# Supporting Information

## Identification, Synthesis and Biological Evaluation of Pyrazine Ring Compounds from *Talaromyces minioluteus (Penicillium minioluteum)*

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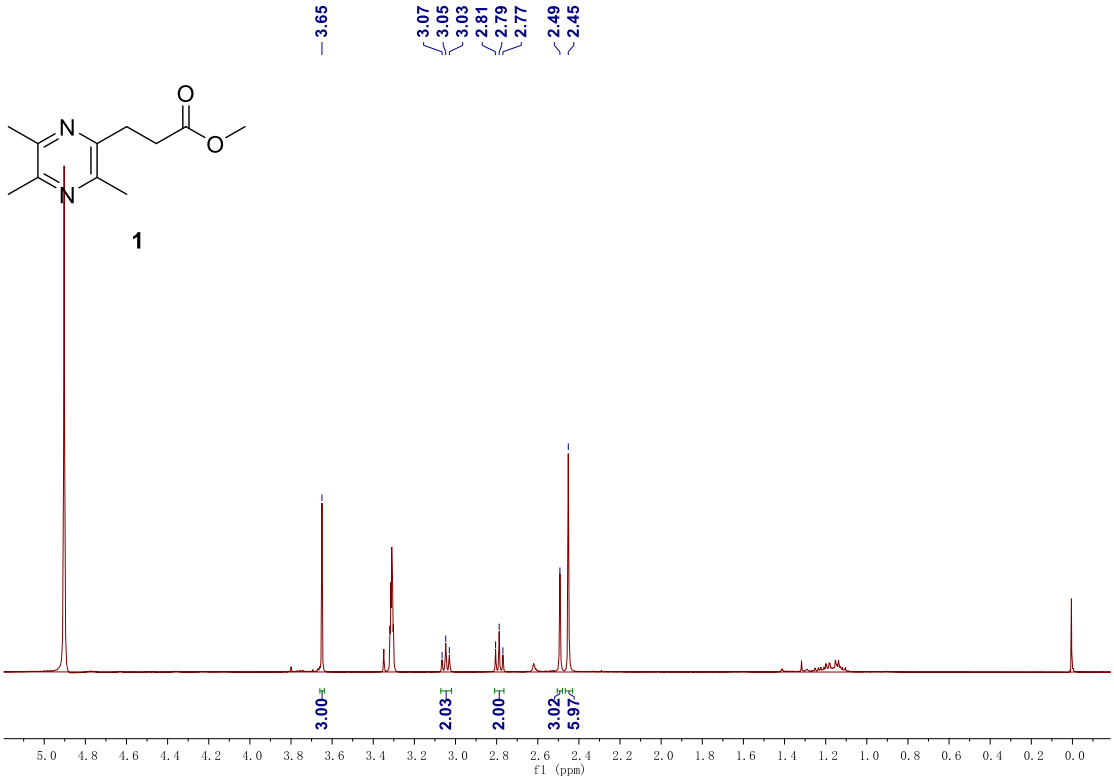



**Figure S2.** $^{13}$C NMR and DEPT NMR spectra of **1** (100MHz, $CD_3OD$)

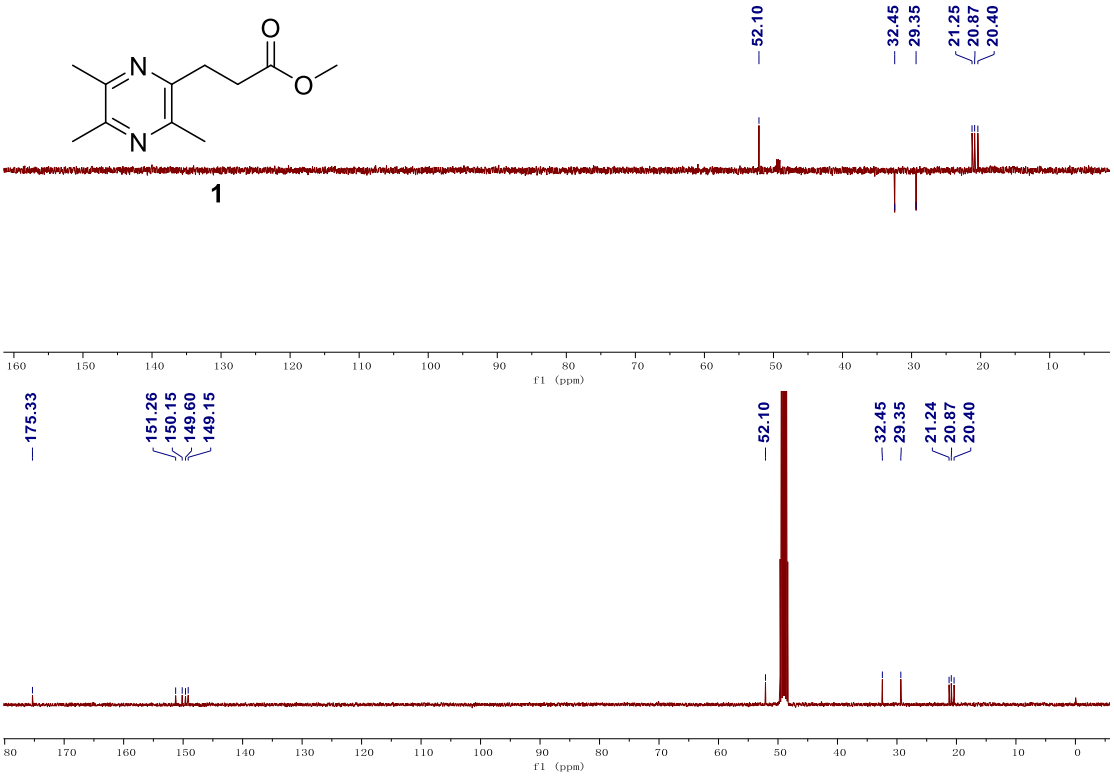


**Figure S3.** HSQC NMR spectra of **1** ($CD_3OD$)

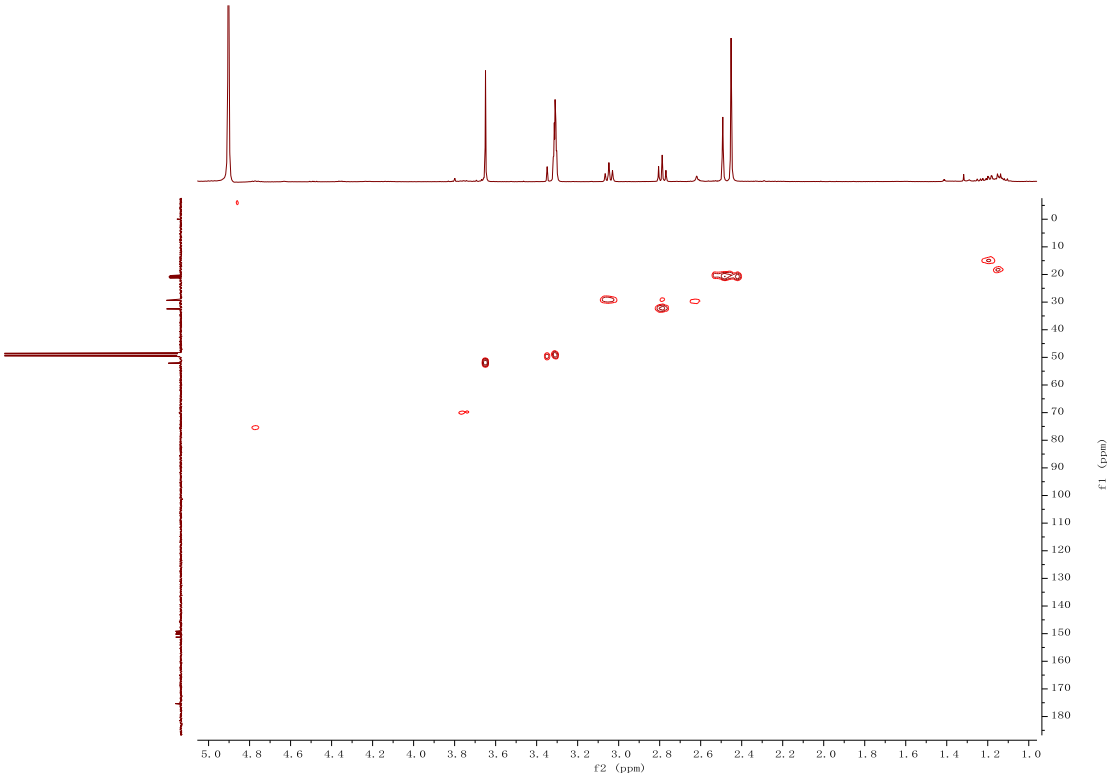



**Figure S4.** HMBC spectra of **1** ($CD_3OD$)

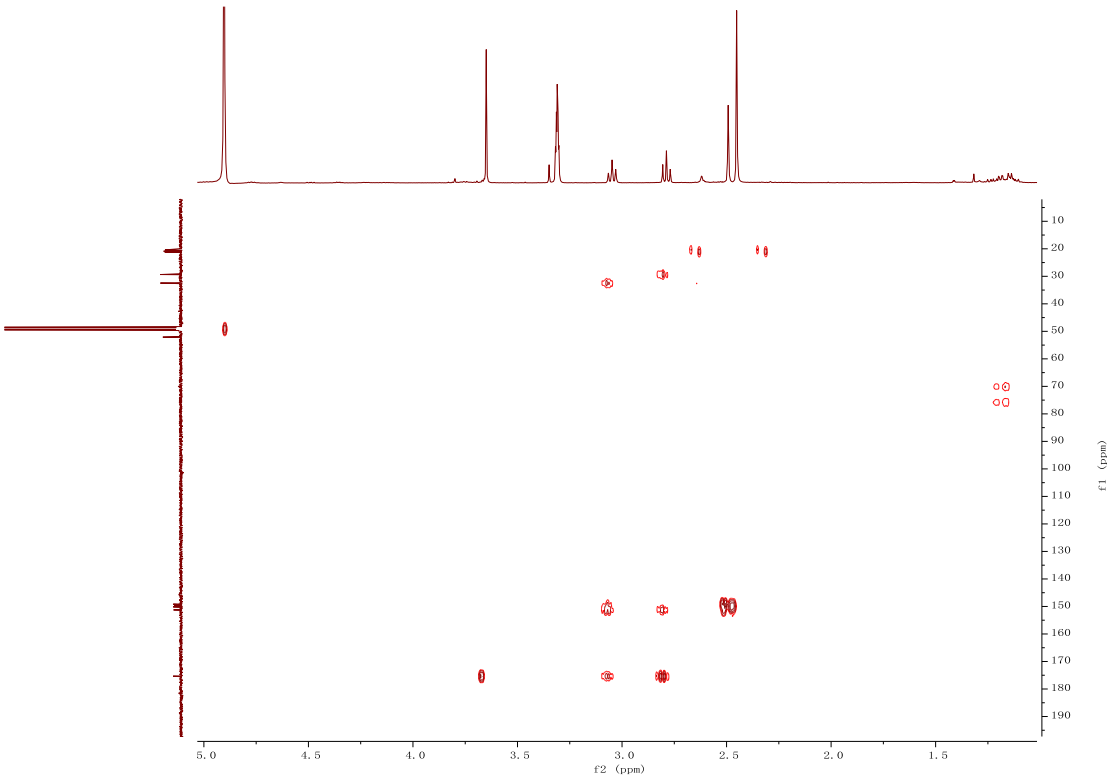


**Figure S5.** $^{1}H$-$^{1}H$ COSY spectra of **1** (100MHz, $CD_3OD$)

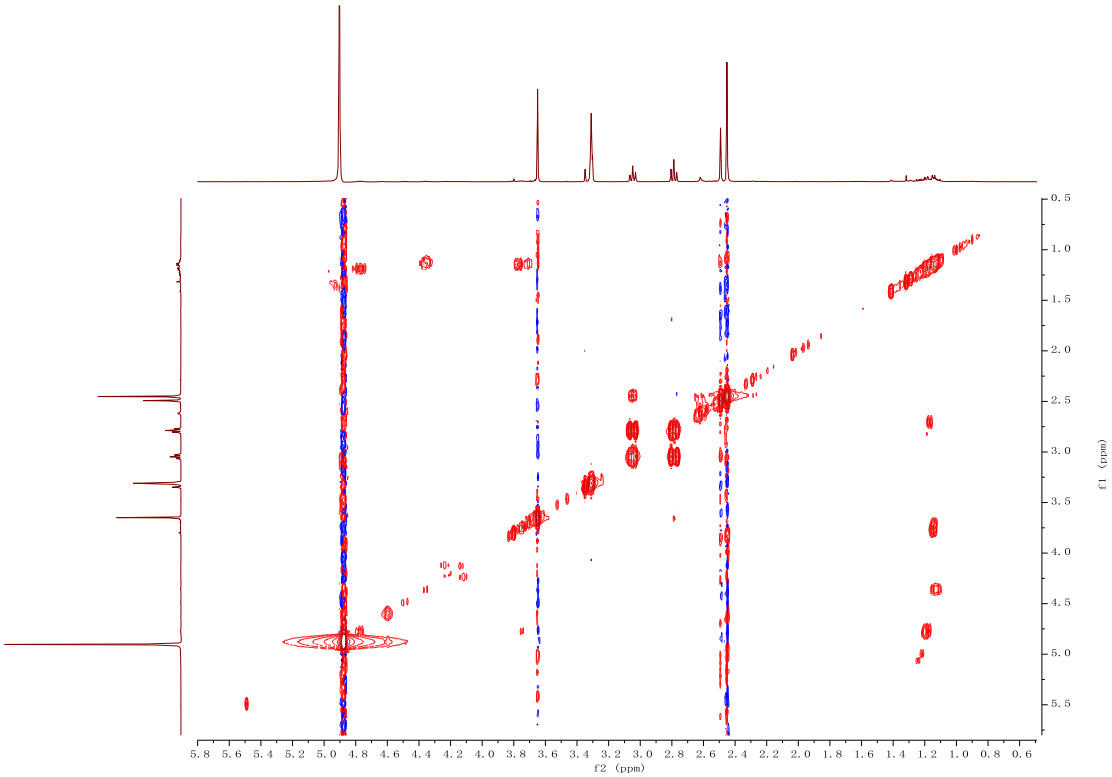



**Figure S6.** HRESIMS spectrum of **1**

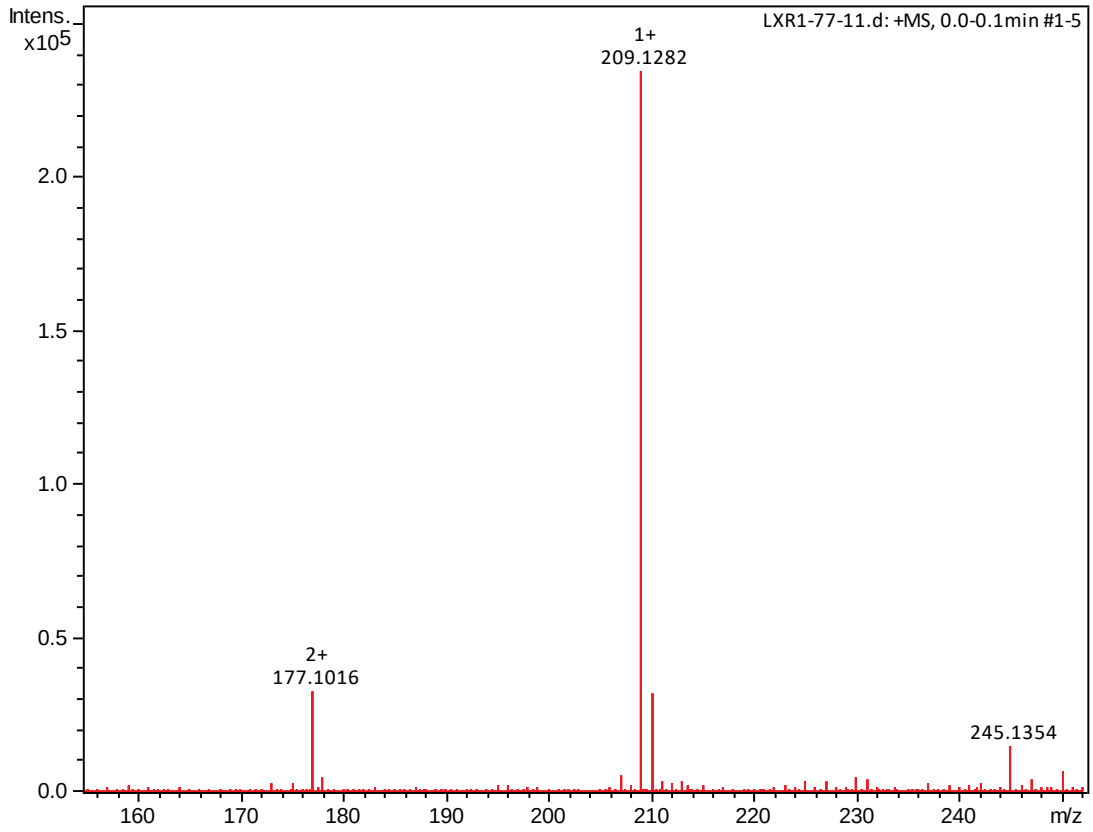


**Figure S7.** IR spectrum of **1**

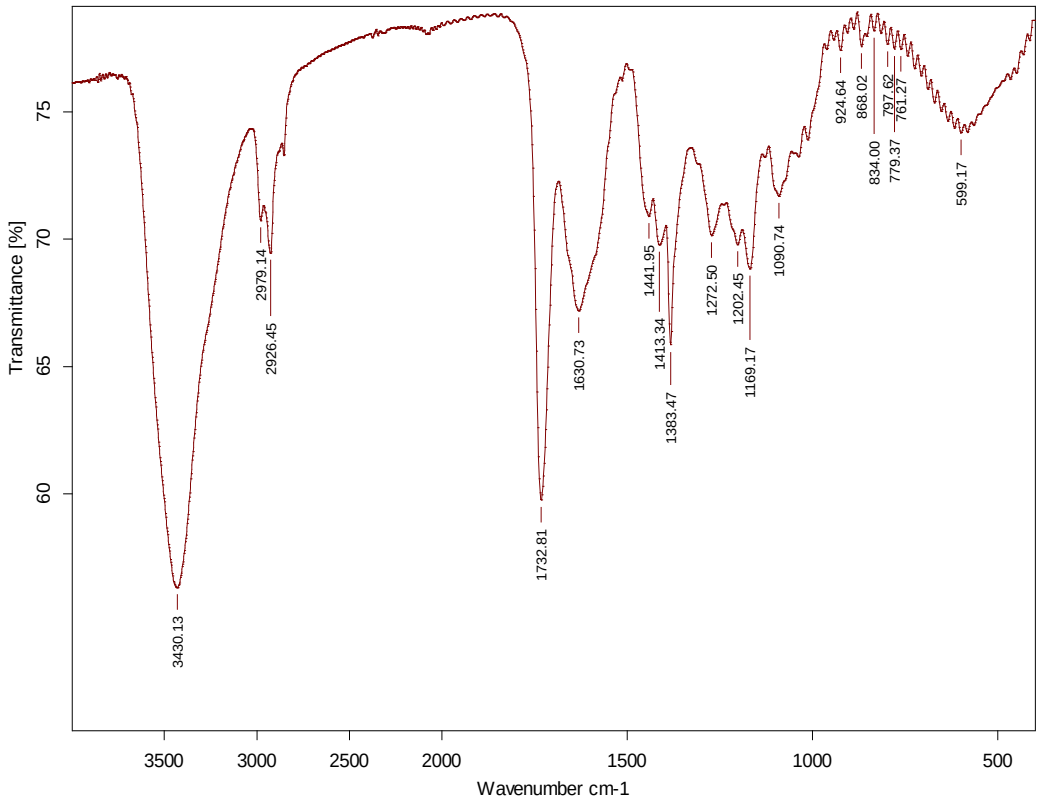



**Figure S8.** $^{1}$H NMR spectra of **2** (400MHz, $CD_3OD$)

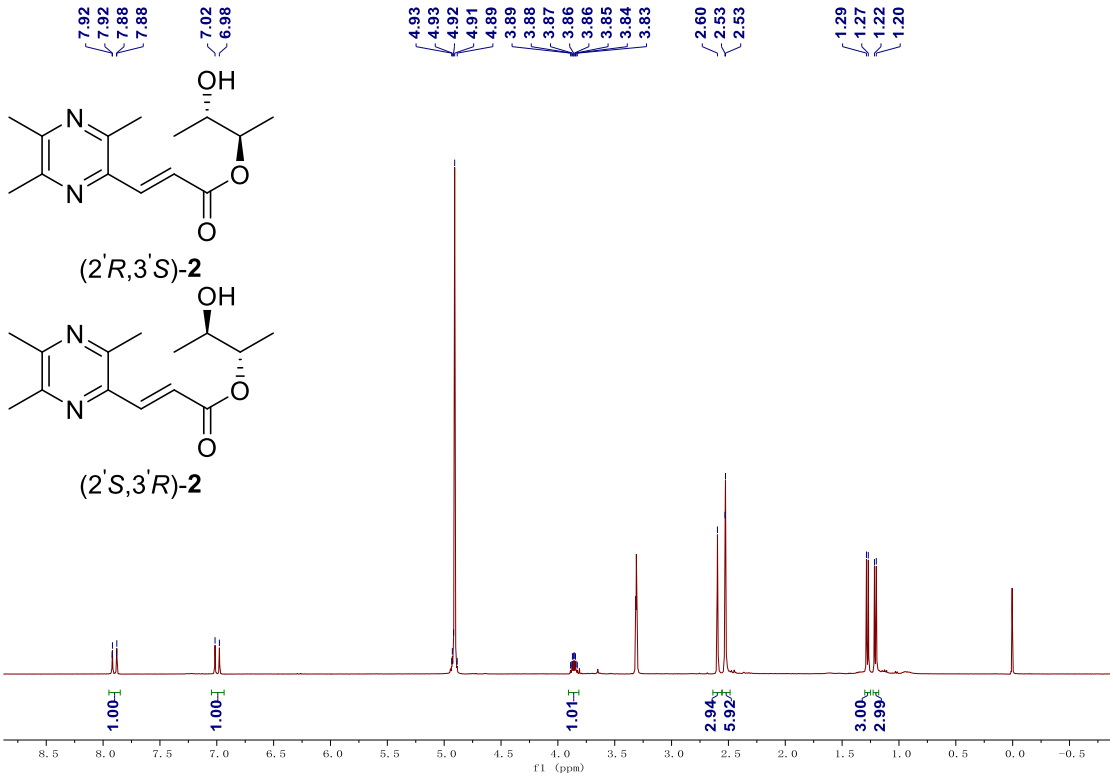


**Figure S9.** $^{13}$C NMR and DEPT NMR spectra of **2** (100MHz, $CD_3OD$)

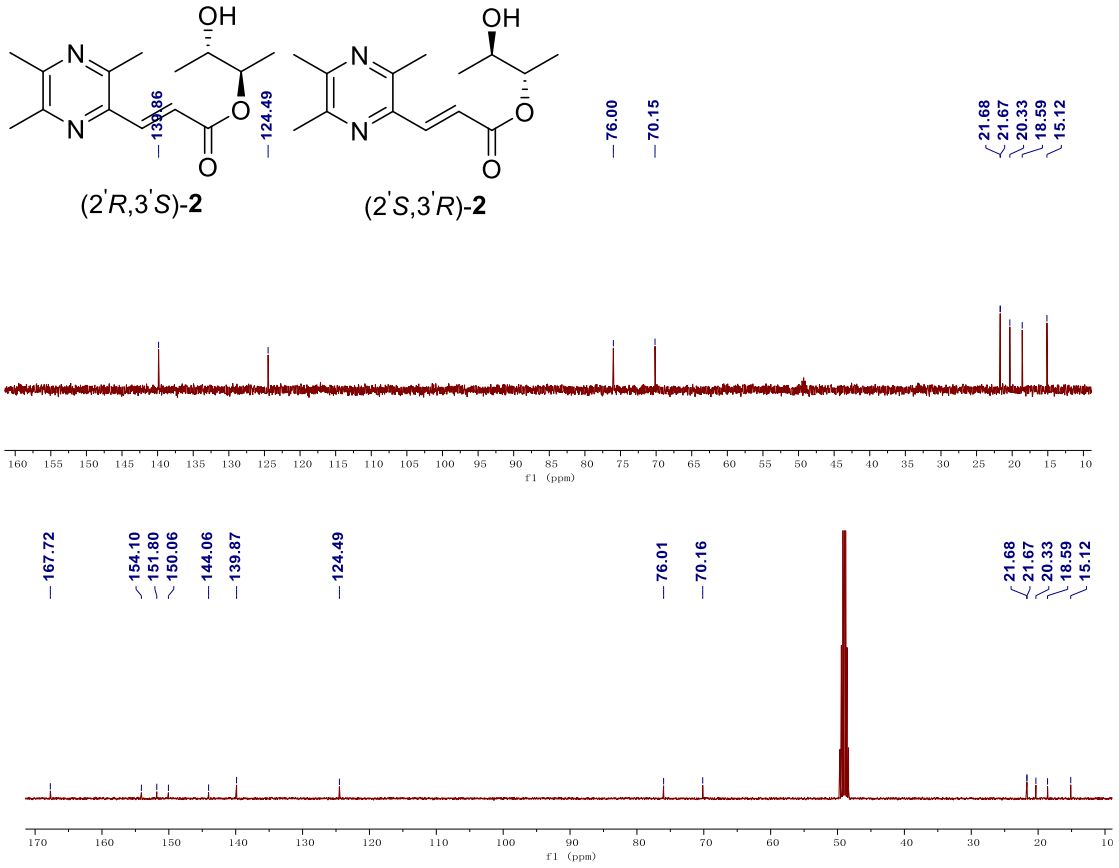



**Figure S10.** HSQC spectra of **2** ($CD_3OD$)

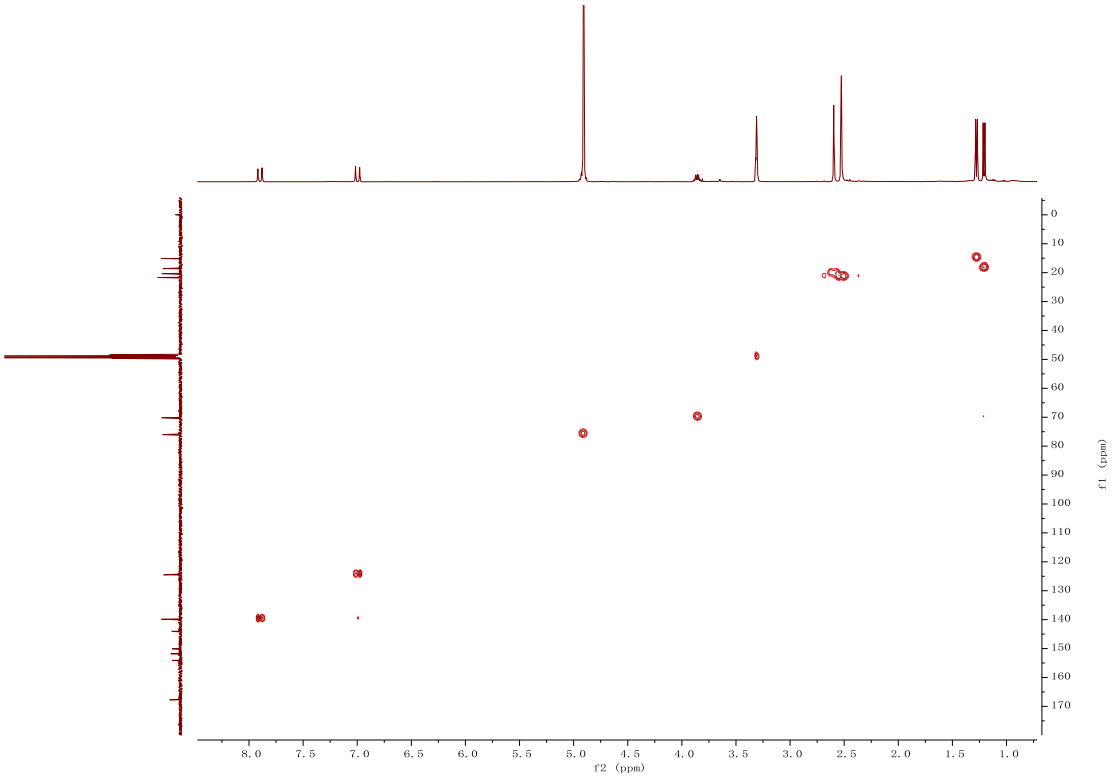


**Figure S11.** HMBC spectra of **2** ($CD_3OD$)

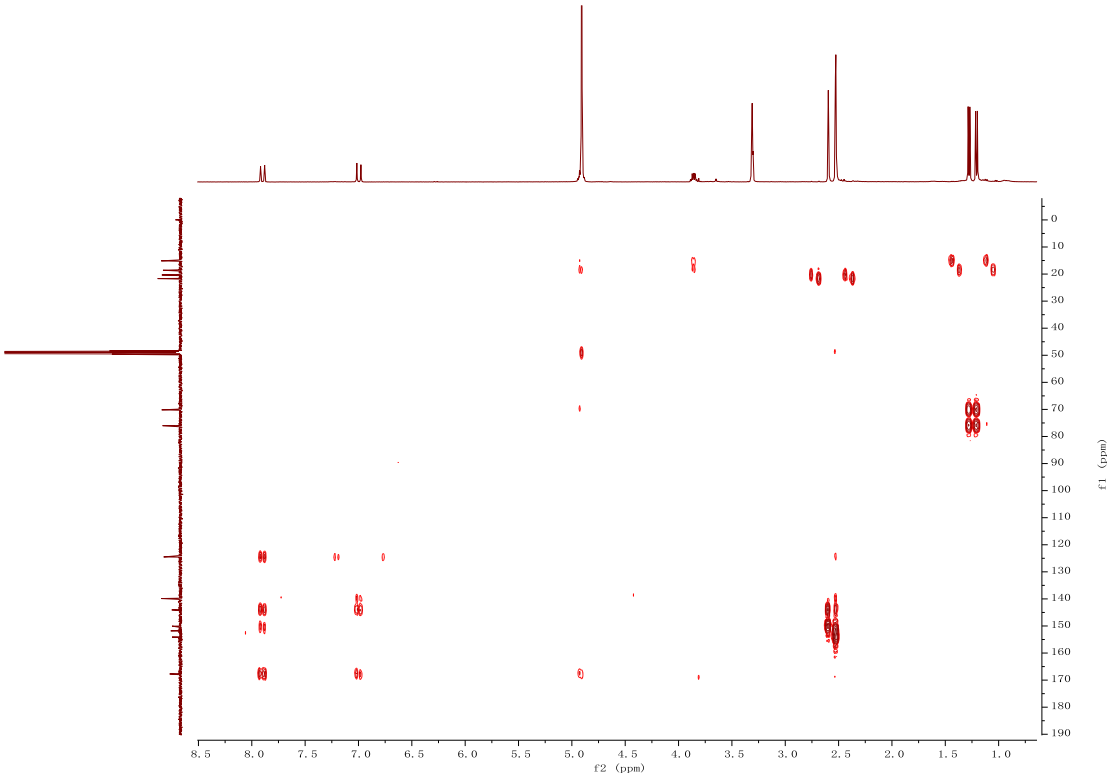



**Figure S12.** $^{1}H$-$^{1}H$ COSY spectra of **2** ($CD_3OD$)

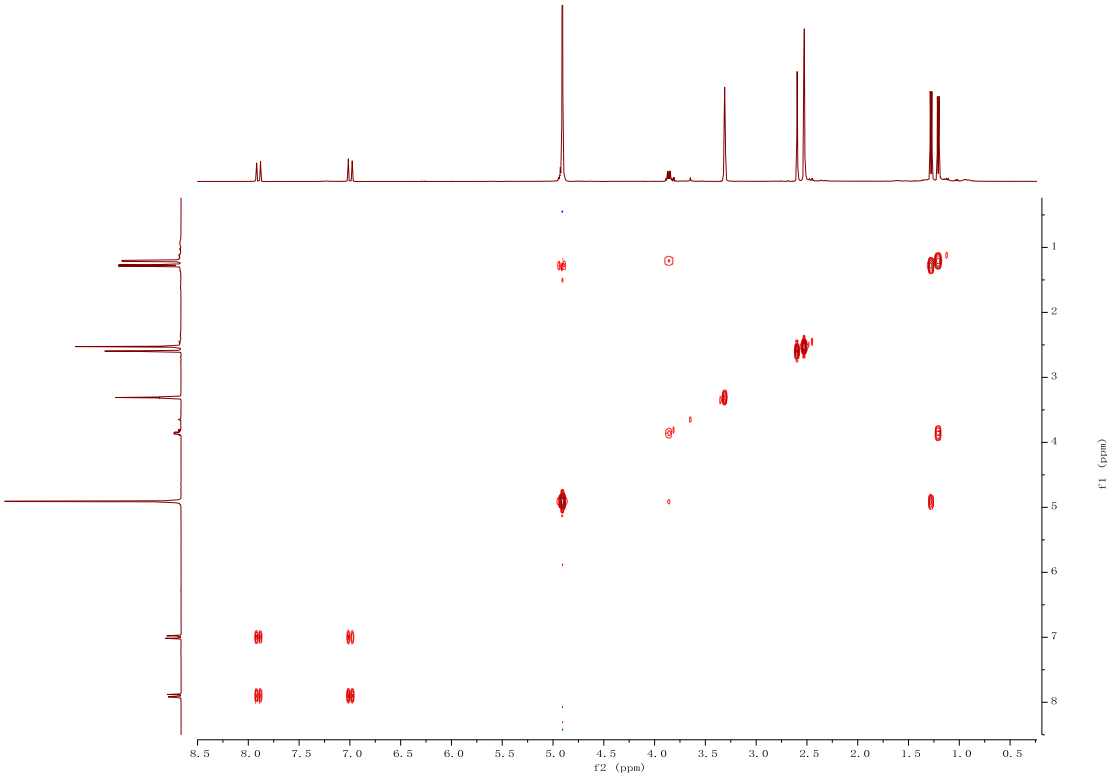


**Figure S13.** NOESY spectra of **2** ($CD_3OD$)

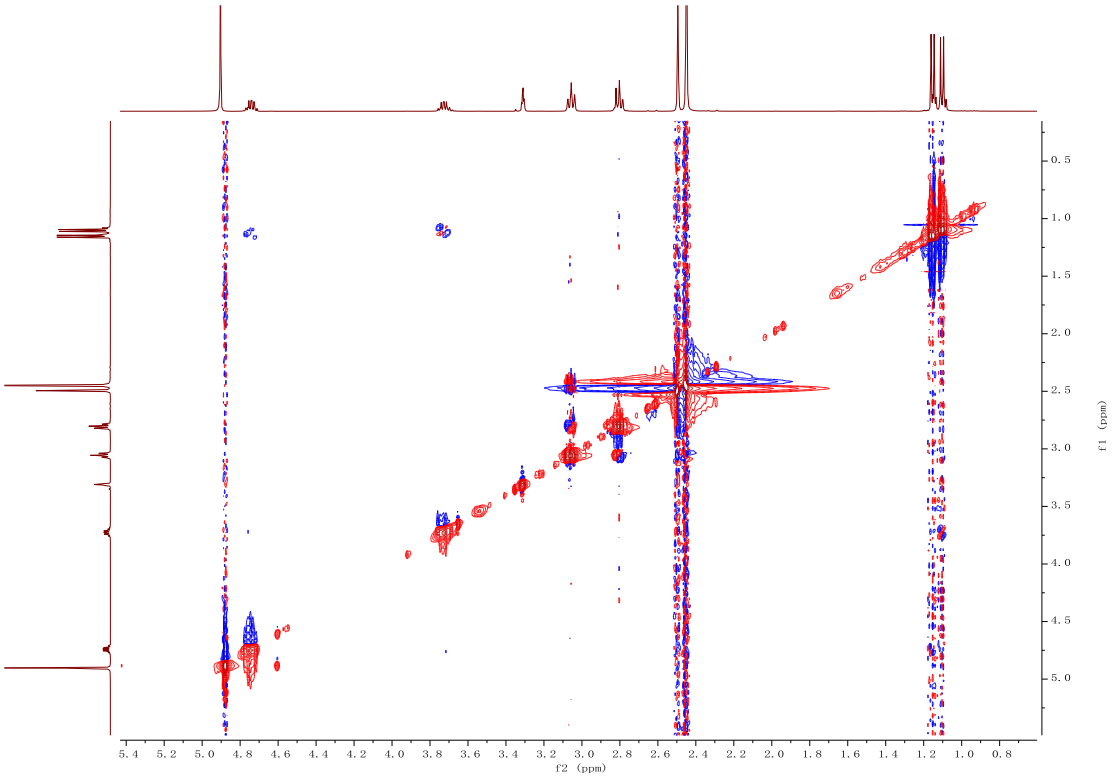



**Figure S14.** HRESIMS spectrum of **2**

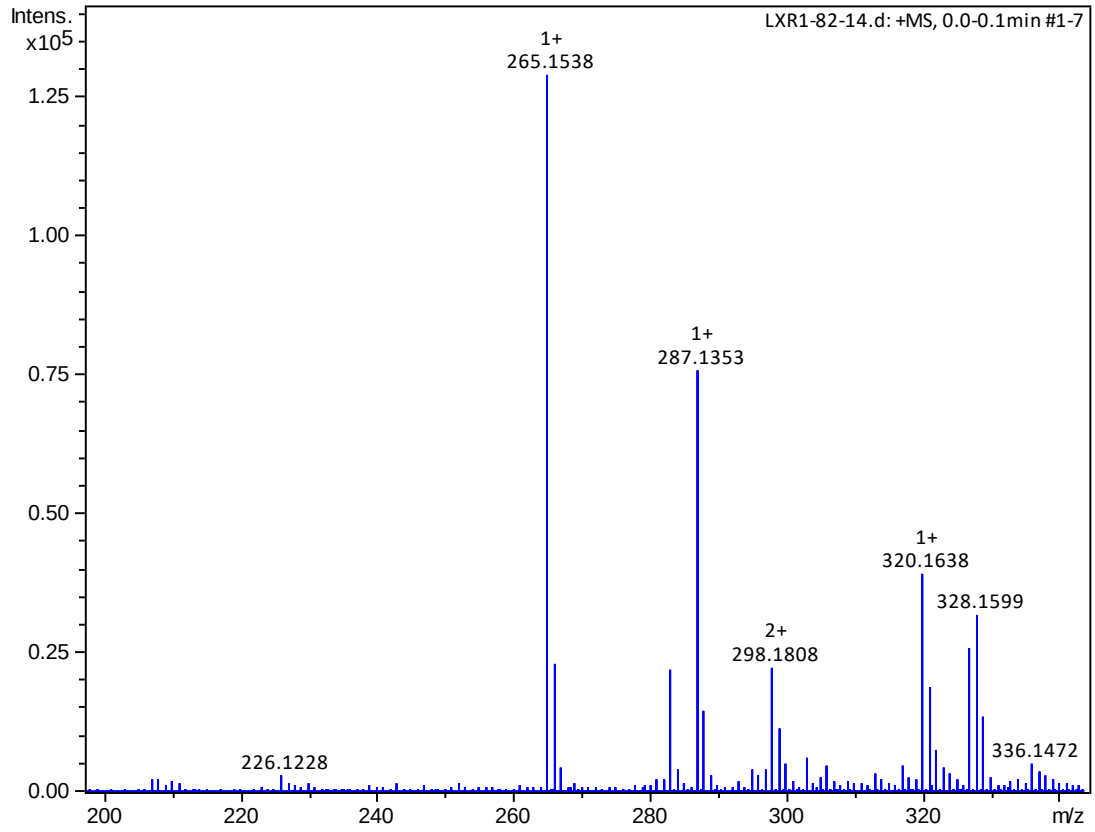


**Figure S15.** IR spectrum of **2**

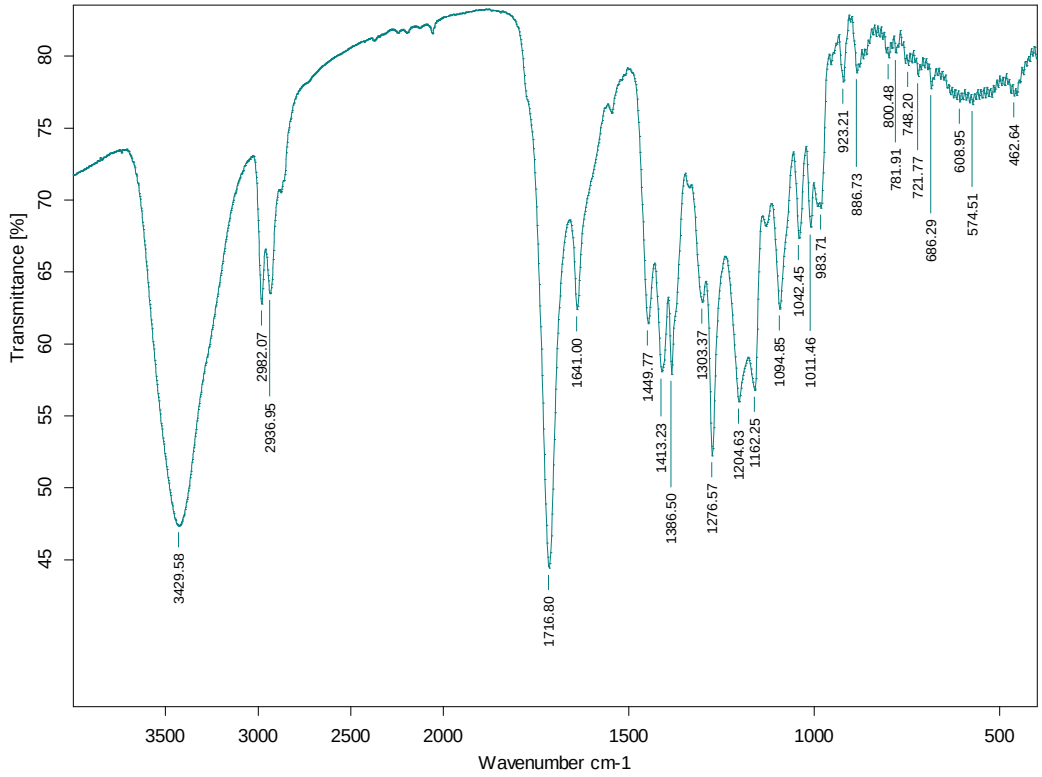



**Figure S16.** $^{1}$H NMR spectra of **3** (400MHz, $CD_3OD$)

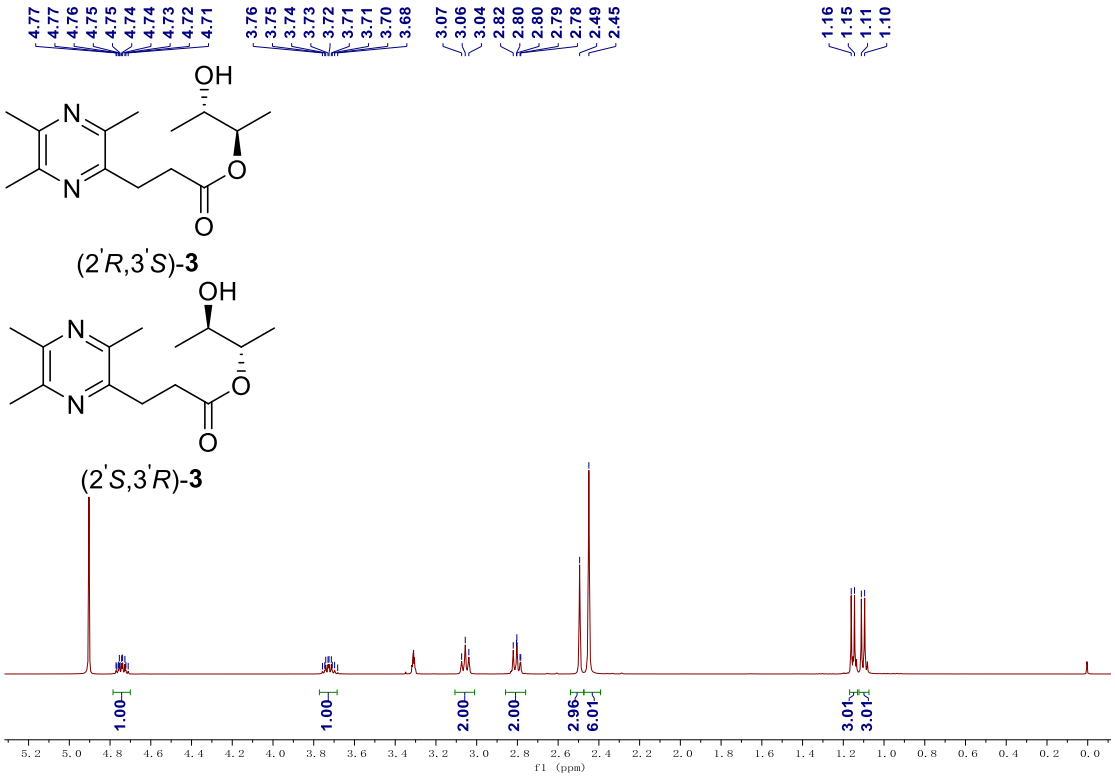


**Figure S17.** $^{13}$C NMR and DEPT NMR spectra of **3** (100MHz, $CD_3OD$)

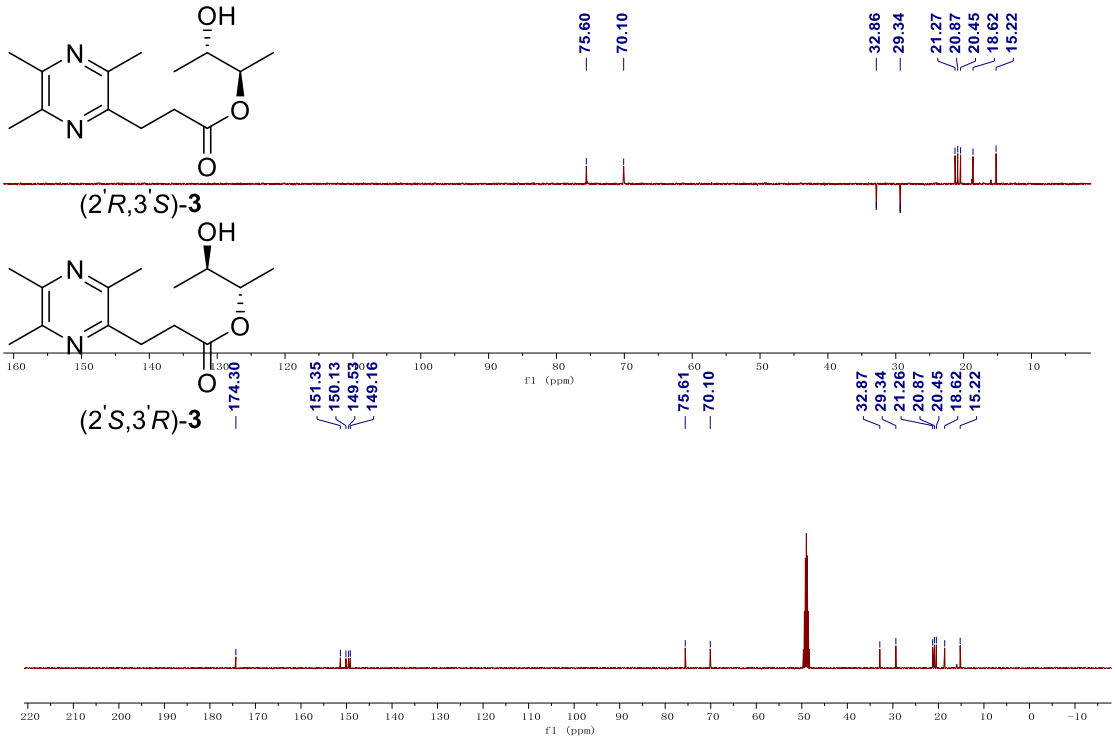



**Figure S18.** HSQC spectra of **3** ($CD_3OD$)

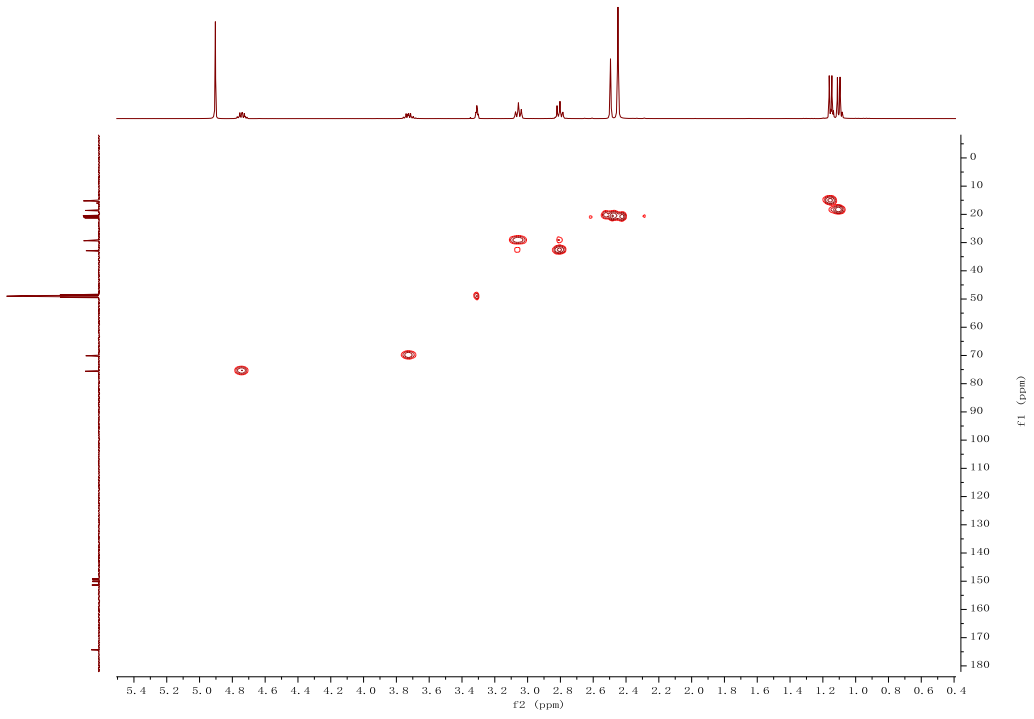
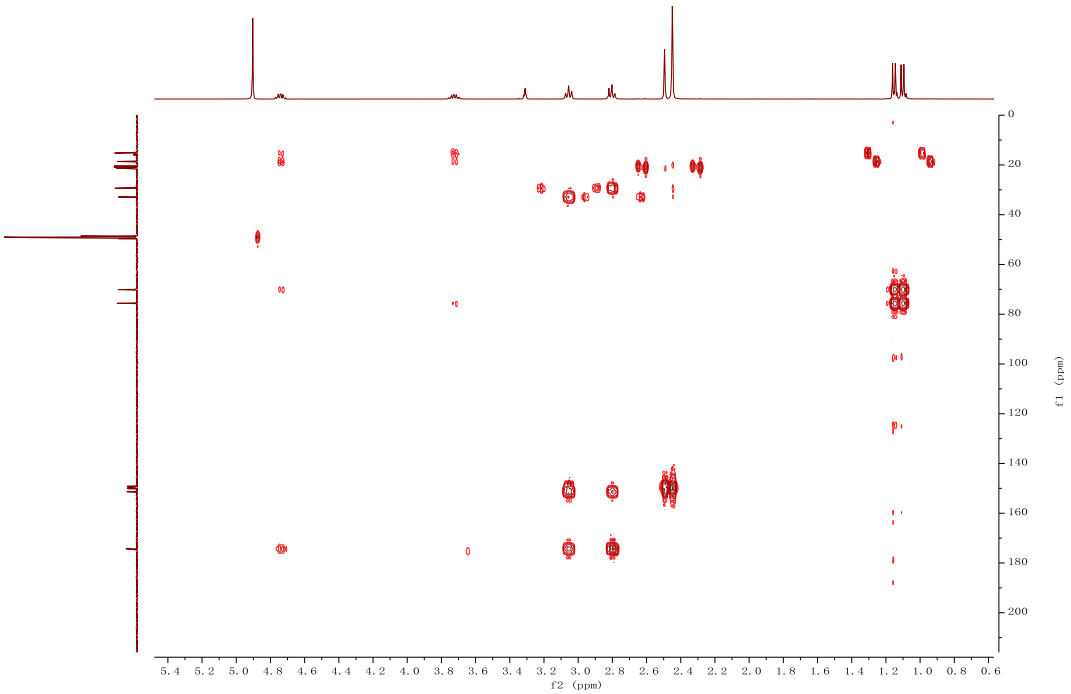


**Figure S19.** HMBC spectra of **3** ($CD_3OD$)

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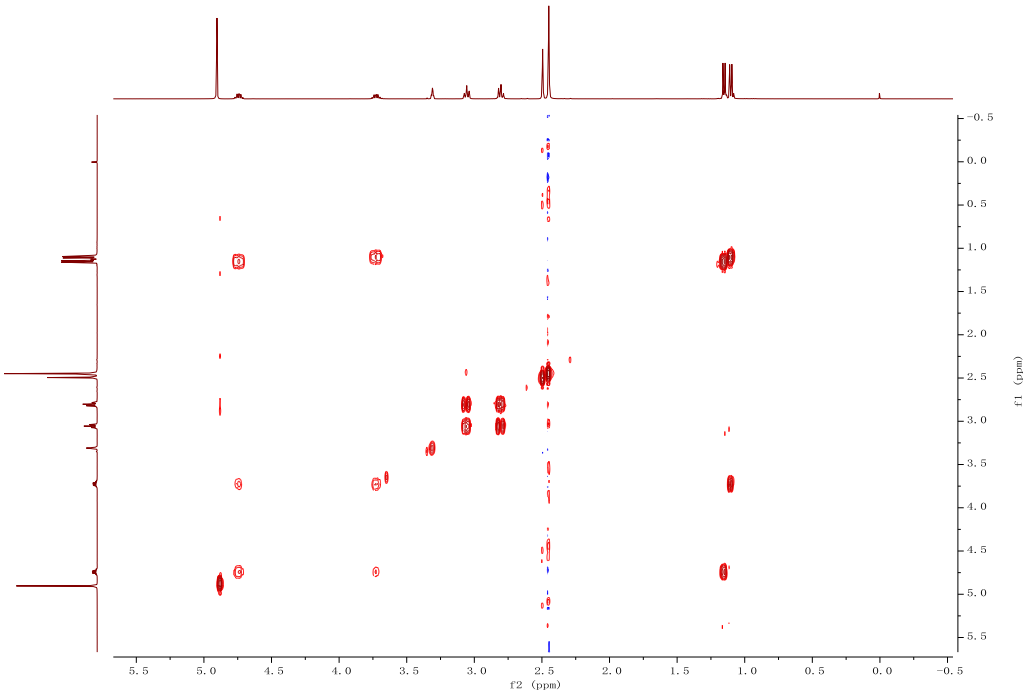

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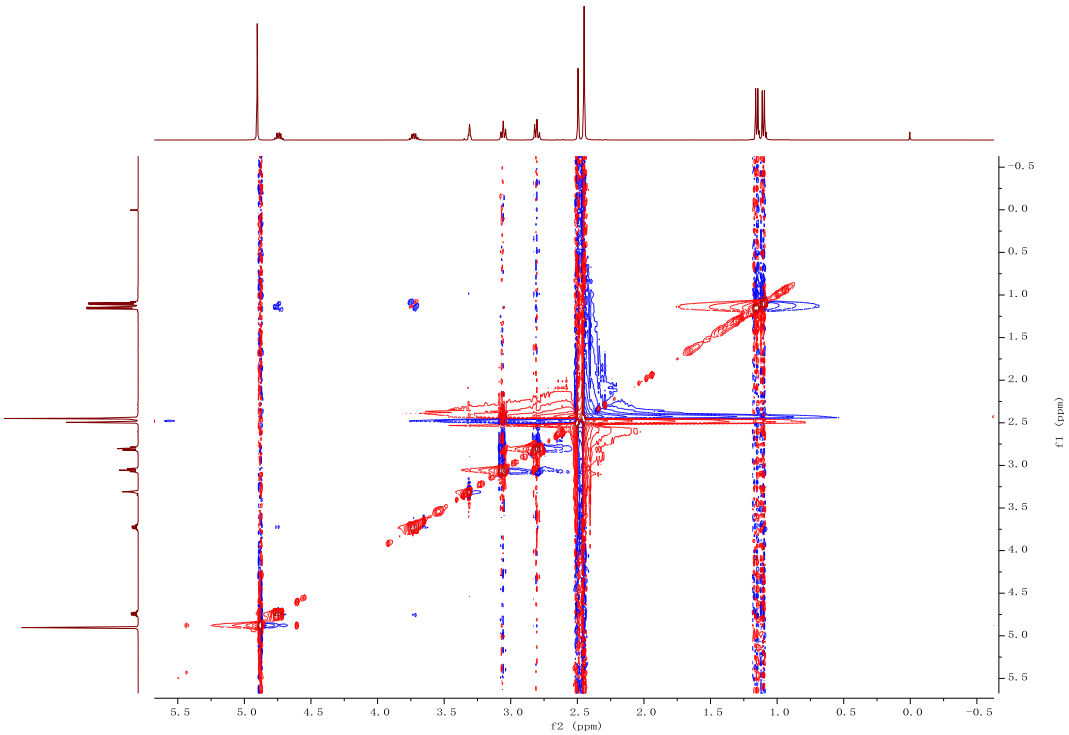


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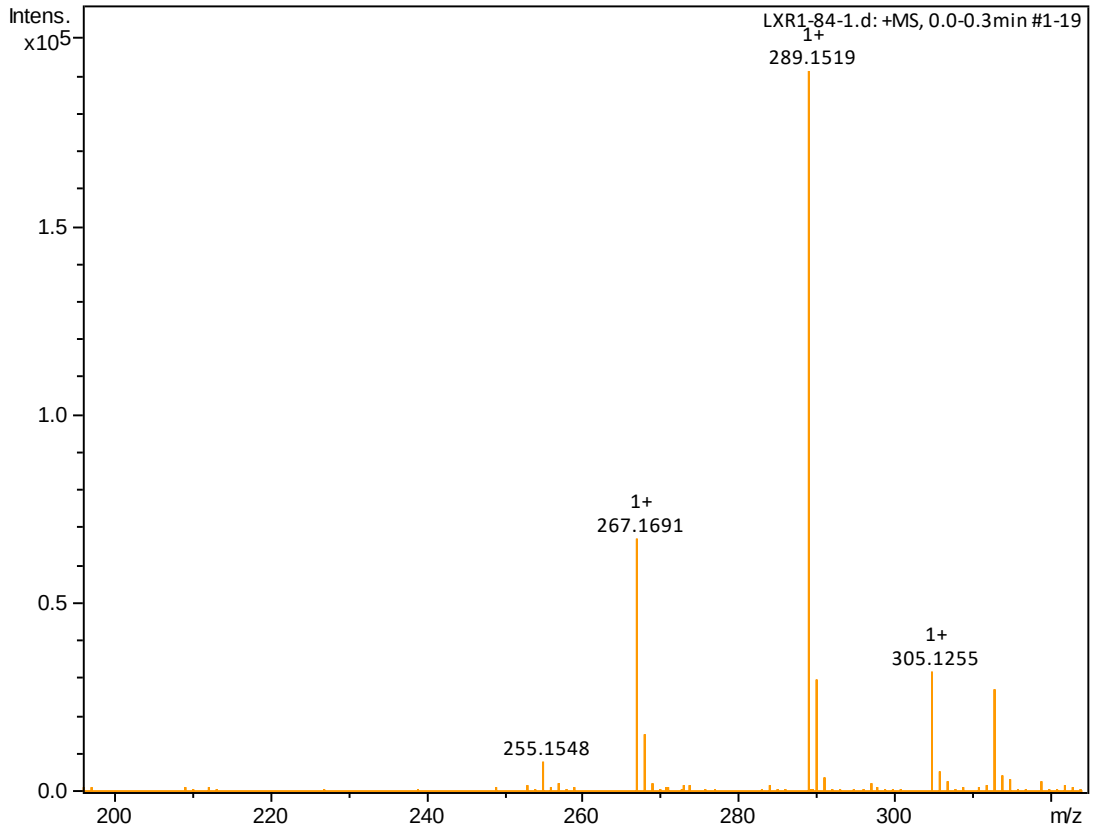

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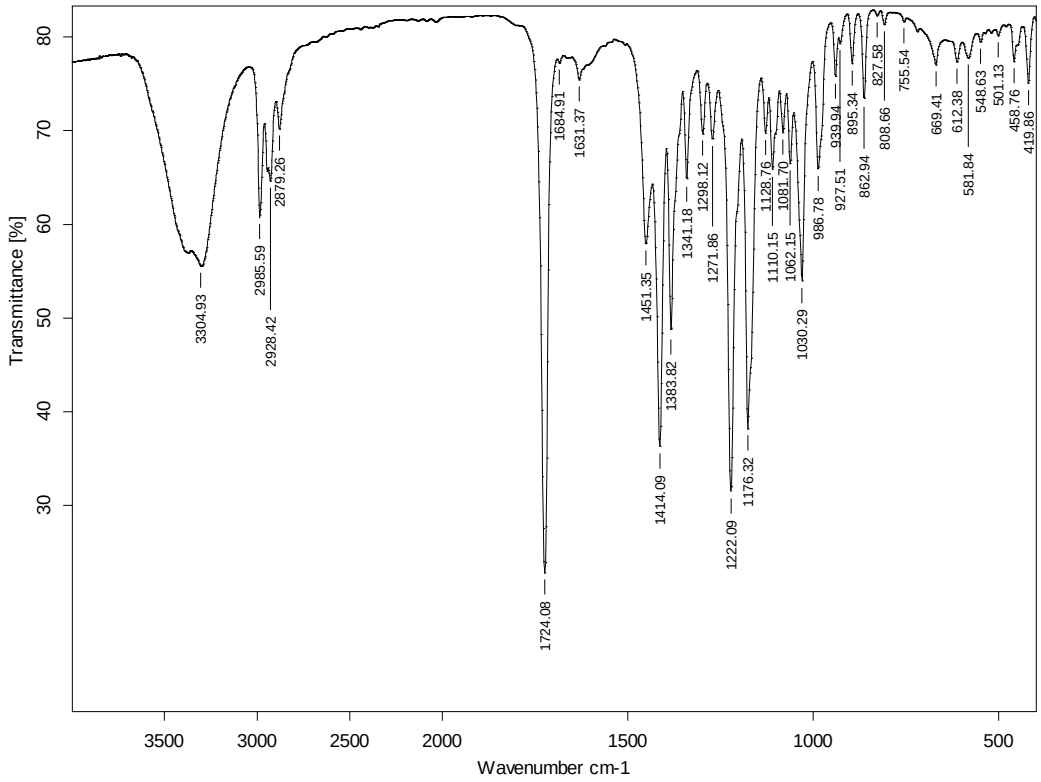
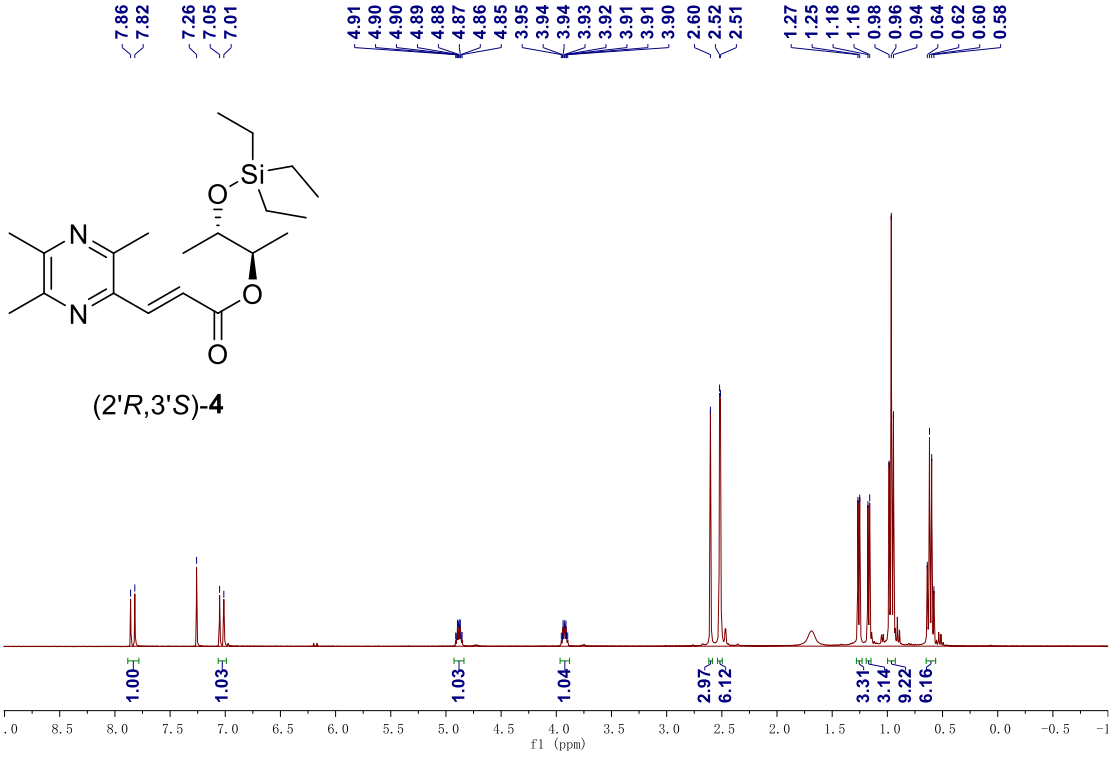



**Figure S24.** $^{1}$H NMR spectra of (2'*R*,3'*S*)-**4** (400MHz, Chloroform-*d*)



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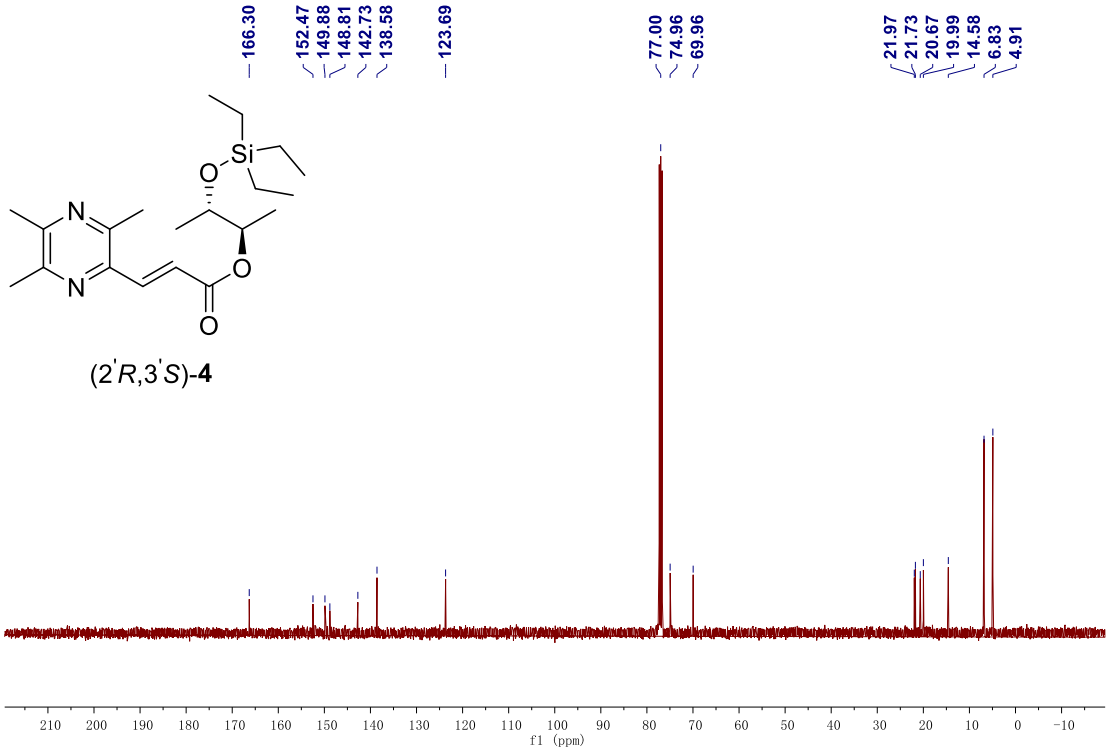
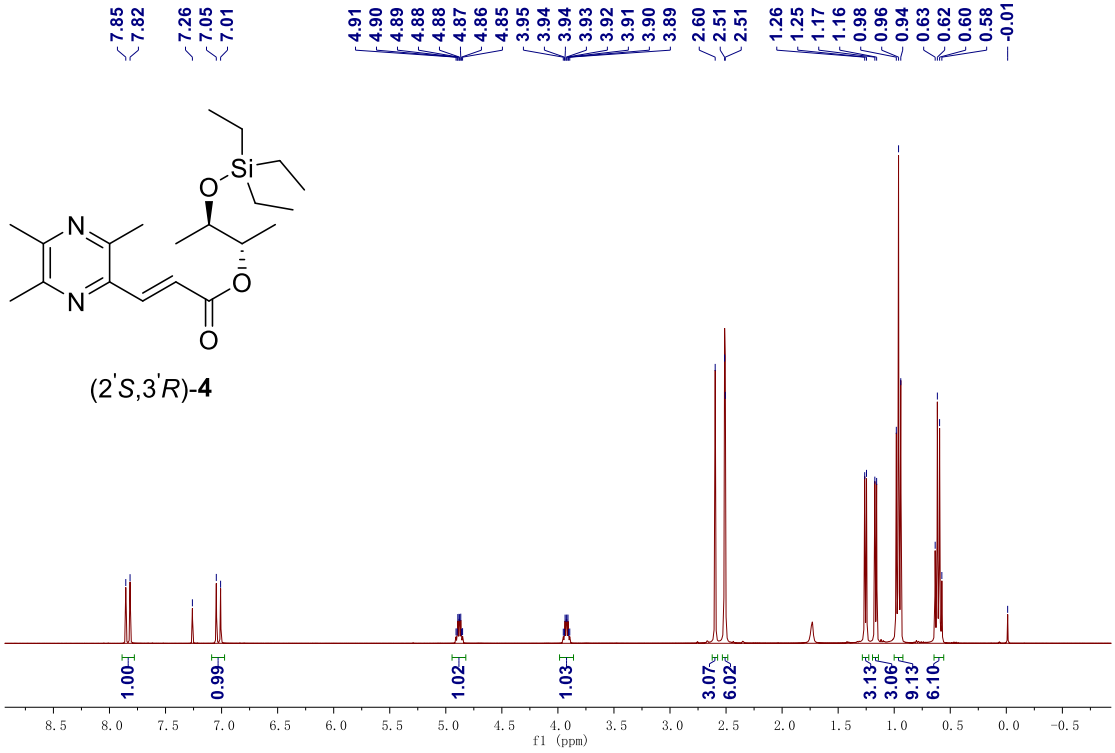



**Figure S26.** $^{1}$H NMR spectra of (2'*S*,3'*R*)-**4** (400MHz, Chloroform-*d*)



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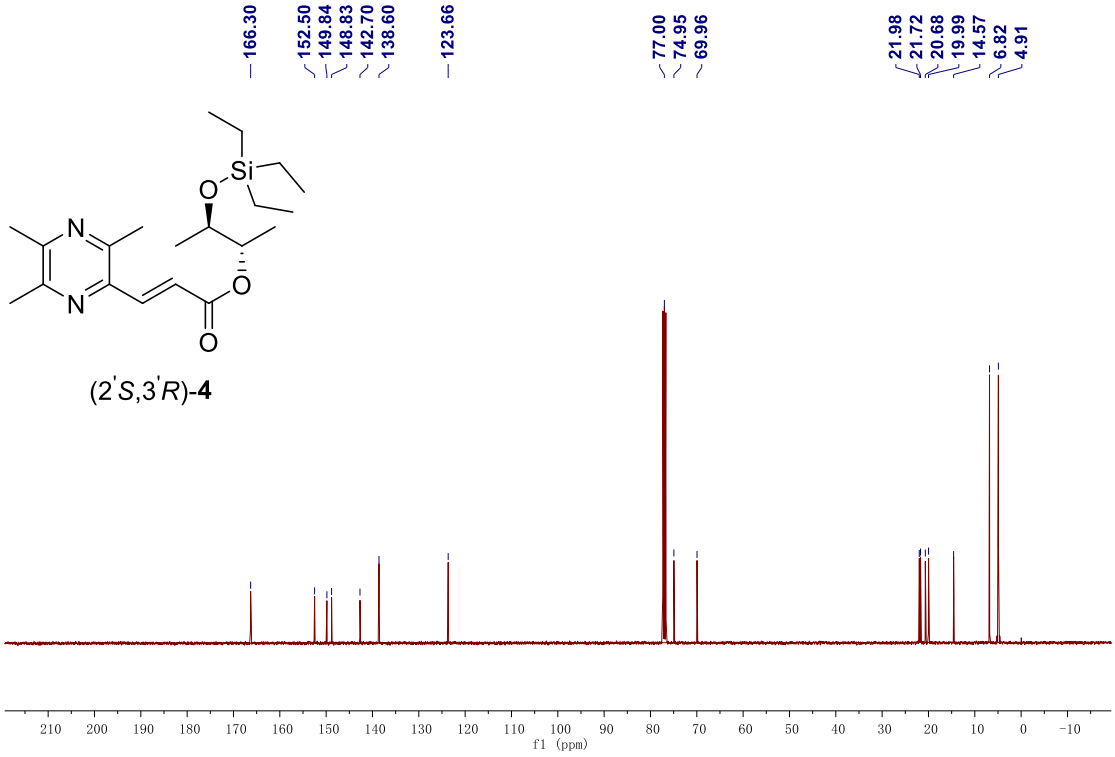


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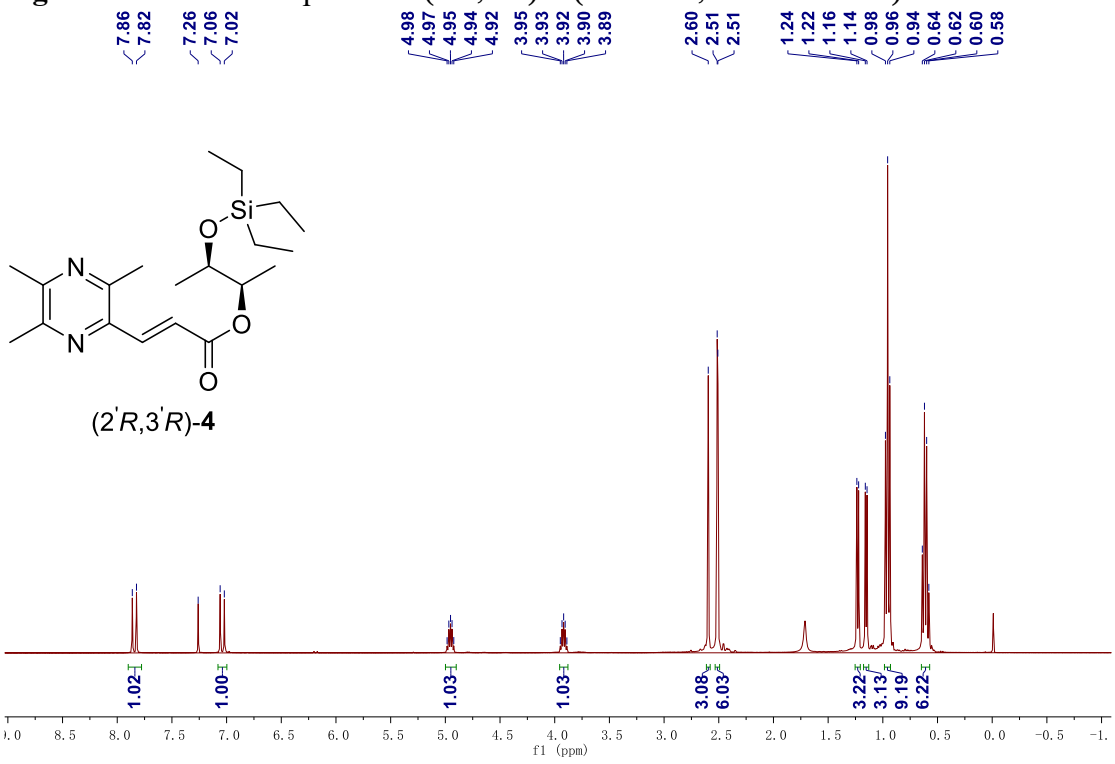


**Figure S29.** $^{13}$C NMR spectra of (2'*R*,3'*R*)-**4** (100MHz, Chloroform-*d*)

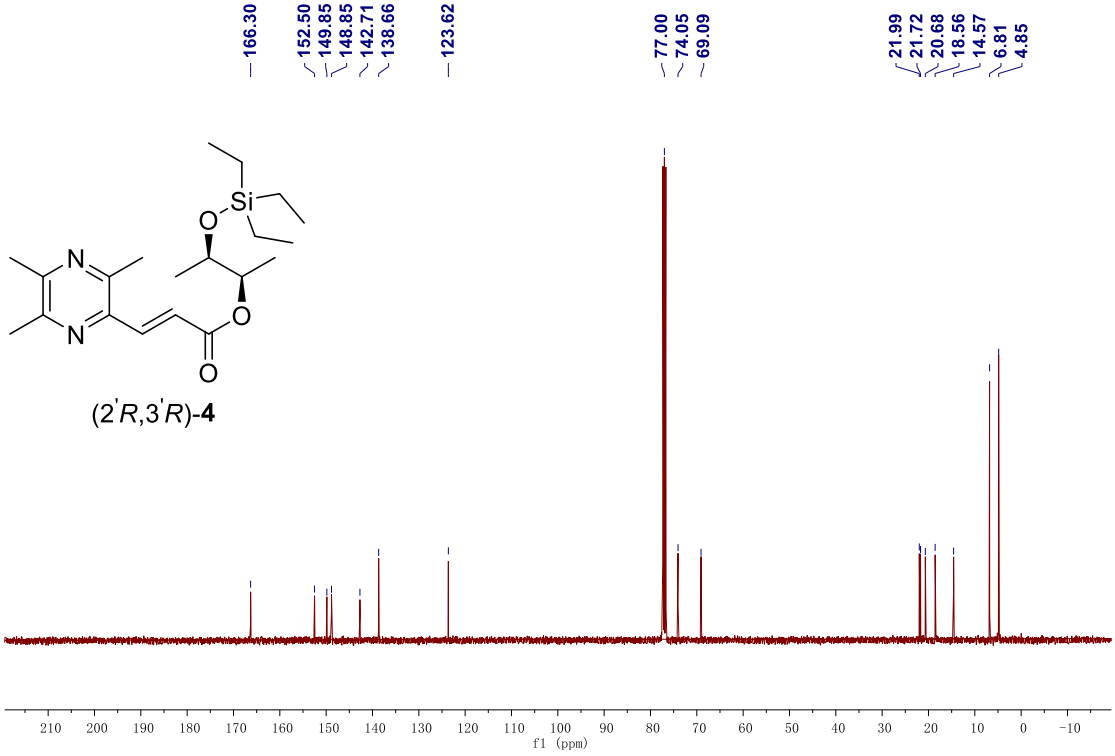



**Figure S30.** $^{1}$H NMR spectra of (2'*S*,3'*S*)-**4** (400MHz, Chloroform-*d*)

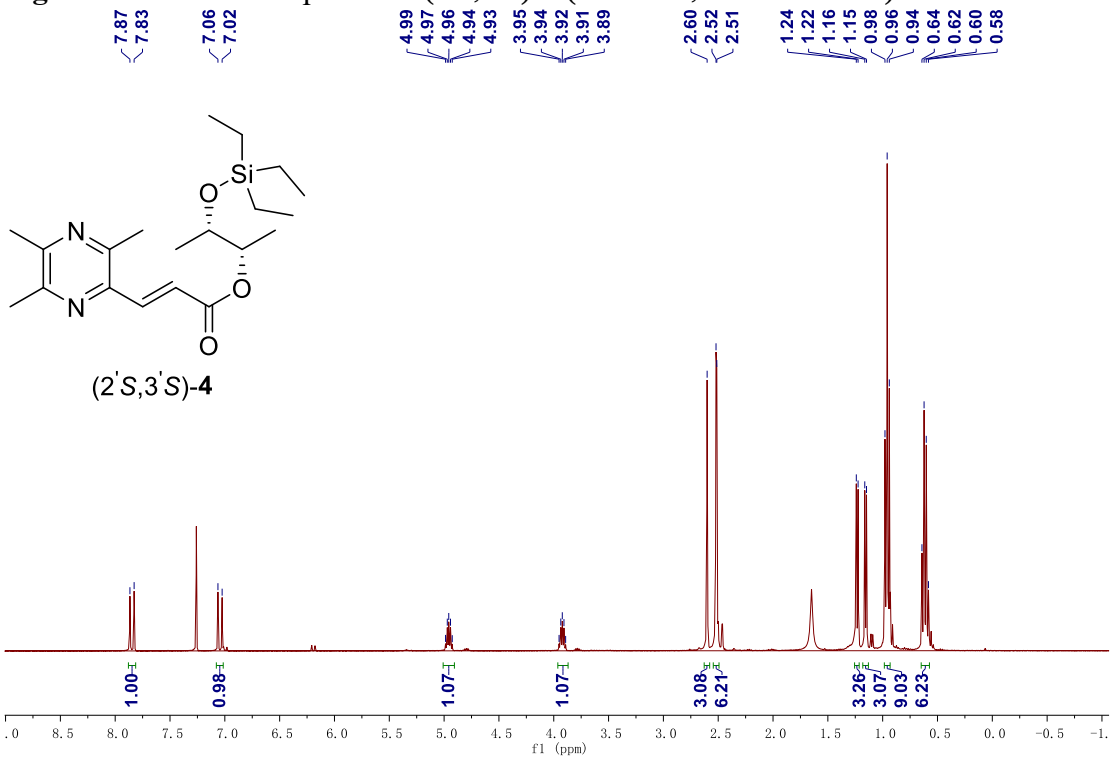


**Figure S31.** $^{13}$C NMR spectra of (2'*S*,3'*S*)-**4** (100MHz, Chloroform-*d*)

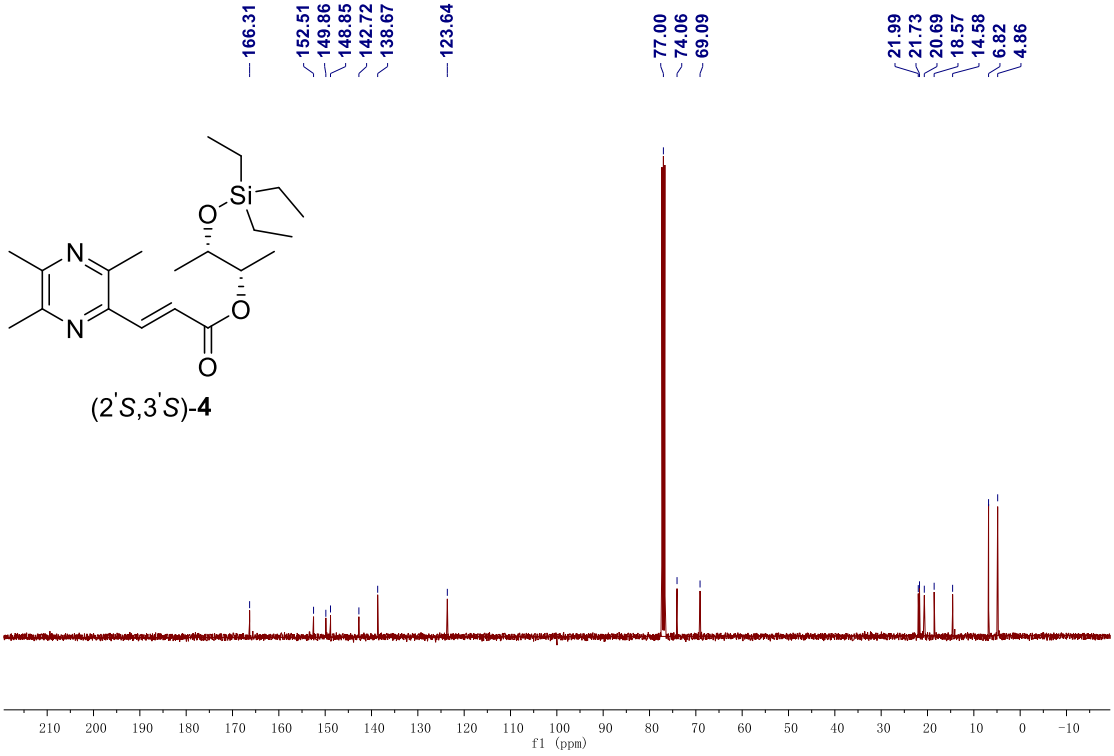



**Figure S32.** $^{1}$H NMR spectra of (2'*R*,3'*S*)-**2** (400MHz, Chloroform-*d*)

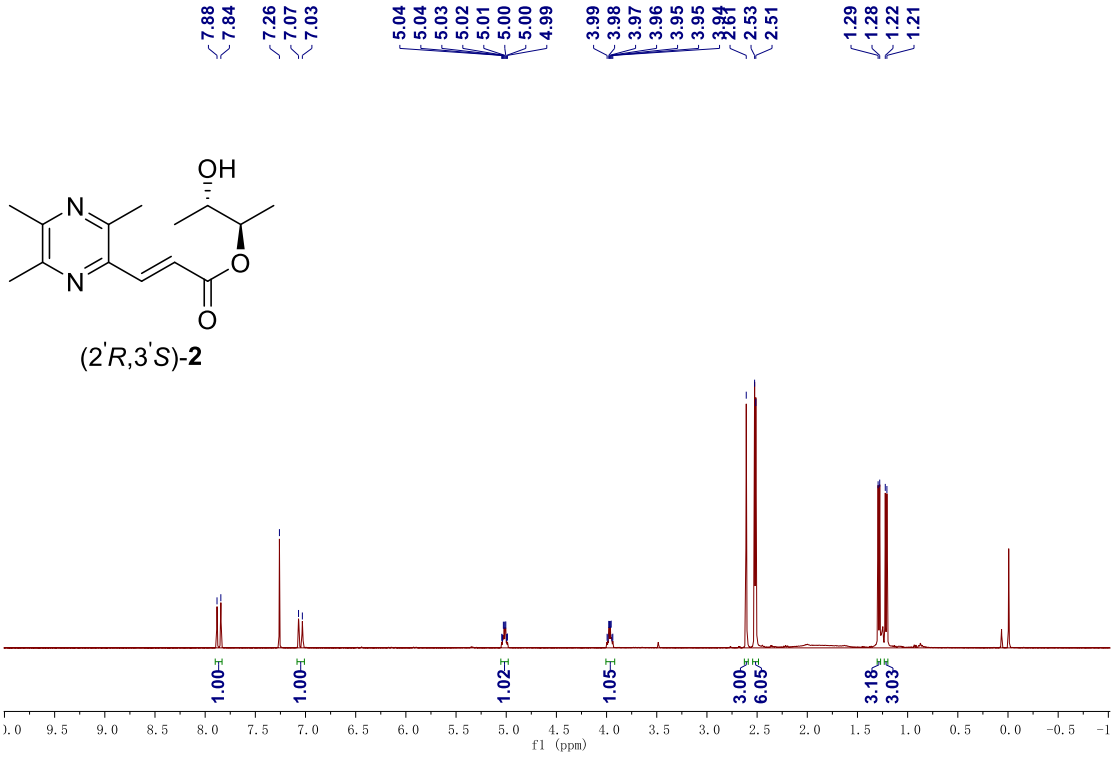


**Figure S33.** $^{13}$C NMR spectra of (2'*R*,3'*S*)-**2** (100MHz, Chloroform-*d*)

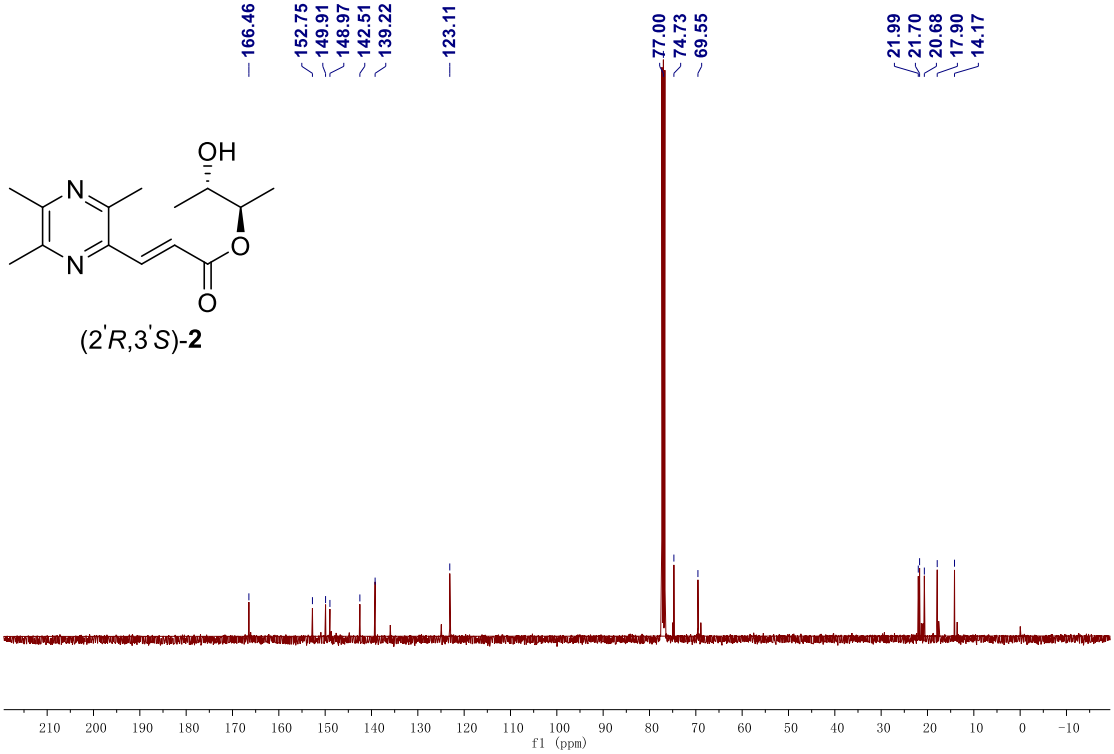



**Figure S34.** $^{1}$H-$^{1}$H COSY spectrum of (2'*R*,3'*S*)-**2** (Chloroform-*d*)

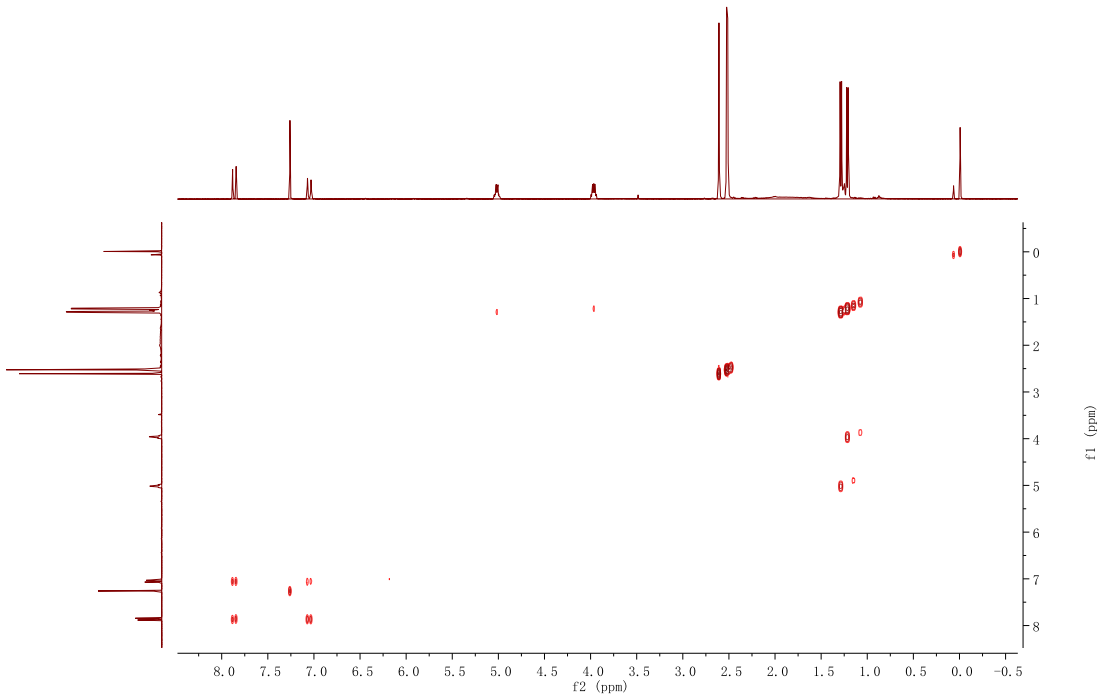


**Figure S35.** HSQC spectrum of (2'*R*,3'*S*)-**2** (Chloroform-*d*)

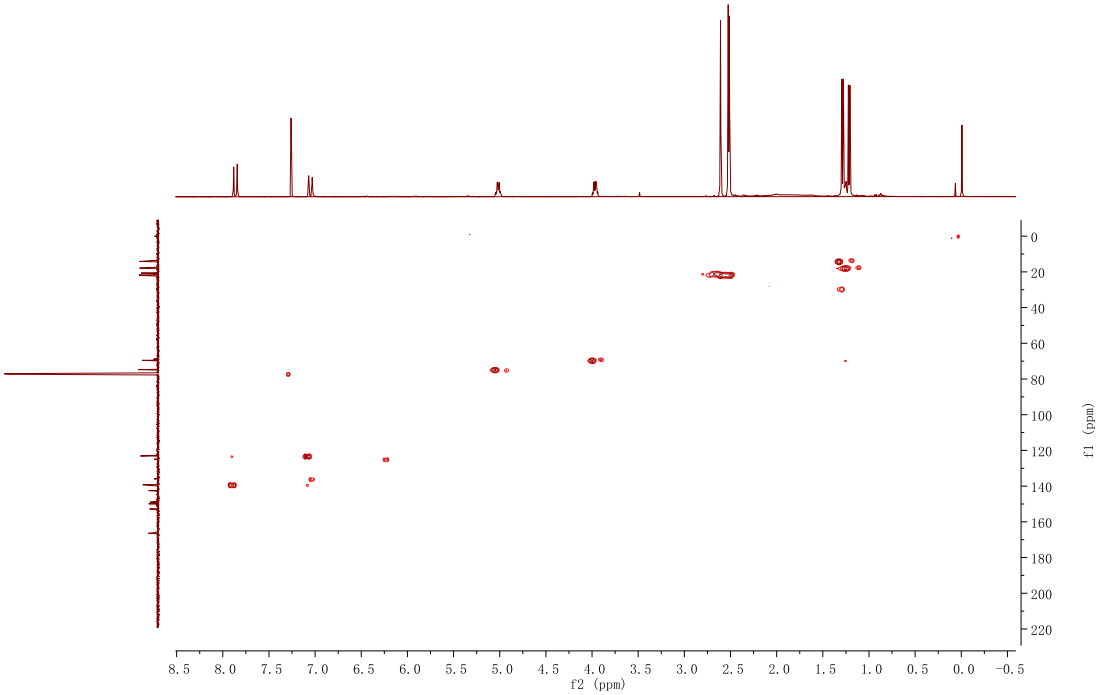



**Figure S36.** HMBC spectrum of (2'*R*,3'*S*)-**2** (Chloroform-*d*)

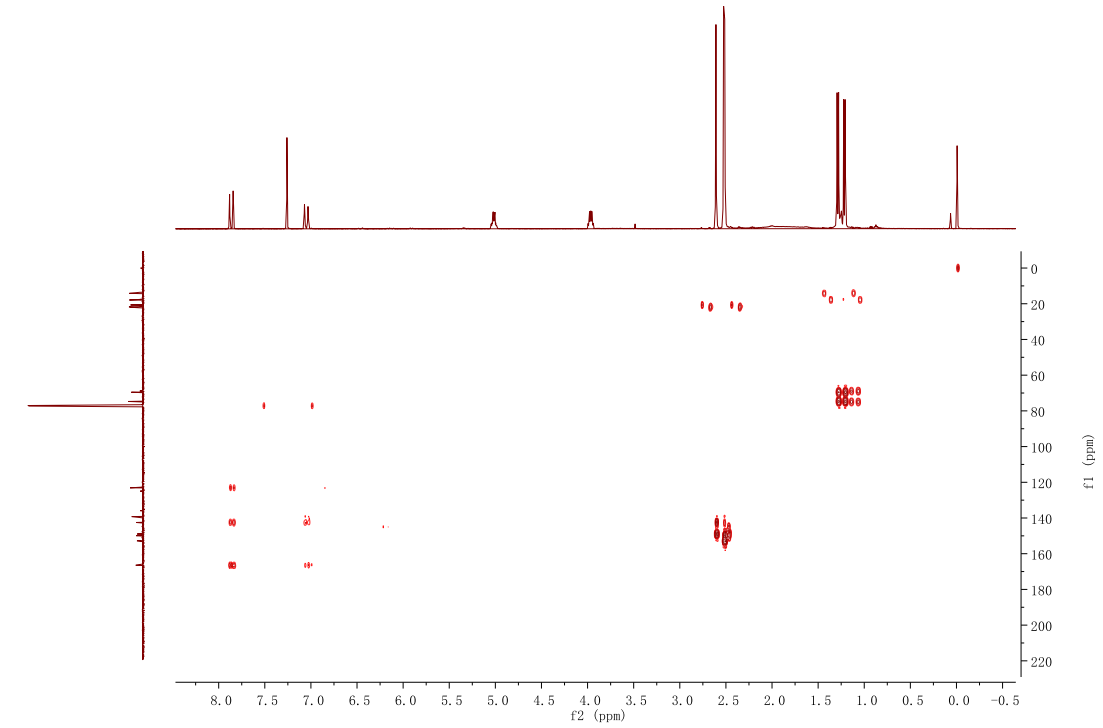


**Figure S37.** NOESY spectrum of (2'*R*,3'*S*)-**2** (Chloroform-*d*)

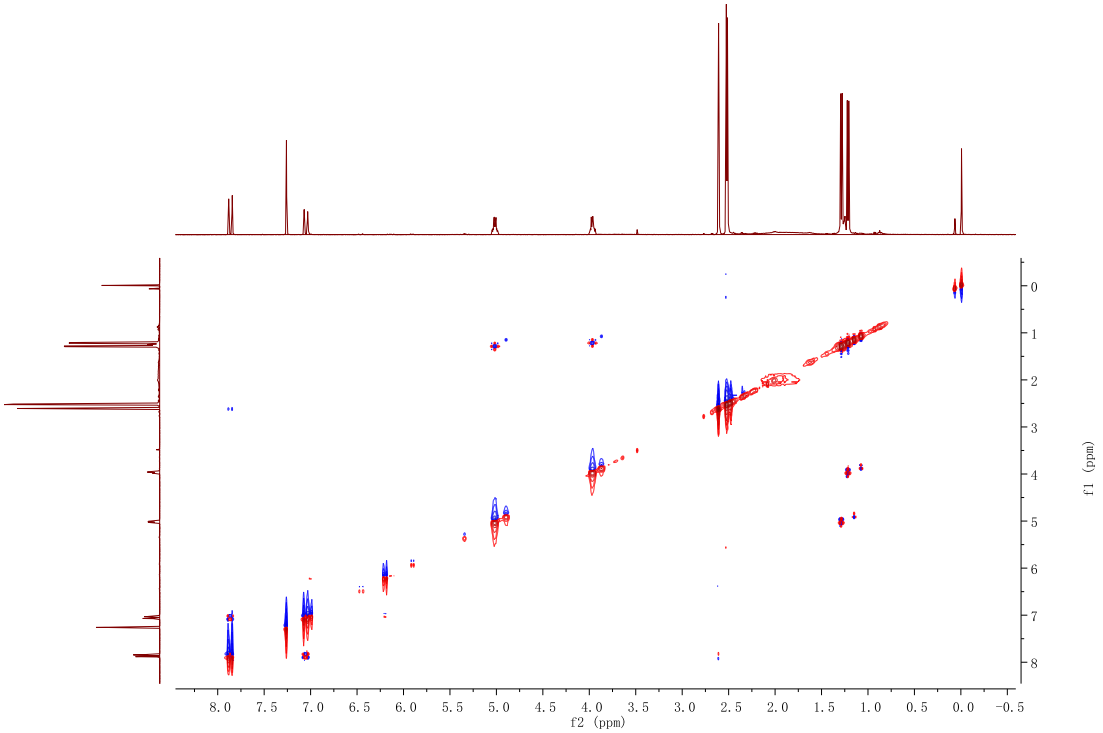



**Figure S38.** $^{1}$H NMR spectra of (2'*S*,3'*R*)-**2** (400MHz, Chloroform-*d*)

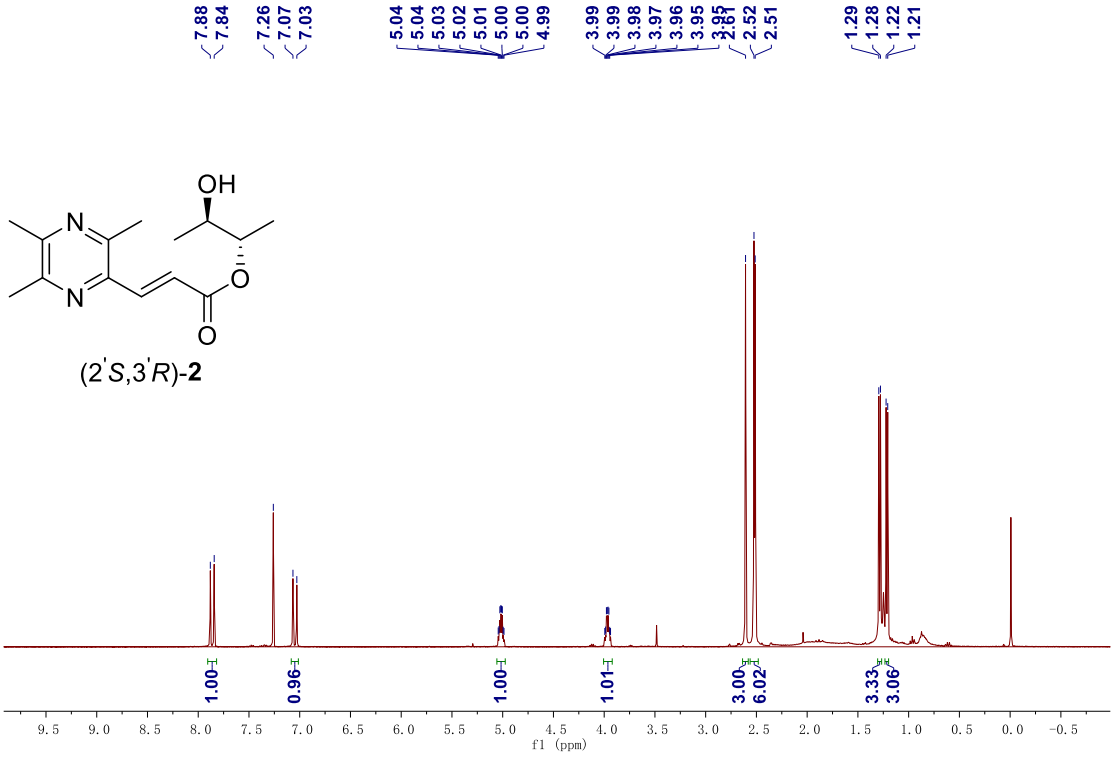


**Figure S39.** $^{13}$C NMR spectra of (2'*S*,3'*R*)-**2** (100MHz, Chloroform-*d*)

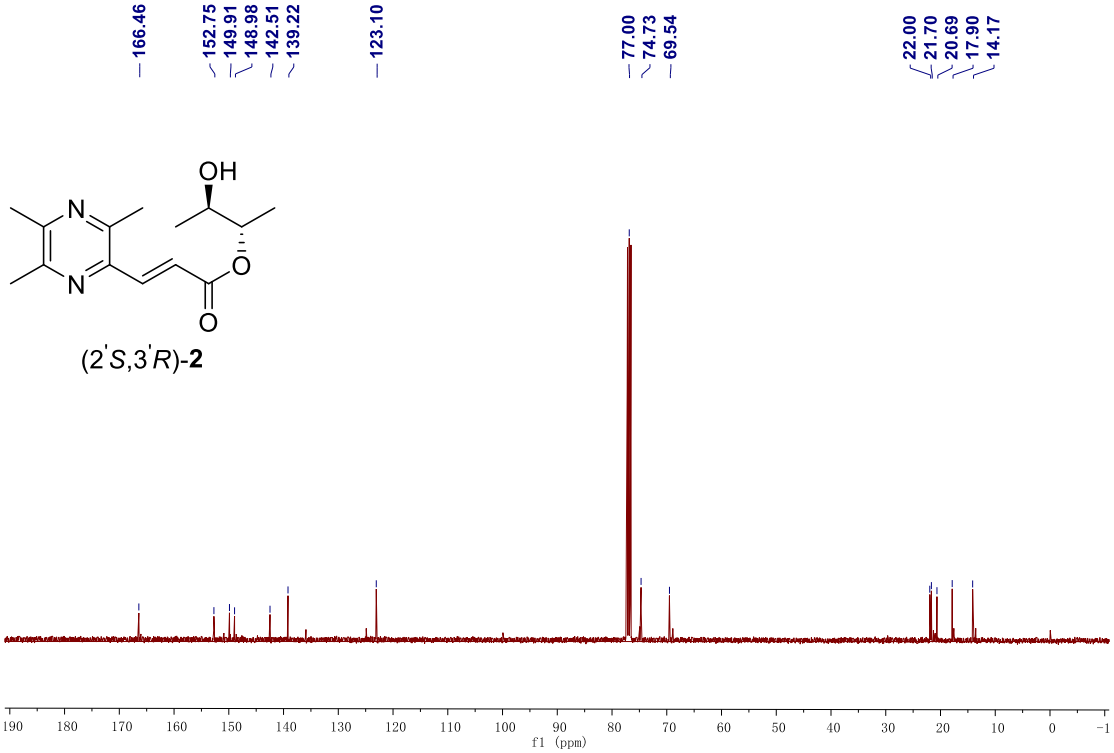



**Figure S40.** $^{1}$H-$^{1}$H COSY spectrum of (2'*S*,3'*R*)-**2** (Chloroform-*d*)

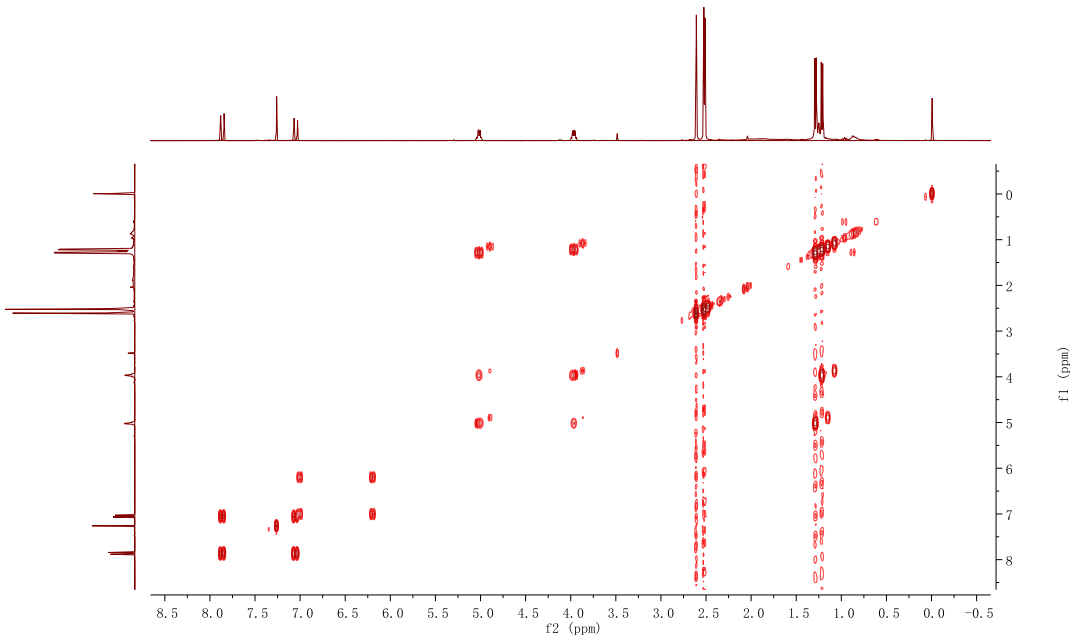


**Figure S41.** HSQC spectrum of (2'*S*,3'*R*)-**2** (Chloroform-*d*)

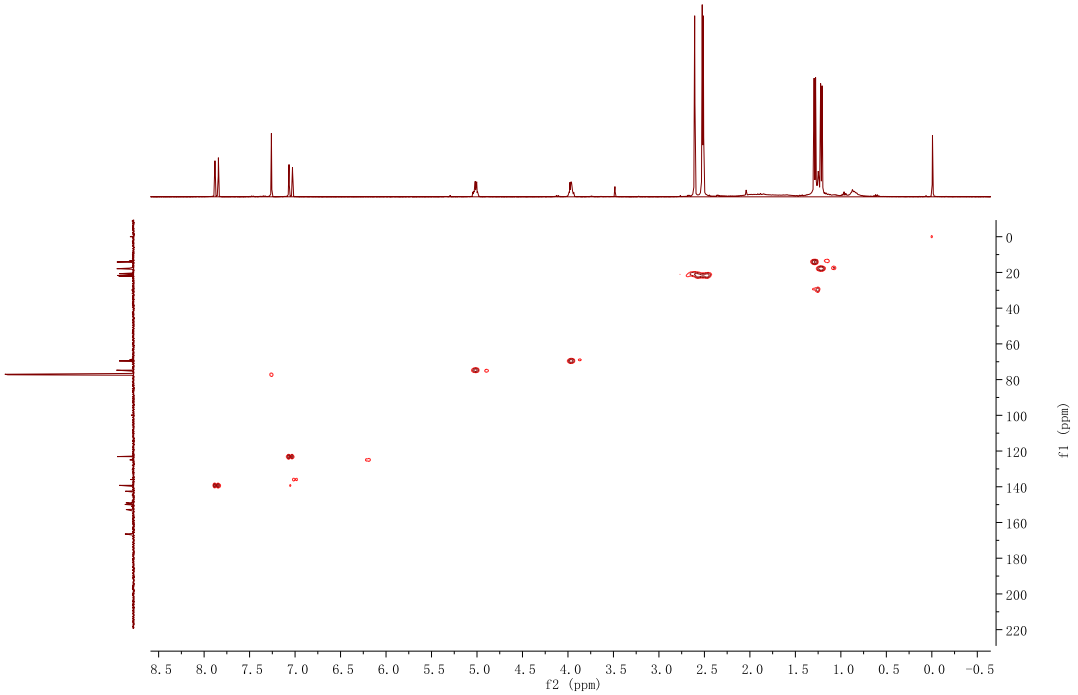



**Figure S42.** HMBC spectrum of (2'*S*,3'*R*)-**2** (Chloroform-*d*)

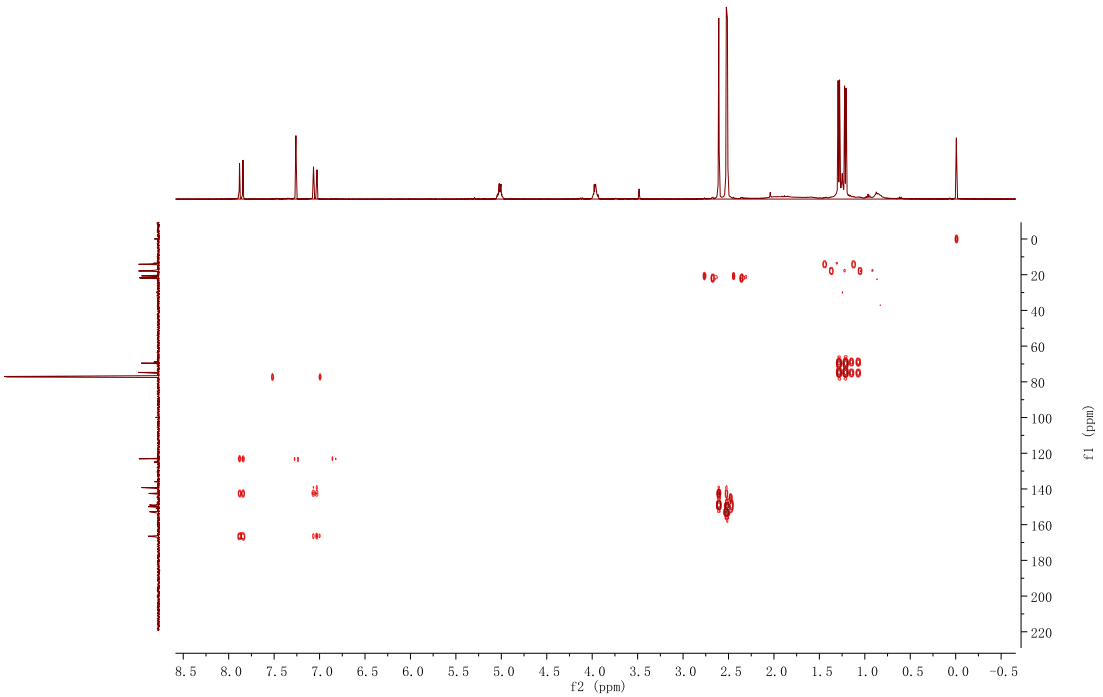


**Figure S43.** NOESY spectrum of (2'*S*,3'*R*)-**2** (Chloroform-*d*)

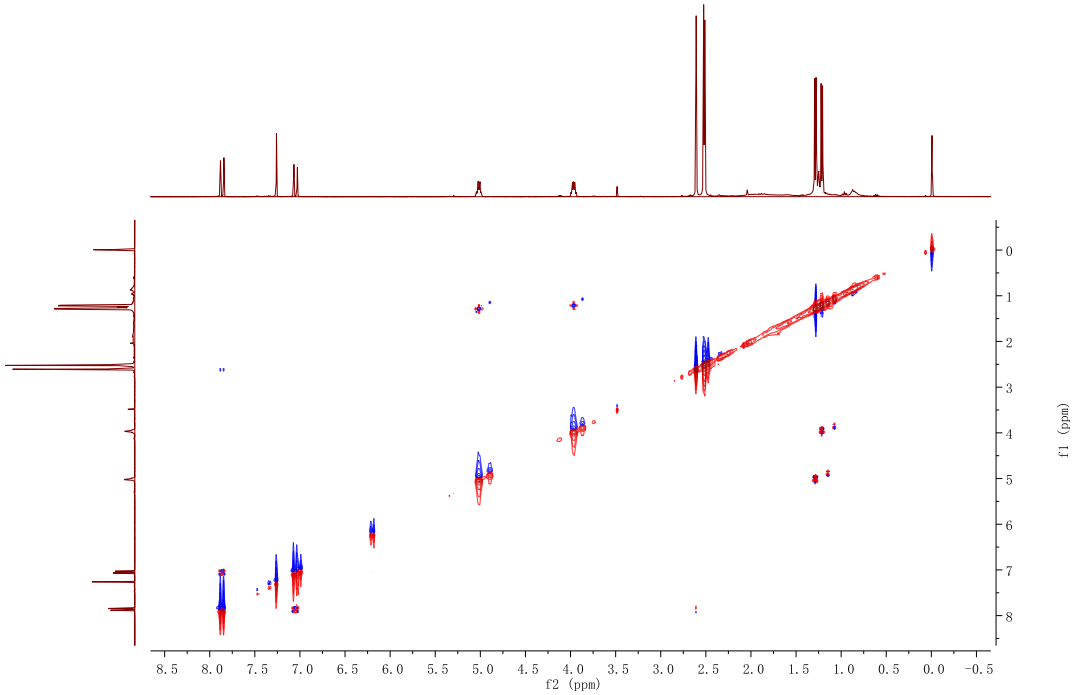



**Figure S44.** $^{1}$H NMR spectra of (2'*R*,3'*R*)-**2** (400MHz, Chloroform-*d*)

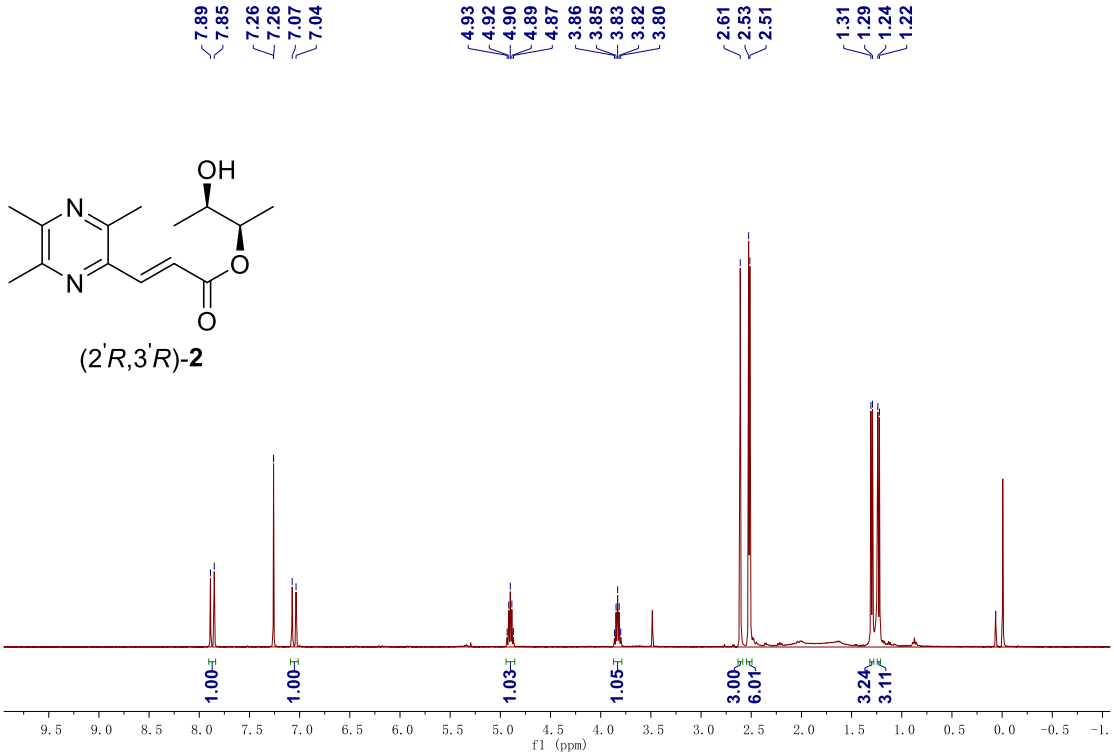


**Figure S45.** $^{13}$C NMR spectra of (2'*R*,3'*R*)-**2** (100MHz, Chloroform-*d*)

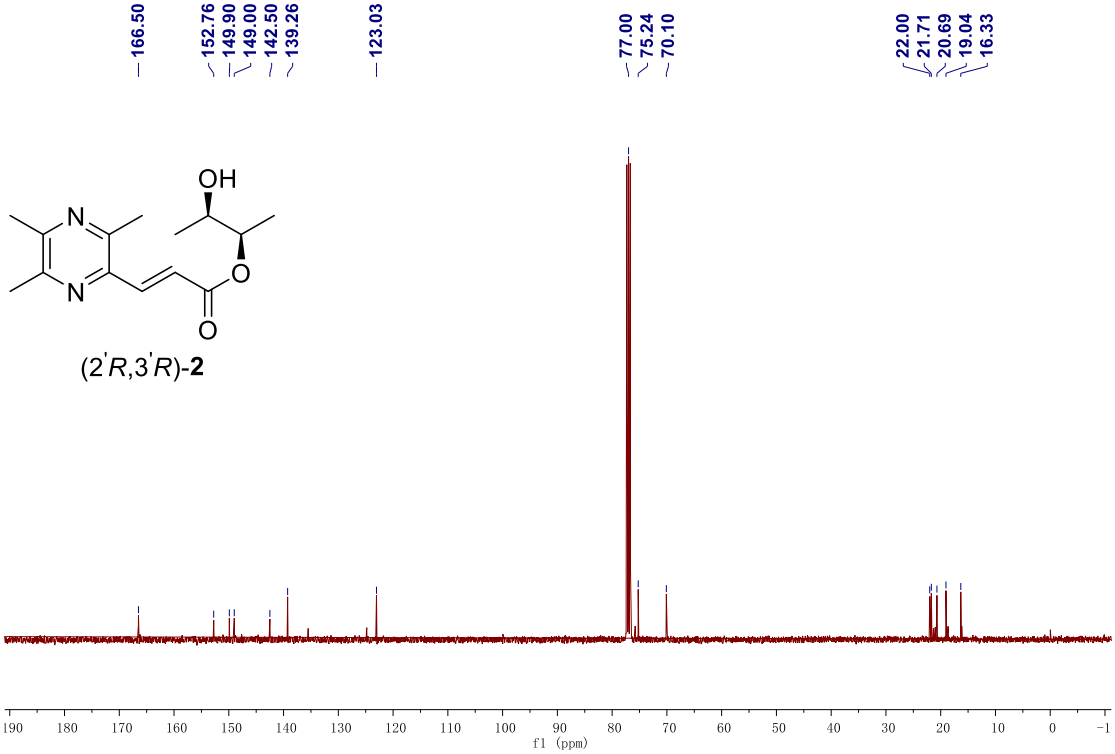



**Figure S46.** $^{1}$H-$^{1}$H COSY spectrum of (2'*R*,3'*R*)-**2** (Chloroform-*d*)

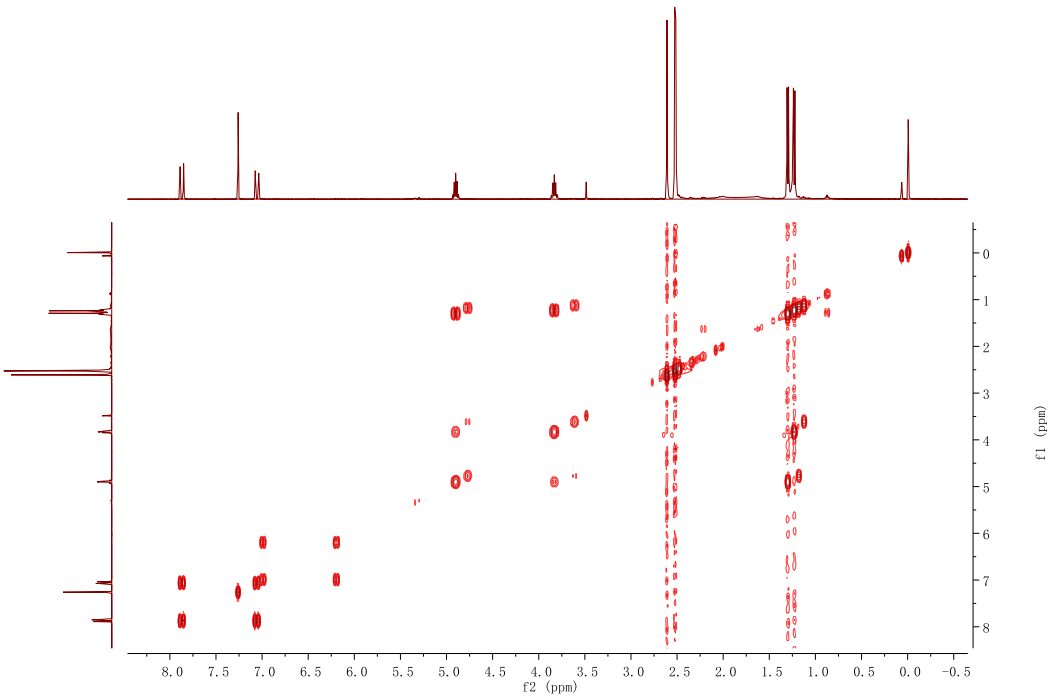


**Figure S47.** HSQC spectrum of (2'*R*,3'*R*)-**2** (Chloroform-*d*)

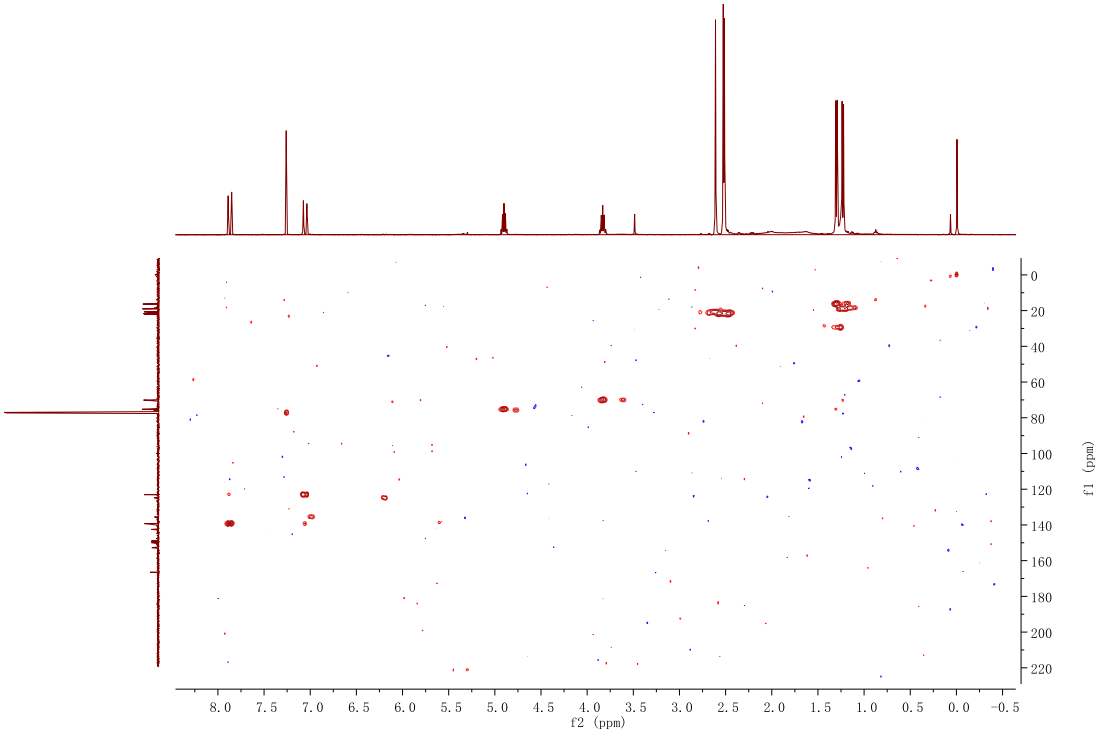



**Figure S48.** HMBC spectrum of (2'*R*,3'*R*)-**2** (Chloroform-*d*)

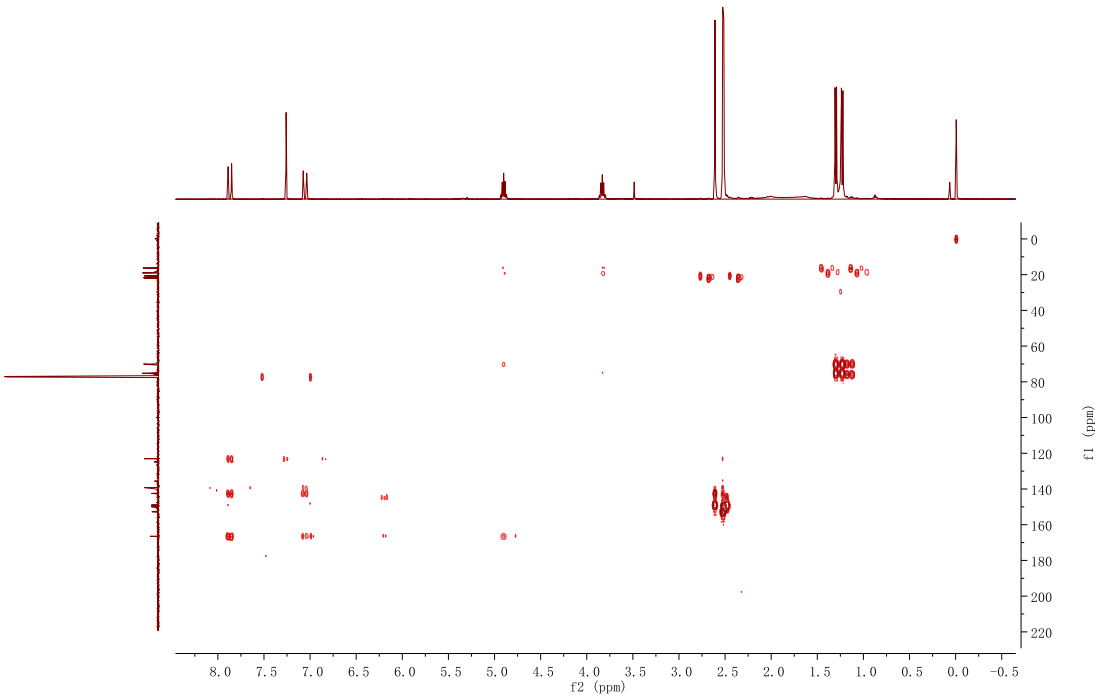


**Figure S49.** NOESY spectrum of (2'*R*,3'*R*)-**2** (Chloroform-*d*)

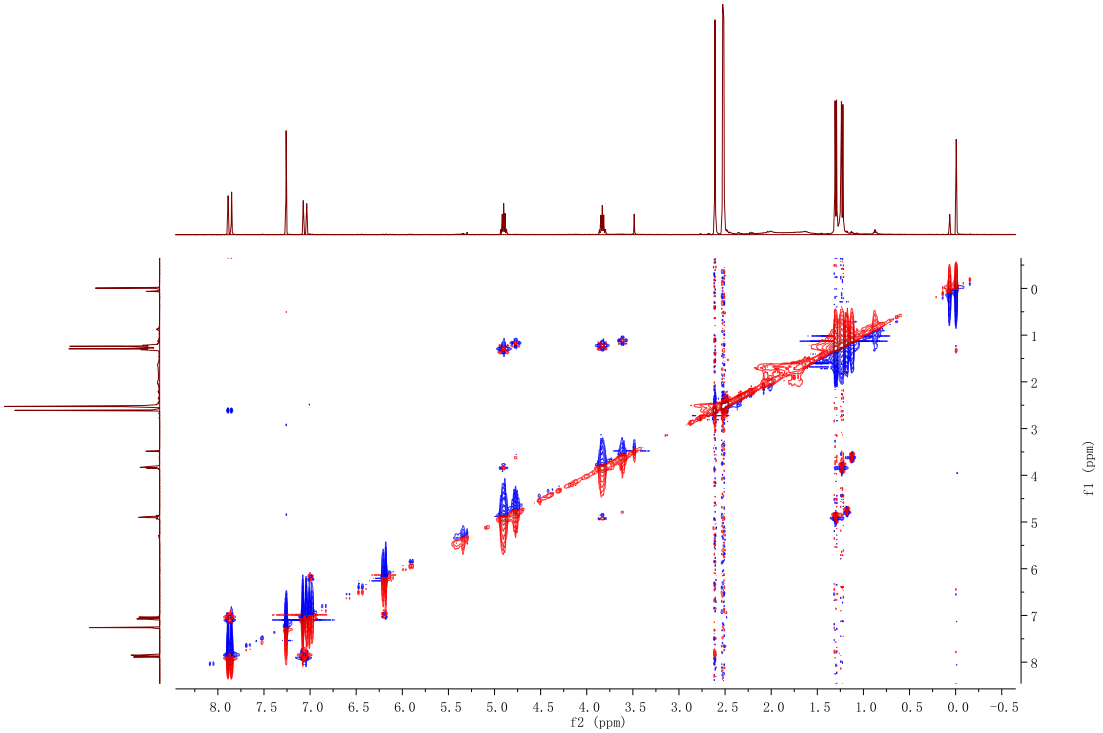
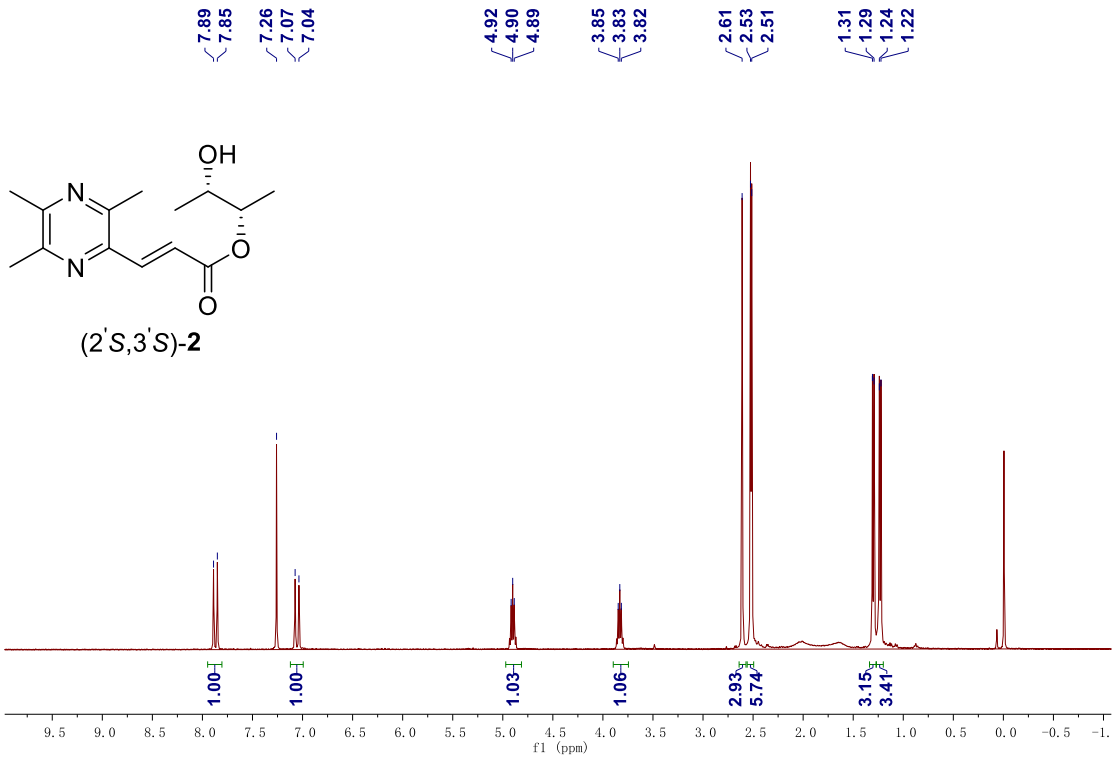



**Figure S50.** $^{1}$H NMR spectra of (2'*S*,3'*S*)-**2** (400MHz, Chloroform-*d*)




(2'*S*,3'*S*)-**2**

**Figure S51.** $^{13}$C NMR spectra of (2'*S*,3'*S*)-**2** (100MHz, Chloroform-*d*)

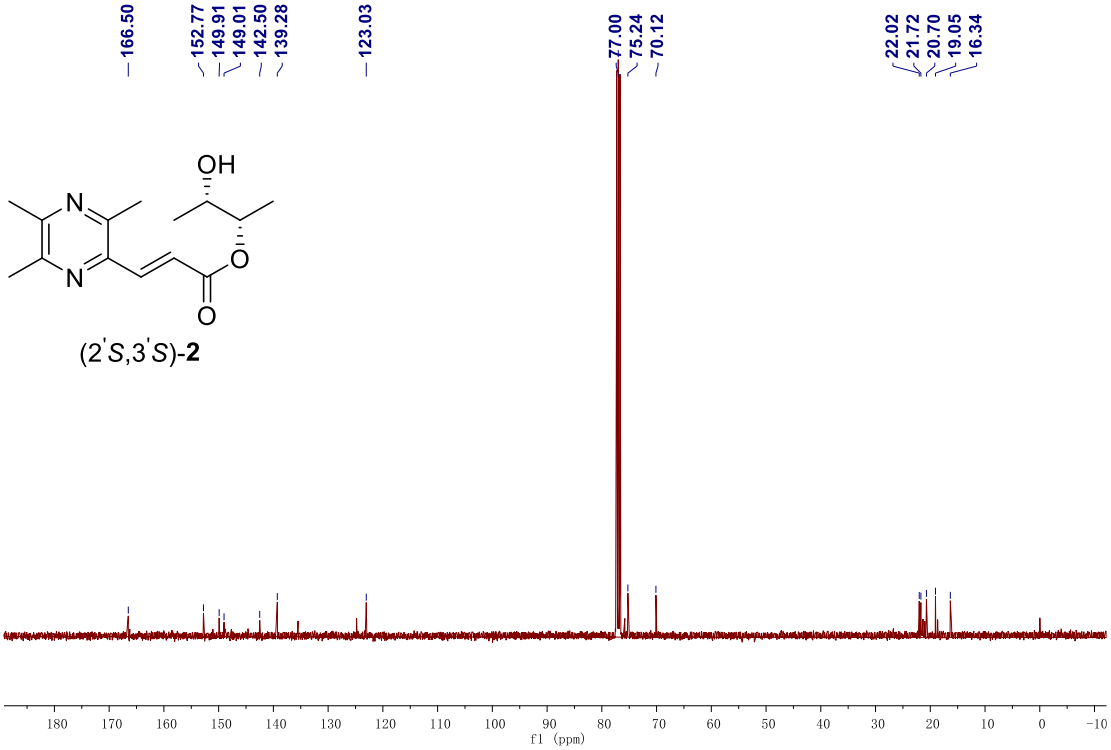



**Figure S52.** $^{1}$H-$^{1}$H COSY spectrum of (2'*S*,3'*S*)-**2** (Chloroform-*d*)

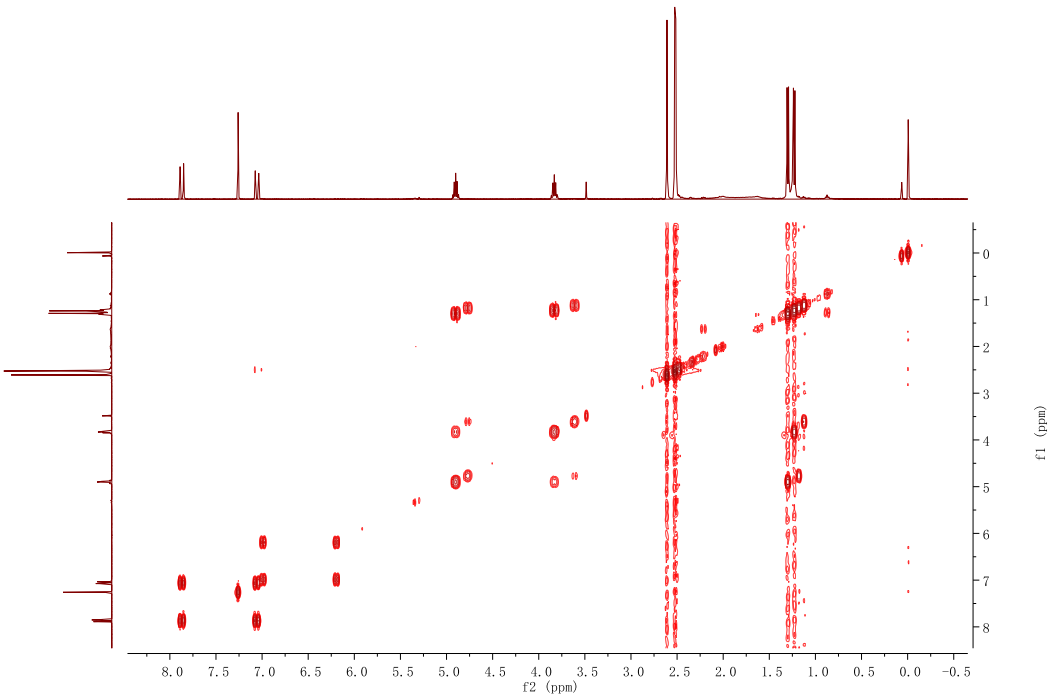


**Figure S53.** HSQC spectrum of (2'*S*,3'*S*)-**2** (Chloroform-*d*)

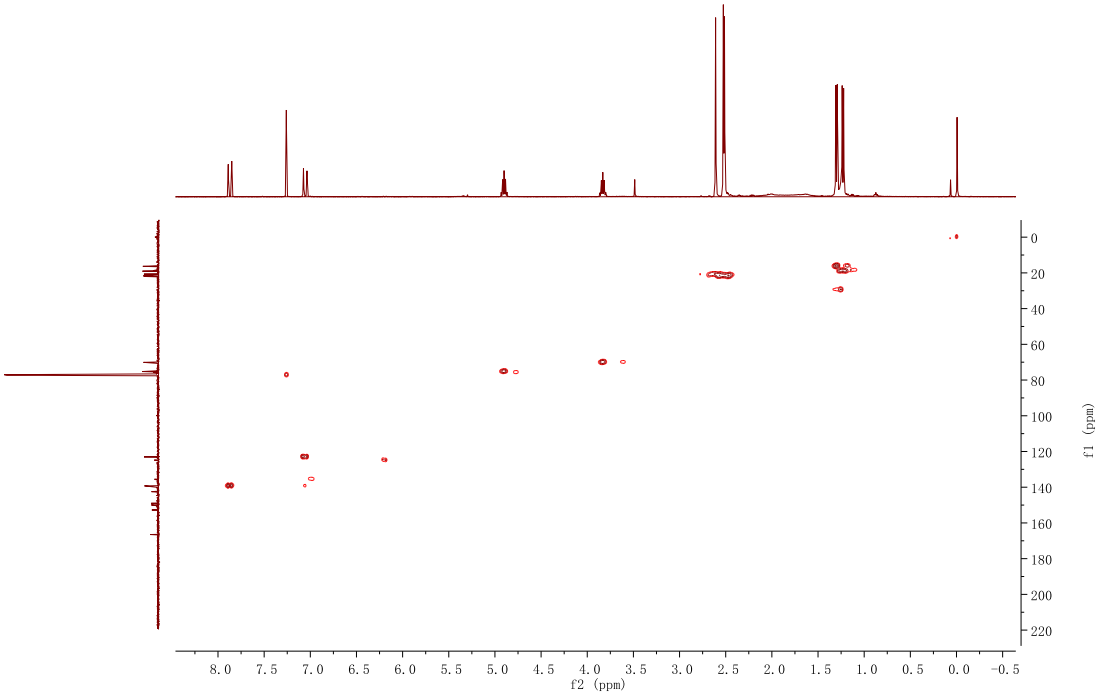



**Figure S54.** HMBC spectrum of (2'*S*,3'*S*)-**2** (Chloroform-*d*)

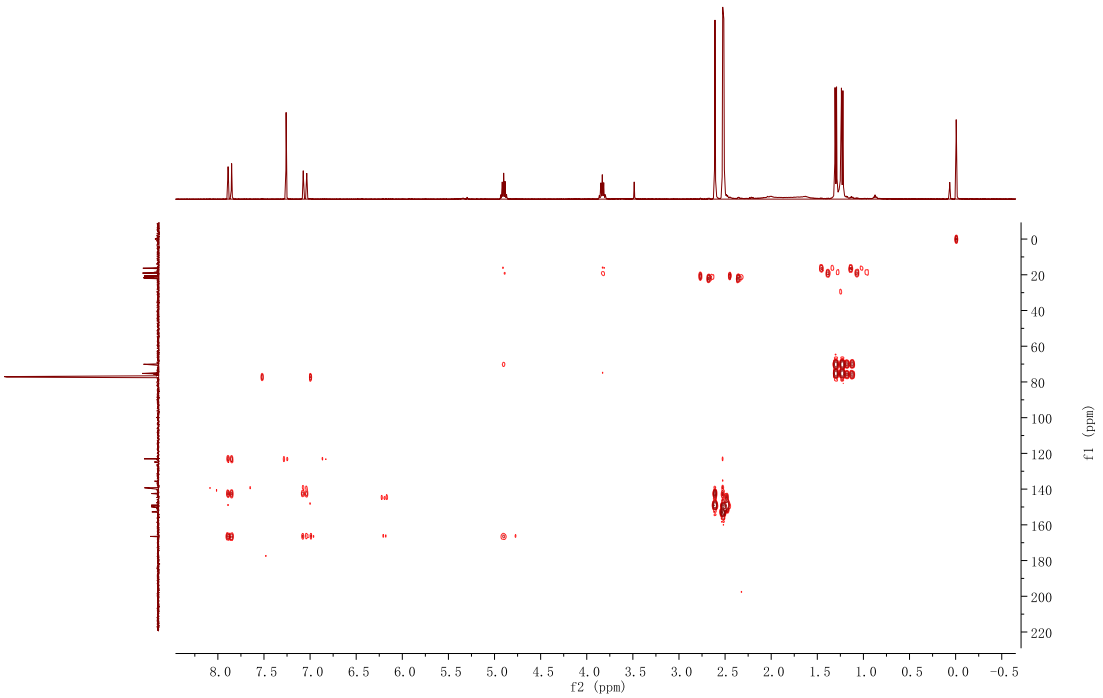


**Figure S55.** NOESY spectrum of (2'*S*,3'*S*)-**2** (Chloroform-*d*)

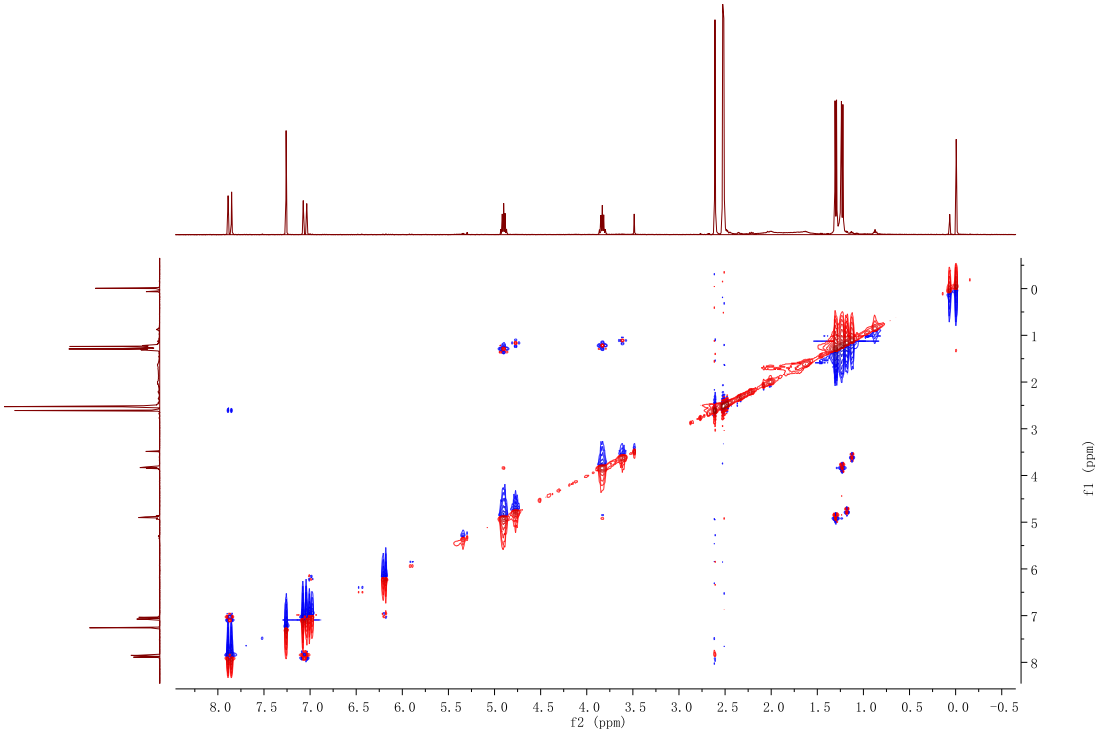



**Figure S56.** $^{1}$H NMR spectra of (2'*R*,3'*S*)-**3** and (2'*S*,3'*R*)-**3** (400MHz, Chloroform-*d*)

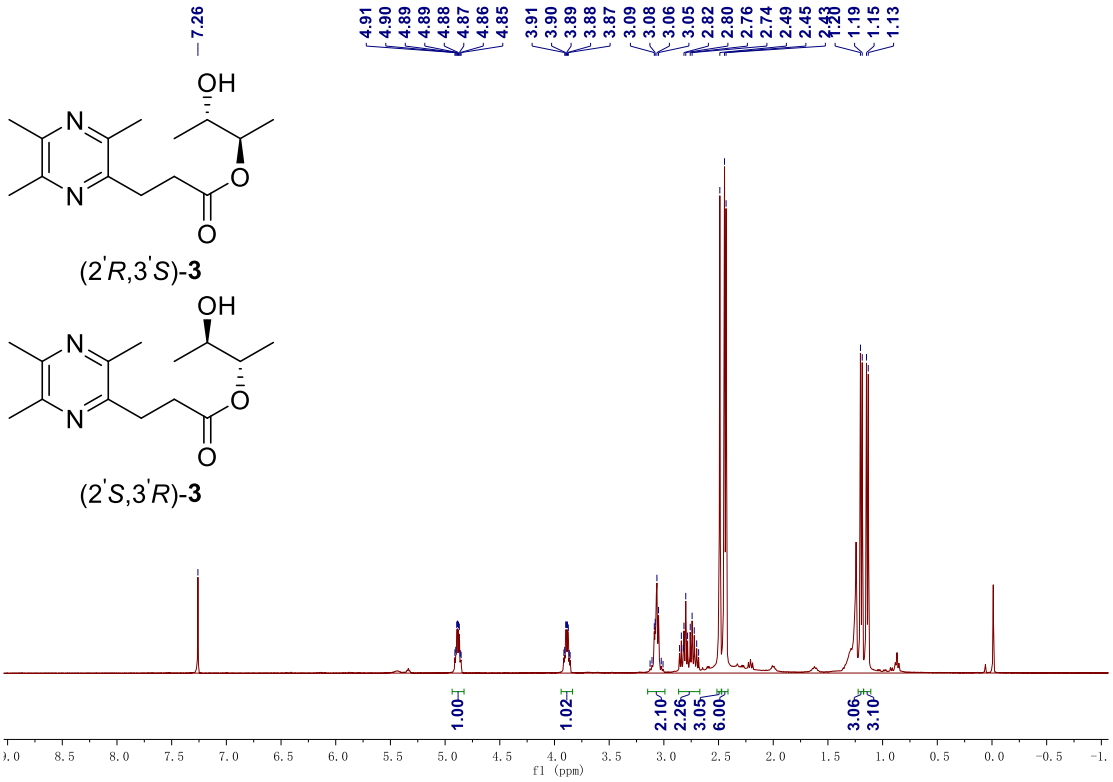


**Figure S57.** $^{13}$C NMR spectra of (2'*R*,3'*S*)-**3** and (2'*S*,3'*R*)-**3** (100MHz, Chloroform-*d*)

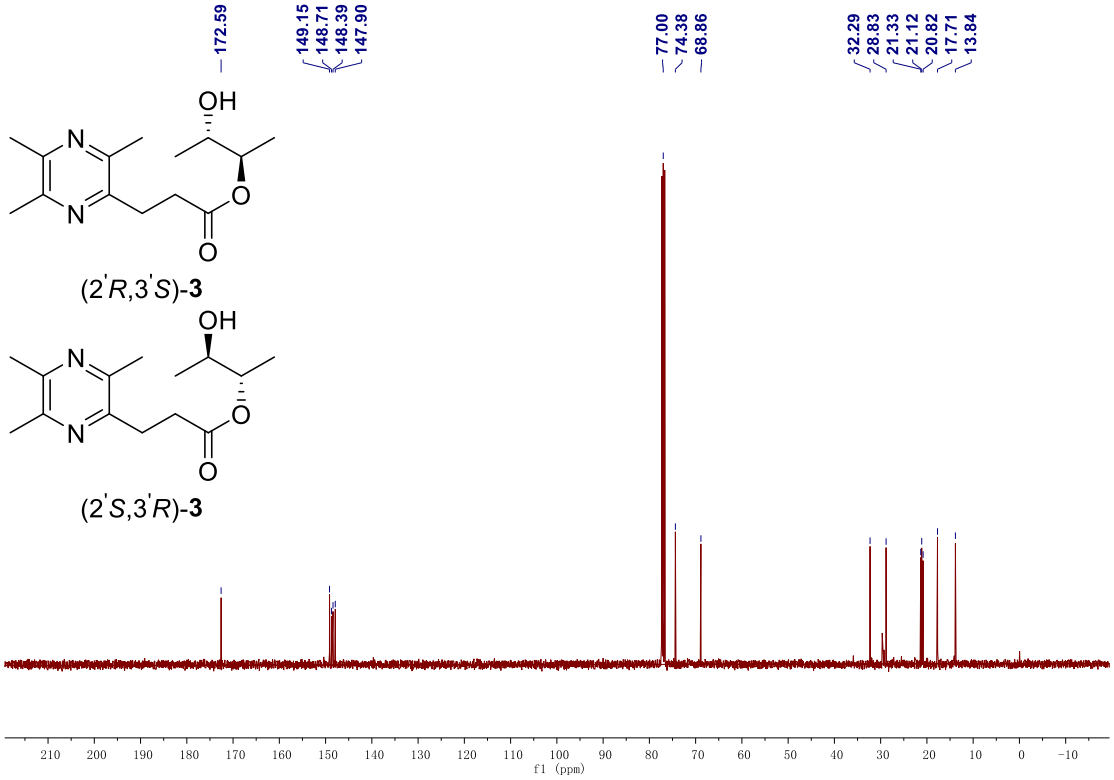



**Figure S58.** $^{1}$H NMR spectra of (2'*R*,3'*R*)-**3** (400MHz, Chloroform-*d*)

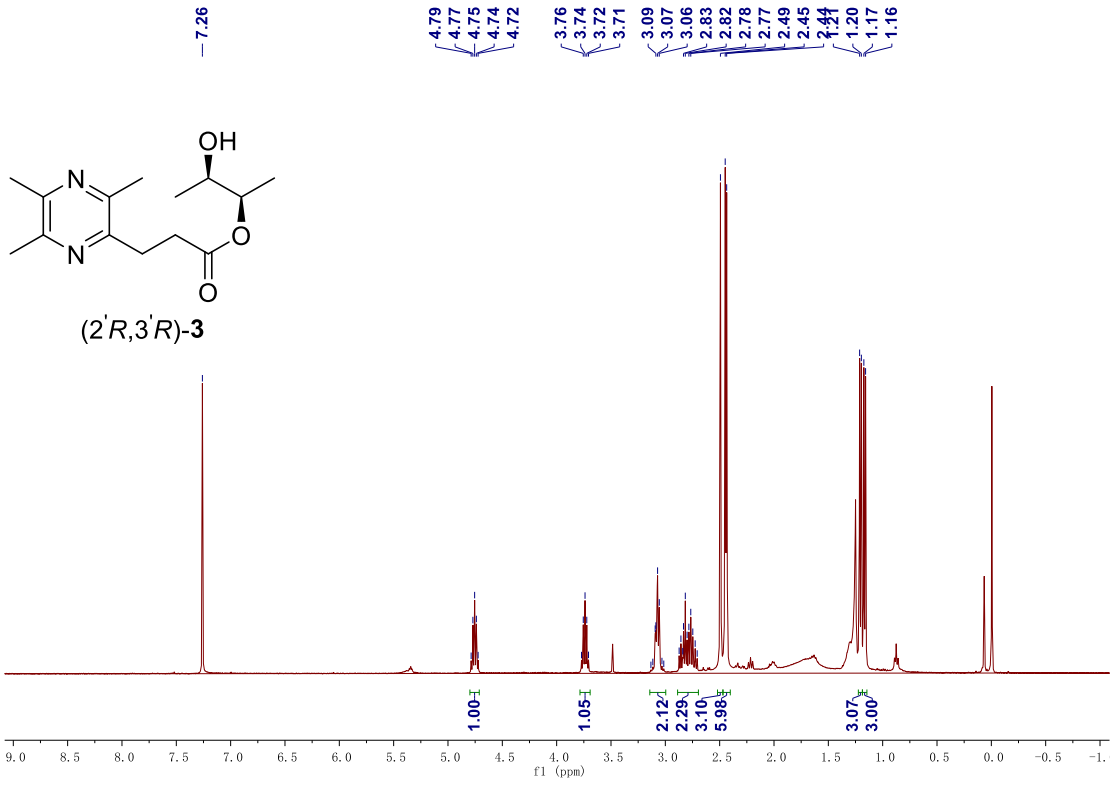


**Figure S59.** $^{13}$C NMR spectra of (2'*R*,3'*R*)-**3** (100MHz, Chloroform-*d*)

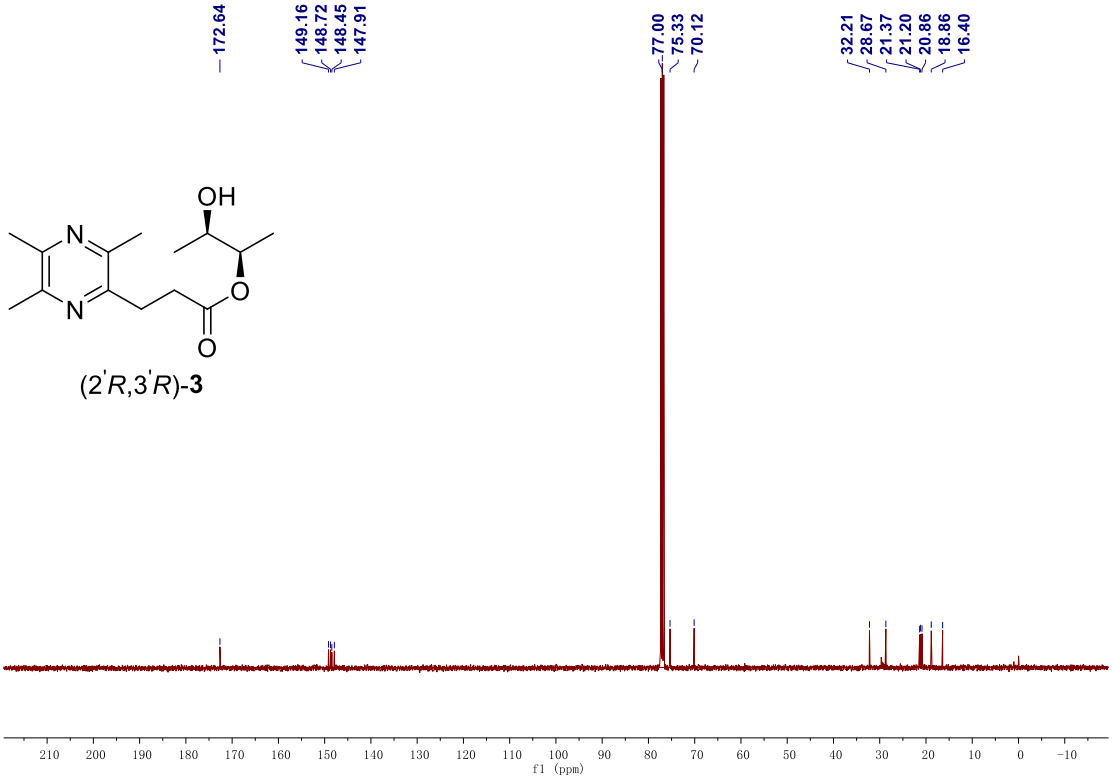



**Figure S60.** $^{1}$H NMR spectra of (2'*S*,3'*S*)-**3** (400MHz, Chloroform-*d*)

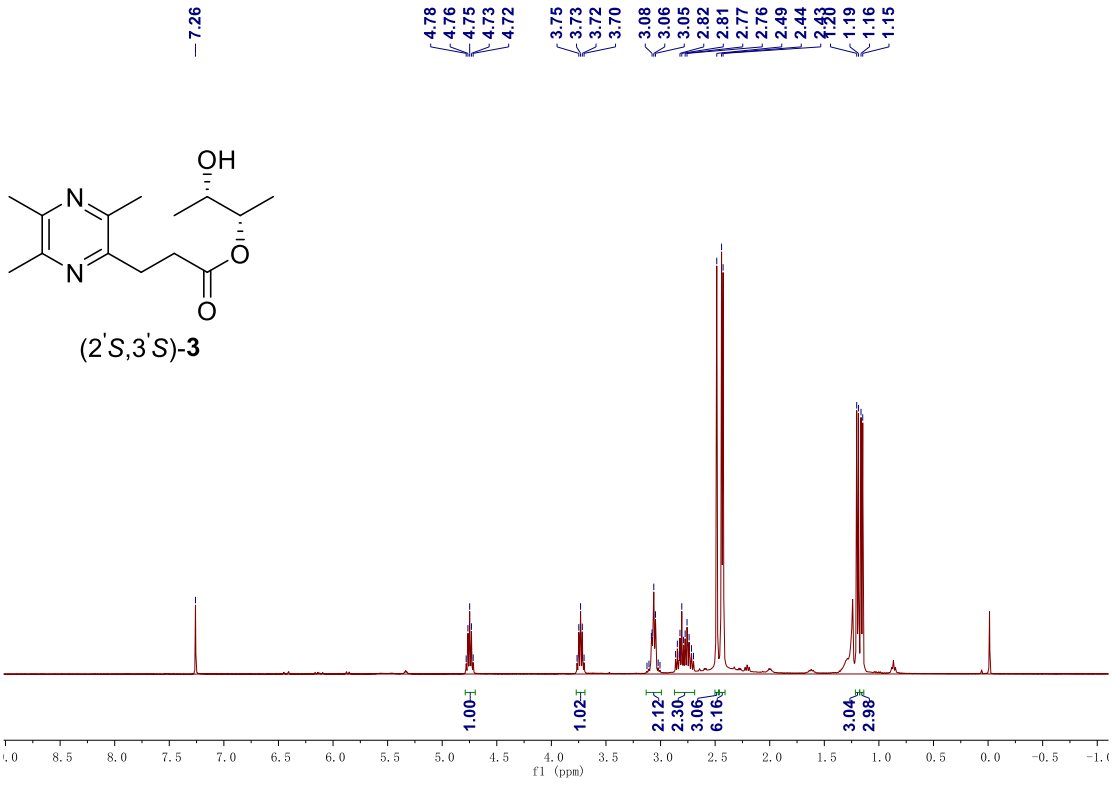
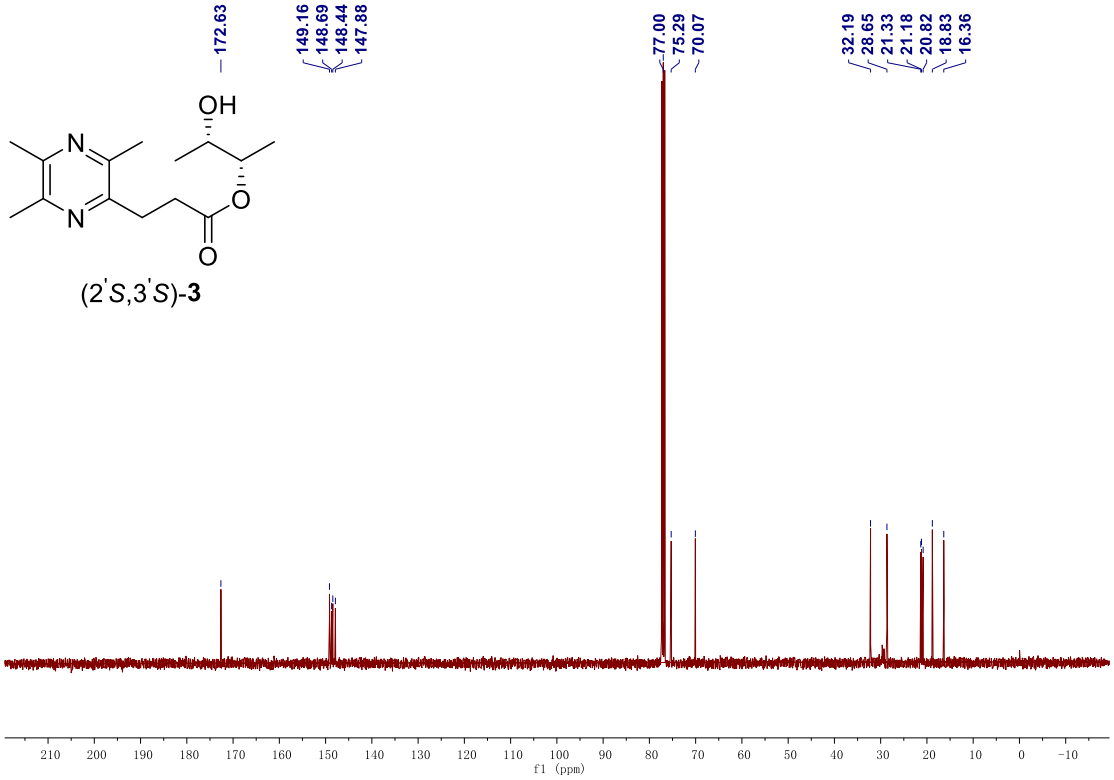


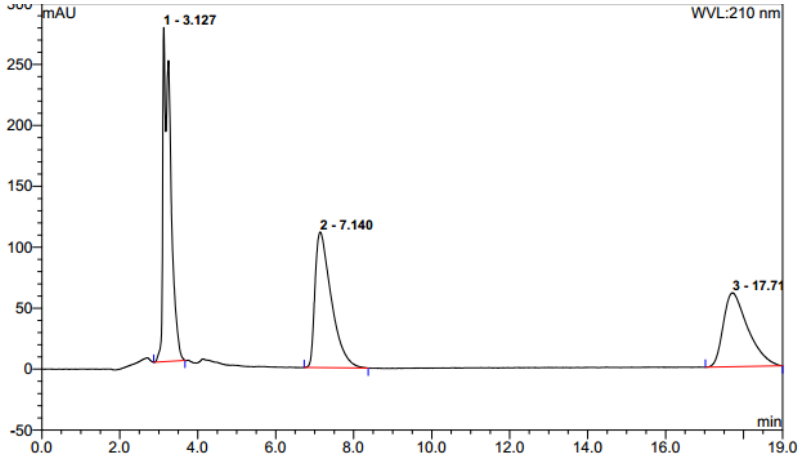
**Figure S61.** $^{13}$C NMR spectra of (2'*S*,3'*S*)-**3** (100MHz, Chloroform-*d*)



**HPLC Traces of natural compound 2 and 3**

Analysis of natural **2** was performed on an Agilent 1220 infinity (Chiralpak IG column, 5 $\mu$m, 4.6 × 250 mm, MeCN: $H_2O$= 100:0, 1.0 mL/min, $t_1$= 7.140 min, $t_2$=17.717 min).

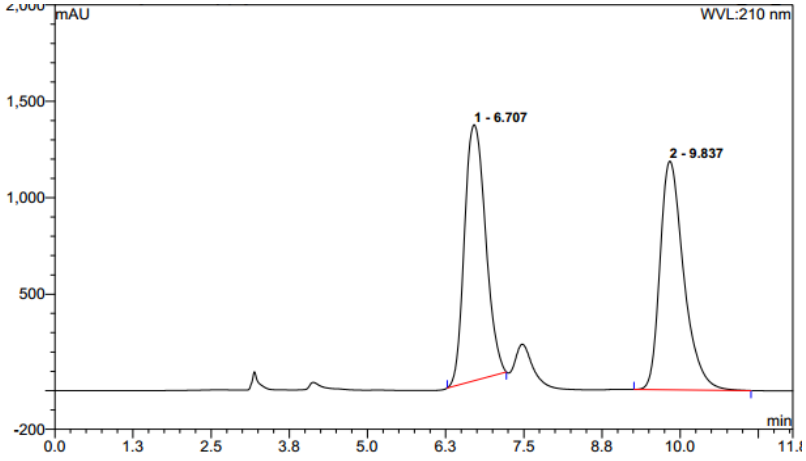
**Figure S62.** Natural **2** HPLC traces




| No. | Ret.Time min | Height mAU | Area mAU*min | Rel.Area % |
|---|---|---|---|---|
| 2 | 7.14 | 111.38465 | 53.8768 | 33.6857 |
| 3 | 17.716667 | 60.69636 | 44.37326 | 27.74375 |

Analysis of natural **3** was performed on an Agilent 1220 infinity (Chiralpak IG column, 5 $\mu$m, 4.6 × 250 mm, MeCN: $H_2O$= 100:0, 1.0 mL/min, $t_1$= 6.707 min, $t_2$=9.837 min).

**Figure S63.** Natural **3** HPLC traces

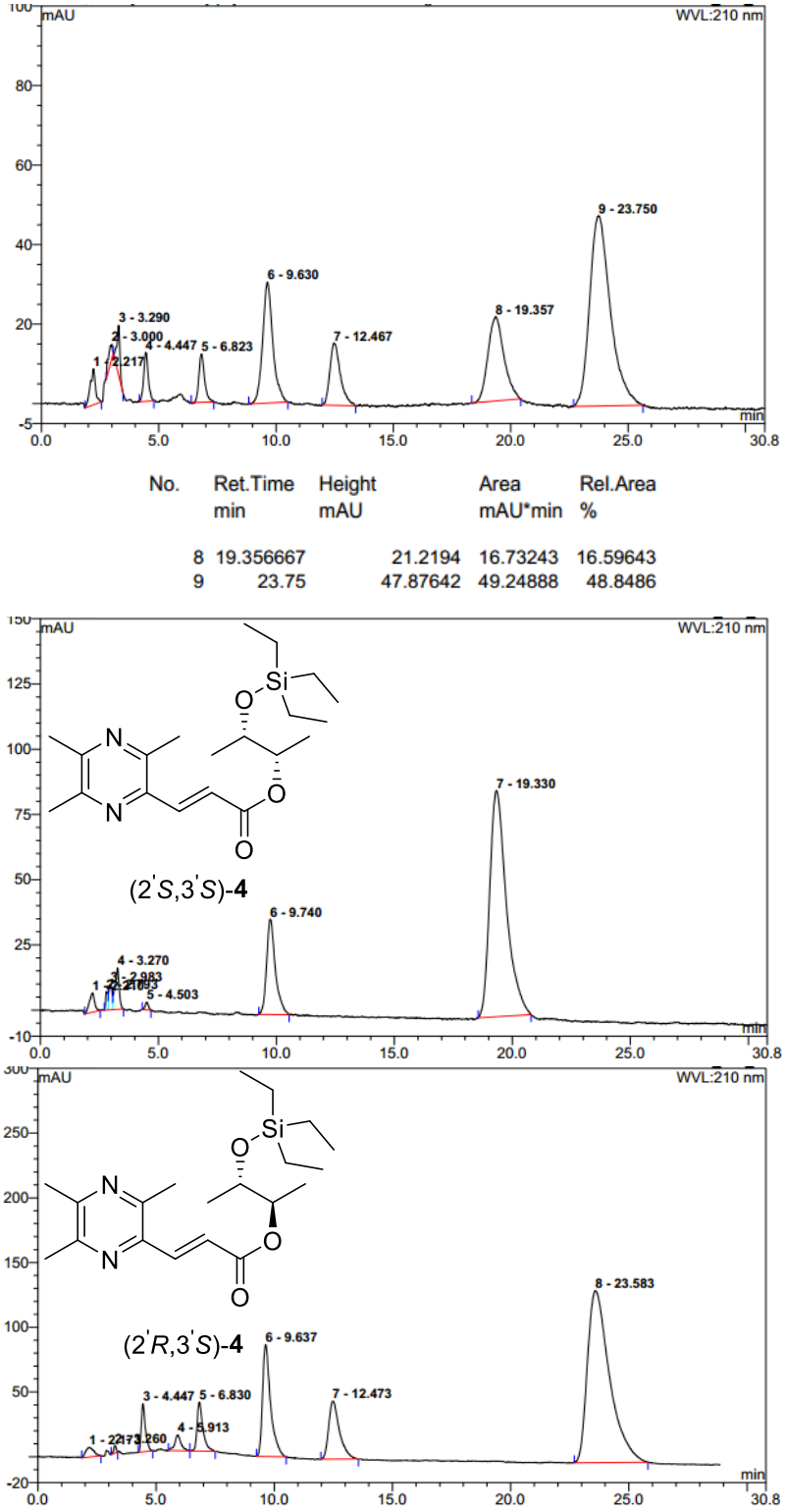



| No. | Ret.Time min | Height mAU | Area mAU*min | Rel.Area % |
|---|---|---|---|---|
| 1 | 6.7066667 | 1327.10101 | 518.1675 | 49.84557 |
| 2 | 9.8366667 | 1184.93849 | 521.3782 | 50.15443 |

**HPLC Traces of four isomers of compound 4, 2 and 3**

Analysis and Semi-prep of (2'*S*,3'*S*)-**4** and (2'*R*,3'*S*)-**4** was performed on an Agilent 1220 infinity (Chiralpak IG column, 5 $\mu$m, 4.6 × 250 mm, MeOH: $H_2O$= 85:15, 1.0 mL/min, $t_1$ = 19.357 min, $t_2$ = 23.750 min).

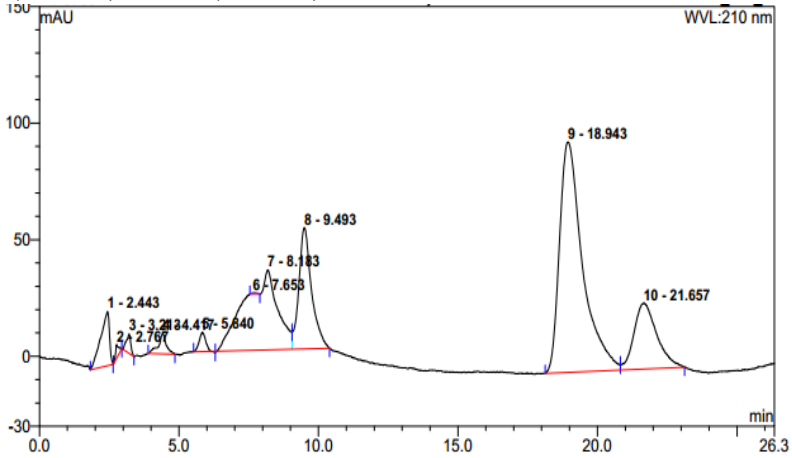
**Figure S64.** (2'*S*,3'*S*)-**4** and (2'*R*,3'*S*)-**4** HPLC traces



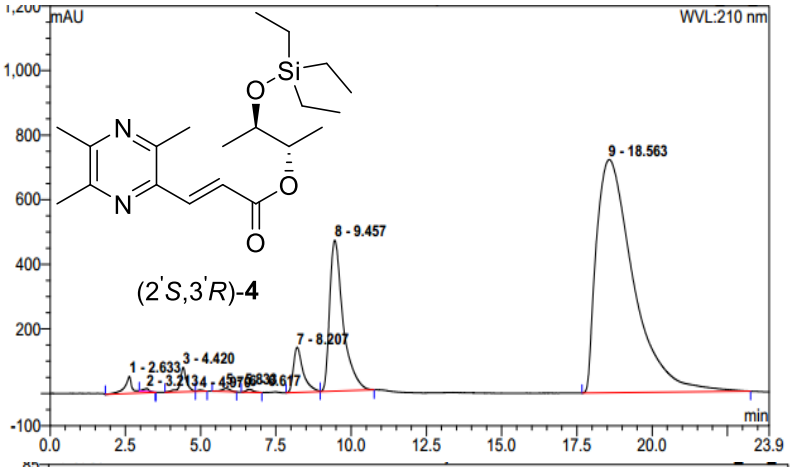

| No. | Ret.Time min | Height mAU | Area mAU*min | Rel.Area % |
|---|---|---|---|---|
| 8 | 19.356667 | 21.2194 | 16.73243 | 16.59643 |
| 9 | 23.75 | 47.87642 | 49.24888 | 48.8486 |

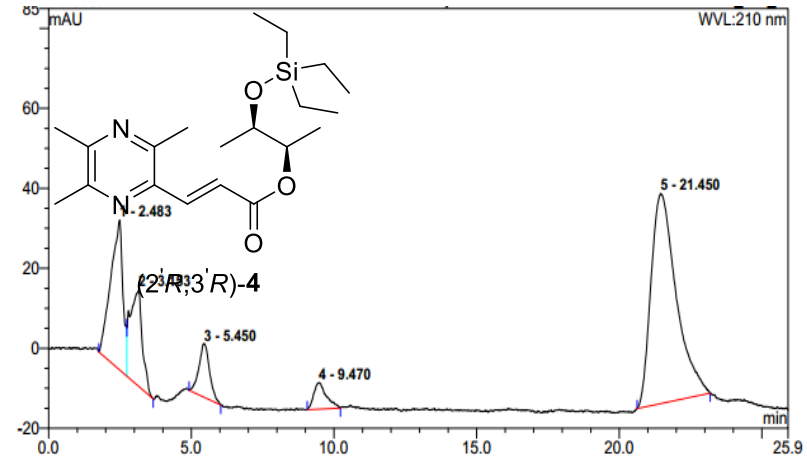
Analysis and Semi-prep of (2'*S*,3'*R*)-**4** and (2'*R*,3'*R*)-**4** was performed on an Agilent 1220 infinity (Chiralpak IG column, 5 $\mu$m, 4.6 × 250 mm, MeOH: $H_2O$= 85:15, 1.0 mL/min, $t_1$ = 18.943 min, $t_2$ = 21.657 min).

**Figure S65.** (2'*S*,3'*R*)-**4** and (2'*R*,3'*R*)-**4** HPLC traces



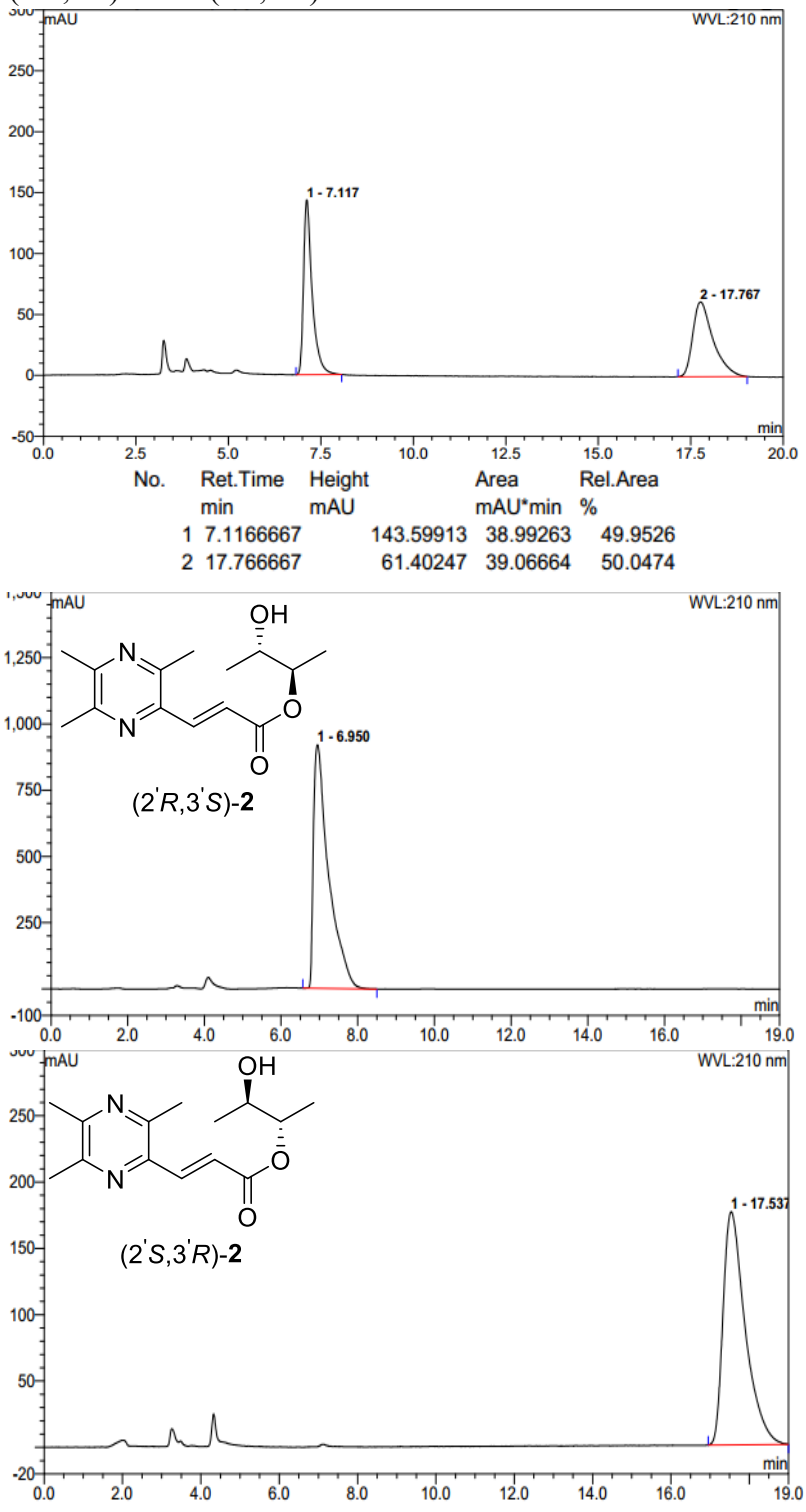

| No. | Ret.Time min | Height mAU | Area mAU*min | Rel.Area % |
|---|---|---|---|---|
| 9 | 18.943333 | 98.72185 | 94.24292 | 43.56771 |
| 10 | 21.656667 | 28.23658 | 26.80444 | 12.39147 |



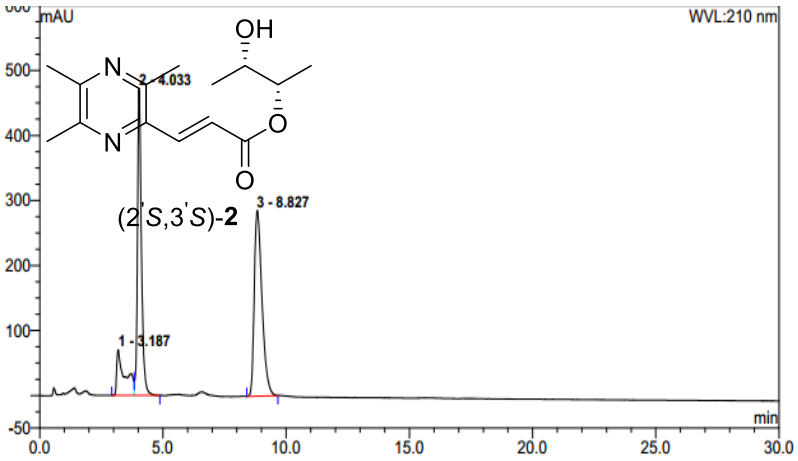
Analysis and Semi-prep of (2'*R*,3'*S*)-**2** and (2'*S*,3'*R*)-**2** was performed on an Agilent 1220 infinity (Chiralpak IG column, 5 $\mu$m, 4.6 × 250 mm, MeCN: $H_2O$= 100:0, 1.0 mL/min, $t_1$ = 7.117 min, $t_2$ = 17.767 min).

**Figure S66.** (2'*R*,3'*S*)-**2** and (2'*S*,3'*R*)-**2** HPLC traces



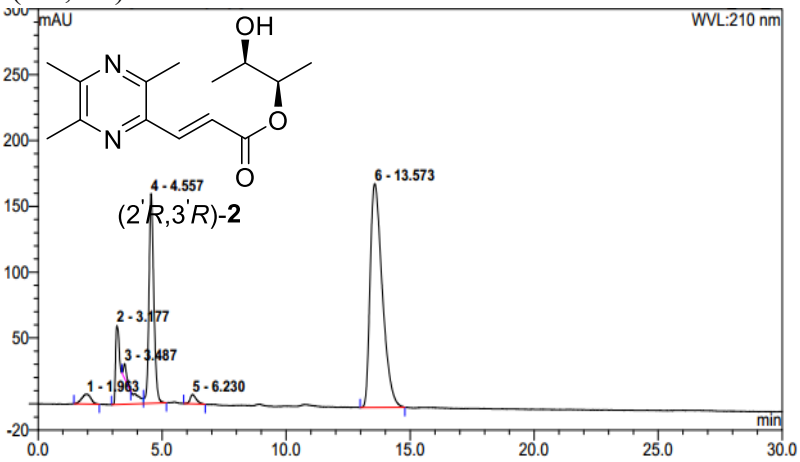
Analysis and Semi-prep of (2'*S*,3'*S*)-**2** was performed on an Agilent 1220 infinity (Chiralpak IG column, 5 $\mu$m, 4.6 × 250 mm, MeCN: $H_2O$= 100:0, 1.0 mL/min, t = 8.827 min).

**Figure S67.** (2'*S*,3'*S*)-**2** HPLC traces



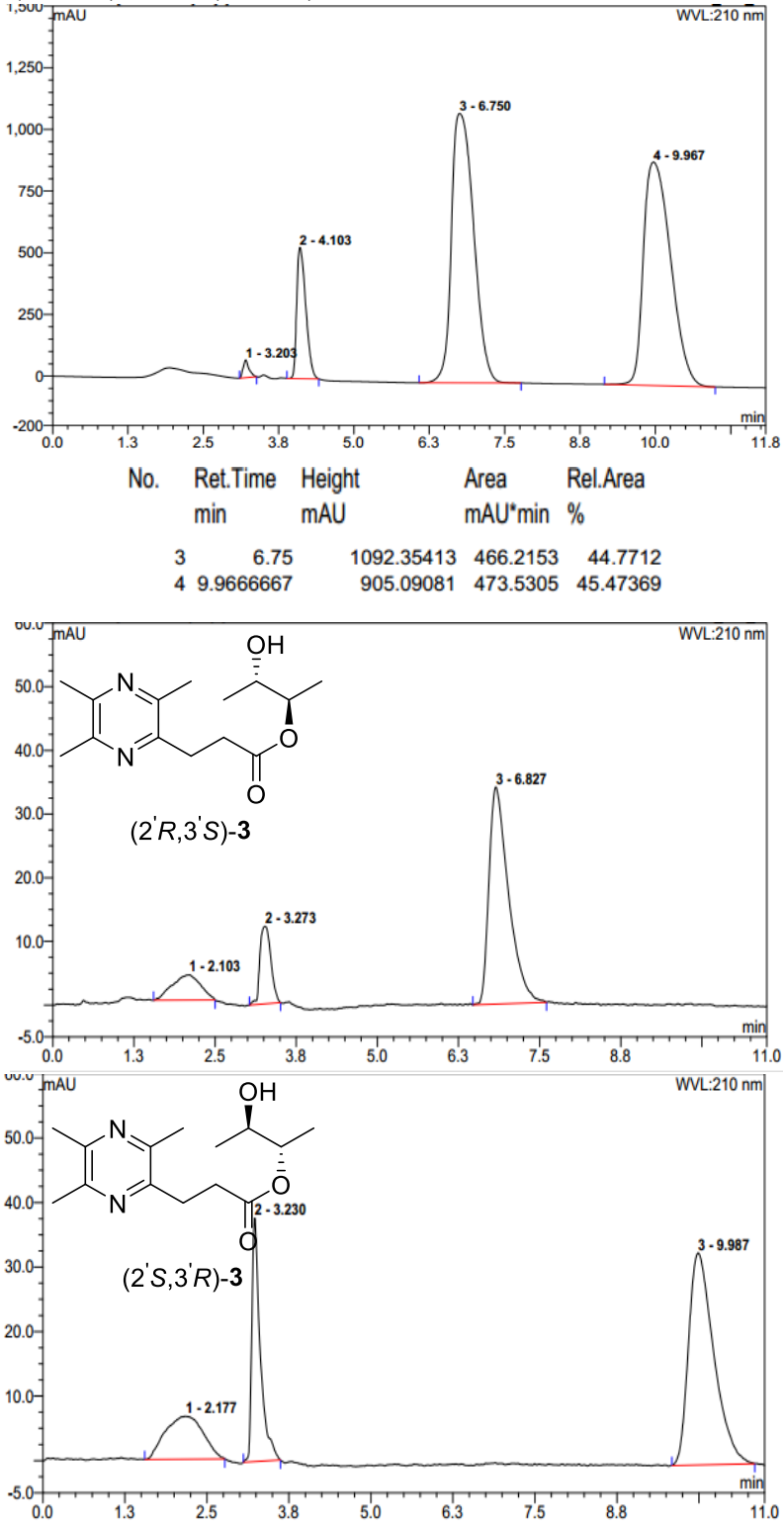

Analysis and Semi-prep of (2'*R*,3'*R*)-**2** was performed on an Agilent 1220 infinity (Chiralpak IG column, 5 $\mu$m, 4.6 × 250 mm, MeCN: $H_2O$= 100:0, 1.0 mL/min, t = 13.573 min).

**Figure S68.** (2'*R*,3'*R*)-**2** HPLC traces



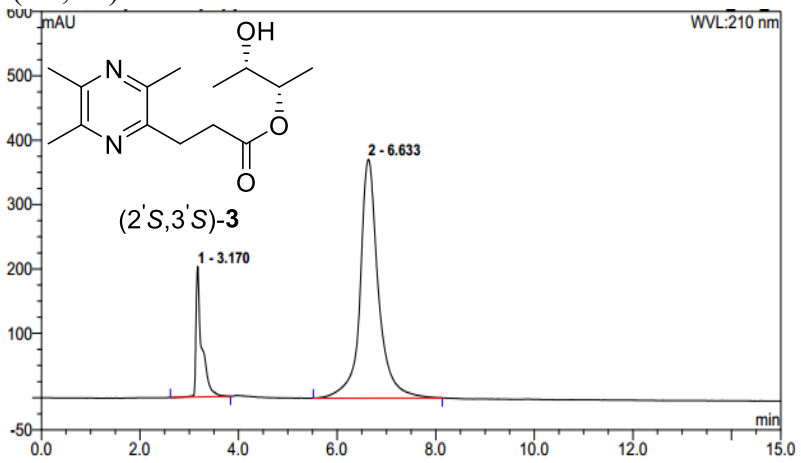
Analysis and Semi-prep of (2'*R*,3'*S*)-**3** and (2'*S*,3'*R*)-**3** was performed on an Agilent 1220 infinity (Chiralpak IG column, 5 $\mu$m, 4.6 × 250 mm, MeCN: $H_2O$= 100:0, 1.0 mL/min, $t_1$ = 6.750 min, $t_2$ = 9.967 min).

**Figure S69.** (2'*R*,3'*S*)-**3** and (2'*S*,3'*R*)-**3** HPLC traces



Analysis and Semi-prep of (2'*S*,3'*S*)-**3** was performed on an Agilent 1220 infinity (Chiralpak IG column, 5 $\mu$m, 4.6 × 250 mm, MeCN: $H_2O$= 100:0, 1.0 mL/min, t = 6.633 min).

**Figure S70.** (2'*S*,3'*S*)-**3** HPLC traces




Analysis and Semi-prep of (2'*R*,3'*R*)-**3** was performed on an Agilent 1220 infinity (Chiralpak IG column, 5 $\mu$m, 5 × 250 mm, MeCN: $H_2O$= 100:0, 1.0 mL/min, t = 7.640 min).

**Figure S71.** (2'*R*,3'*R*)-**3** HPLC traces