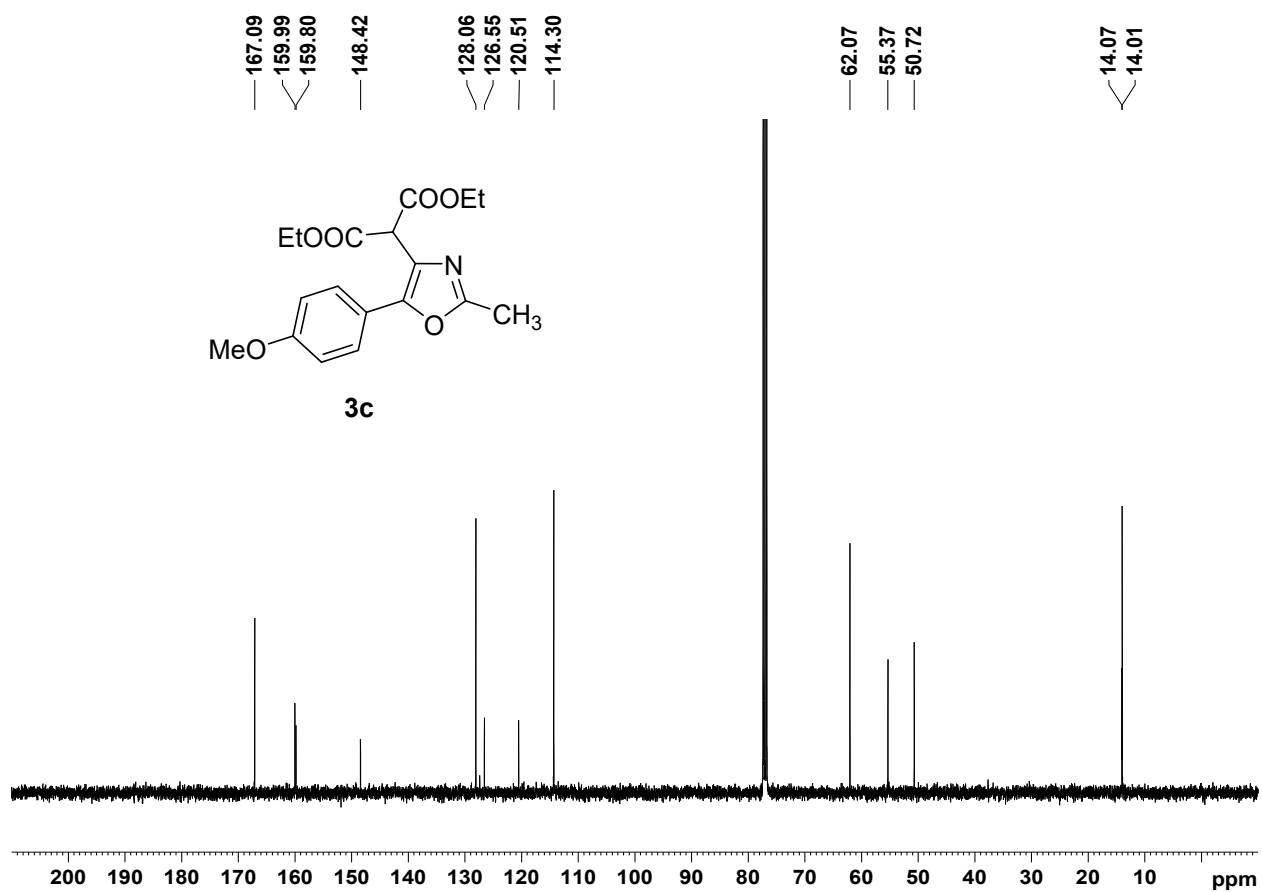


Figure S16. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of **3c**

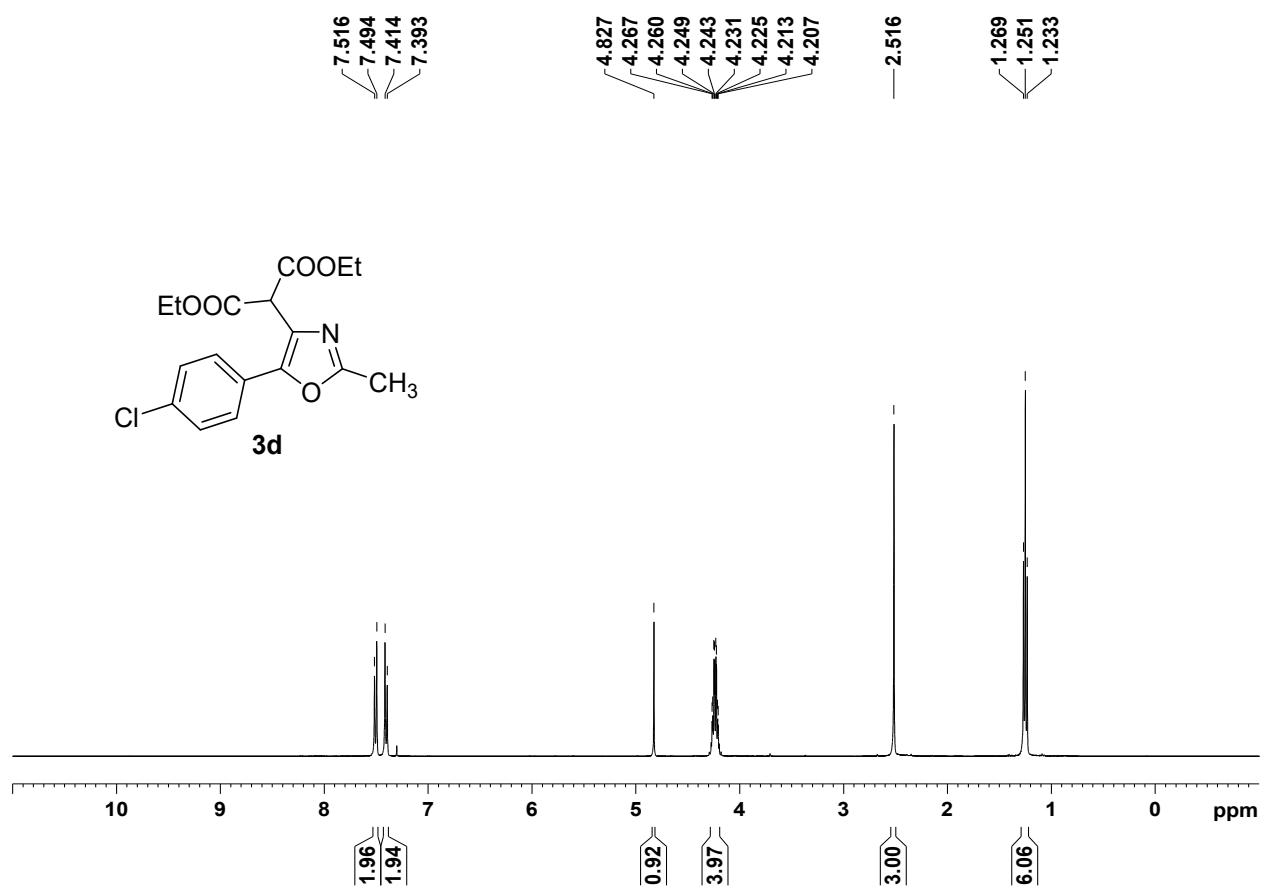


Figure S17. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of **3d**

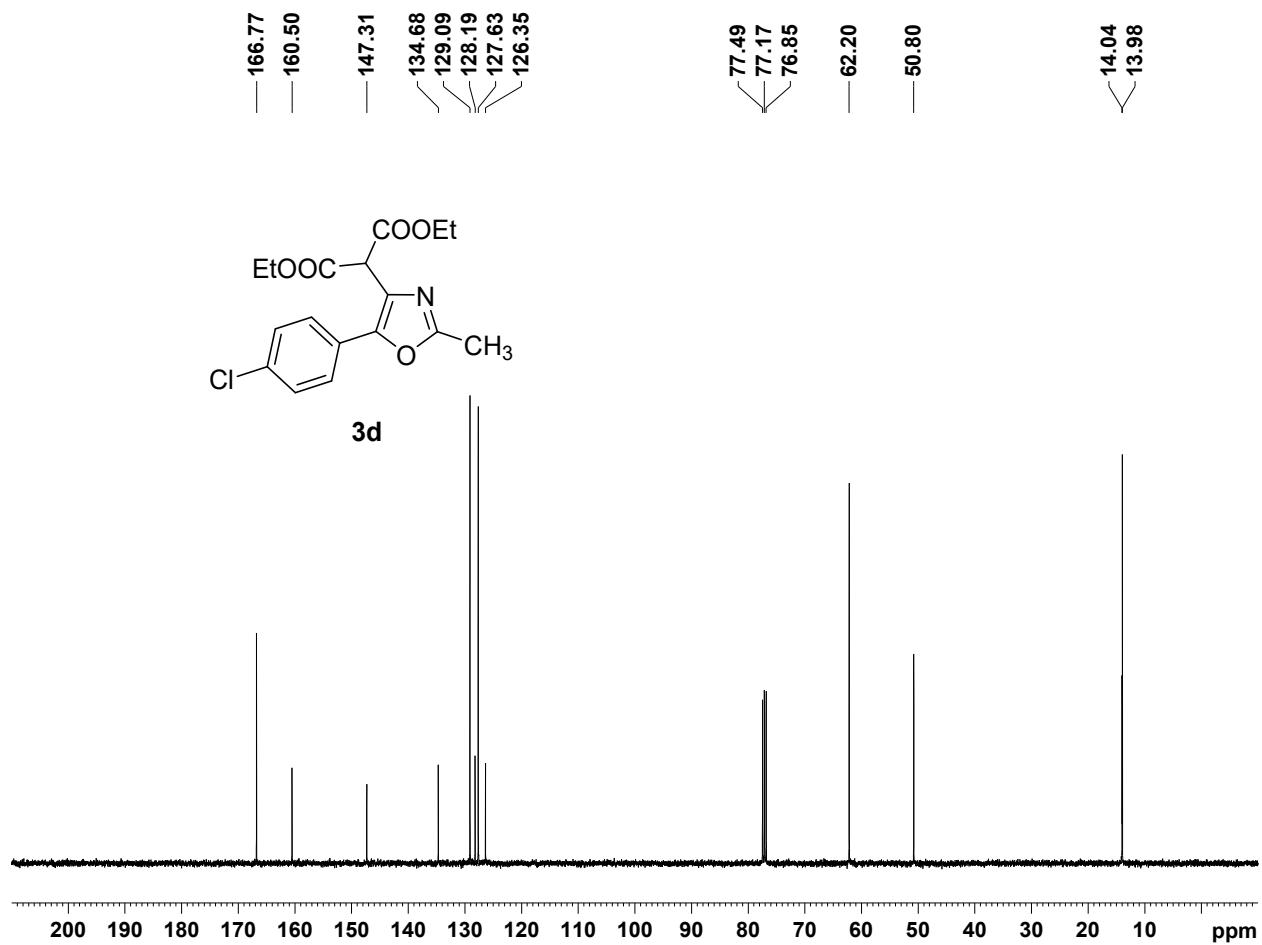


Figure S18. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of **3d**

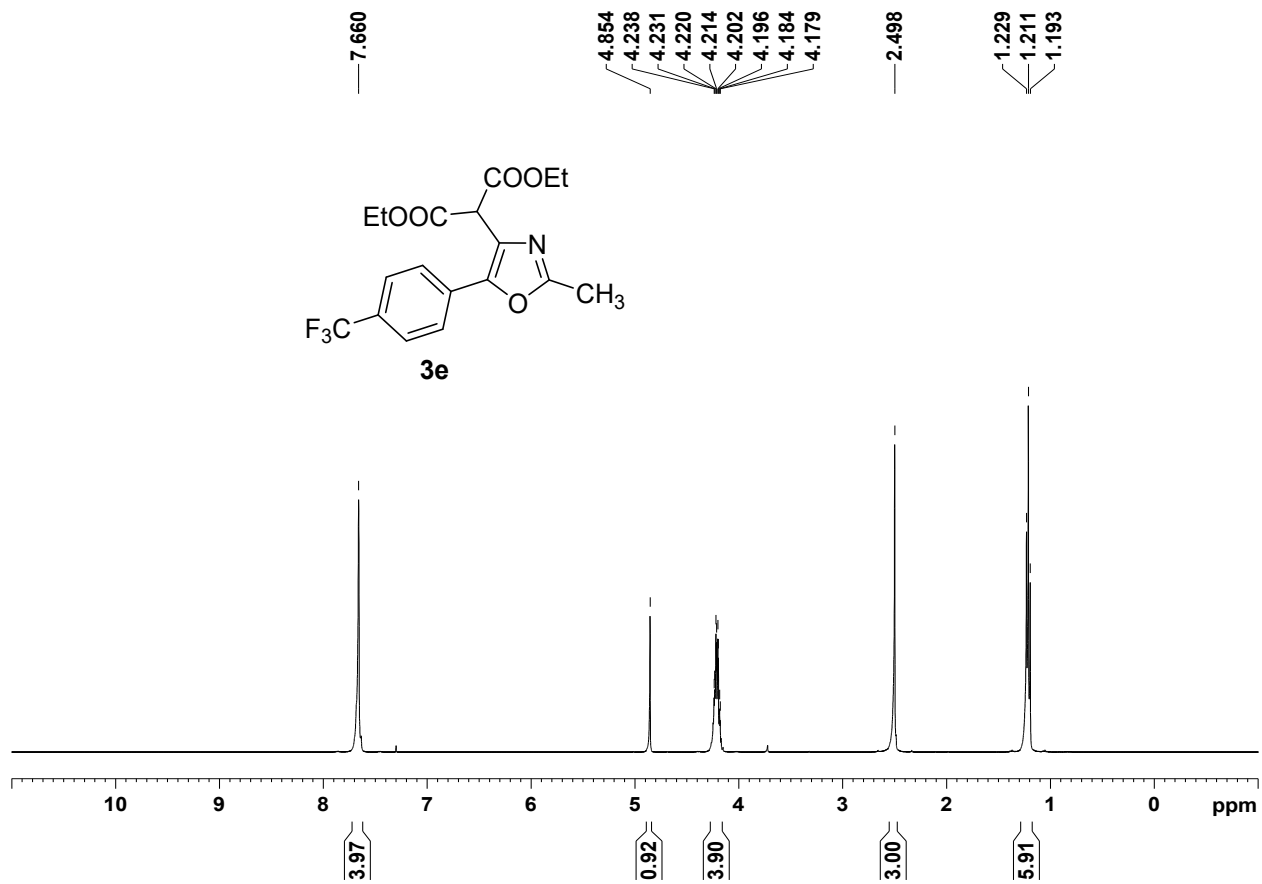


Figure S19. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of **3e**

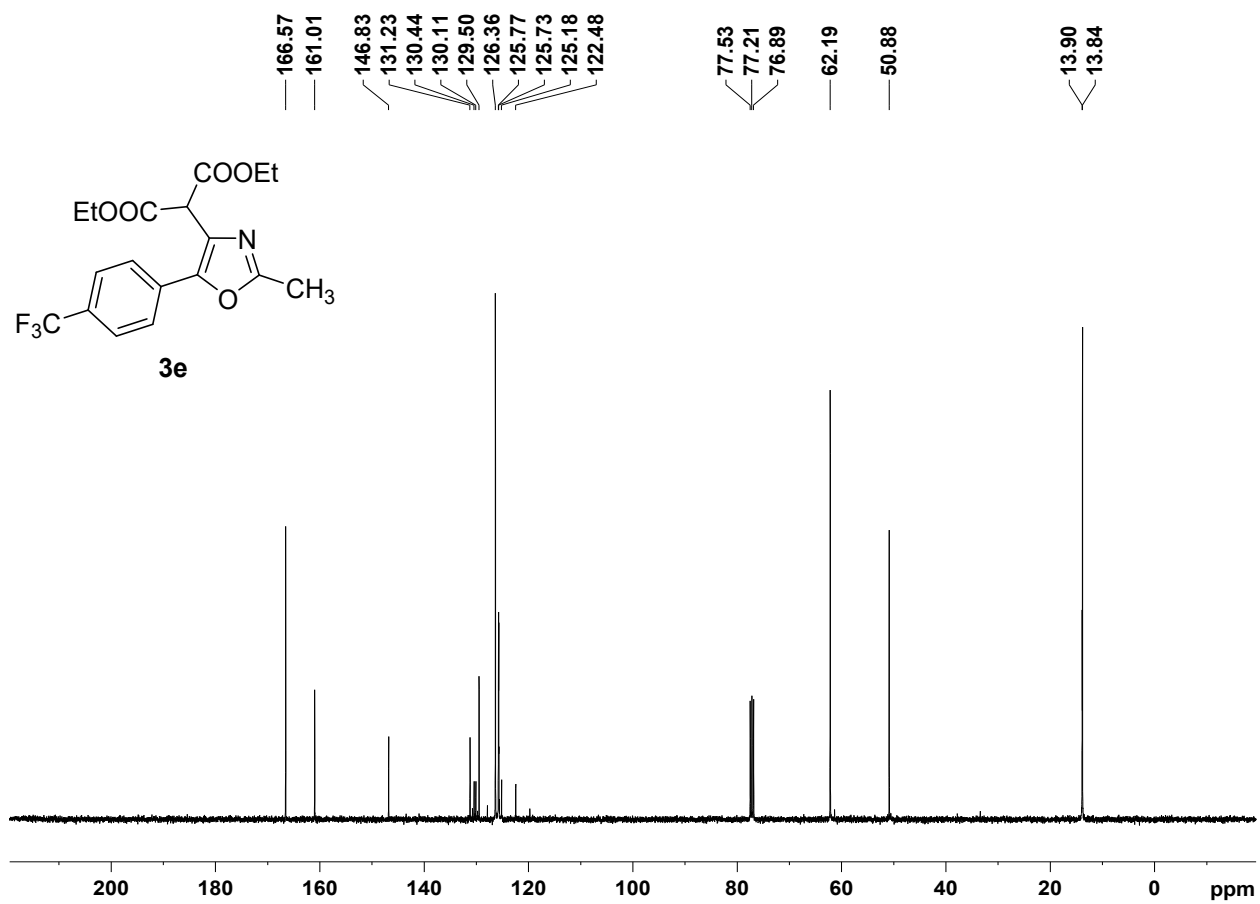


Figure S20. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of **3e**

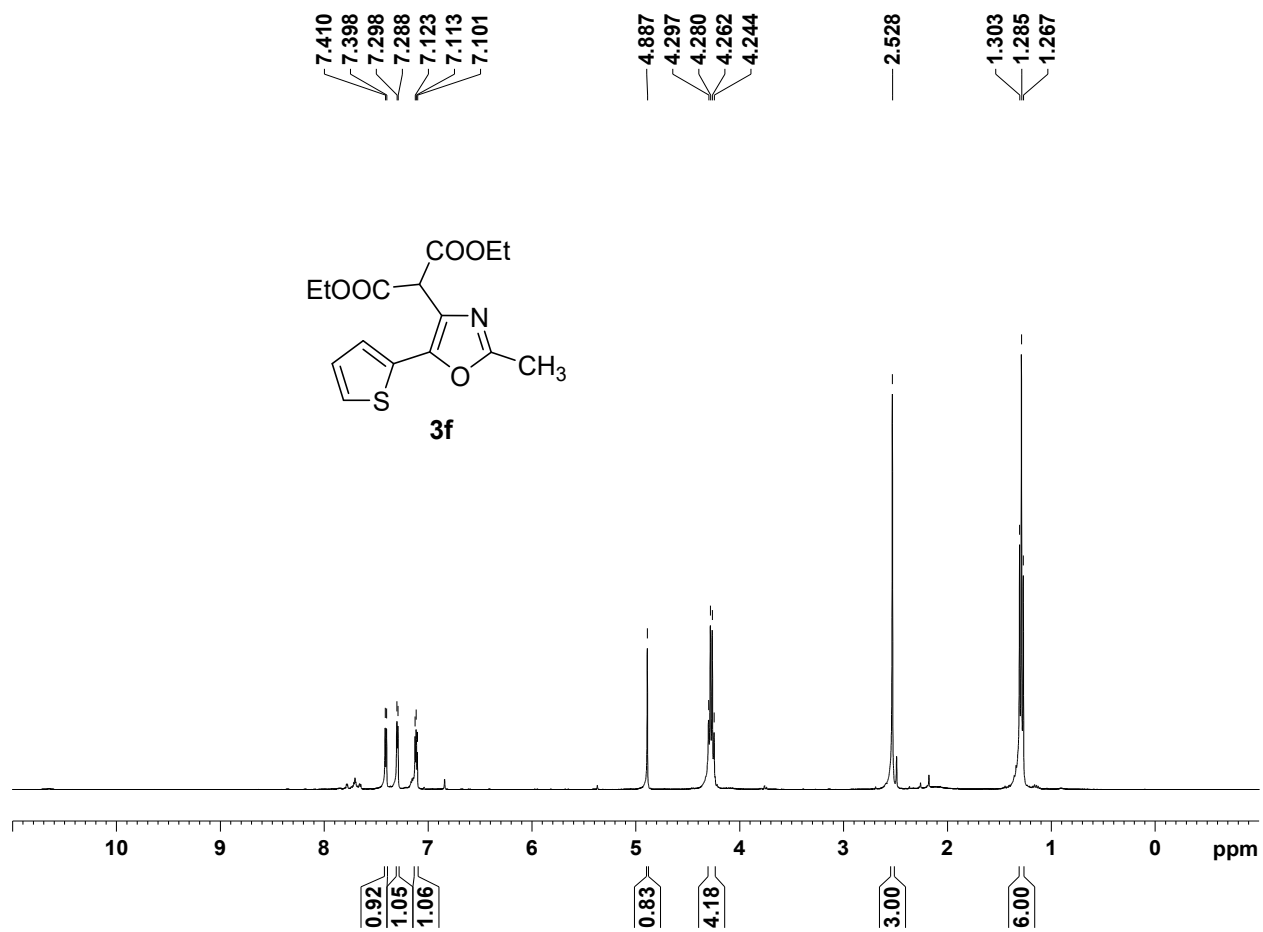


Figure S21. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of **3f**

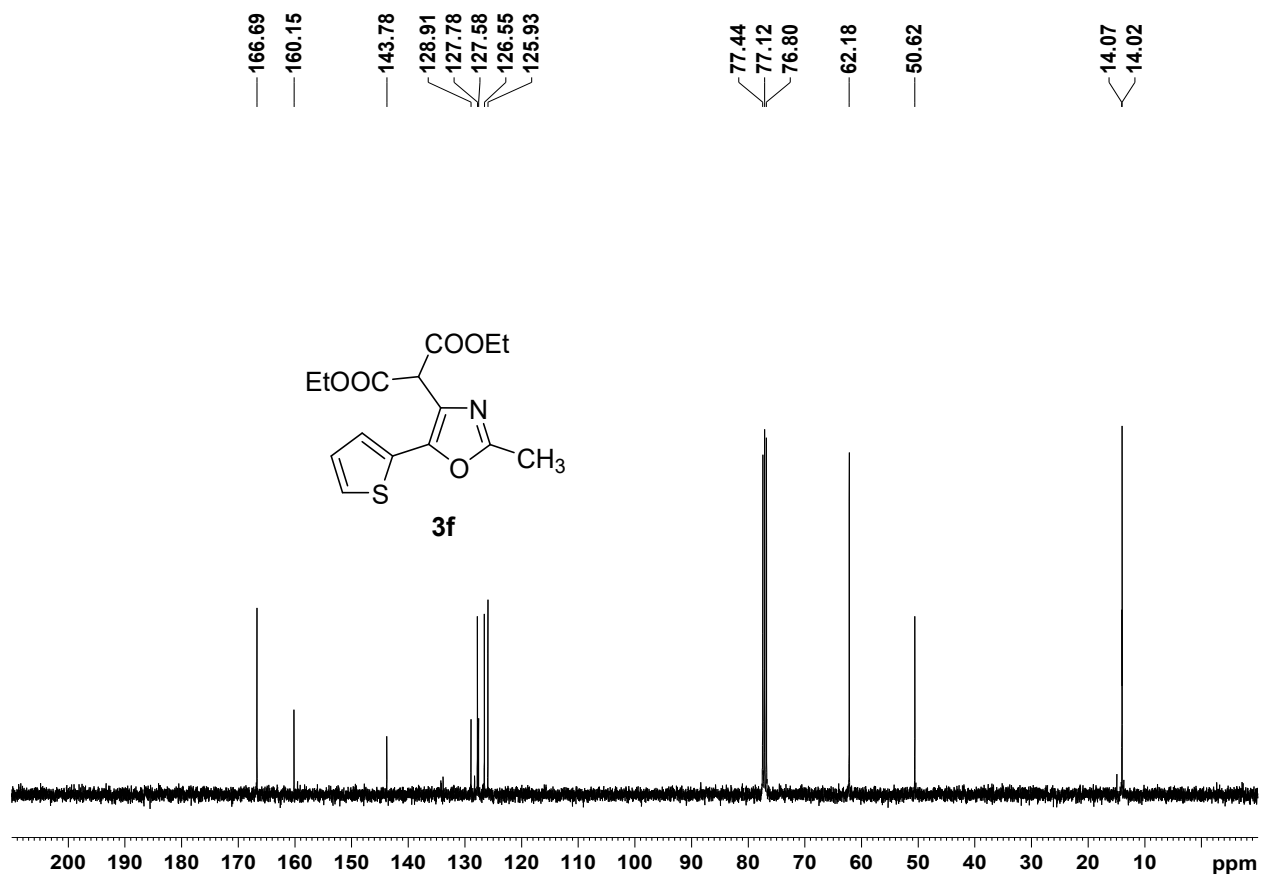


Figure S22. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of **3f**

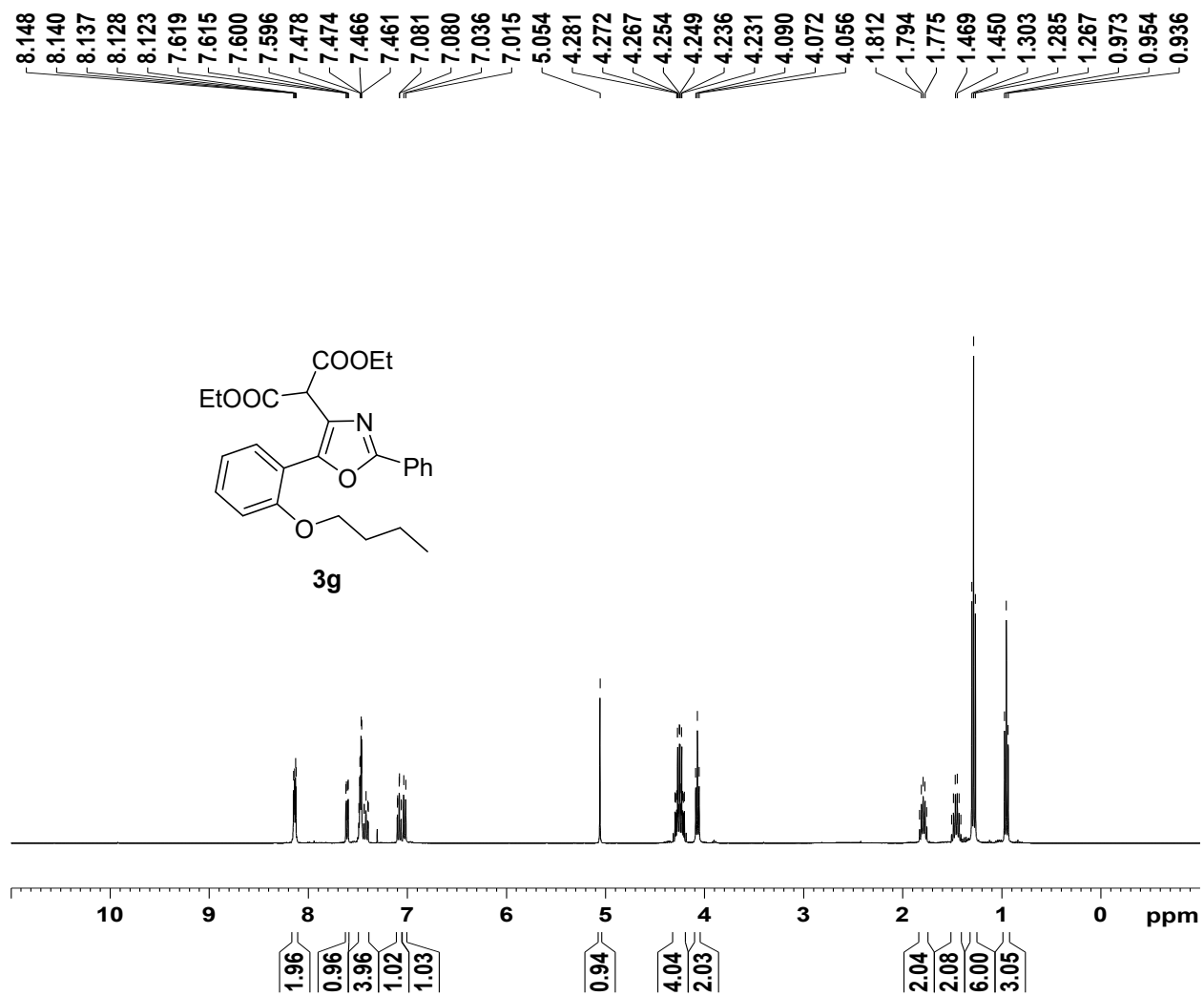


Figure S23. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of **3g**



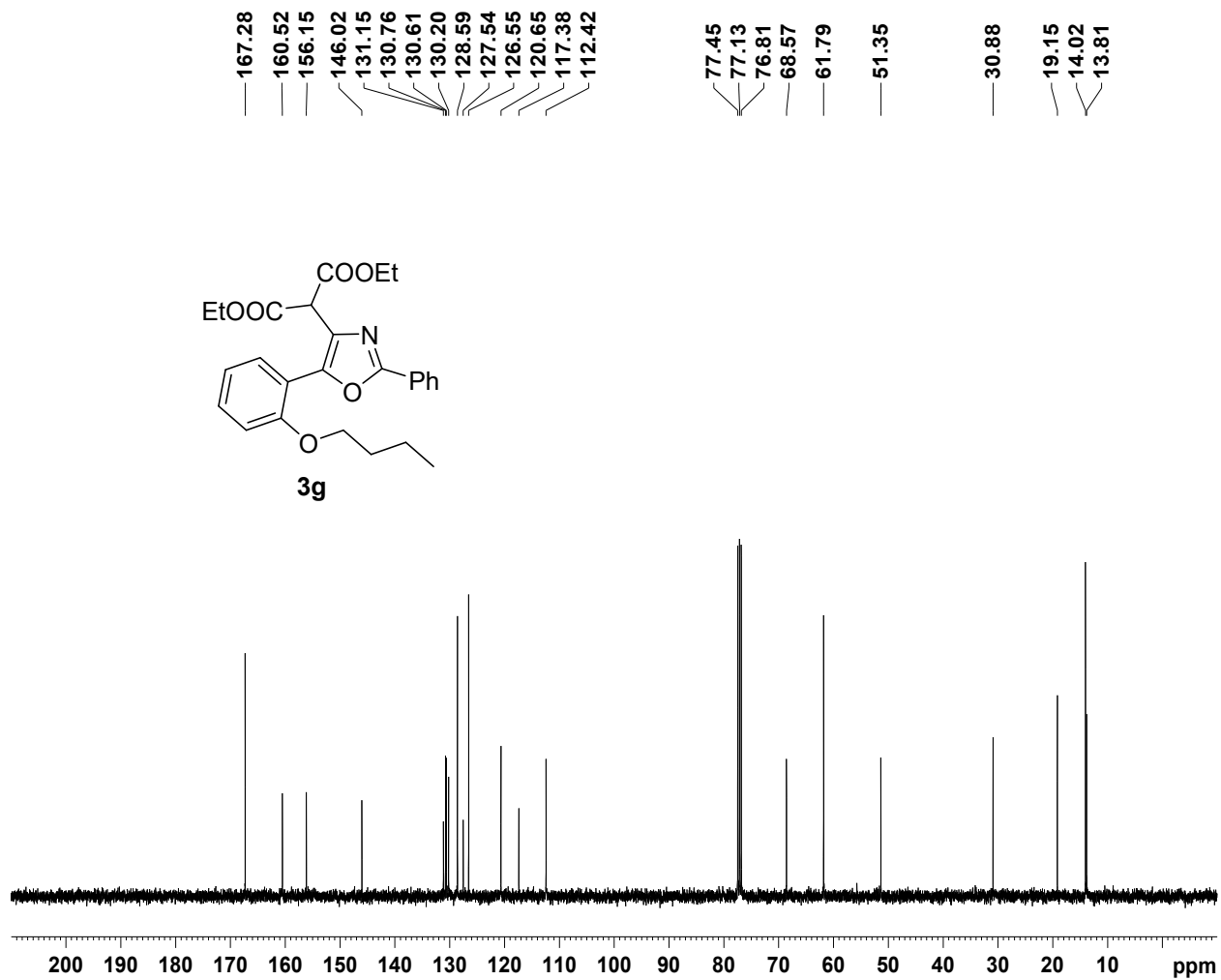


Figure S24. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of **3g**

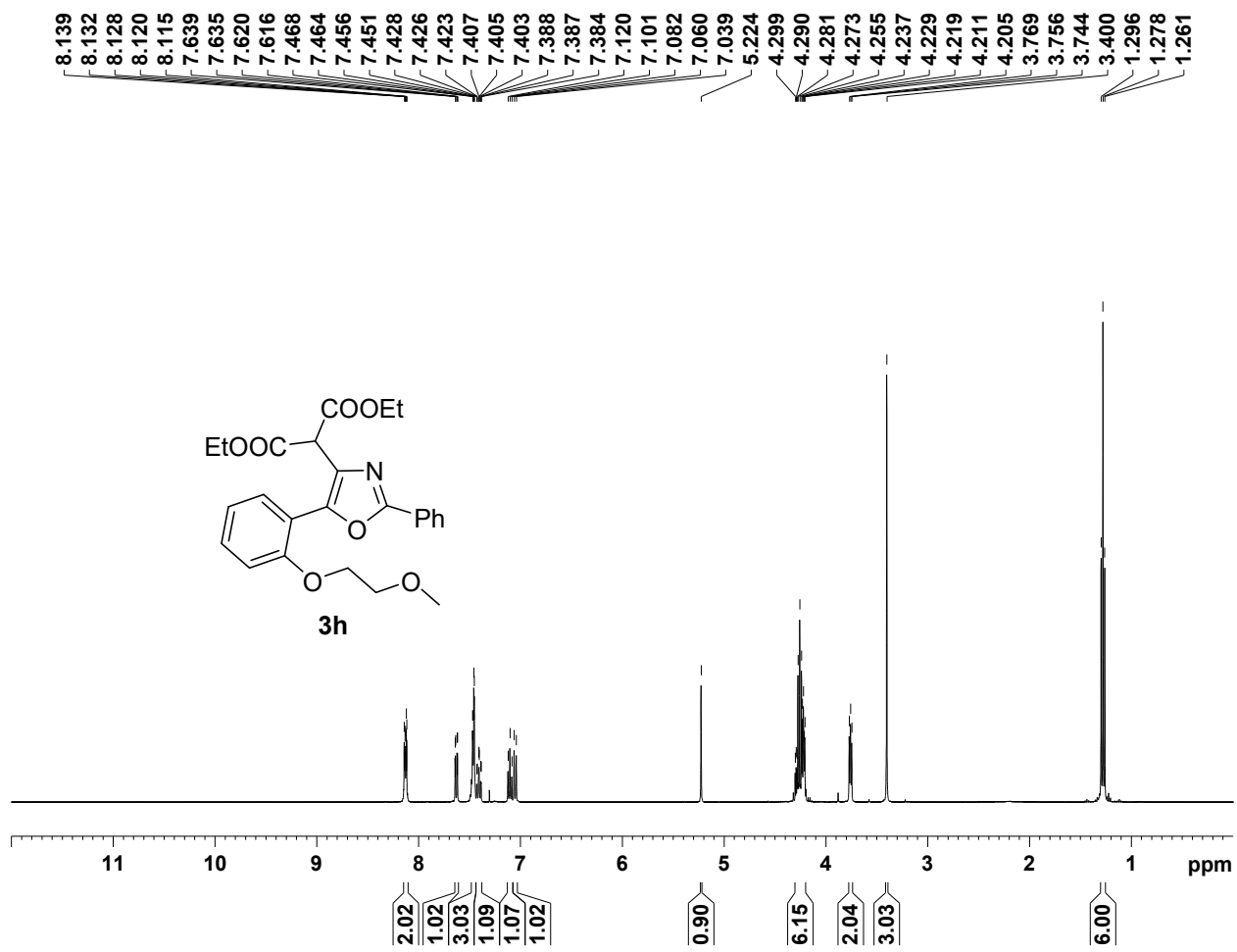


Figure S25. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of **3h**

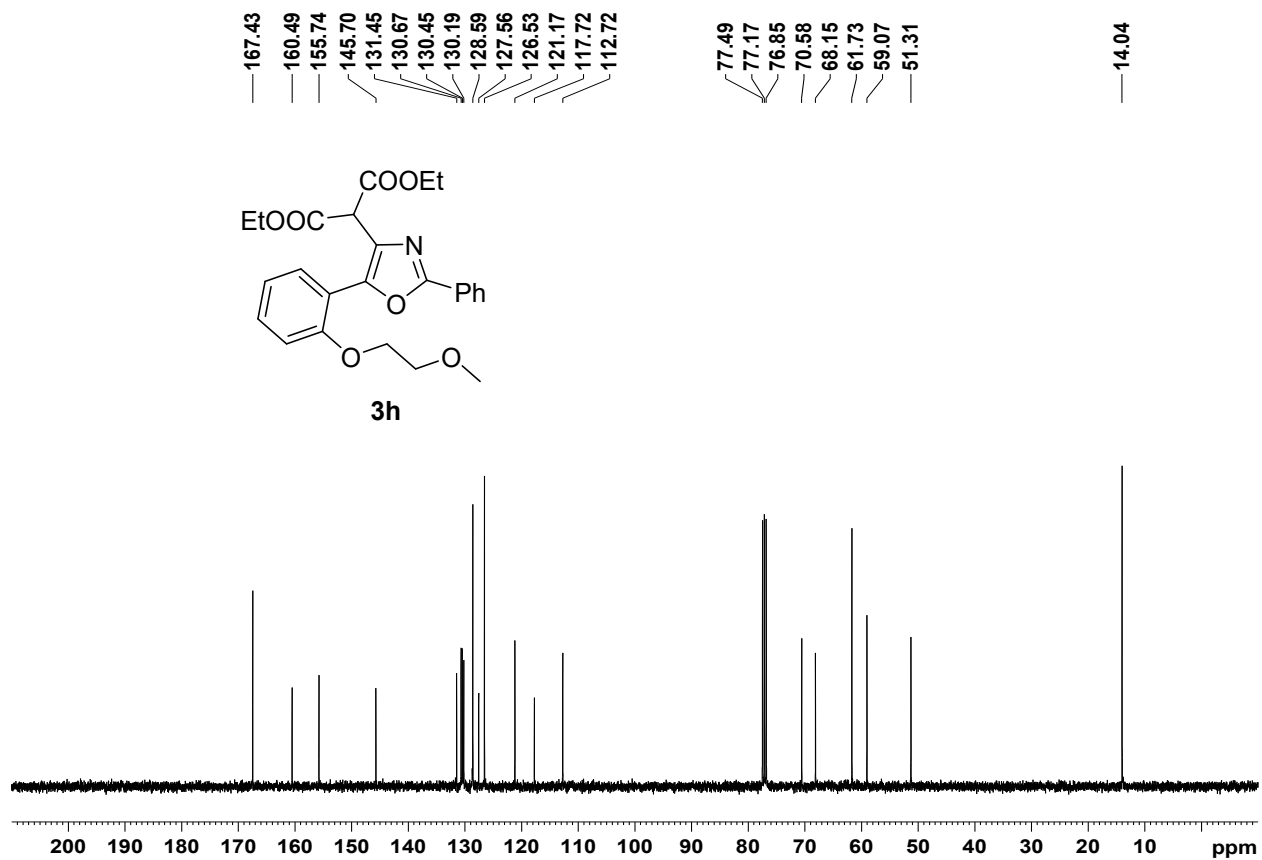


Figure S26. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of **3h**

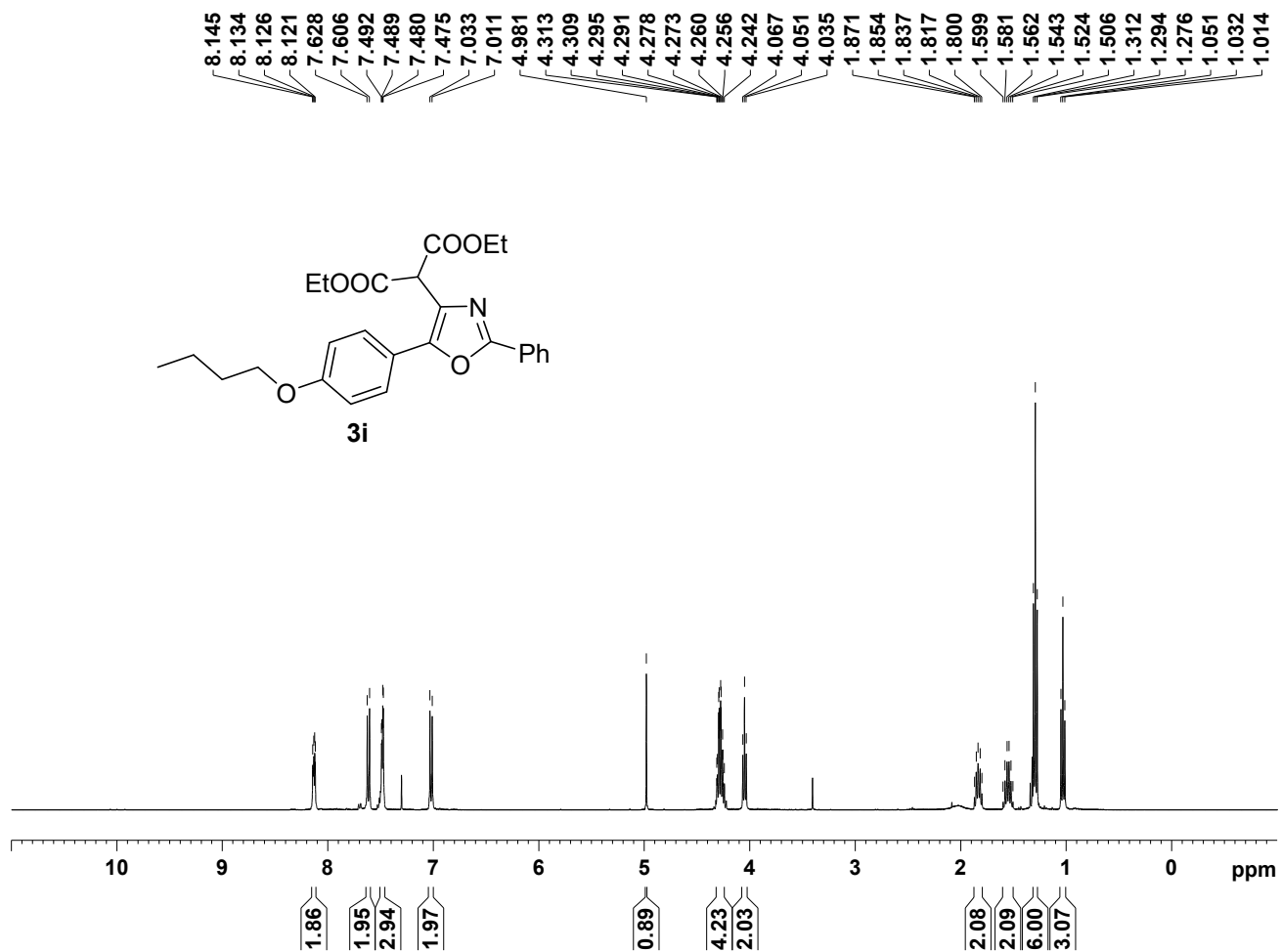


Figure S27. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of **3i**

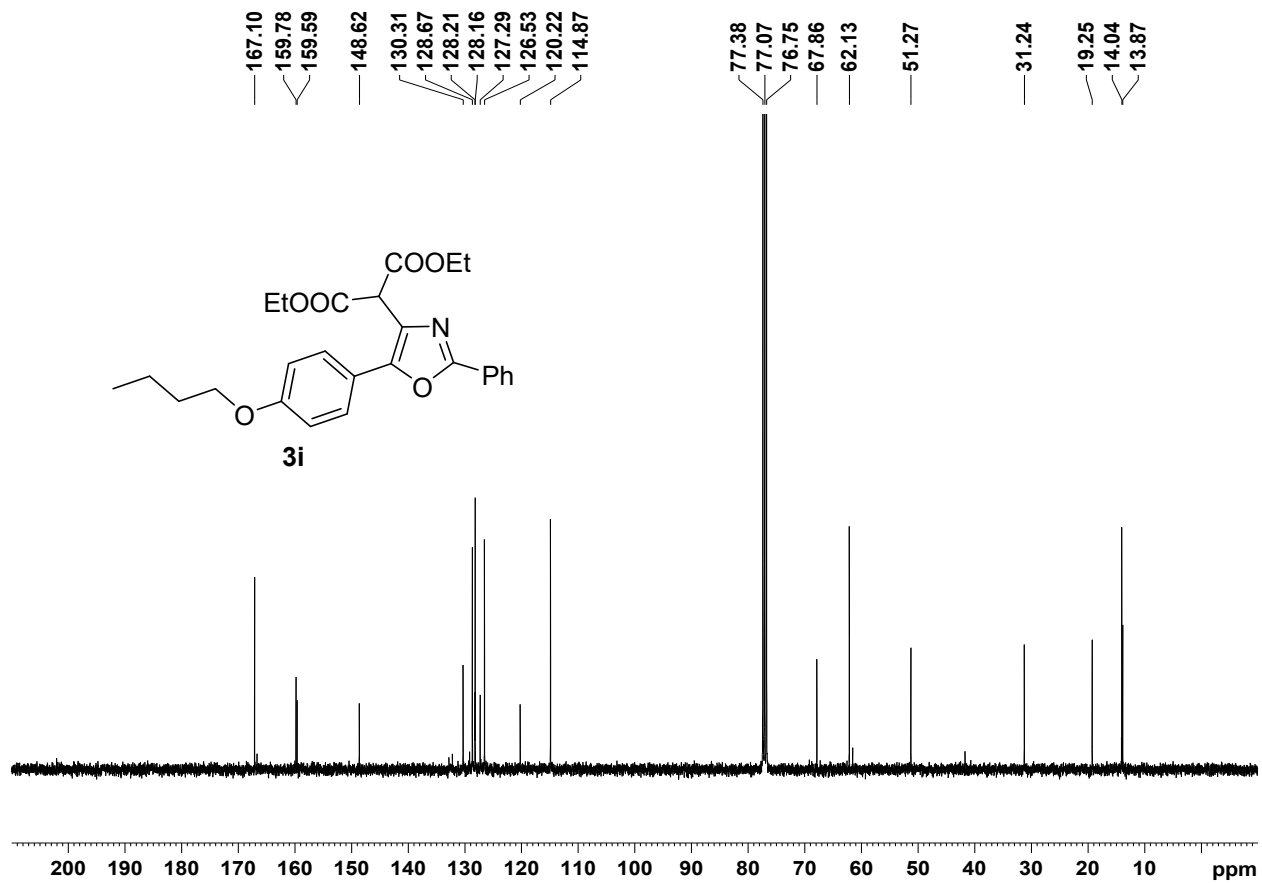


Figure S28. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of **3i**

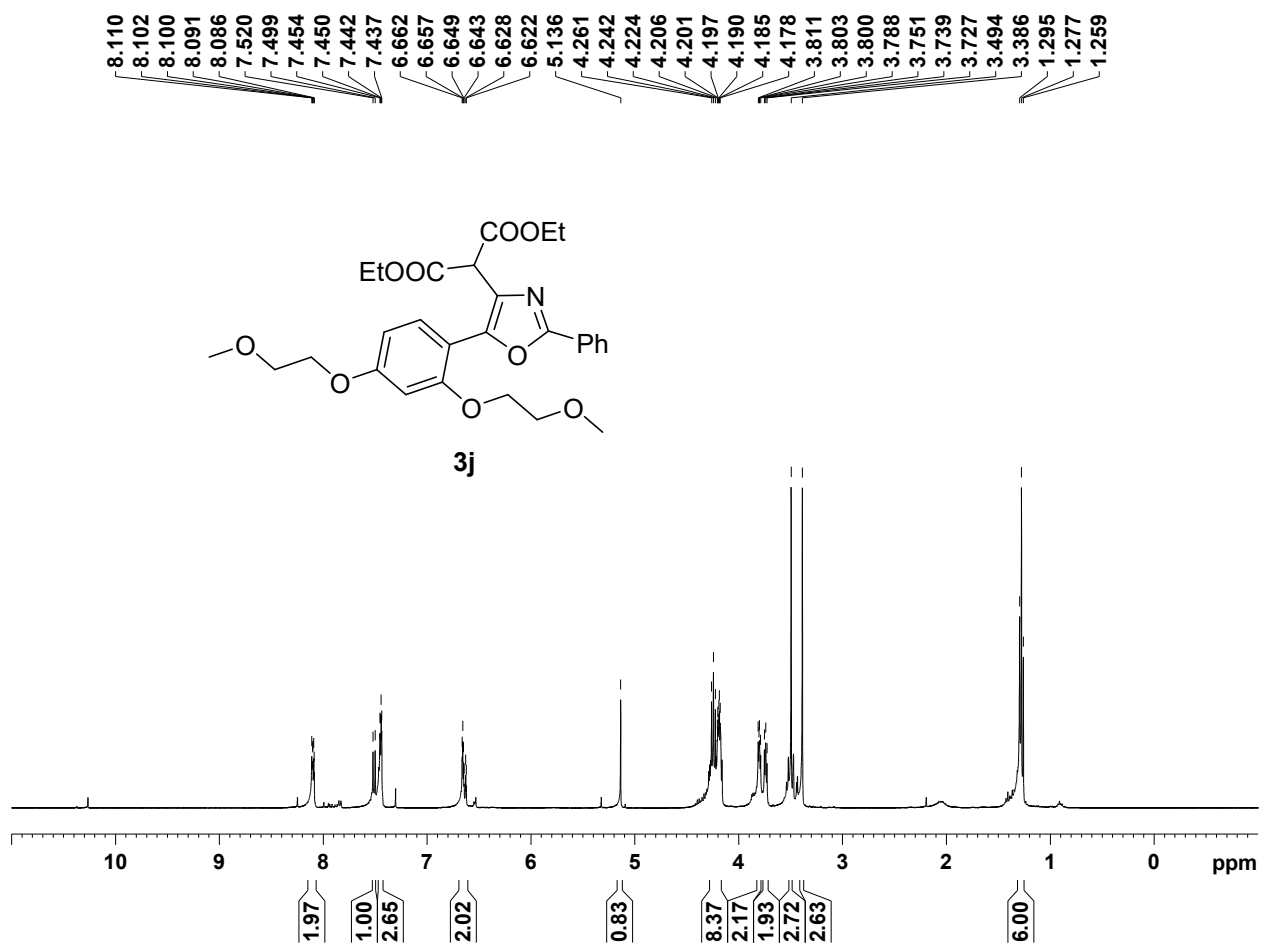


Figure S29. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of **3j**

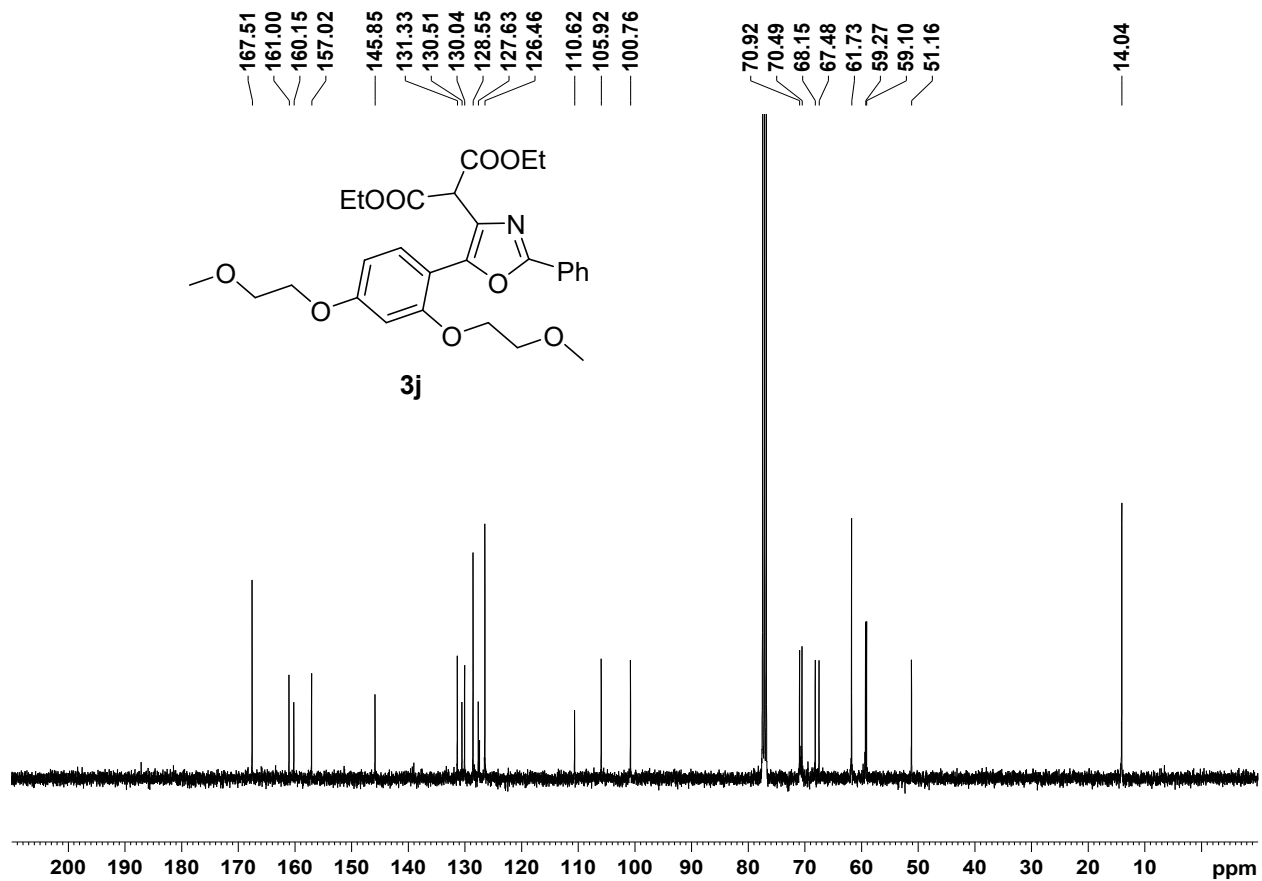


Figure S30. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of **3j**

# C. Copies of HRMS

## Spectrum Plot Report



Name	ON-1	Rack Pos.		Instrument	QTOF	Operator	
Inj. Vol. (ul)	2	Plate Pos.		IRM Status	Success	Acq. Time (Local)	07-12-2022 14:51:39
Data File	ON-1.d	Method (Acq)	GCN-NORMAL1.m	Comment		(UTC-08:00)	

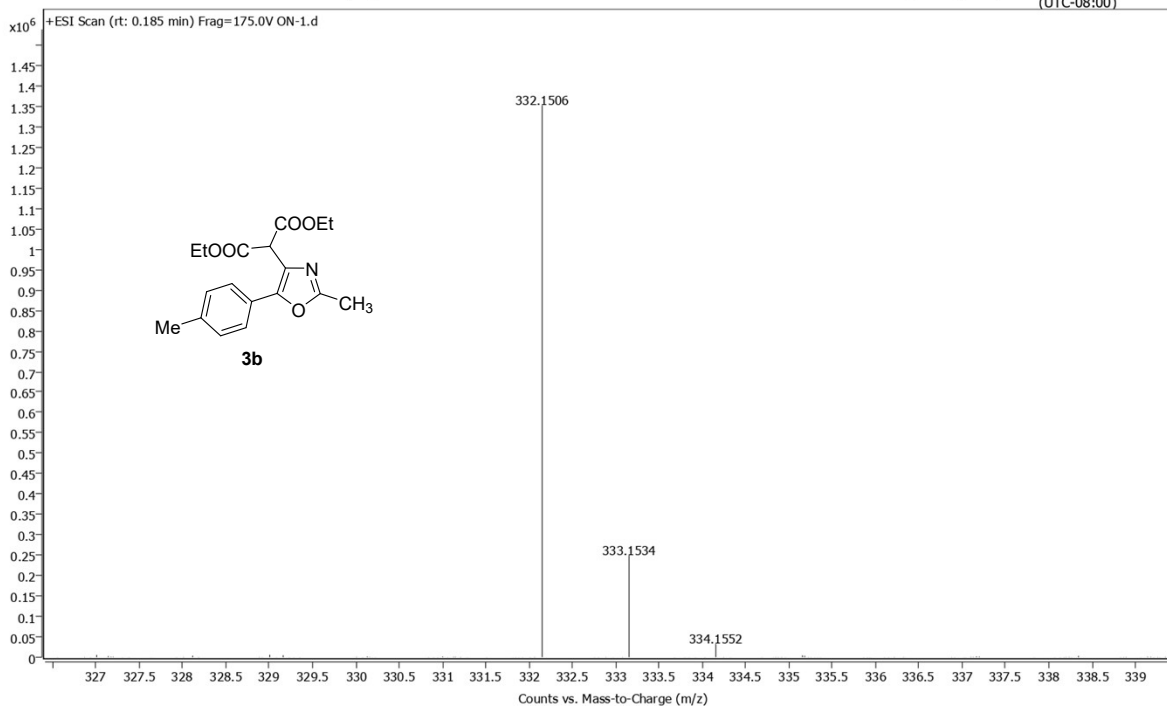


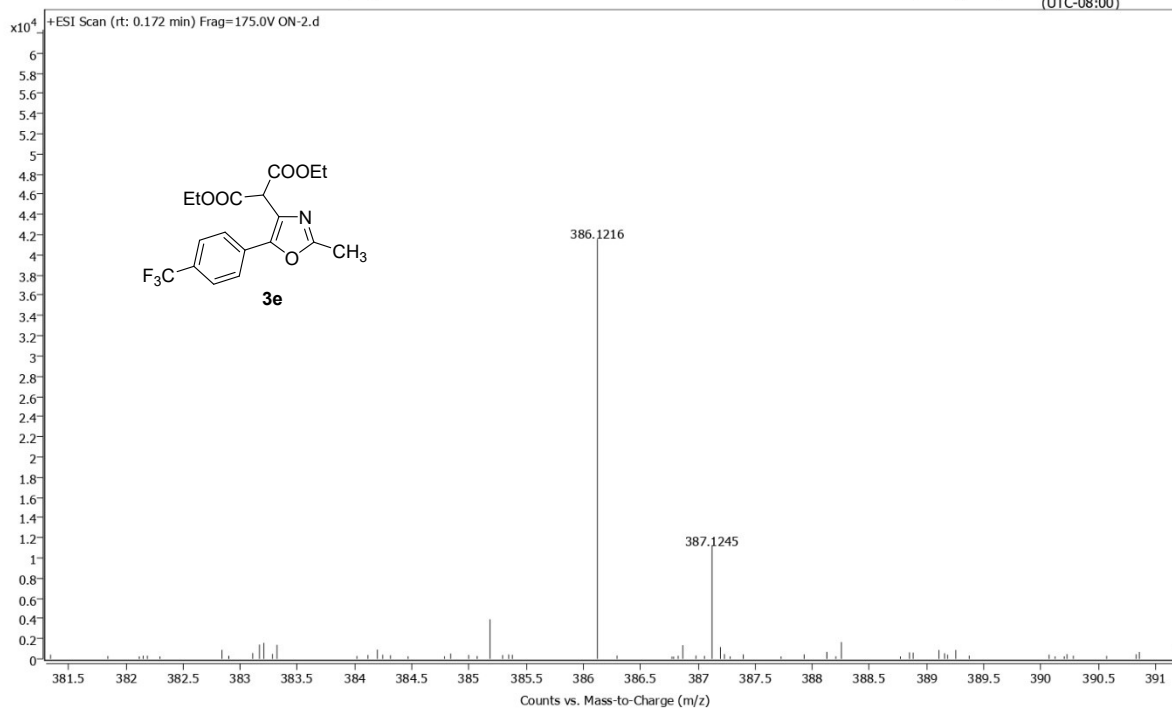
Figure S31. Mass spectrum of **3b**



# User Spectrum Plot Report



Name	ON-2	Rack Pos.		Instrument	QTOF	Operator	
Inj. Vol. (ul)	2	Plate Pos.		IRM Status	Success		
Data File	ON-2.d	Method (Acq)	GCN-NORMAL1.m	Comment		Acq. Time (Local)	07-12-2022 14:37:49 (UTC-08:00)

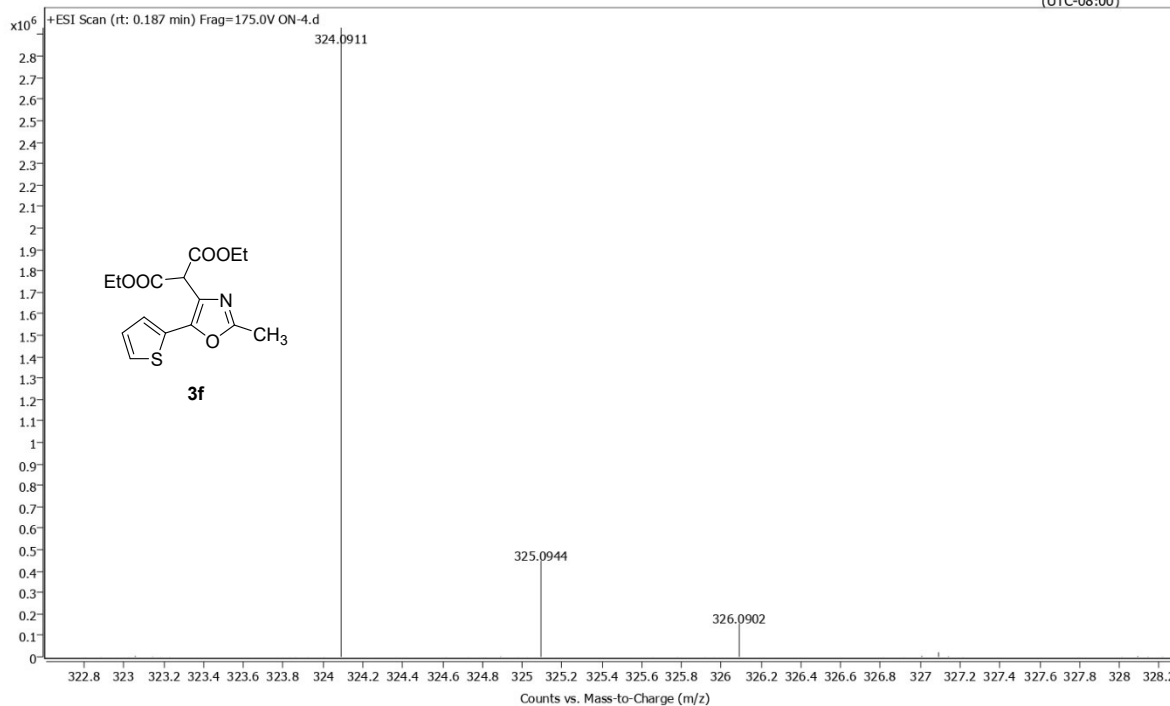


**Figure S32.** Mass spectrum of **3e**

# Spectrum Plot Report



Name	ON-4	Rack Pos.		Instrument	QTOF	Operator	
Inj. Vol. (ul)	2	Plate Pos.		IRM Status	Success	Acq. Time (Local)	07-12-2022 14:41:15
Data File	ON-4.d	Method (Acq)	GCN-NORMAL1.m	Comment		(UTC-08:00)	

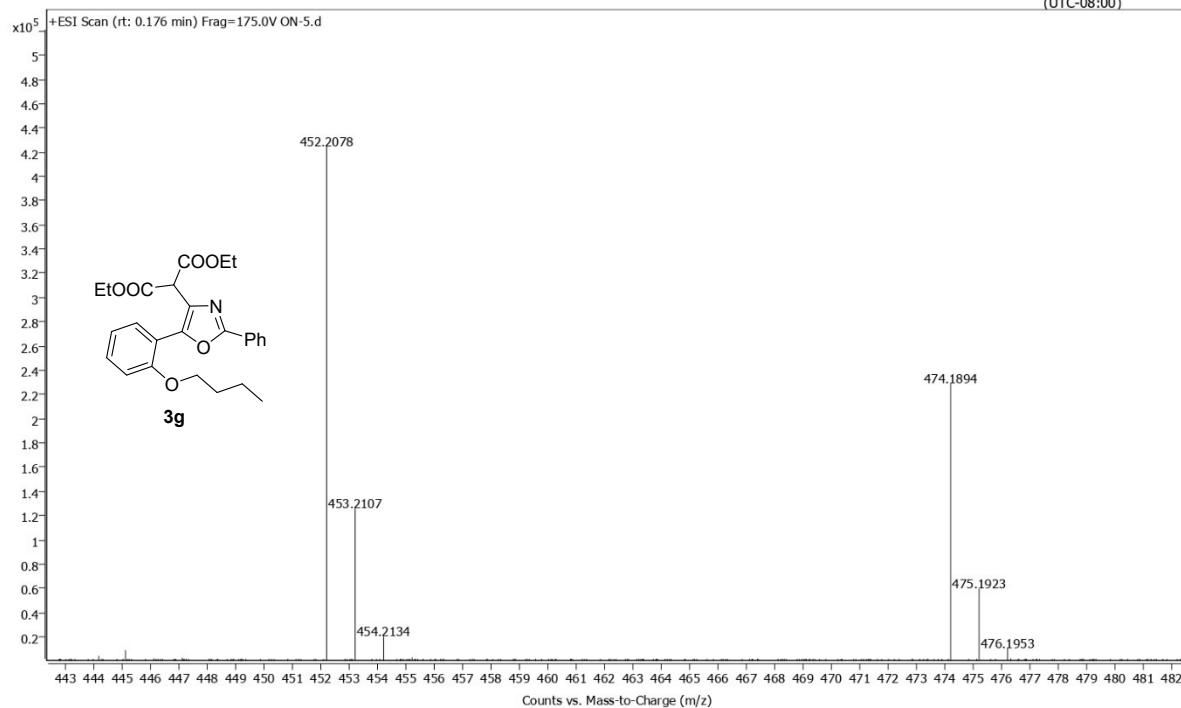


**Figure S33.** Mass spectrum of **3f**

# Spectrum Plot Report



Name	ON-5	Rack Pos.		Instrument	QTOF	Operator	
Inj. Vol. (ul)	2	Plate Pos.		IRM Status	Success	Acq. Time (Local)	07-12-2022 14:42:59
Data File	ON-5.d	Method (Acq)	GCN-NORMAL1.m	Comment		(UTC-08:00)	

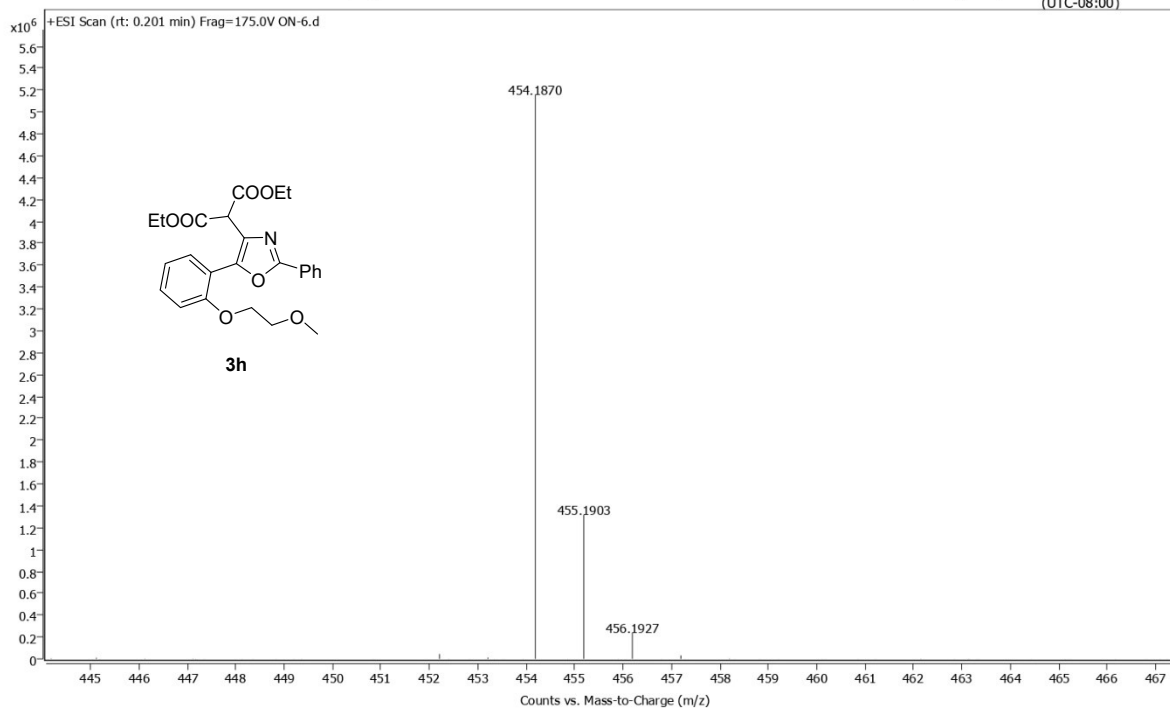


**Figure S34.** Mass spectrum of **3g**

# Spectrum Plot Report



Name	ON-6	Rack Pos.		Instrument	QTOF	Operator	
Inj. Vol. (ul)	2	Plate Pos.		IRM Status	Success	Acq. Time (Local)	07-12-2022 14:44:43
Data File	ON-6.d	Method (Acq)	GCN-NORMAL1.m	Comment		(UTC-08:00)	

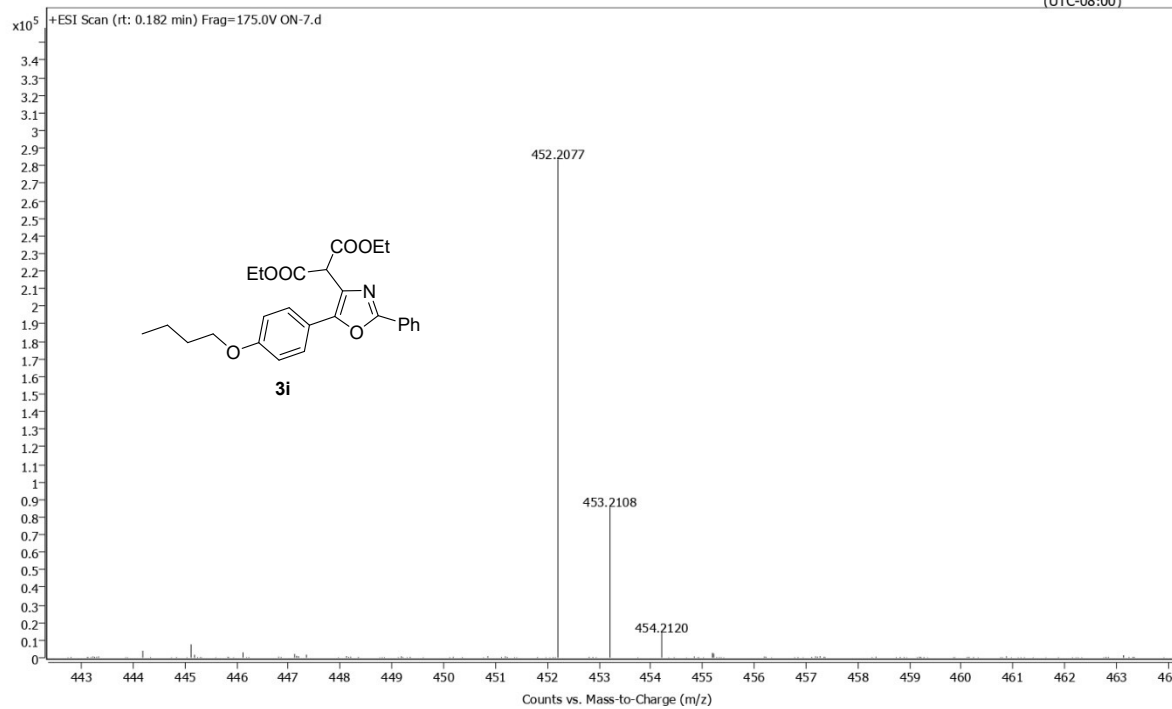


**Figure S35.** Mass spectrum of **3h**

# Spectrum Plot Report



Name	ON-7	Rack Pos.		Instrument	QTOF	Operator	
Inj. Vol. (ul)	2	Plate Pos.		IRM Status	Success	Acq. Time (Local)	07-12-2022 14:46:28
Data File	ON-7.d	Method (Acq)	GCN-NORMAL1.m	Comment		(UTC-08:00)	

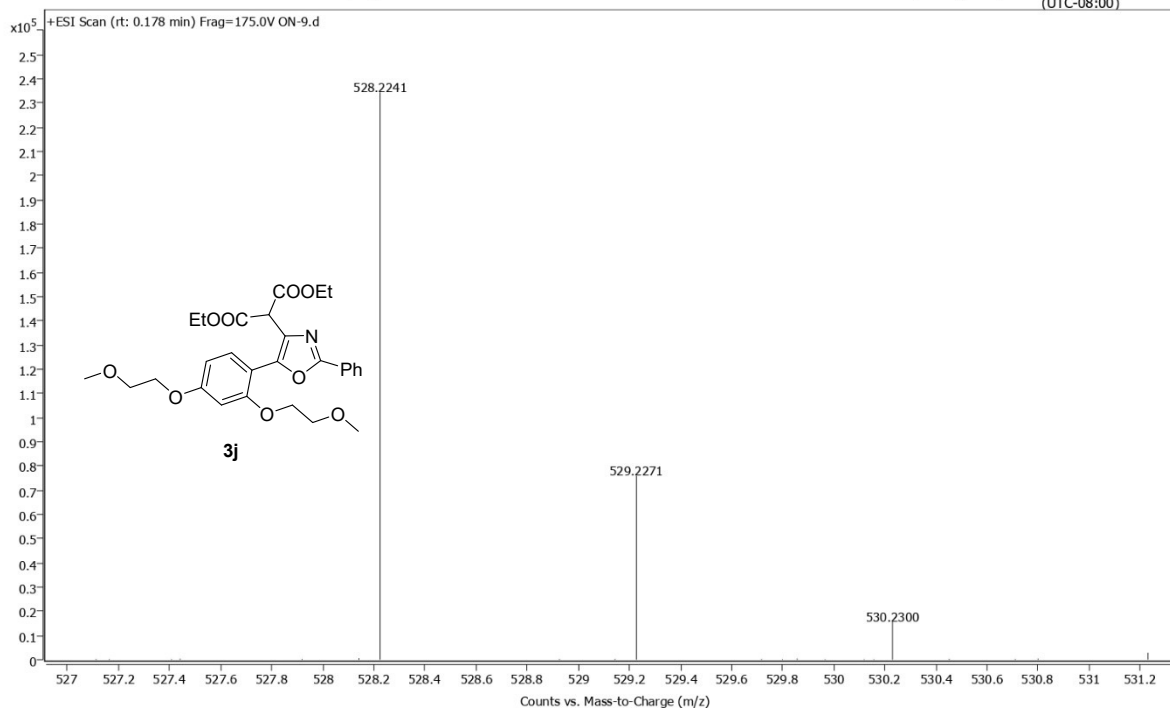


**Figure S36.** Mass spectrum of **3i**

# Spectrum Plot Report



Name	ON-9	Rack Pos.		Instrument	QTOF	Operator	
Inj. Vol. (ul)	2	Plate Pos.		IRM Status	Success	Acq. Time (Local)	07-12-2022 14:49:55
Data File	ON-9.d	Method (Acq)	GCN-NORMAL1.m	Comment		(UTC-08:00)	



**Figure S37.** Mass spectrum of **3j**

## HPLC Analysis of Compound 3a Used for *In-vitro* Analysis

System : Waters Breeze™2  
Waters 1525 Binary HPLC Pump

Detector : 2998 Photodiode Array Detector

Column : Name: Symmetry® C18 3.5µm  
Dimension: 4.6mm x 75 mm coloumn

### Test Method

Mobile phase : 80/20 Acetonitrile /water

Mode : Isocratic system

Flow rate : 1 mL/min

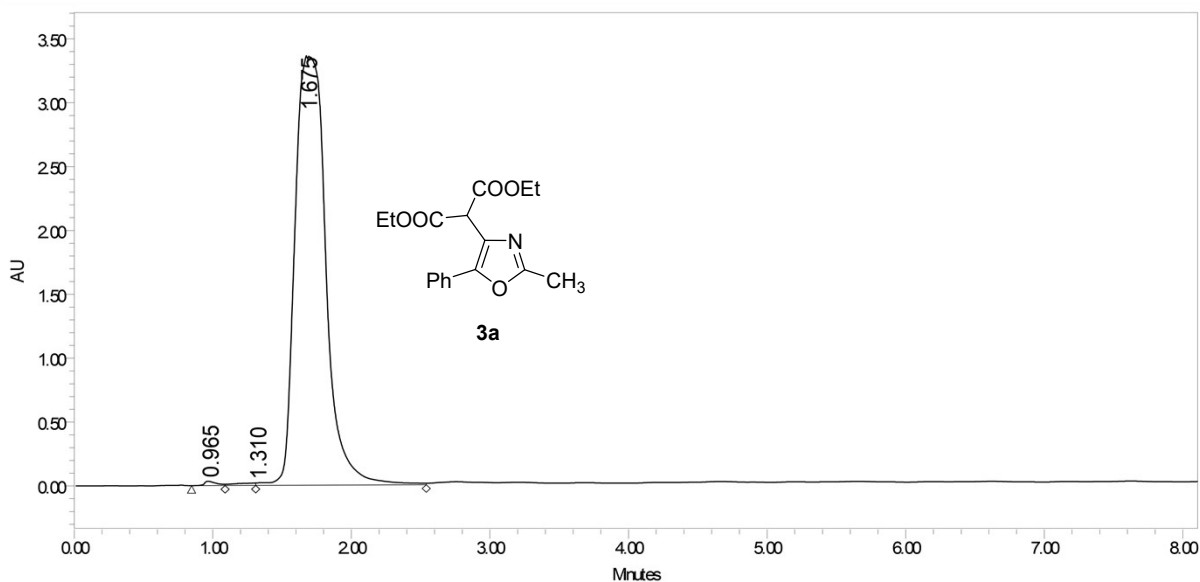
Injection Volume : 10µL

Retention Time : 1.675 min

Purity (area%) : 99.25%

SAMPLE INFORMATION

Sample Name:	3a_26.July	Acquired By:	Breeze
Sample Type:	Unknown	Date Acquired:	7/26/2023 11:08:59 AMIST
Vial:	1	Acq. Method:	80%ACN_20%H <sub>2</sub> O_3a_26JULY
Injection#:	1	Date Processed:	7/26/2023 11:30:28 AMIST
Injection Volume:	10.00 ul	Channel Name:	FDA Max Plot 190.0 - 800.0
Run Time:	10.00 Minutes	Channel Desc.:	2998 (210-400)nm
Column Type:		Sample Set Name:	



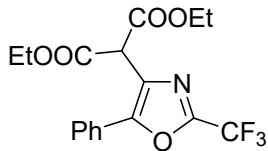
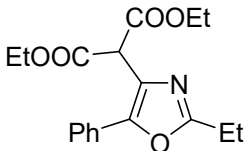
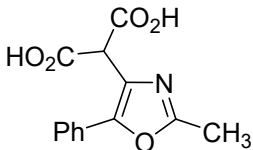
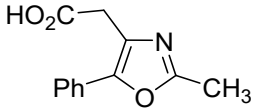
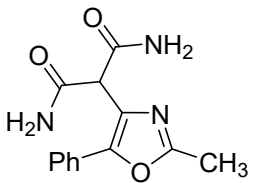
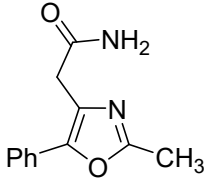
	RT (min)	Area (µV*sec)	%Area	Height (µV)	% Height
1	0.965	200297	0.36	34258	1.00
2	1.310	193691	0.37	19165	0.56
3	1.675	52105844	99.25	3361794	98.44

Figure S38. HPLC chromatogram of 3a



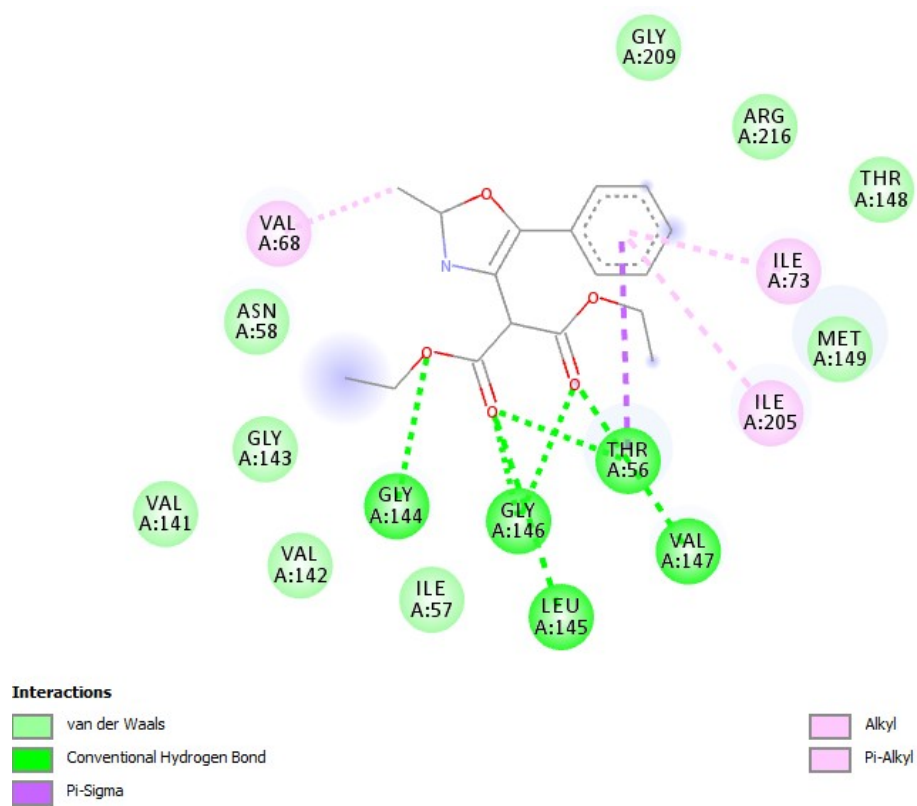
### Results of *In-silico* Analysis of Hypothetical Products 3k-l

**Table 1.** Docking score of hypothetical products 3k-l

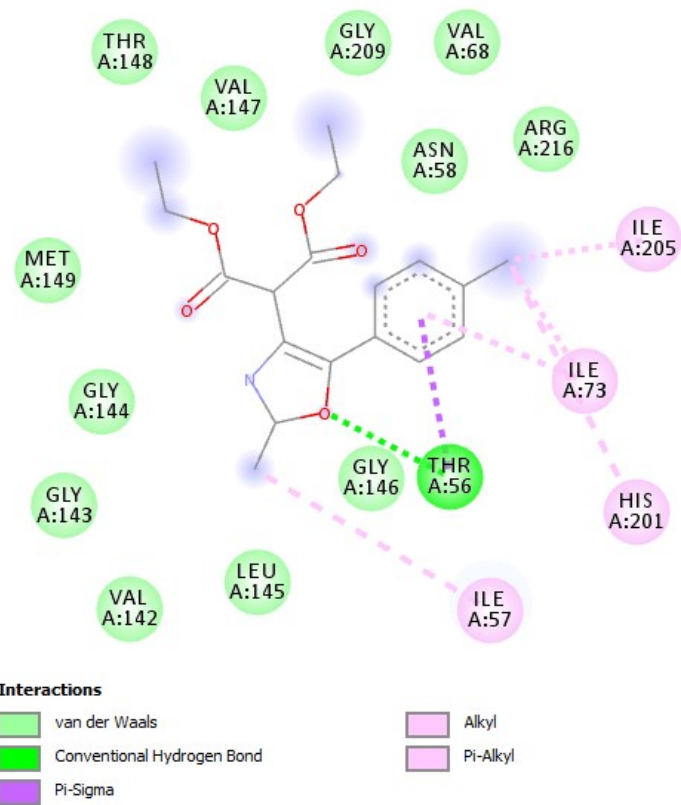
S.NO.	Compound	Molecular Weight (g/mol)	Binding Energy (Kcal/mol)	Interactive Residues
3k		371.3122	-6.6	ARG216, GLY144, GLY146, GLY209, VAL147, VAL68
3l		331.3680	-6.4	ASN58, ASN206, GLY146, ILE57, ILE73, ILE203, THR56, VAL68
3m		261.2330	-6.8	GLY144, ILE73, ILE205, THR56, VAL68, VAL147
3n		217.2240	-6.3	GLY144, ILE73, ILE205, THR56, VAL68
3o		259.2650	-7.0	ASN206, GLY209, HIS201, ILE73, ILE205, MET149, PHE77, VAL68
3p		216.2400	-6.2	GLY209, HIS201, ILE205, ILE73, PHE77, MET149, VAL68

**Table 2.** Physicochemical properties calculated for oxazoles **3k-l** using Qikpro

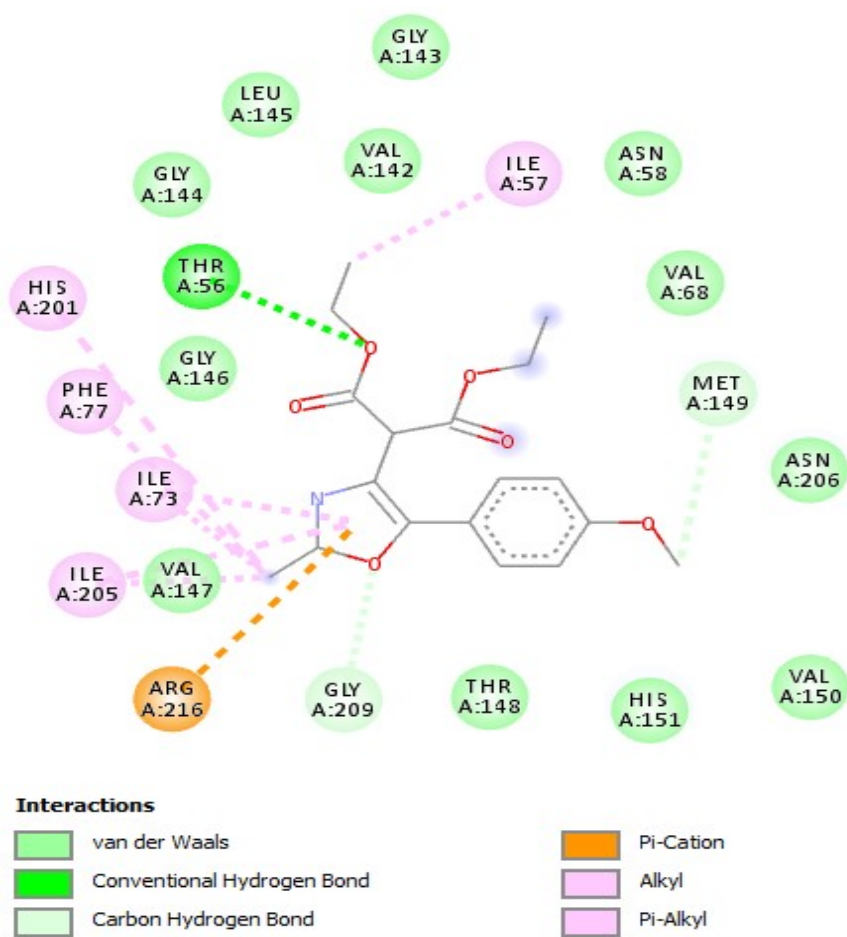
Compound	Molecular Weight	QPlogS	QPlogHERG	QPPCaco	QPPMDCK	QPlogKp	QPlogPo/w	Human Oral Absorption	Rule of Five
<b>3k</b>	371.3122	-5.548	-5.819	1709.024	4092.338	-1.943	3.975	100	0
<b>3l</b>	331.3680	-4.983	-5.826	1629.892	838.768	-1.826	3.625	100	0
<b>3m</b>	261.2330	-2.796	-0.957	11.335	6.314	-3.944	2.617	61.142	0
<b>3n</b>	217.2240	-2.744	-2.574	227.391	126.922	-2.658	2.218	82.116	0
<b>3o</b>	259.2650	-0.863	-1.956	38.472	56.624	-4.170	-0.079	54.856	0
<b>3p</b>	216.2400	-1.556	-3.145	409.513	383.624	-2.754	0.794	78.347	0



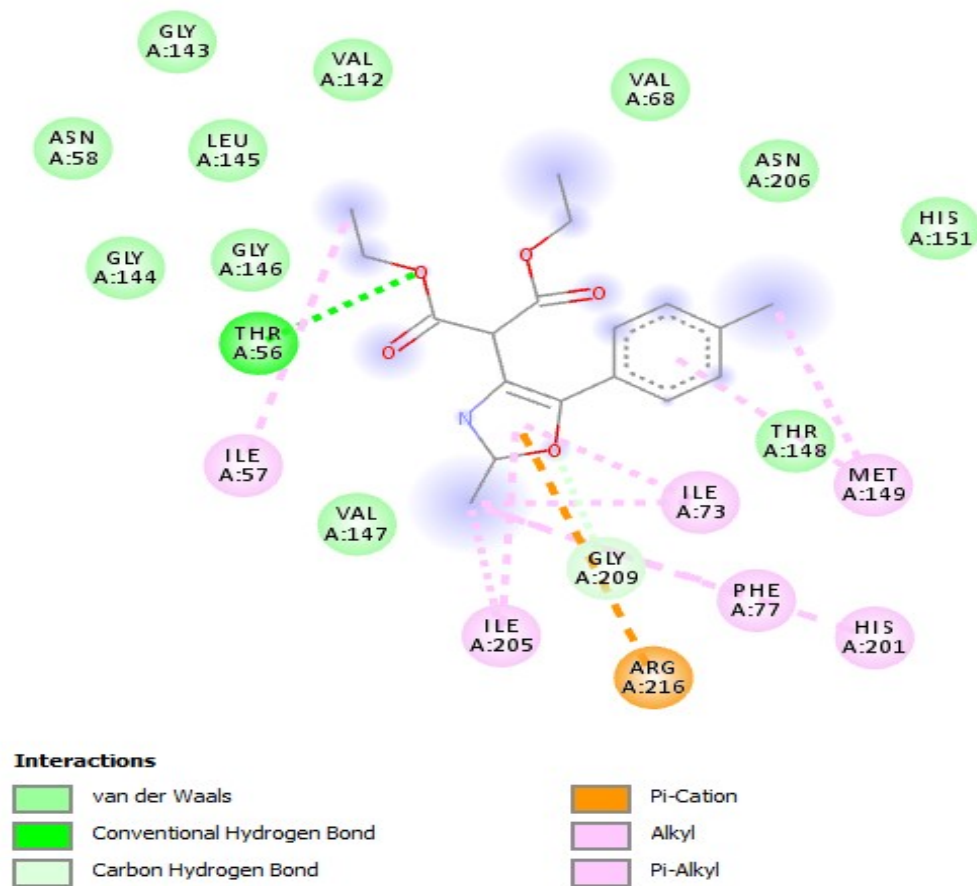
**Figure S39.** 2D interaction diagram of **3a** with AQP4



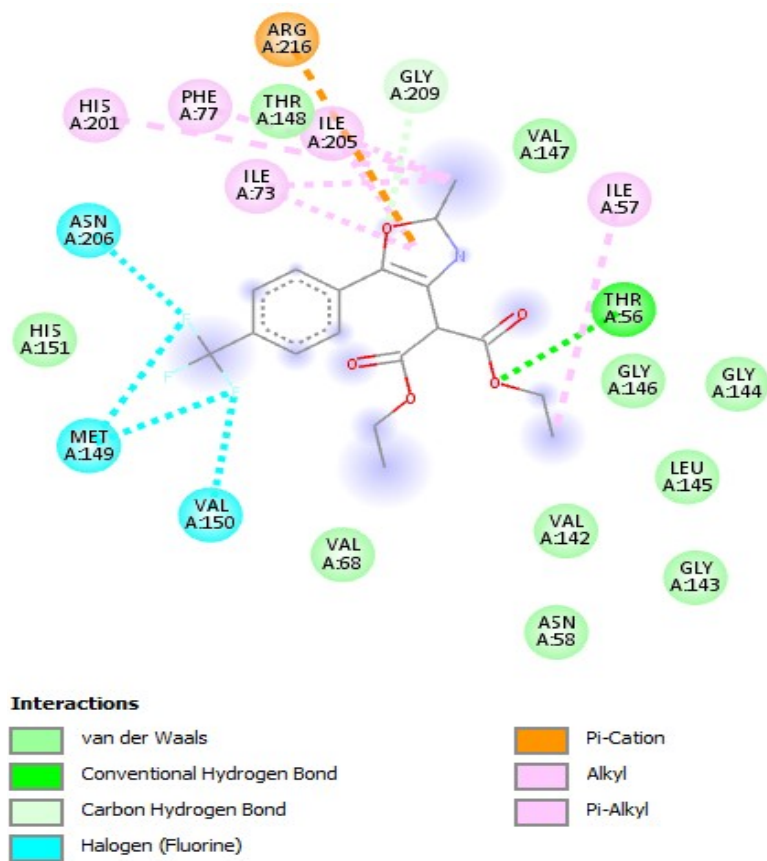
**Figure S40.** 2D interaction diagram of **3b** with AQP4



**Figure S41.** 2D interaction diagram of **3c** with AQP4



**Figure S42.** 2D interaction diagram of **3d** with AQP4



**Figure S43.** 2D interaction diagram of **3e** with AQP4

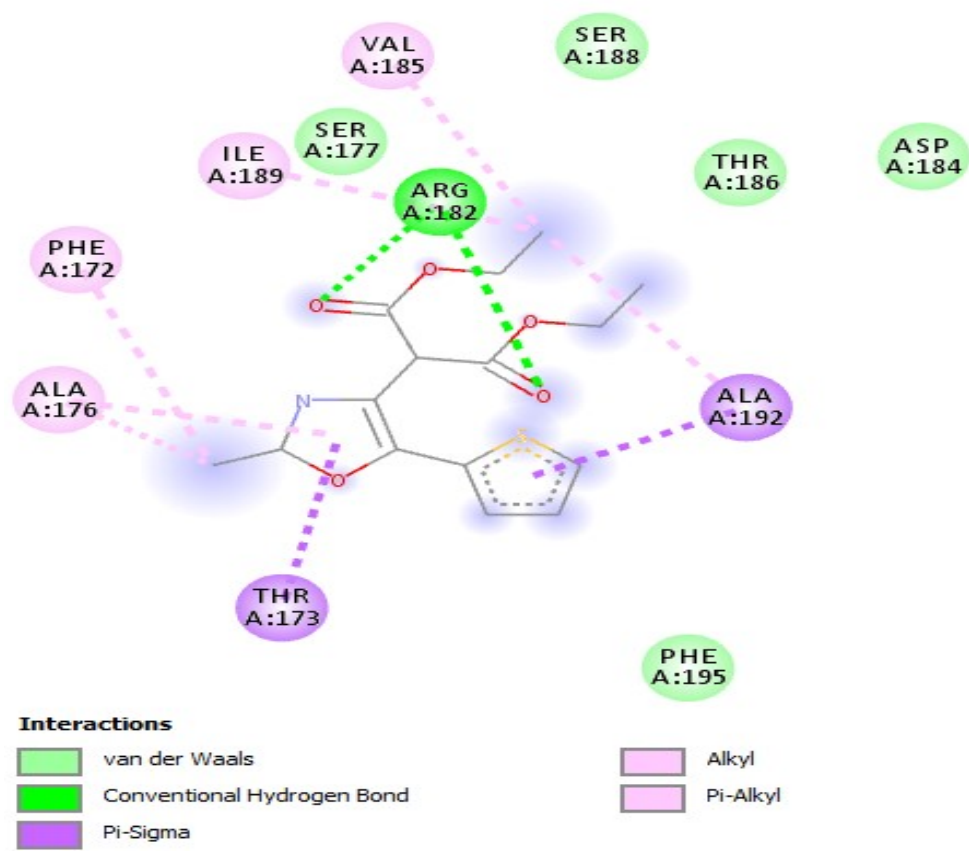
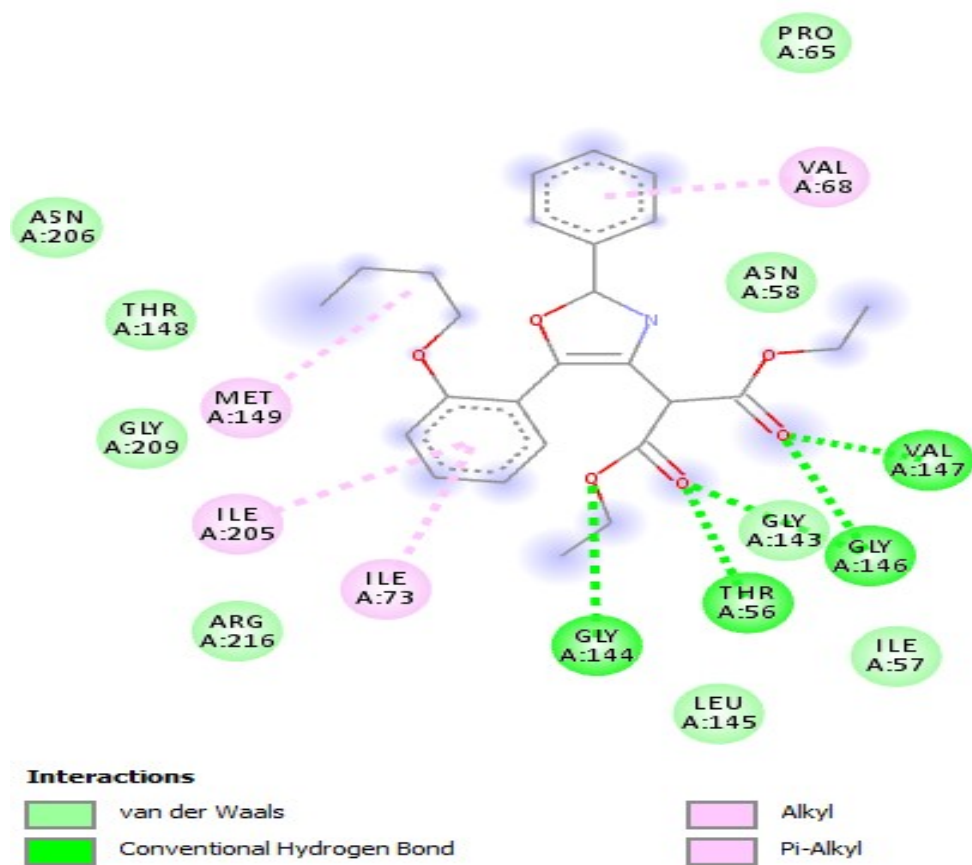
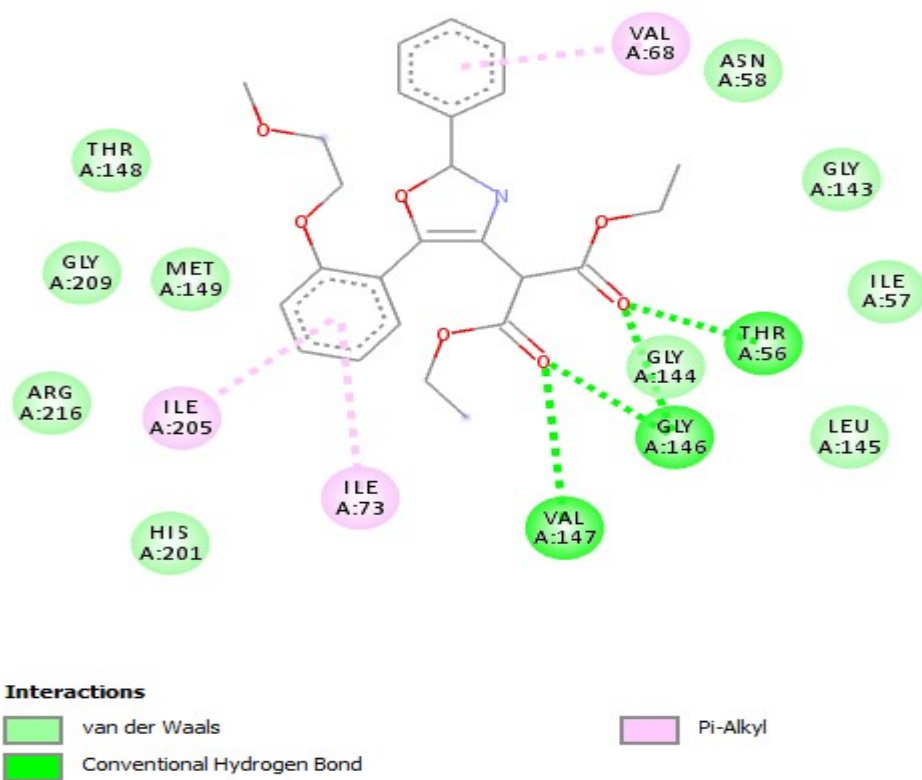


Figure S44. 2D interaction diagram of **3f** with AQP4

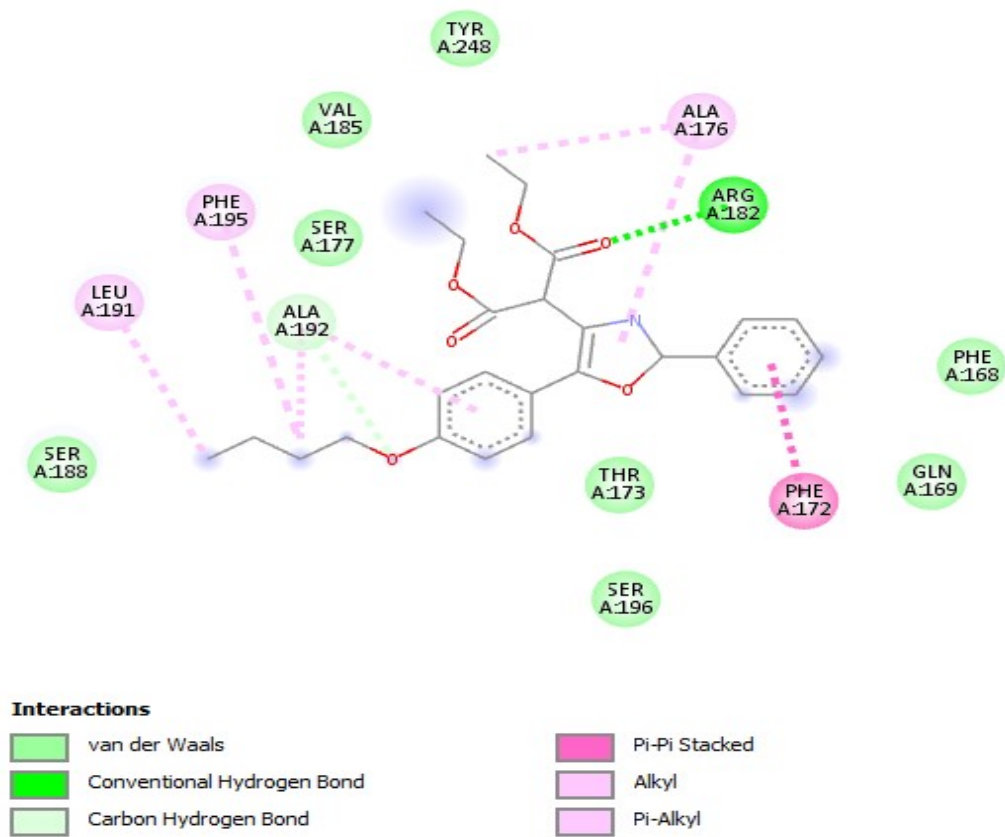




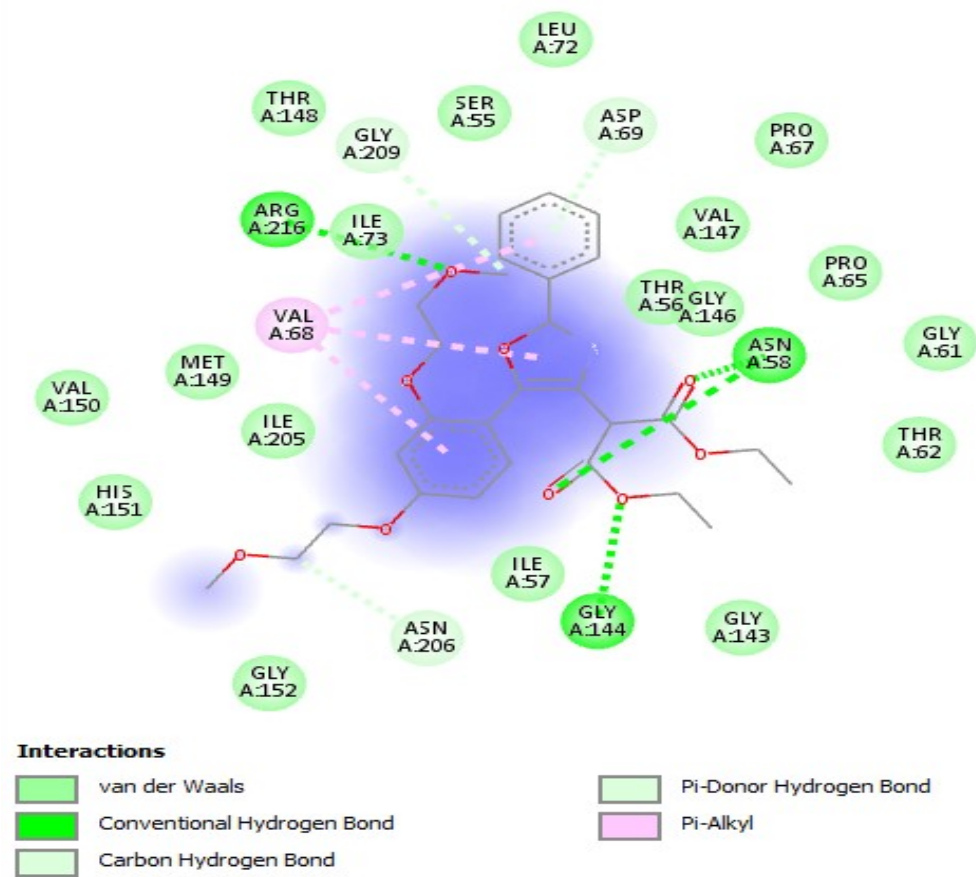
**Figure S45.** 2D interaction diagram of **3g** with AQP4



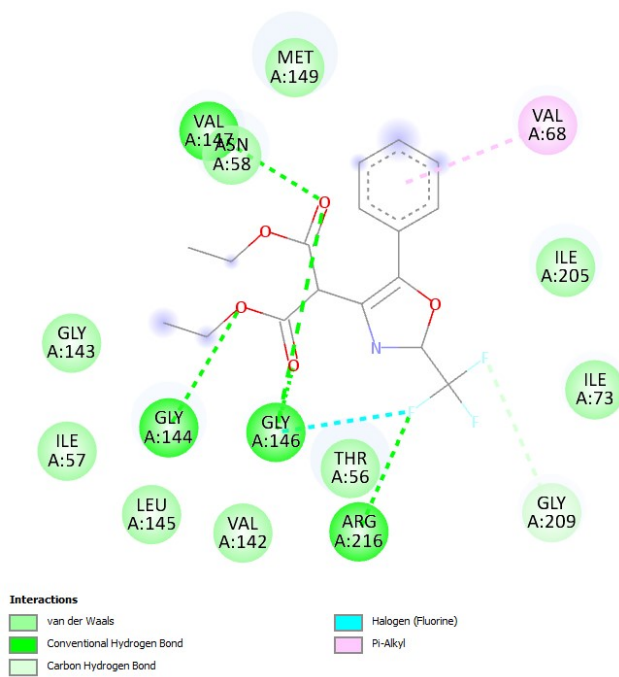
**Figure S46.** 2D interaction diagram of **3h** with AQP4



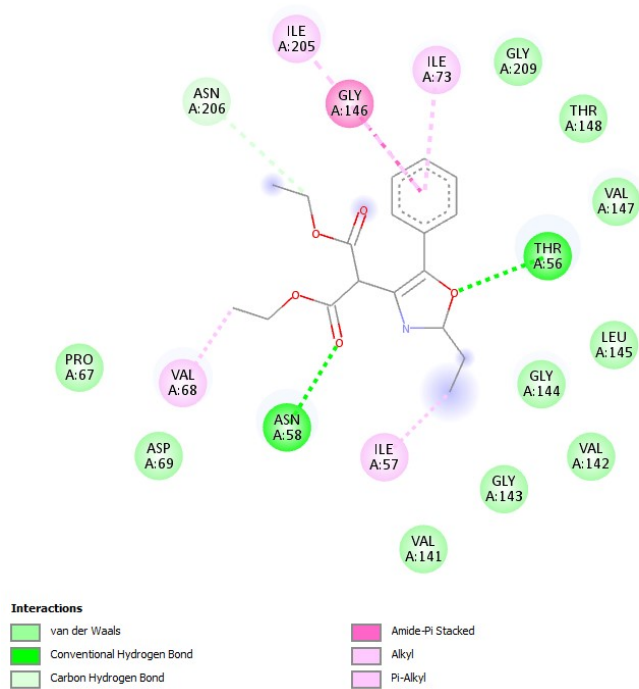
**Figure S47.** 2D interaction diagram of **3i** with AQP4



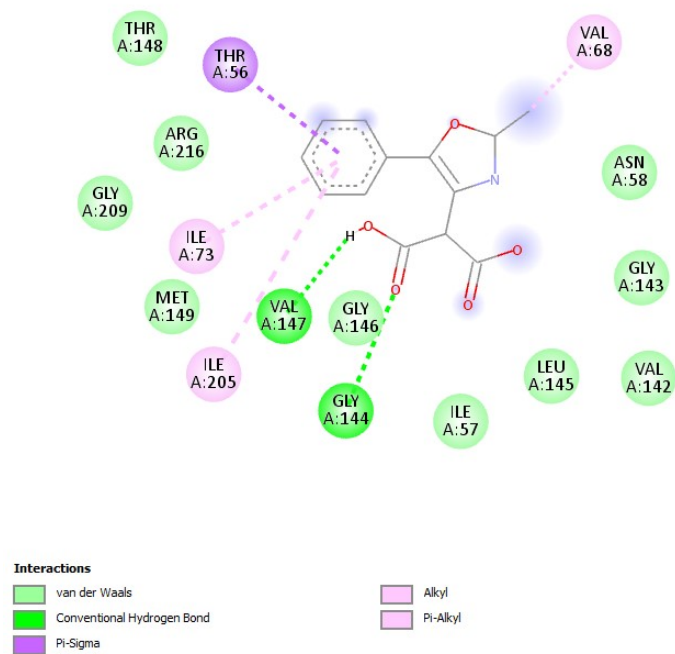
**Figure S48.** 2D interaction diagram of **3j** with AQP4



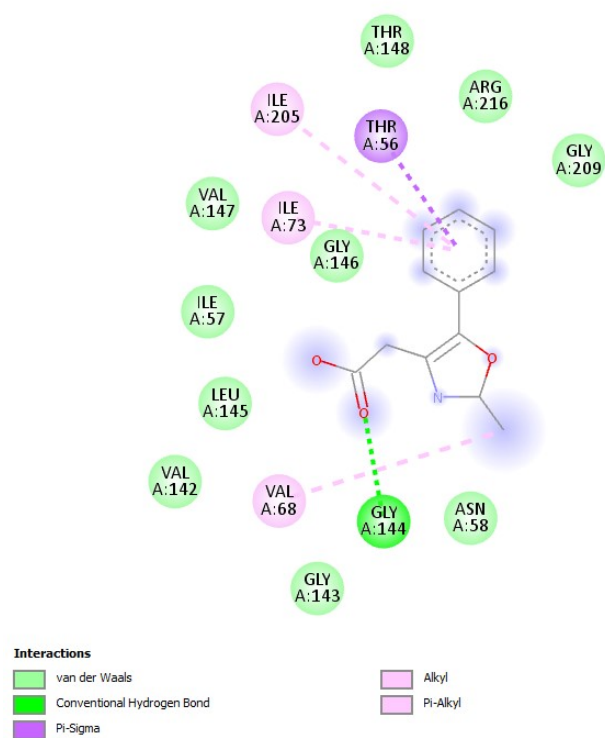
**Figure S49.** 2D interaction diagram of **3k** with AQP4



**Figure S50.** 2D interaction diagram of **31** with AQP4

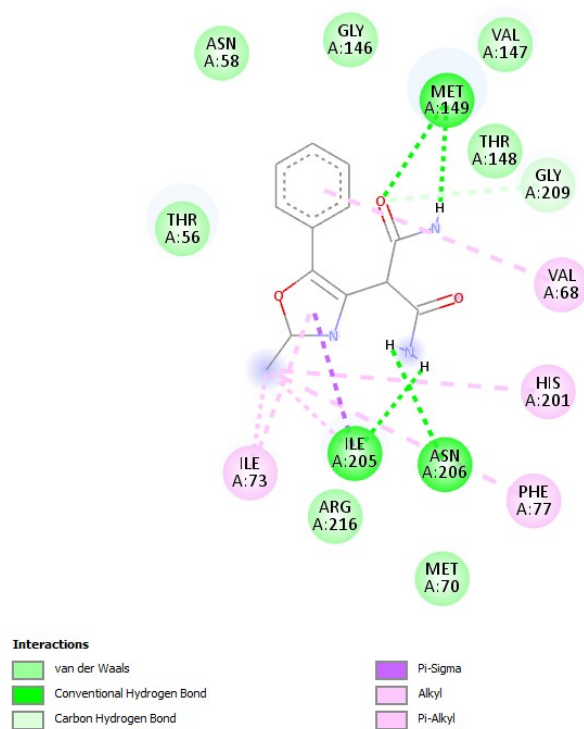


**Figure S51.** 2D interaction diagram of **3m** with AQP4

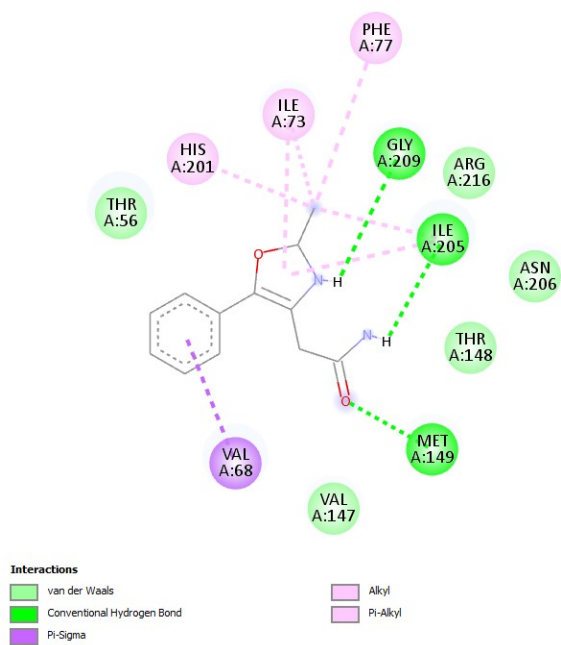


**Figure S52.** 2D interaction diagram of **3n** with AQP4





**Figure S53.** 2D interaction diagram of **3o** with AQP4



**Figure S54.** 2D interaction diagram of **3p** with AQP4