# Supplementary Information

# Isoquinoline alkaloids as protein tyrosine inhibitors from a deep-sea-derived fungus *Aspergillus puniceus*

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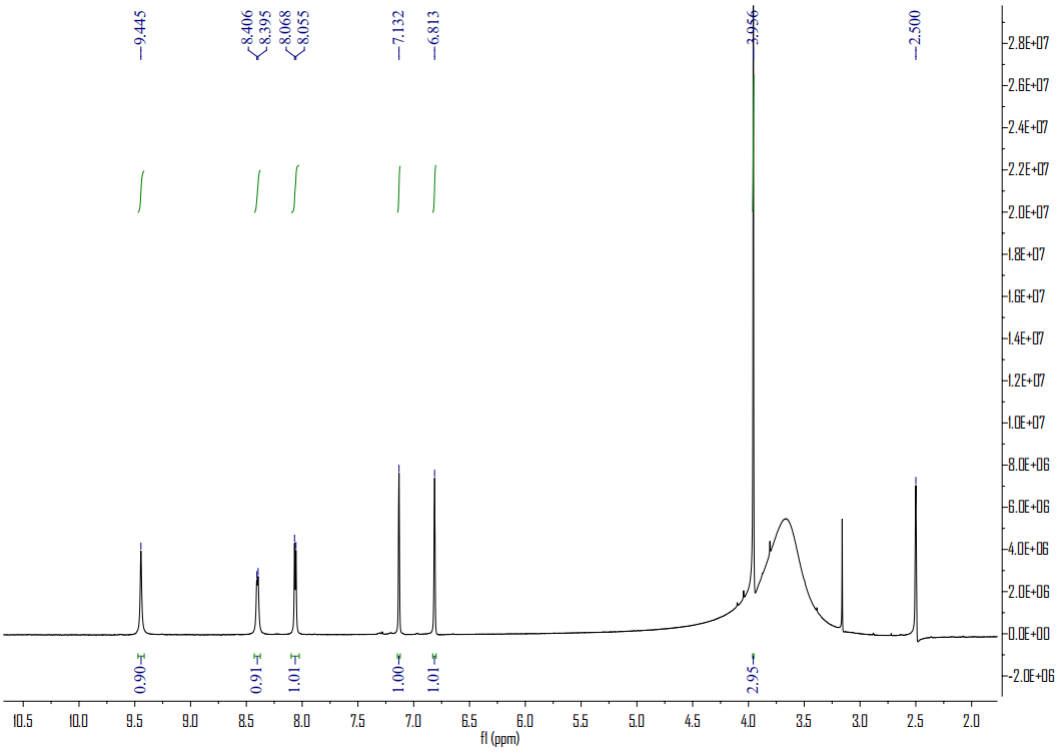



**Figure S1.** $^{1}$H NMR spectrum of **1** in DMSO-$d_6$

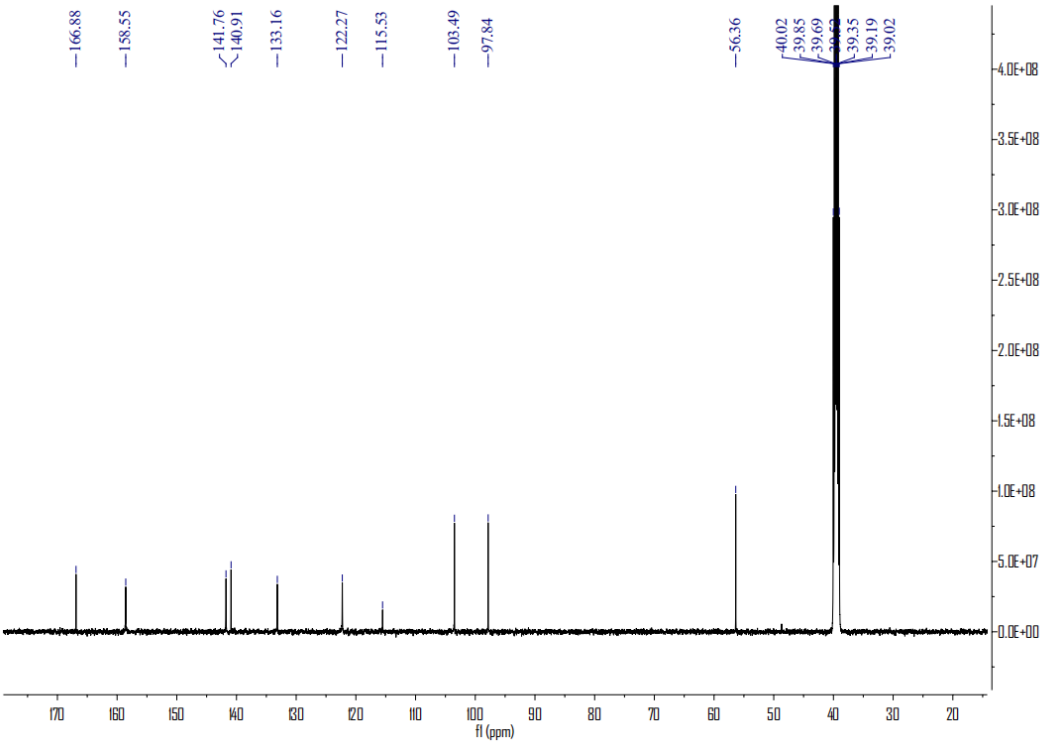



**Figure S2.** $^{13}$C NMR spectrum of **1** in DMSO-$d_6$

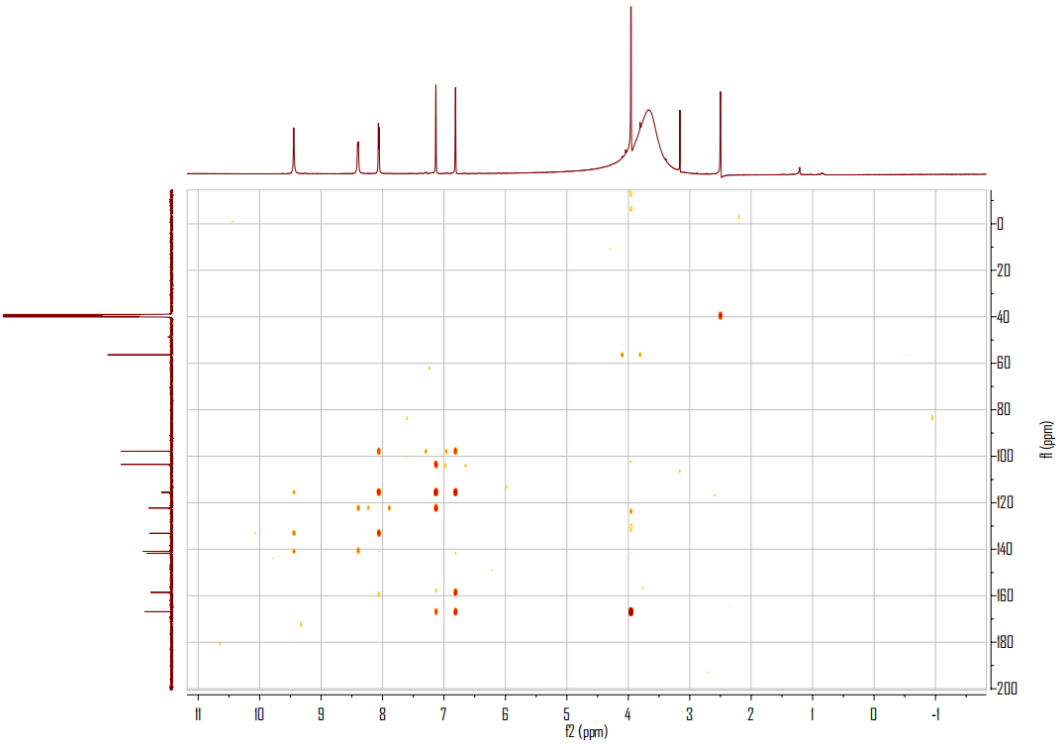



**Figure S3.** HMBC spectrum of **1** in DMSO-$d_6$

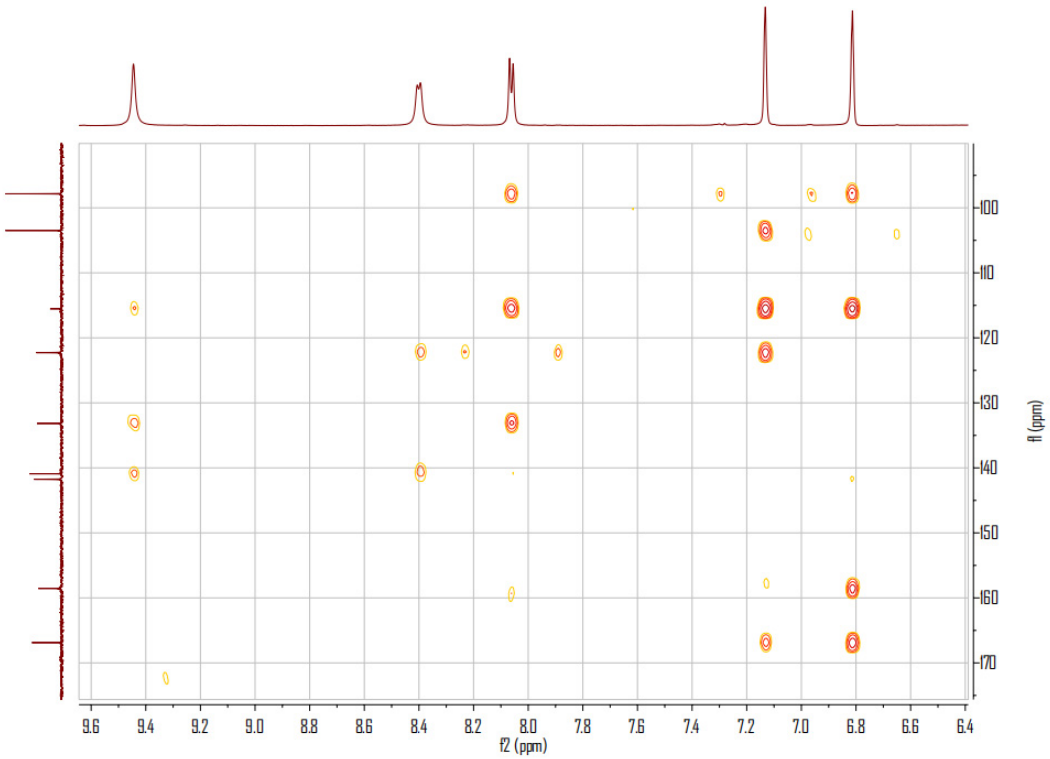



**Figure S4.** Partial HMBC spectrum of **1** in DMSO-$d_6$

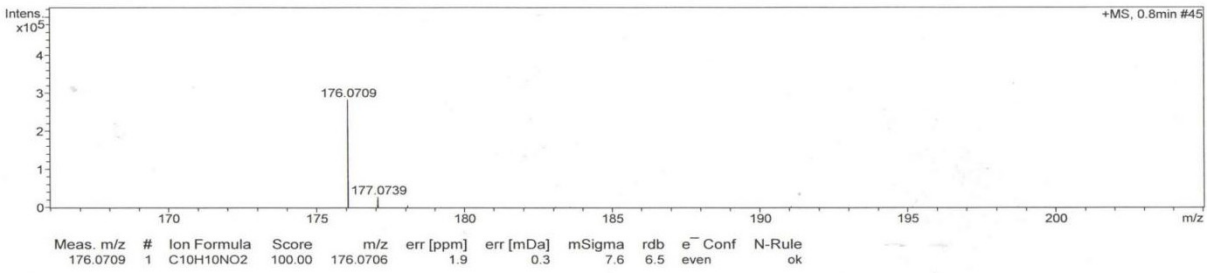



**Figure S5.** HRESIMS spectrum of **1**

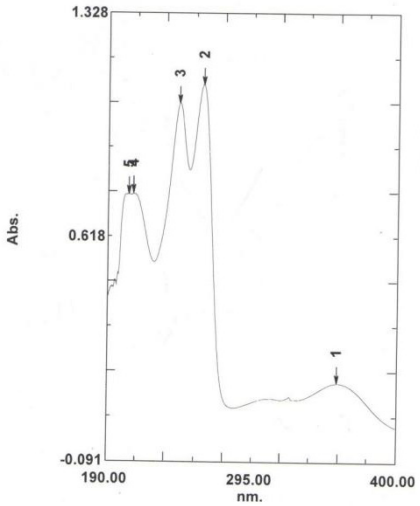



**Figure S6**. UV spectrum of **1**

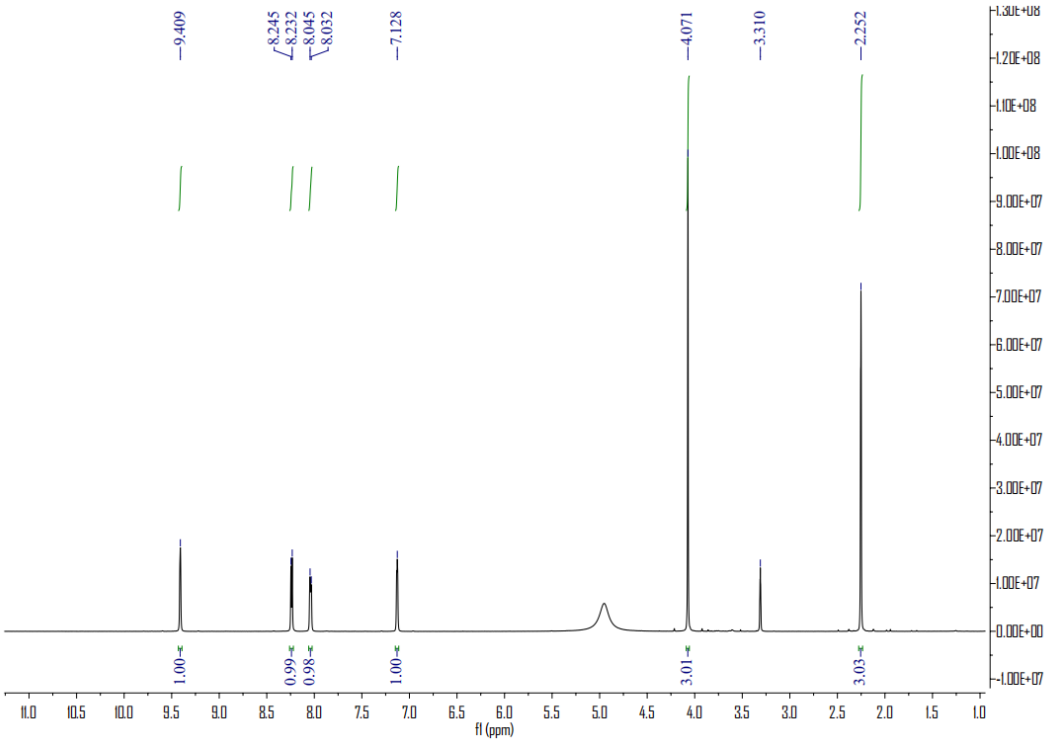



**Figure S7**. $^{1}$H NMR spectrum of **2** in methanol-$d_4$

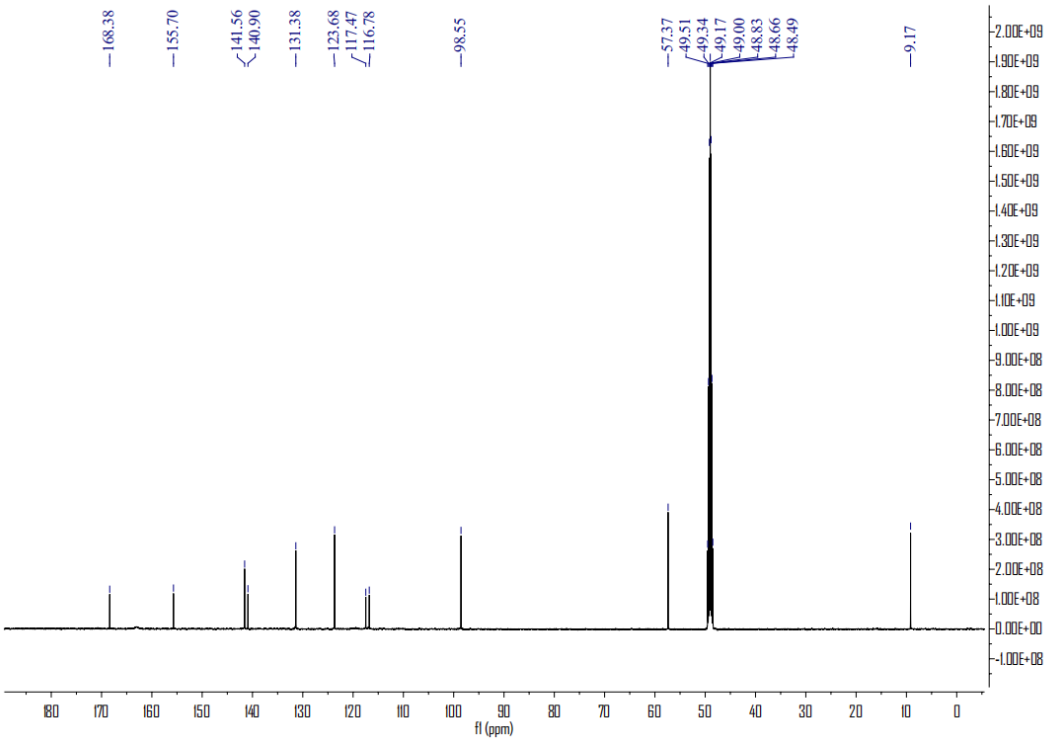



**Figure S8**. $^{13}$C NMR spectrum of **2** in methanol-$d_4$

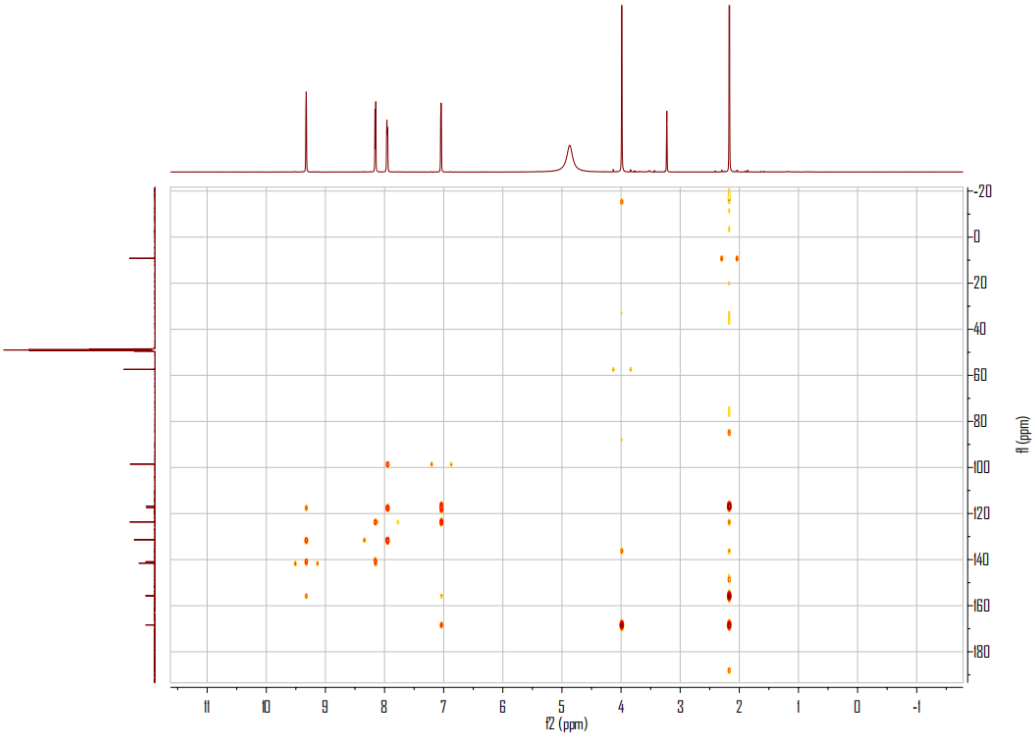



**Figure S9**. HMBC spectrum of **2** in methanol-$d_4$

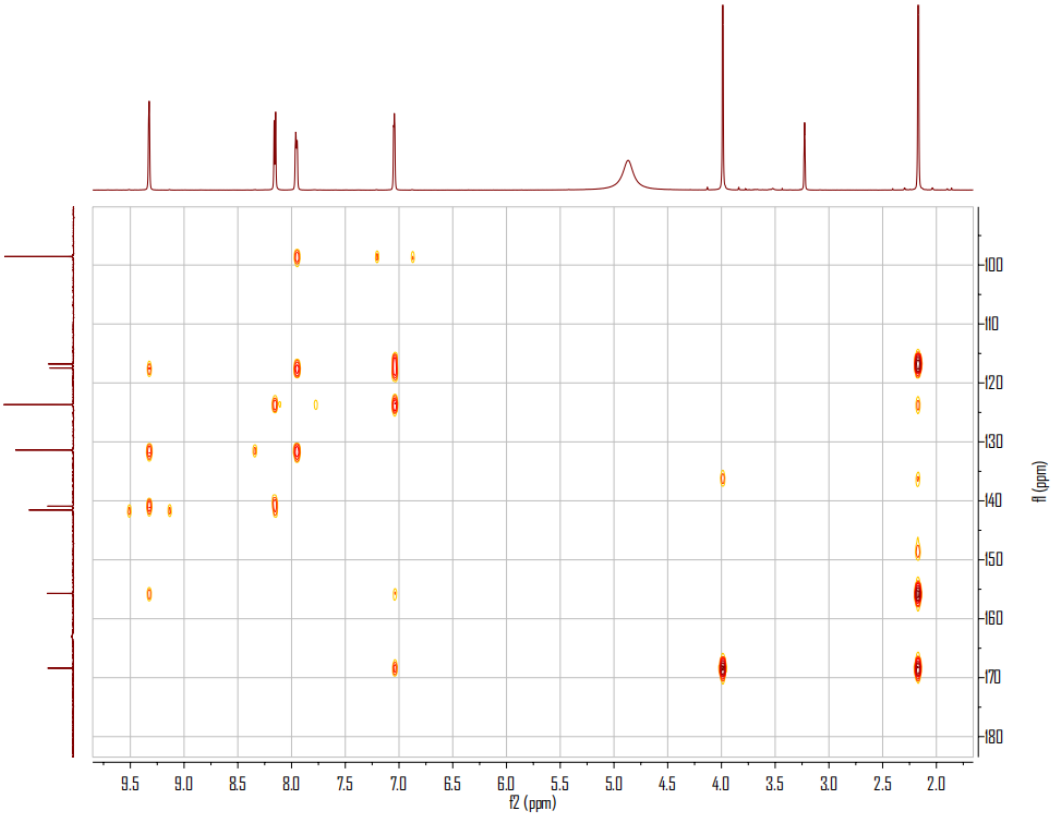



**Figure S10**. Partial HMBC spectrum of **2** in methanol-$d_4$

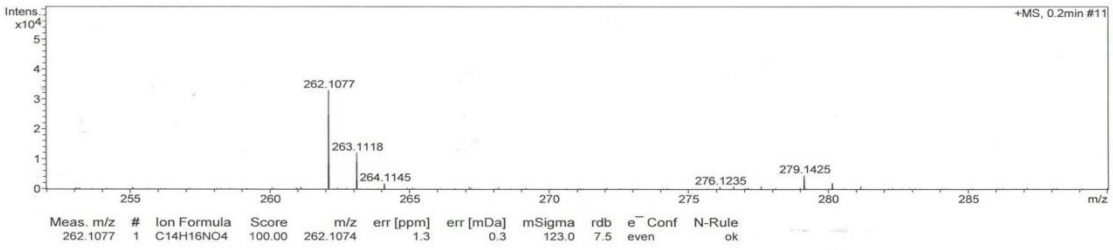



**Figure S11**. HRESIMS spectrum of **2**

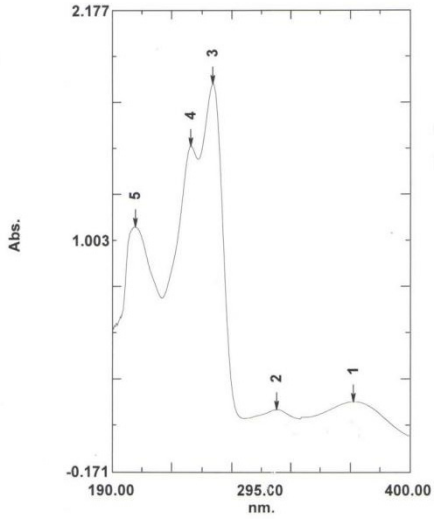



**Figure S12**. UV spectrum of **2.**

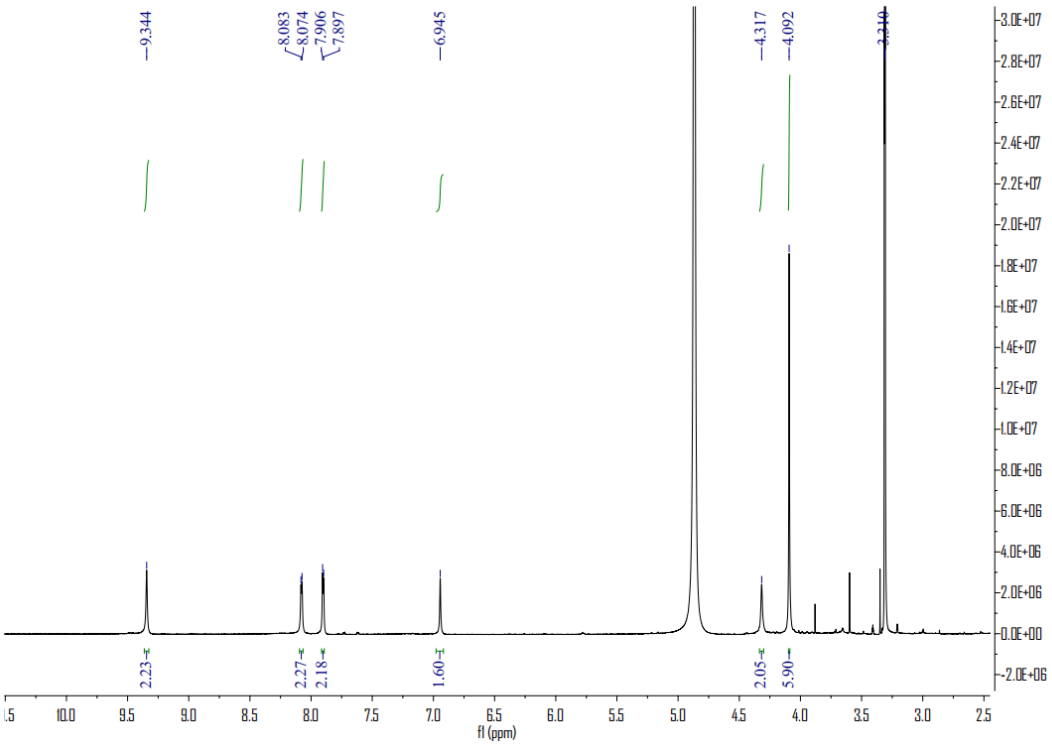



**Figure S13**. $^{1}$H NMR spectrum of **3** in methanol-$d_4$

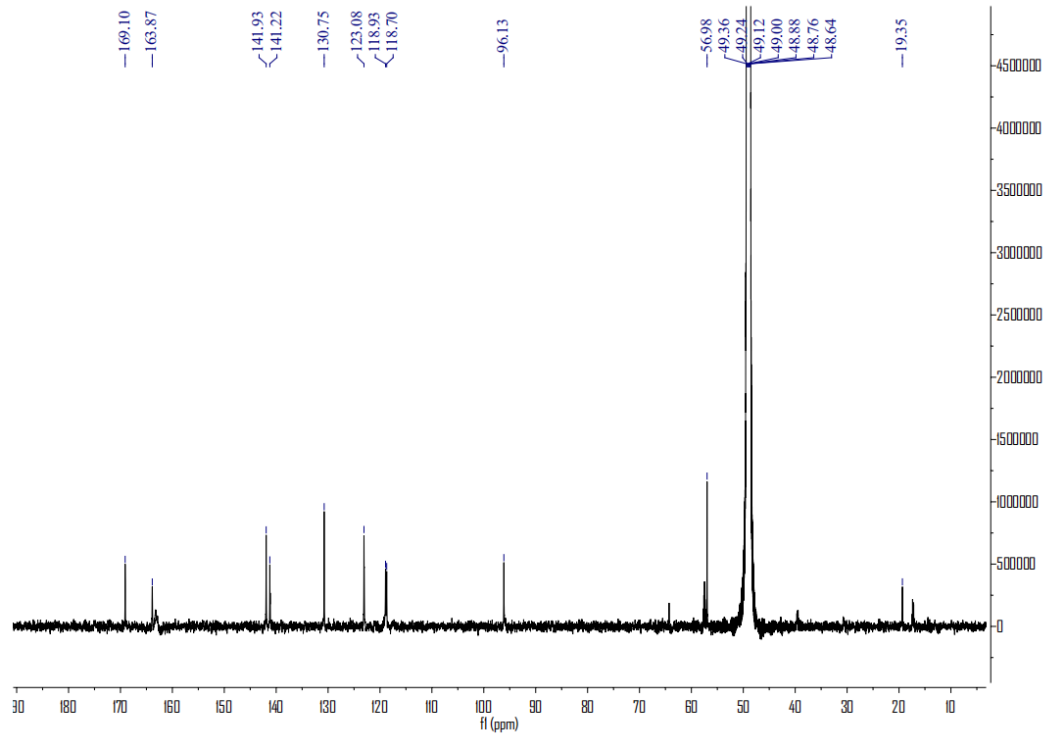



**Figure S14**. $^{13}$C NMR spectrum of **3** in methanol-$d_4$

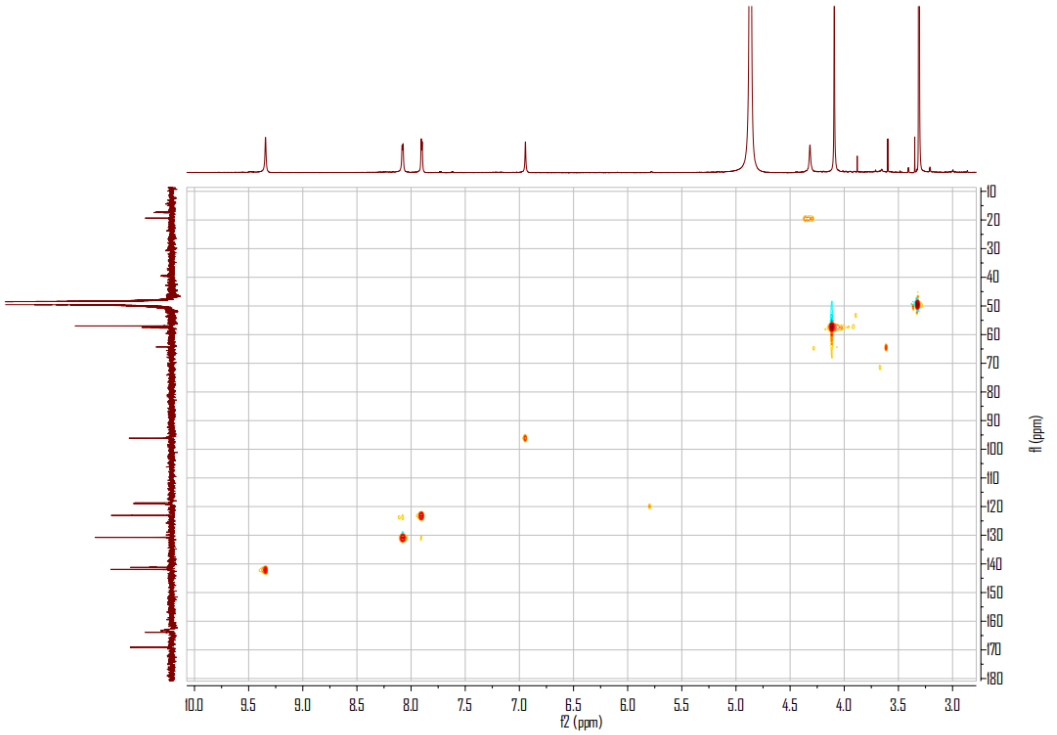



**Figure S15**. HSQC spectrum of **3** in methanol-$d_4$

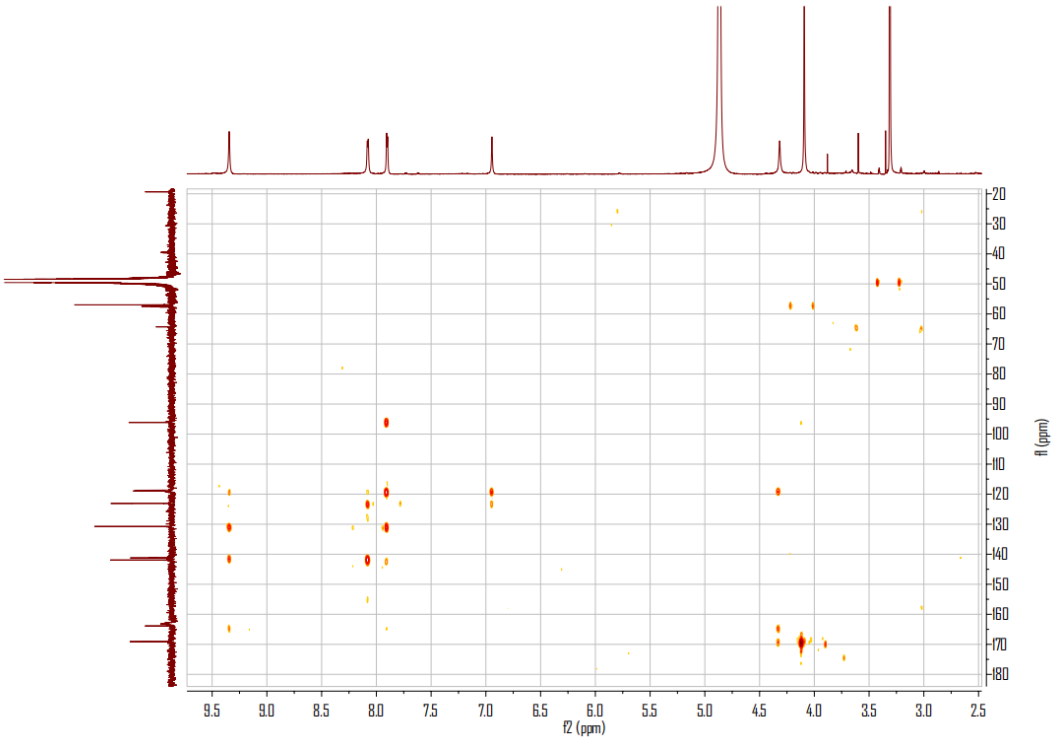



**Figure S16**. HMBC spectrum of **3** in methanol-$d_4$

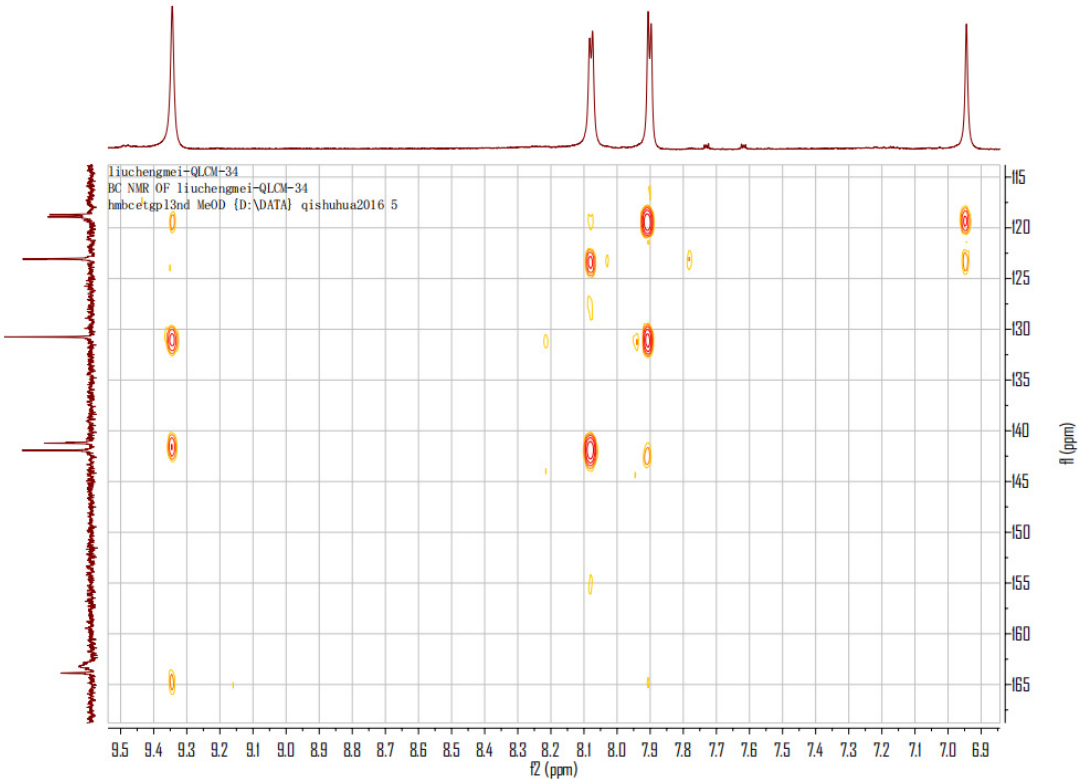



**Figure S17**. Partial HMBC spectrum of **3** in methanol-$d_4$

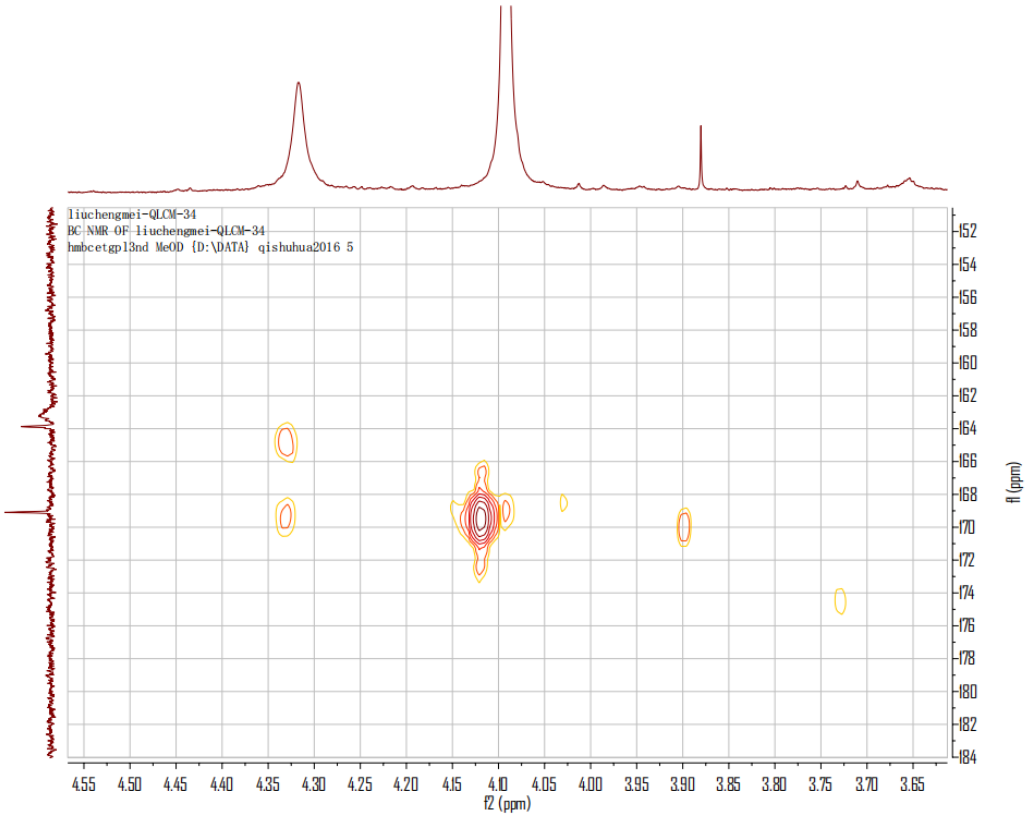



**Figure S18**. Partial HMBC spectrum of **3** in methanol-$d_4$

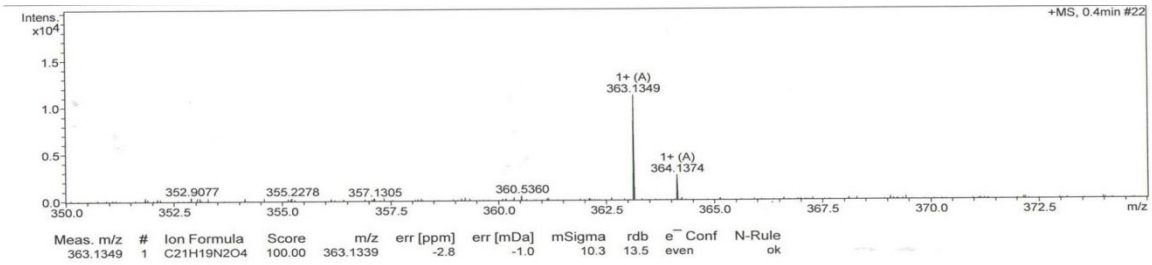



**Figure S19**. HRESIMS spectrum of **3**.

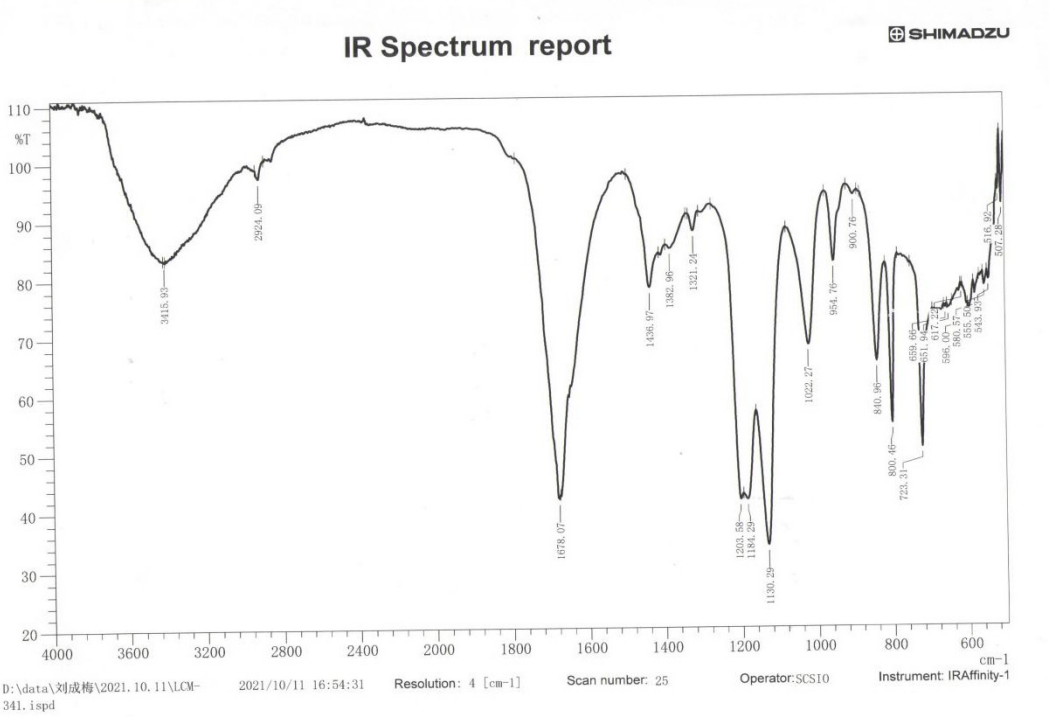



**Figure S20**. IR spectrum of **3**

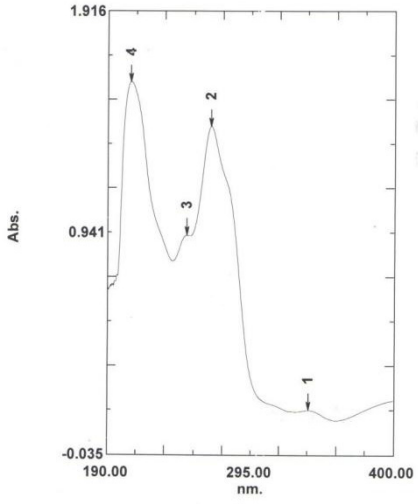



**Figure S21**. UV spectrum of **3**

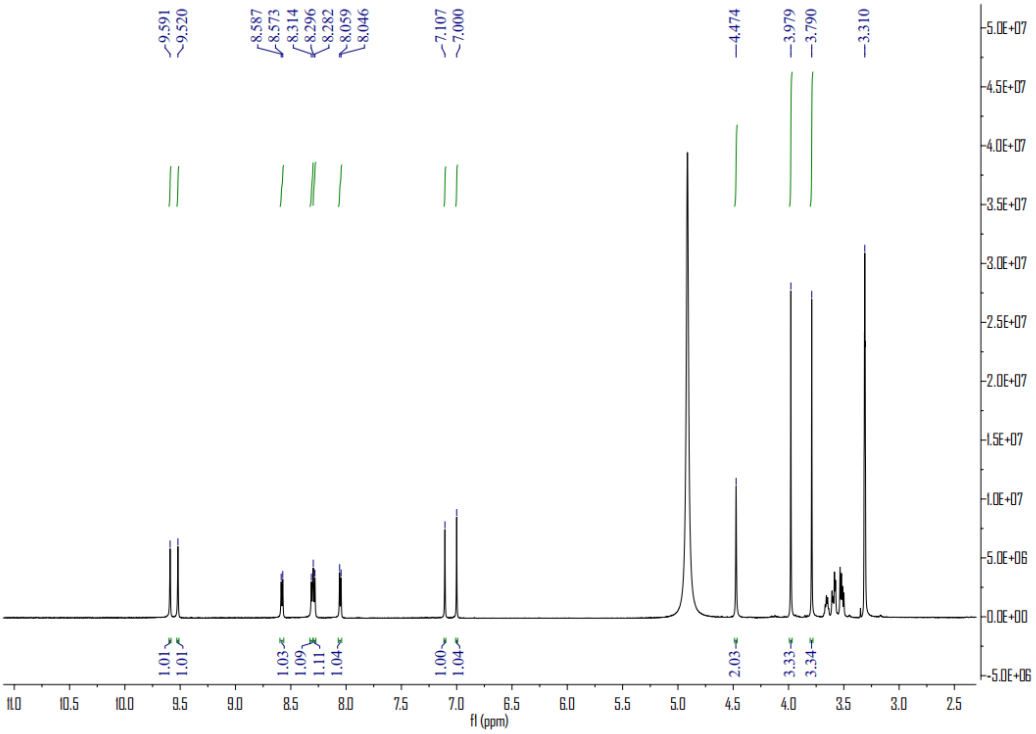



**Figure S22**. $^{1}$H NMR spectrum of **4** in methanol-$d_4$

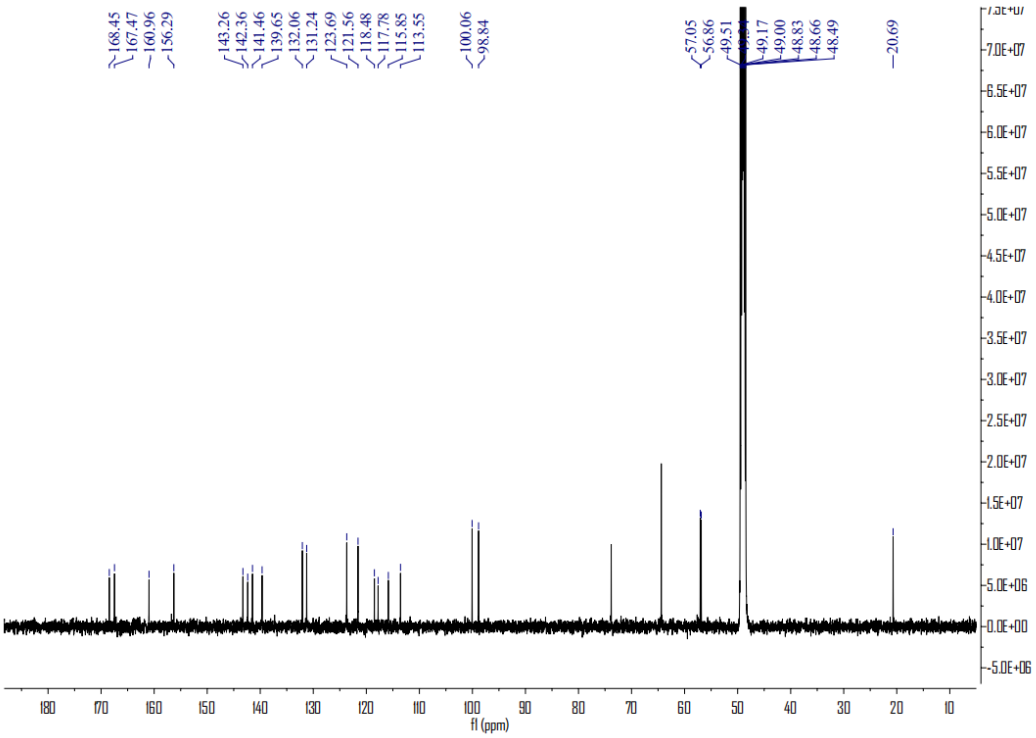



**Figure S23**. $^{13}$C NMR spectrum of **4** in methanol-$d_4$

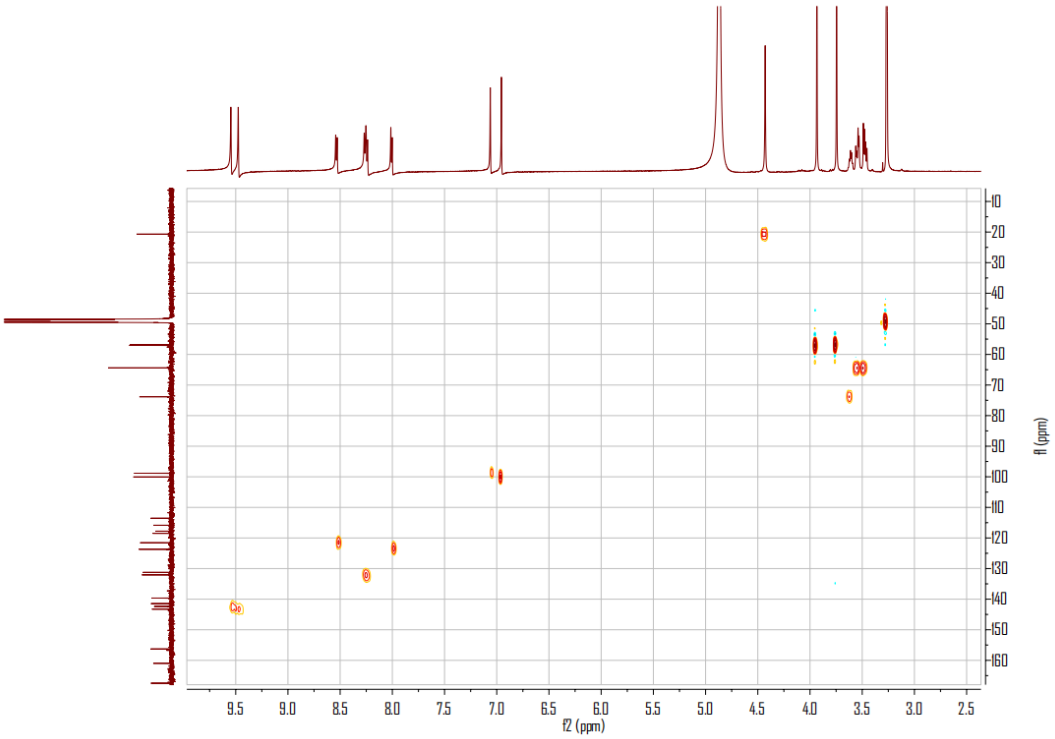



**Figure S24**. HSQC spectrum of **4** in methanol-$d_4$

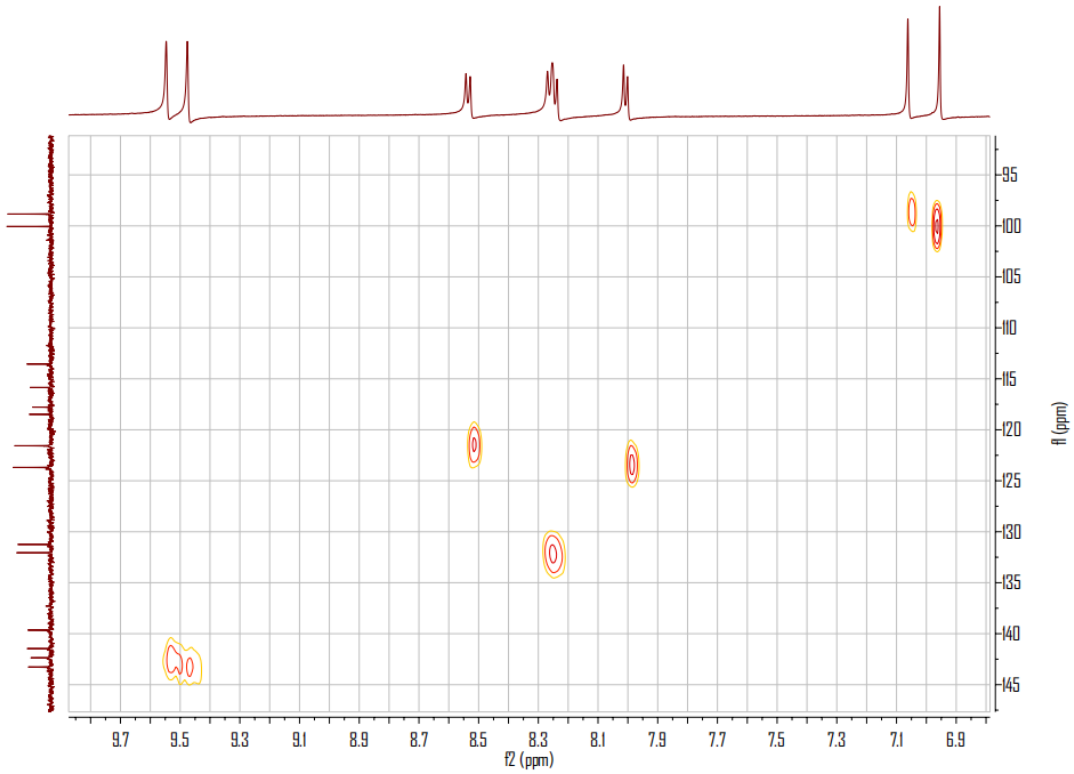



**Figure S25**. Partial HSQC spectrum of **4** in methanol-$d_4$

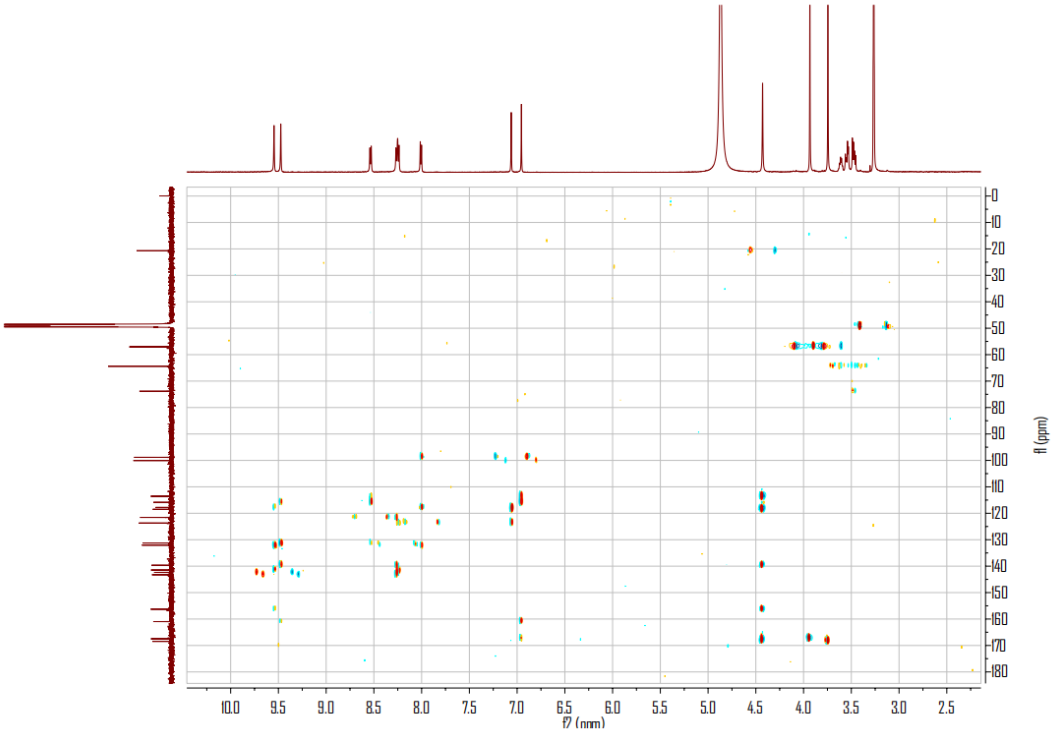



**Figure S26**. HMBC spectrum of **4** in methanol-$d_4$

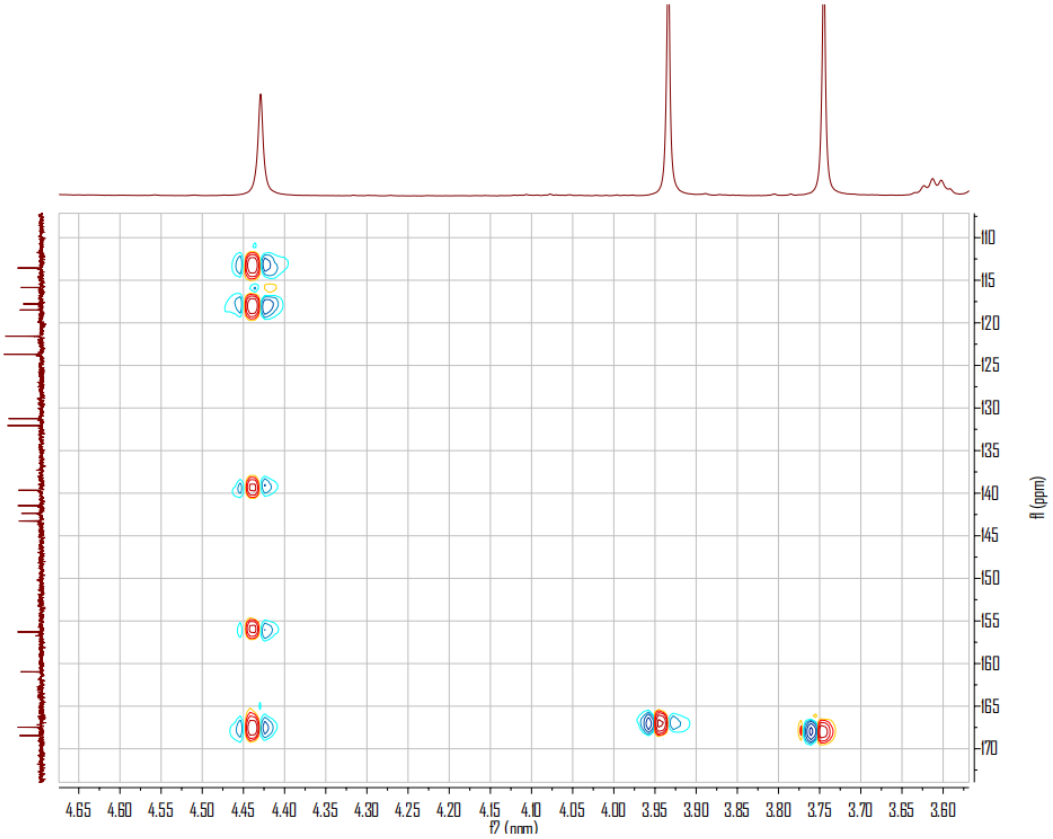



**Figure S27**. Partial HMBC spectrum of **4** in methanol-$d_4$

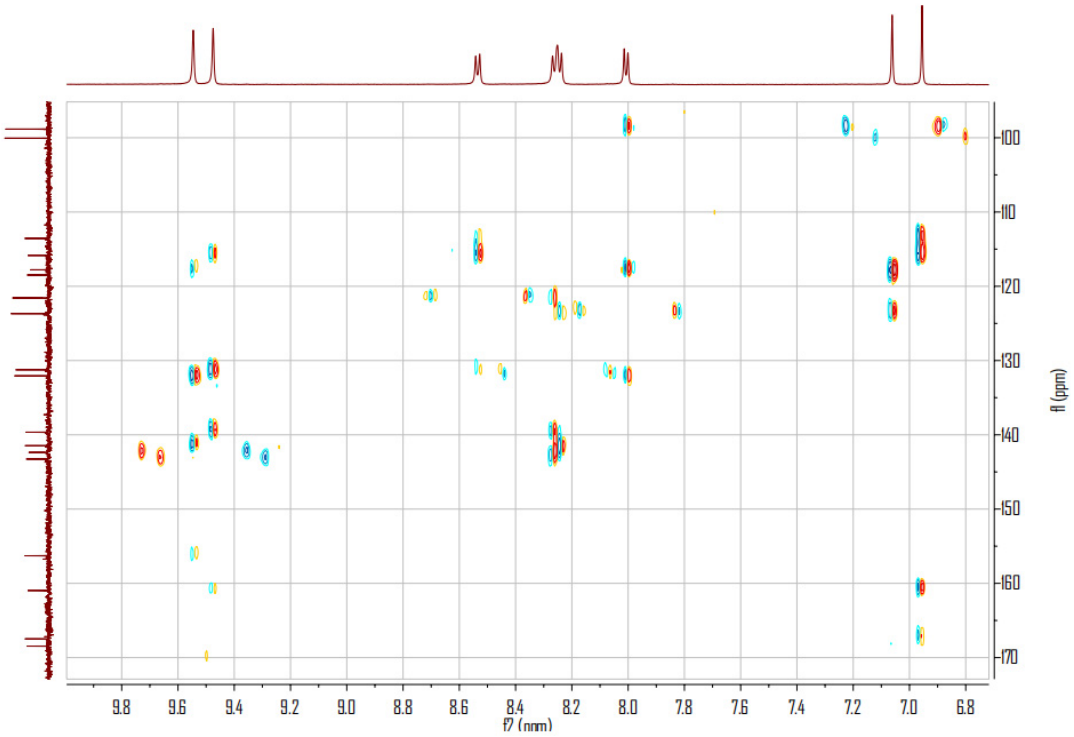



**Figure S28**. Partial HMBC spectrum of **4** in methanol-$d_4$

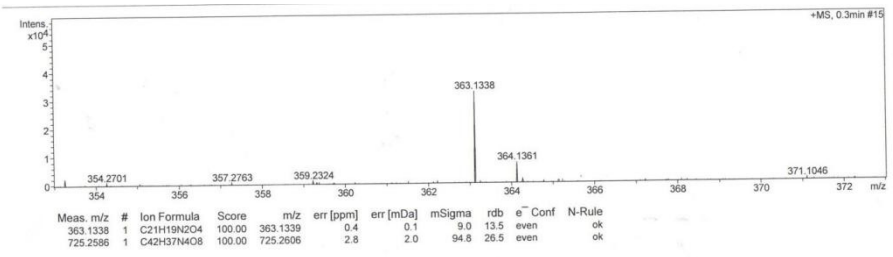



**Figure S29**. HRESIMS spectrum of **4**

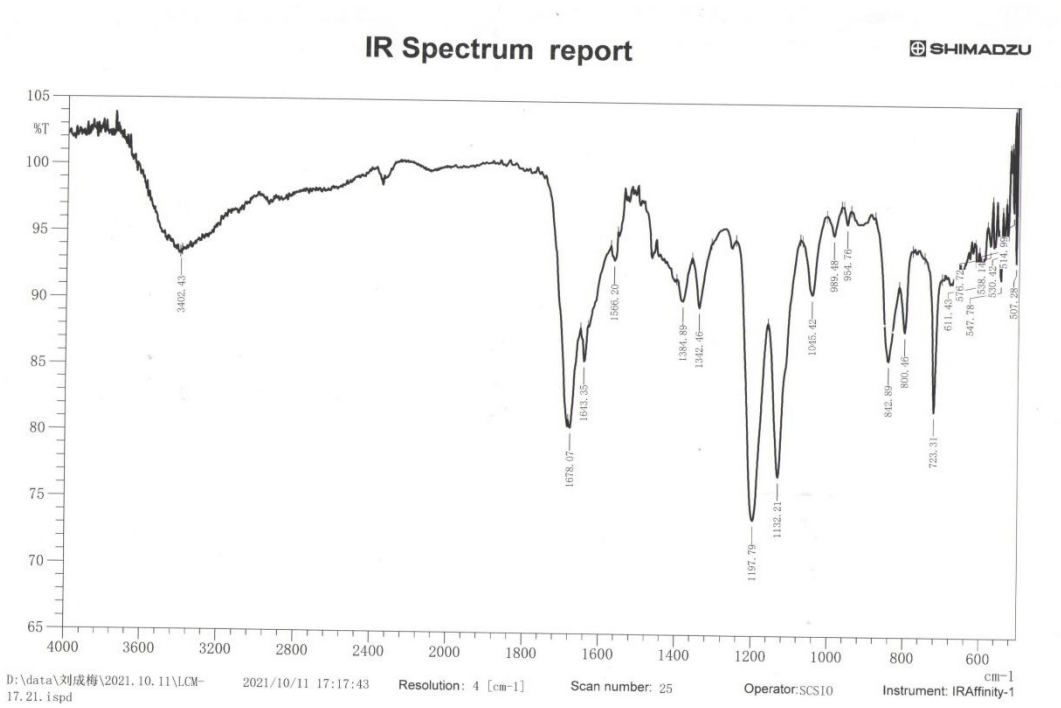



**Figure S30**. IR spectrum of **4**

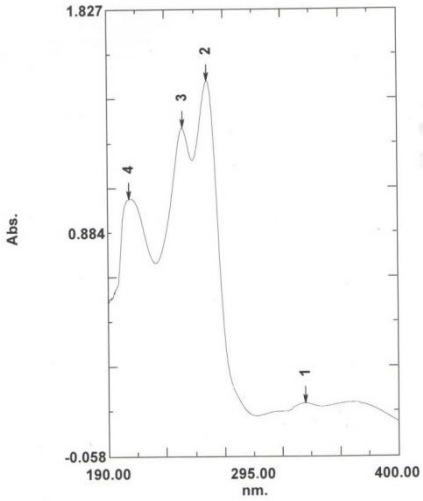



**Figure S31**. UV spectrum of **4**

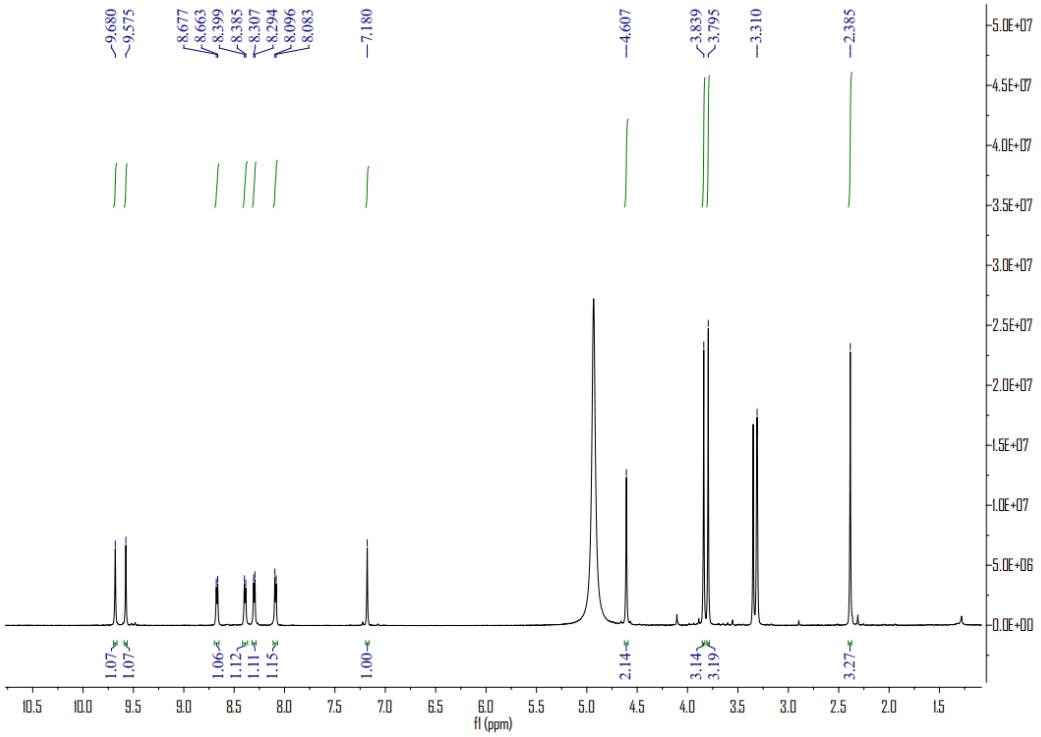



**Figure S32**. $^{1}$H NMR spectrum of **5** in methanol-$d_4$

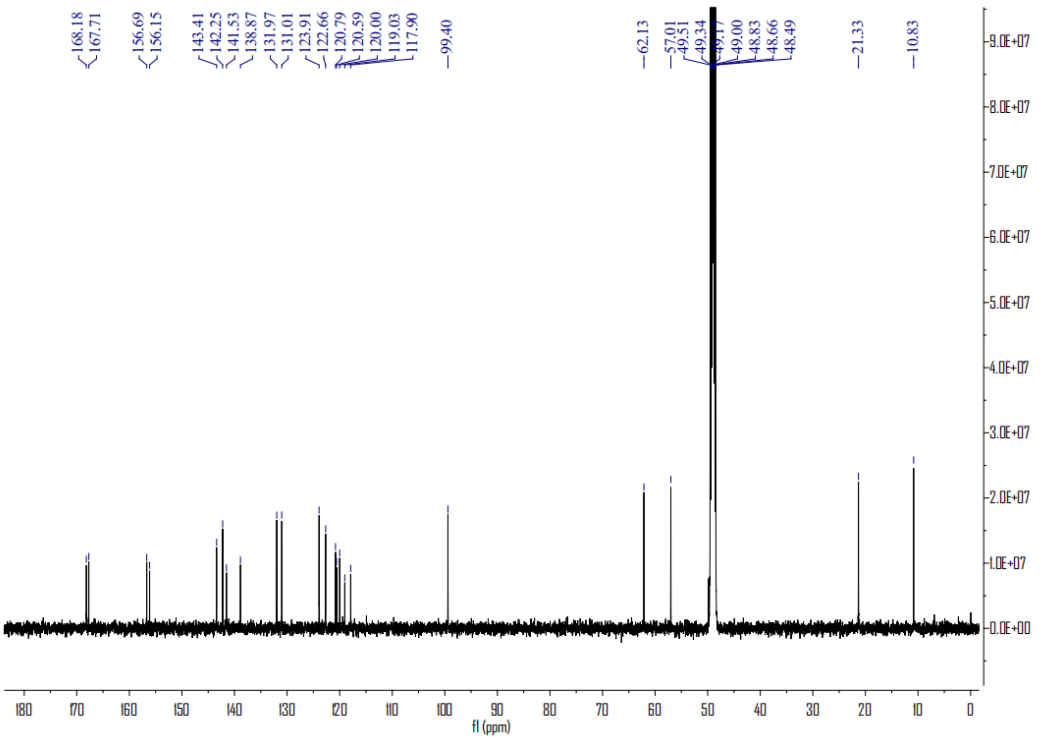



**Figure S33**. $^{13}$C NMR spectrum of **5** in methanol-$d_4$

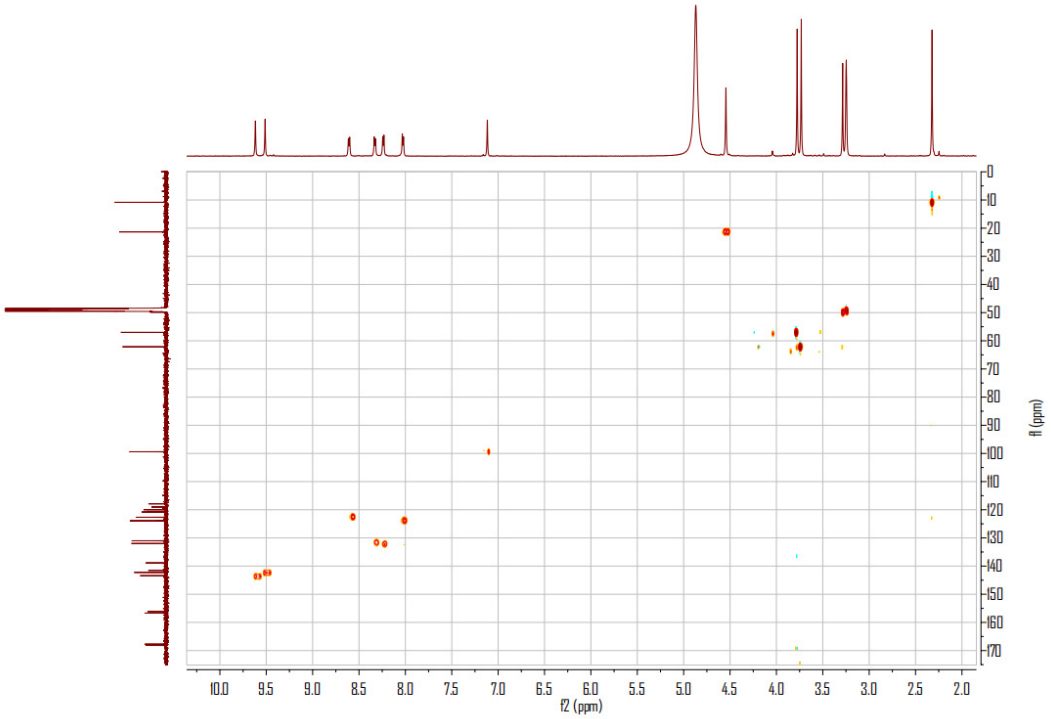



**Figure S34**. HSQC spectrum of **5** in methanol-$d_4$

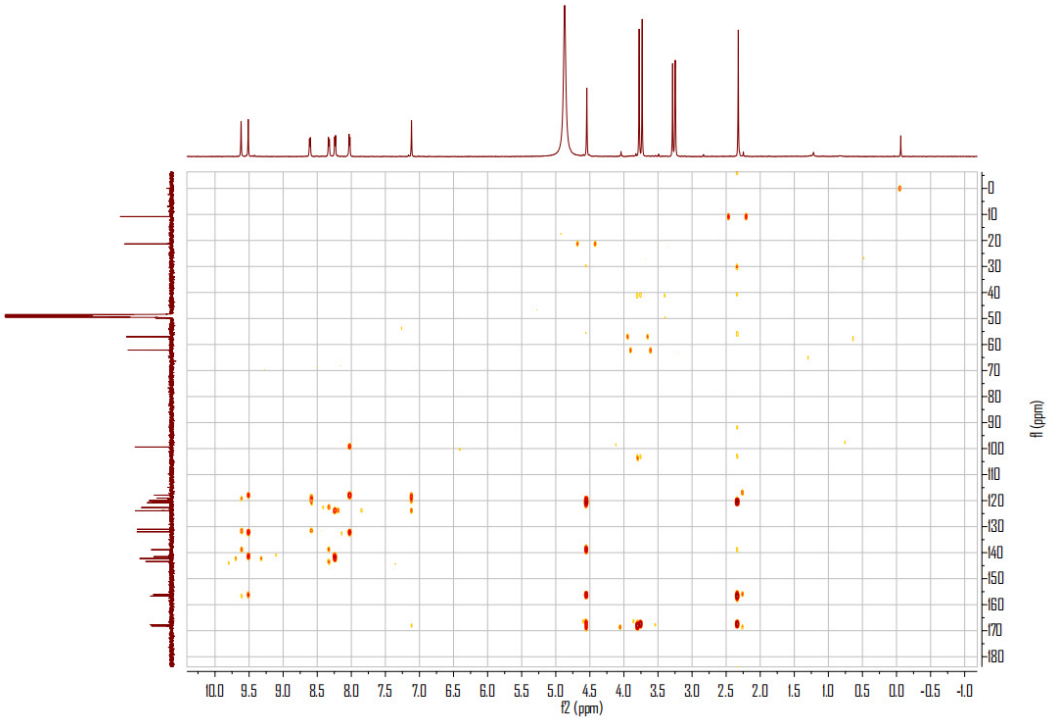



**Figure S35**. HMBC spectrum of **5** in methanol-$d_4$

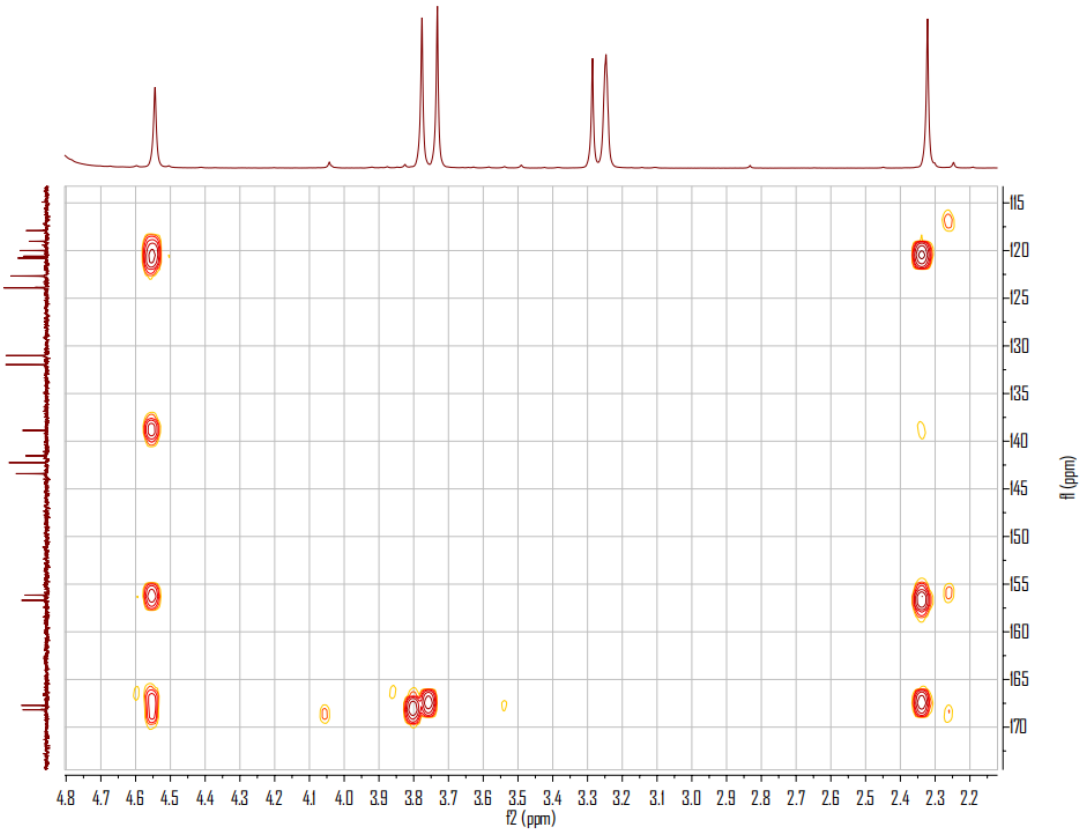



**Figure S36**. Partial HMBC spectrum of **5** in methanol-$d_4$

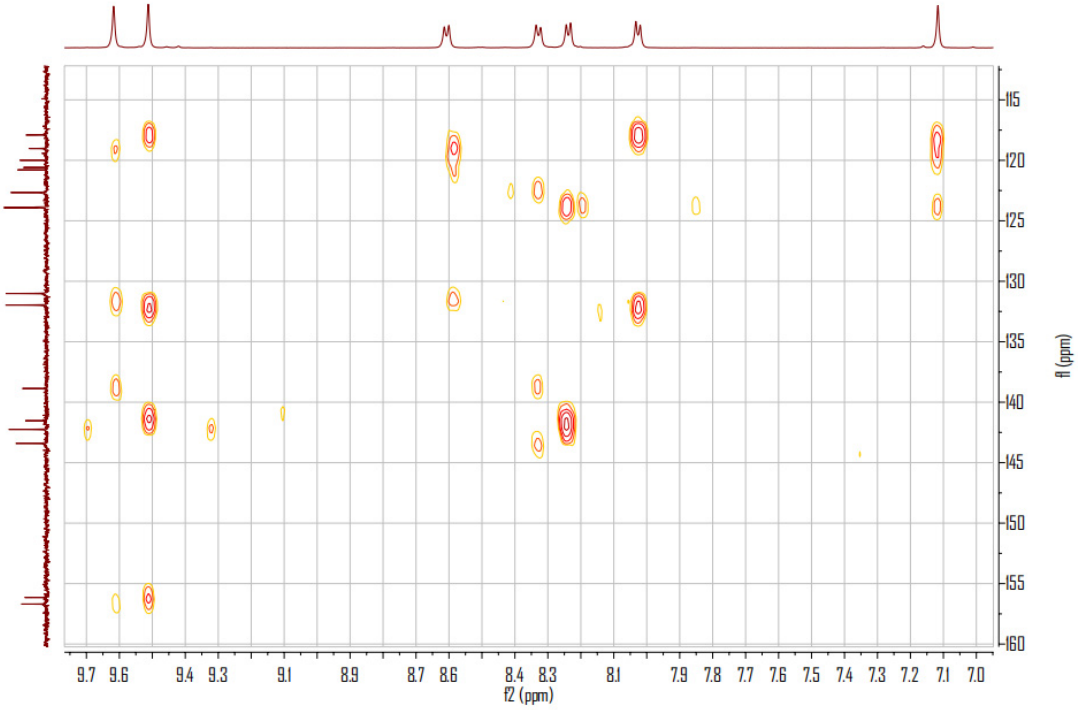



**Figure S37**. Partial HMBC spectrum of **5** in methanol-$d_4$

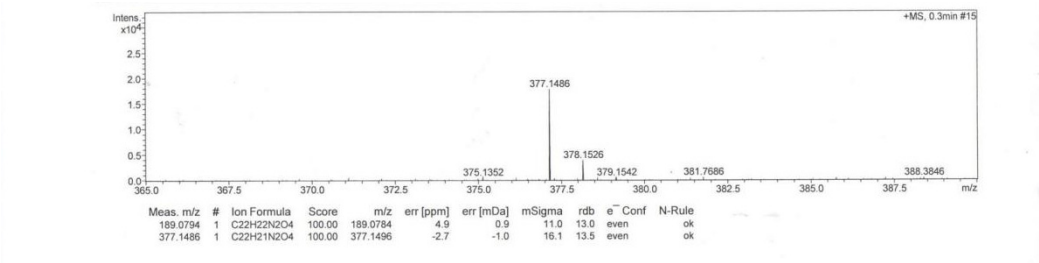



**Figure S38**. HRESIMS spectrum of **5**

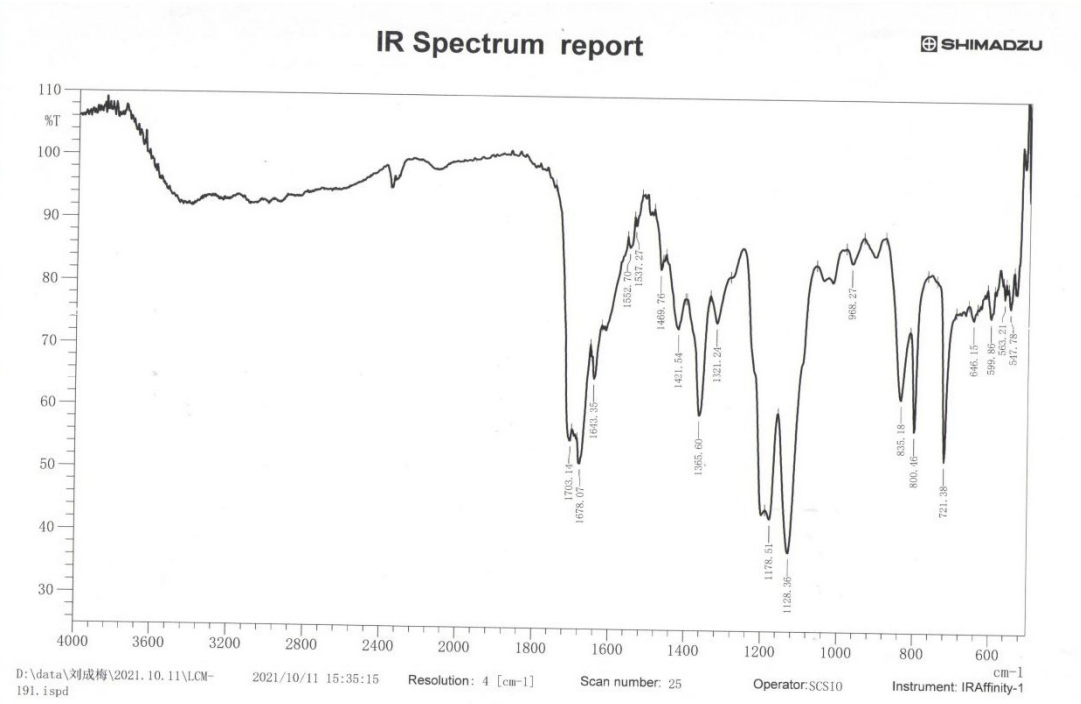



**Figure S39**. IR spectrum of **5**

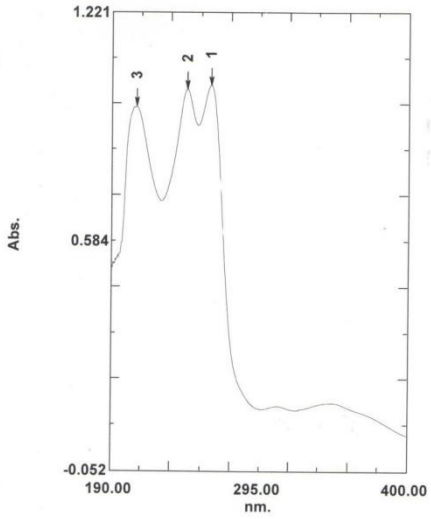



**Figure S40**. UV spectrum of **5**

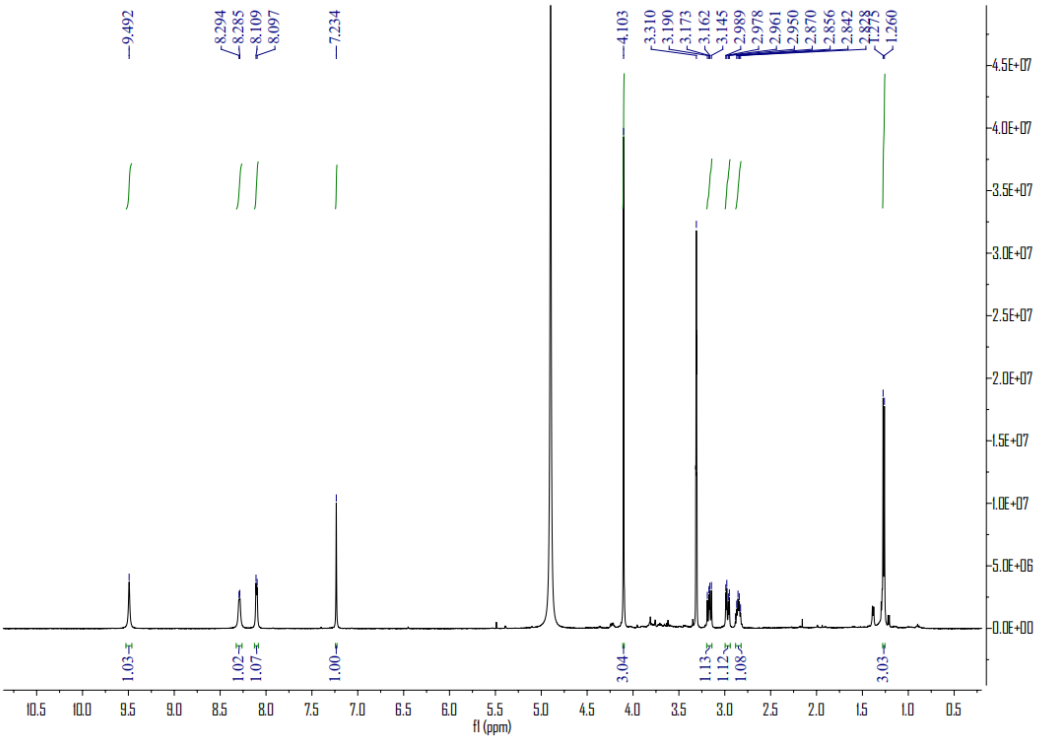



**Figure S41**. $^{1}$H NMR spectrum of **6** in methanol-$d_4$

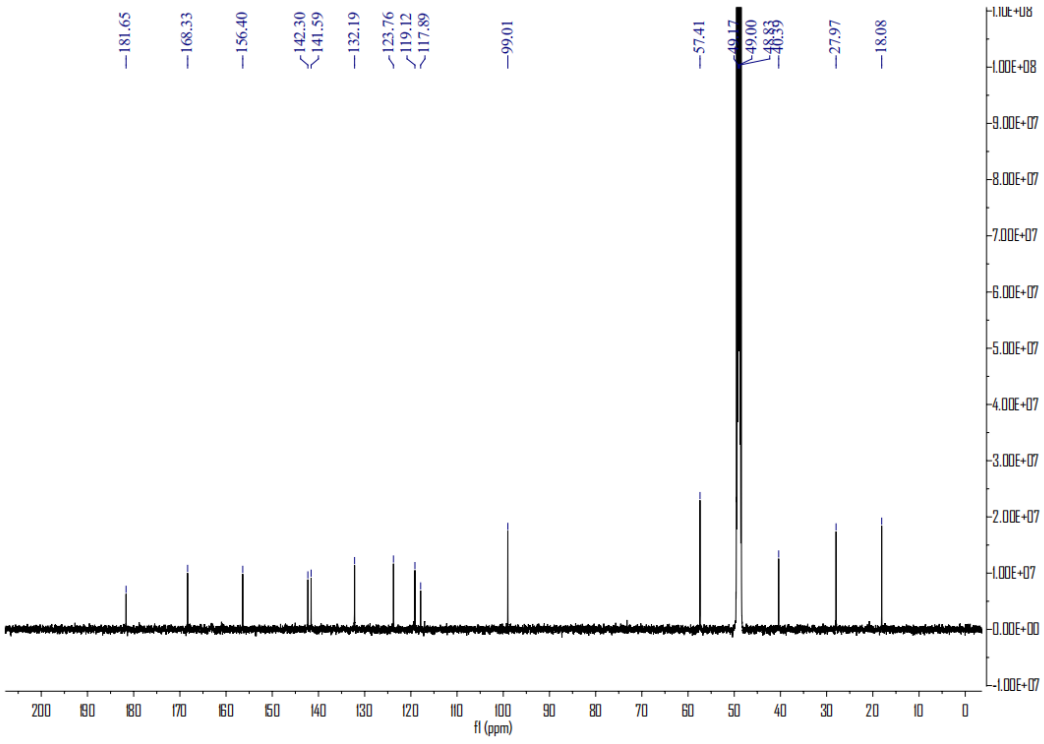



**Figure S42**. $^{13}$C NMR spectrum of **6** in methanol-$d_4$

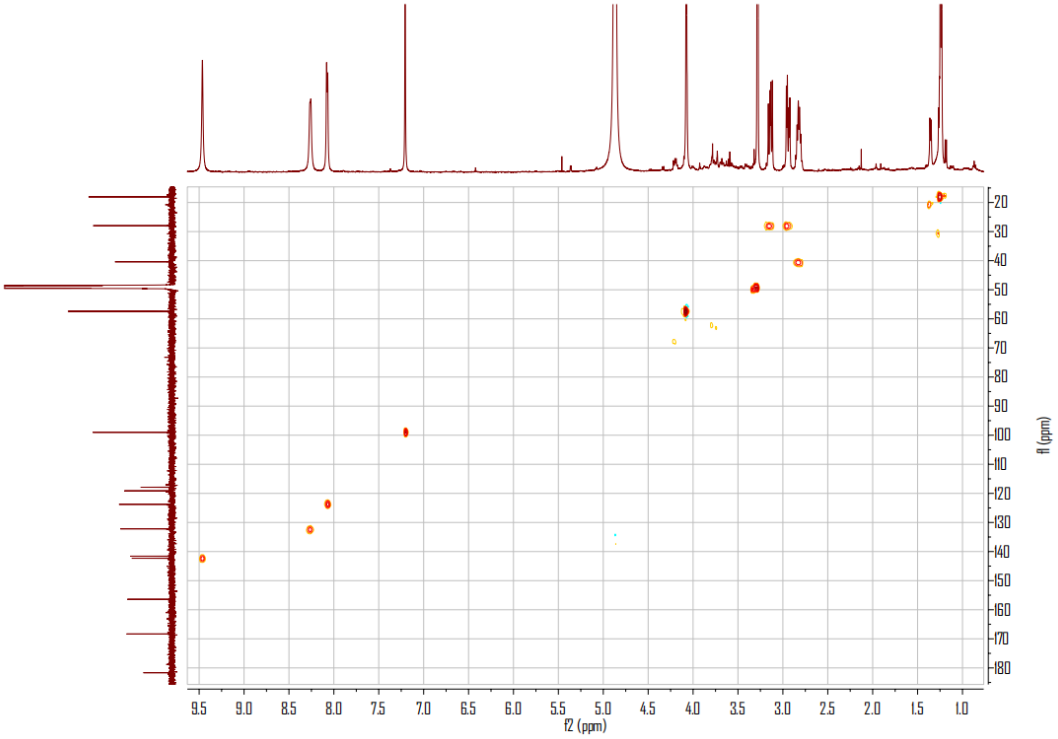



**Figure S43**. HSQC spectrum of **6** in methanol-$d_4$

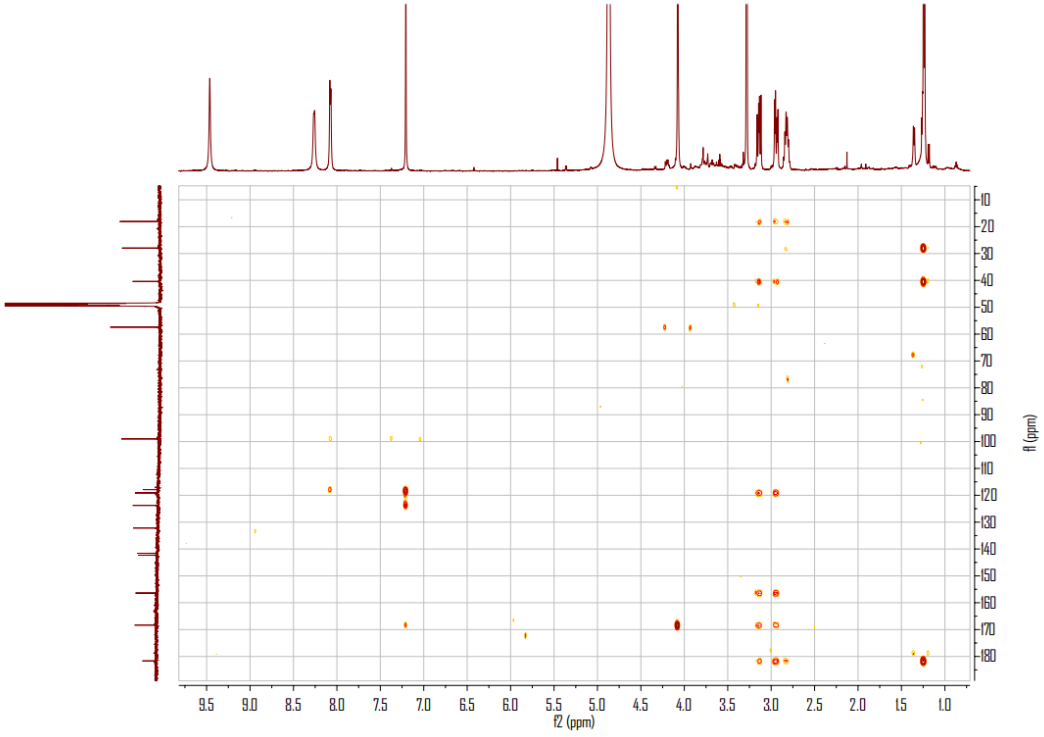



**Figure S44**. HMBC spectrum of **6** in methanol-$d_4$

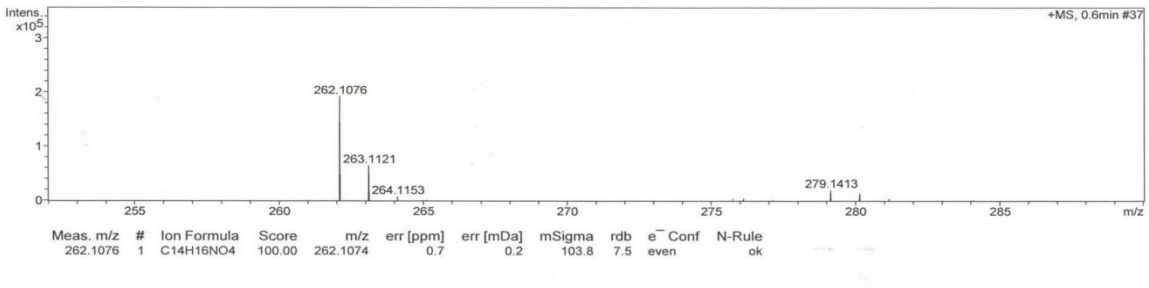



**Figure S45**. HRESIMS spectrum of **6**

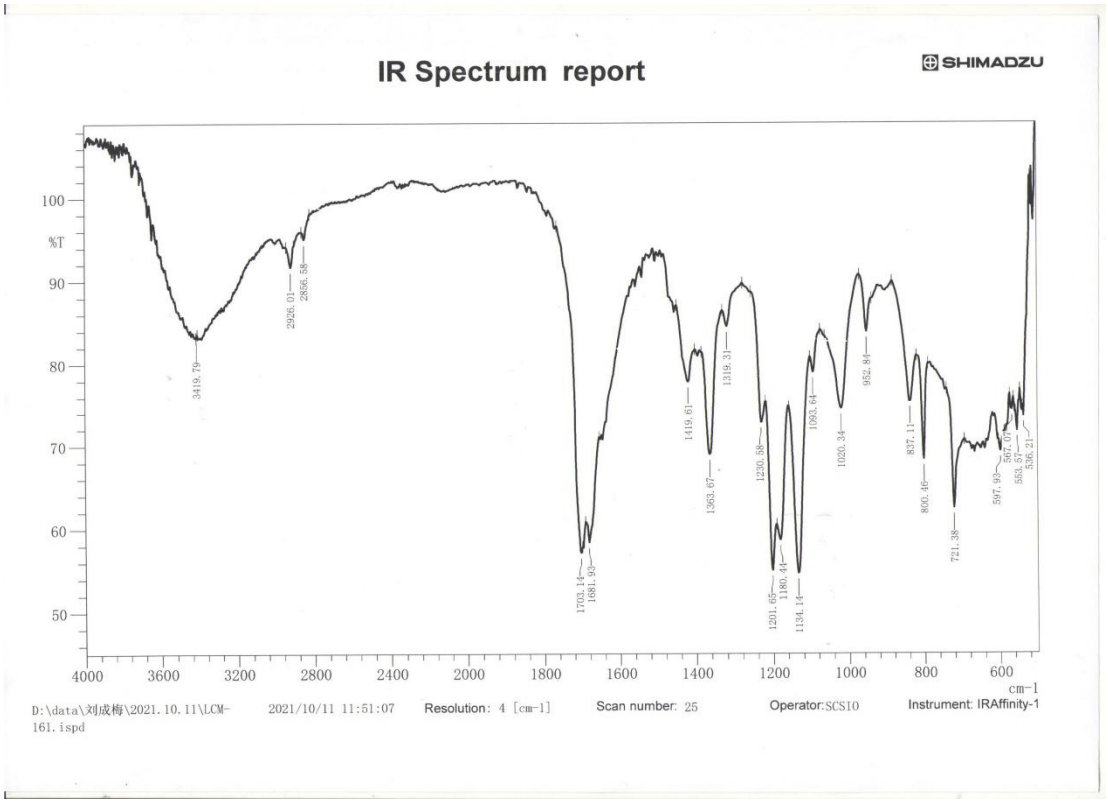



**Figure S46**. IR spectrum of **6**

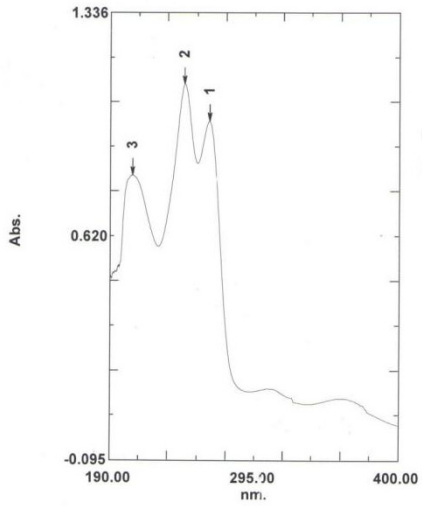



**Figure S47**. UV spectrum of **6**

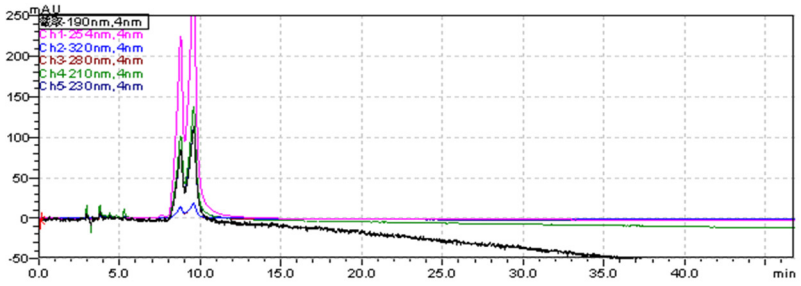



**Figure S48**. Chirality analysis of compound **6**

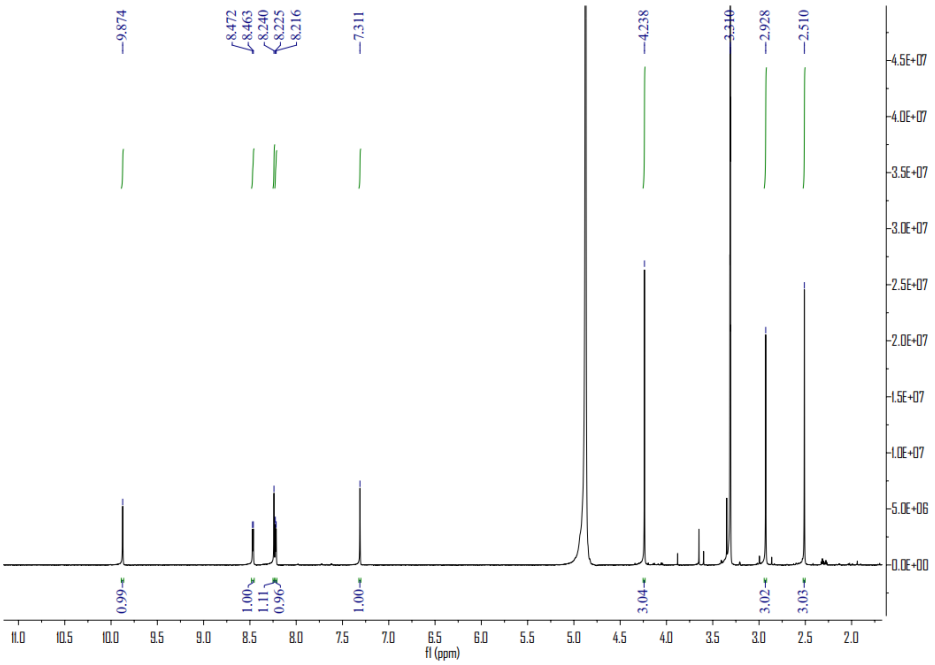



**Figure S49**. $^{1}$H NMR spectrum of **7** in methanol-$d_4$

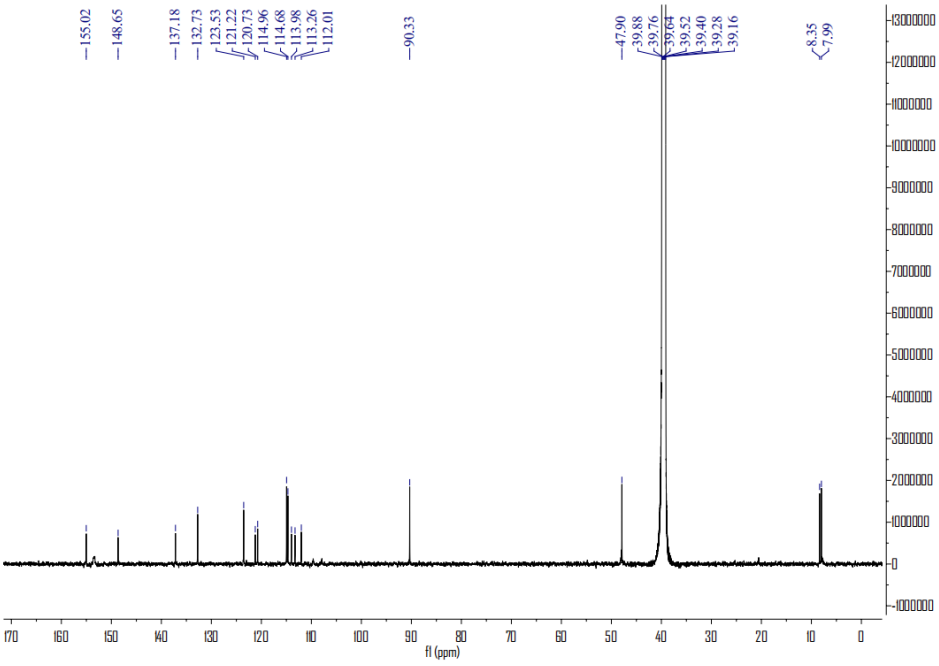



**Figure S50**. $^{13}$C NMR spectrum of **7** in methanol-$d_4$

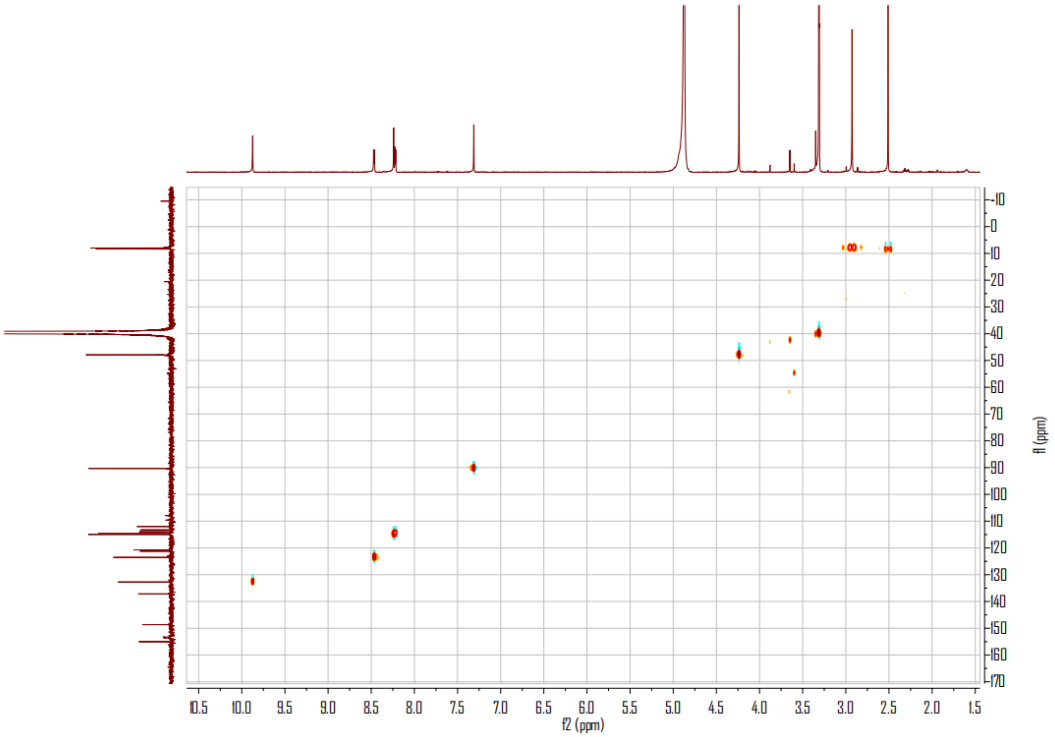



**Figure S51**. HSQC spectrum of **7** in methanol-$d_4$

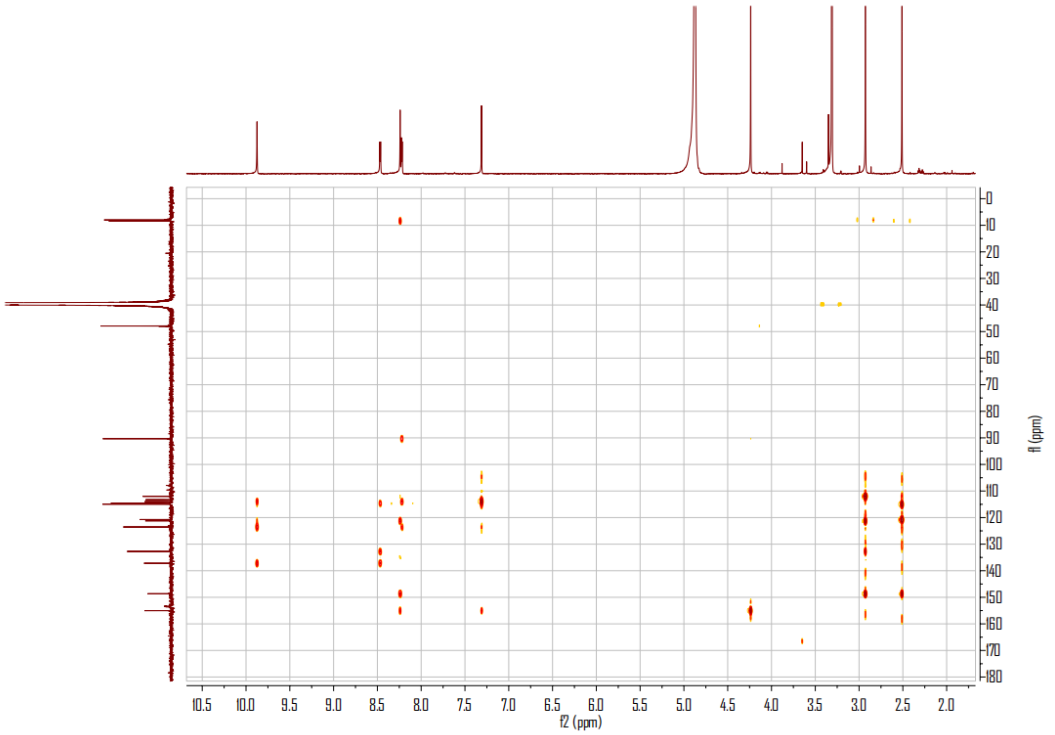



**Figure S52**. HMBC spectrum of **7** in methanol-$d_4$

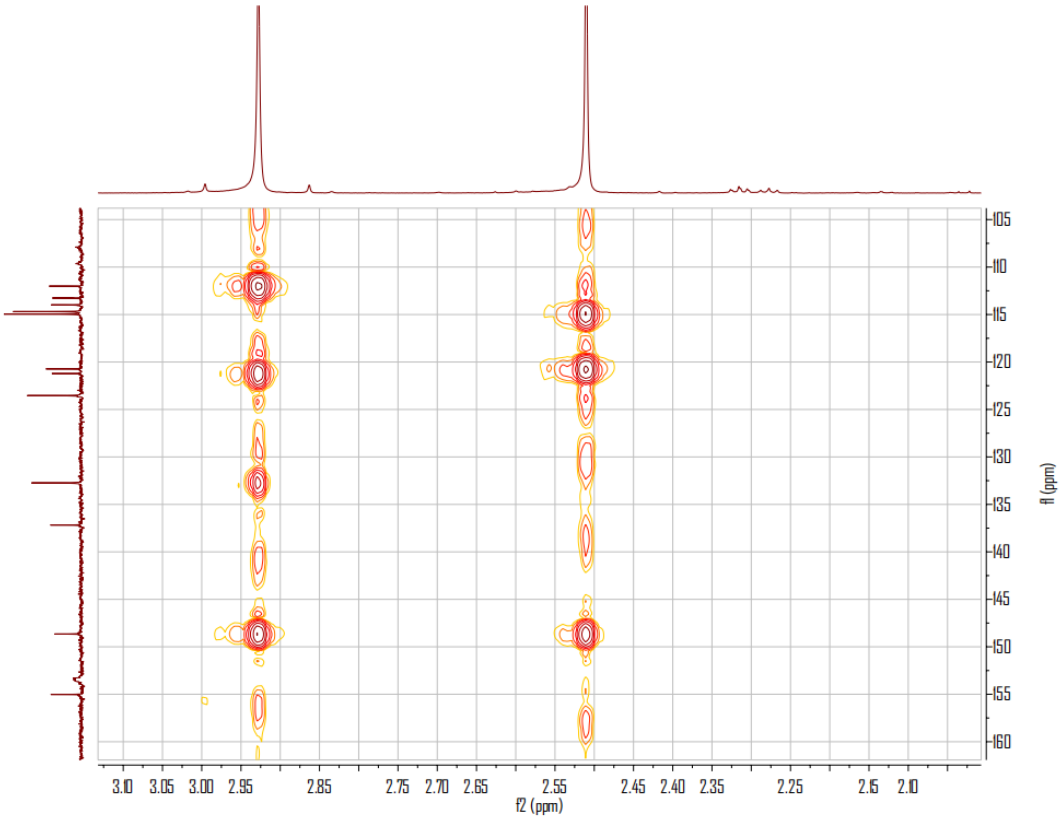



**Figure S53**. Partial HMBC spectrum of **7** in methanol-$d_4$

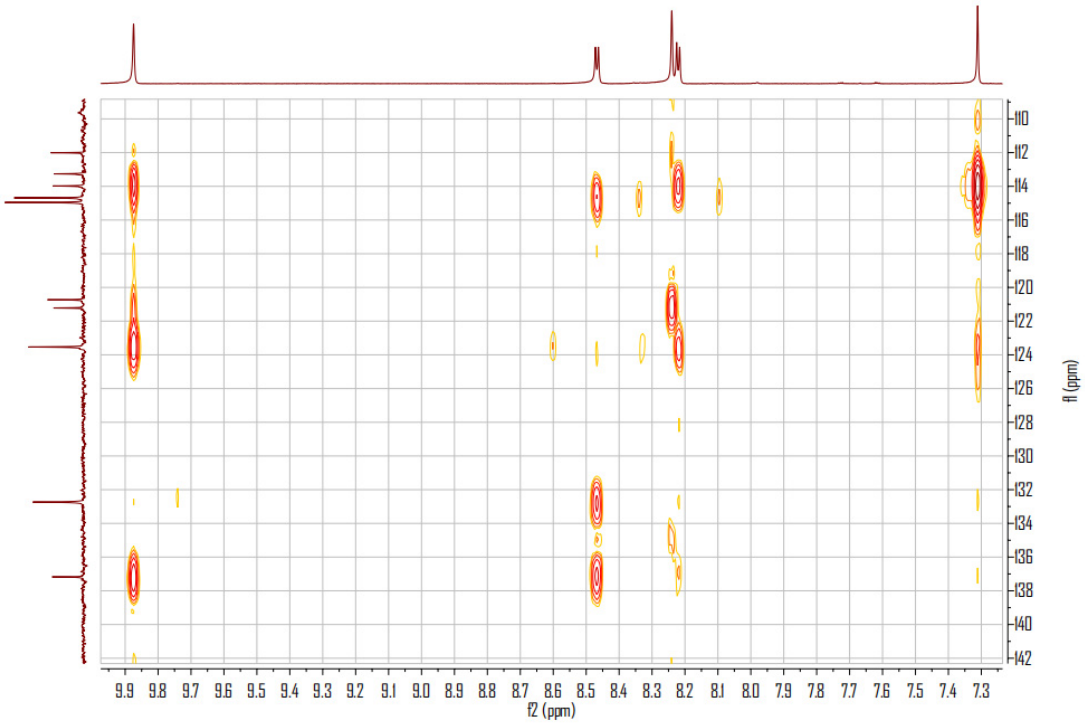



**Figure S54**. Partial HMBC spectrum of **7** in methanol-$d_4$

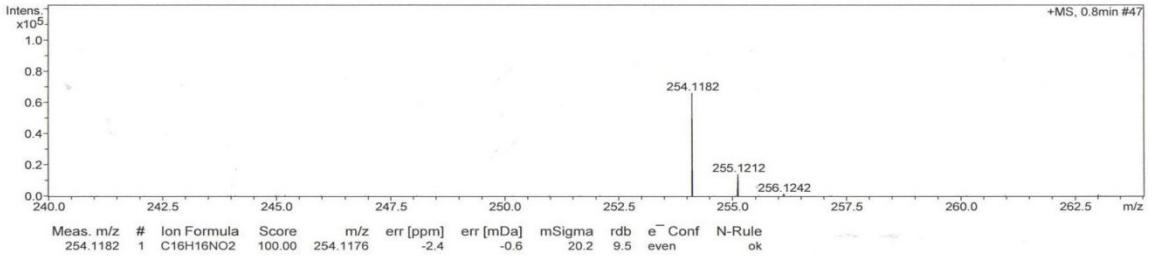



**Figure S55**. HRESIMS spectrum of **7**

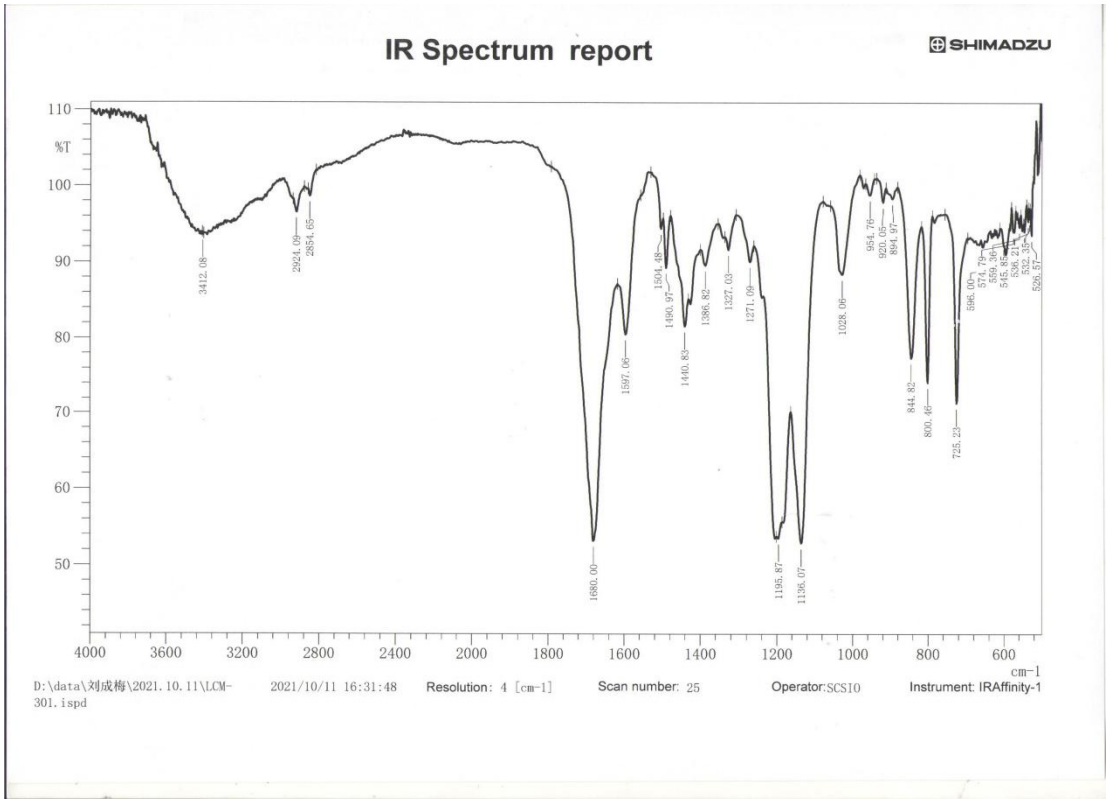



**Figure S56**. IR spectrum of **7**

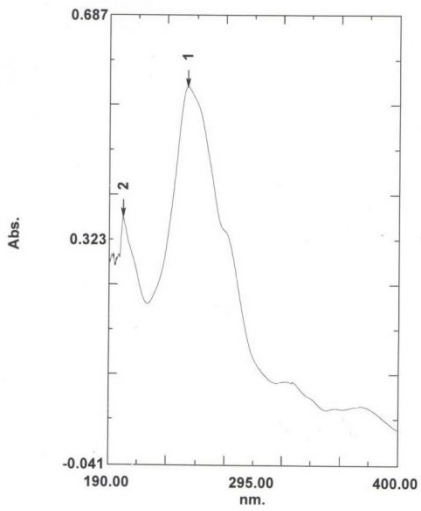



**Figure S57**. UV spectrum of **7**

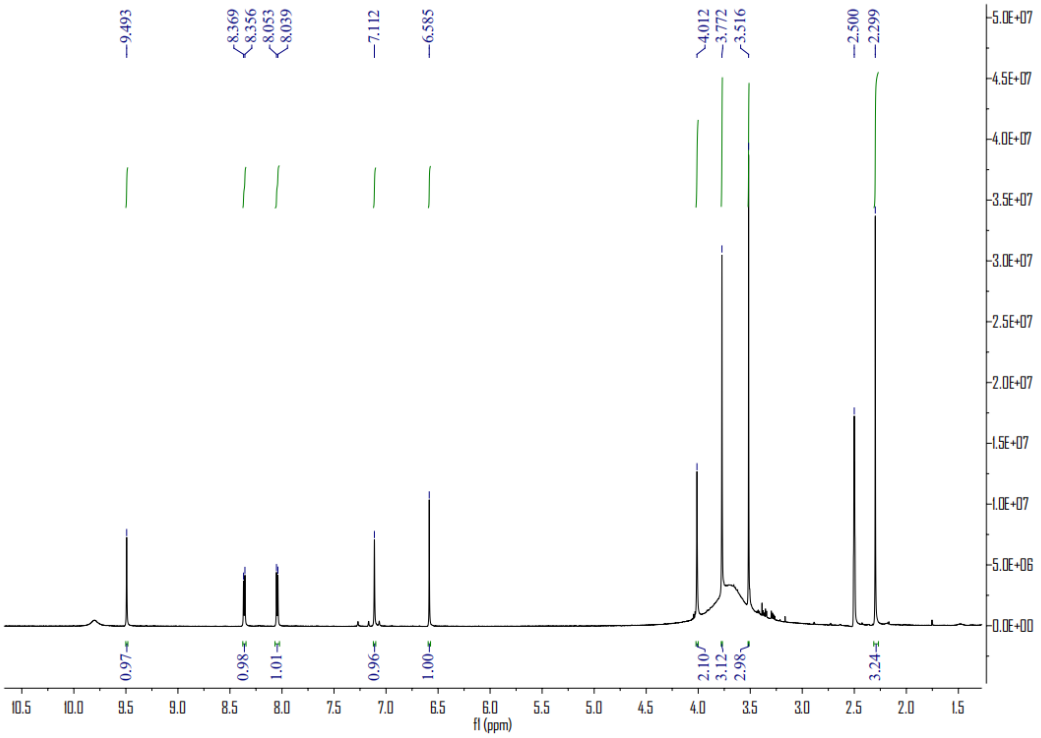



**Figure S58**. $^{1}$H NMR spectrum of **8** in DMSO-$d_6$

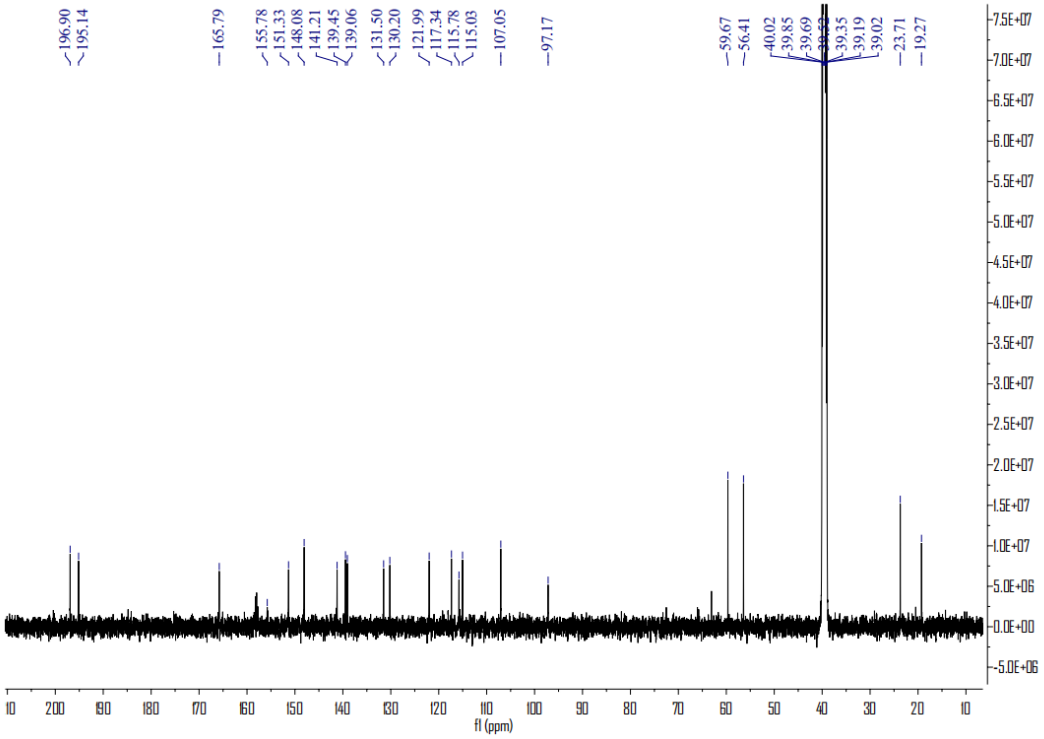



**Figure S59**. $^{13}$C NMR spectrum of **8** in DMSO-$d_6$

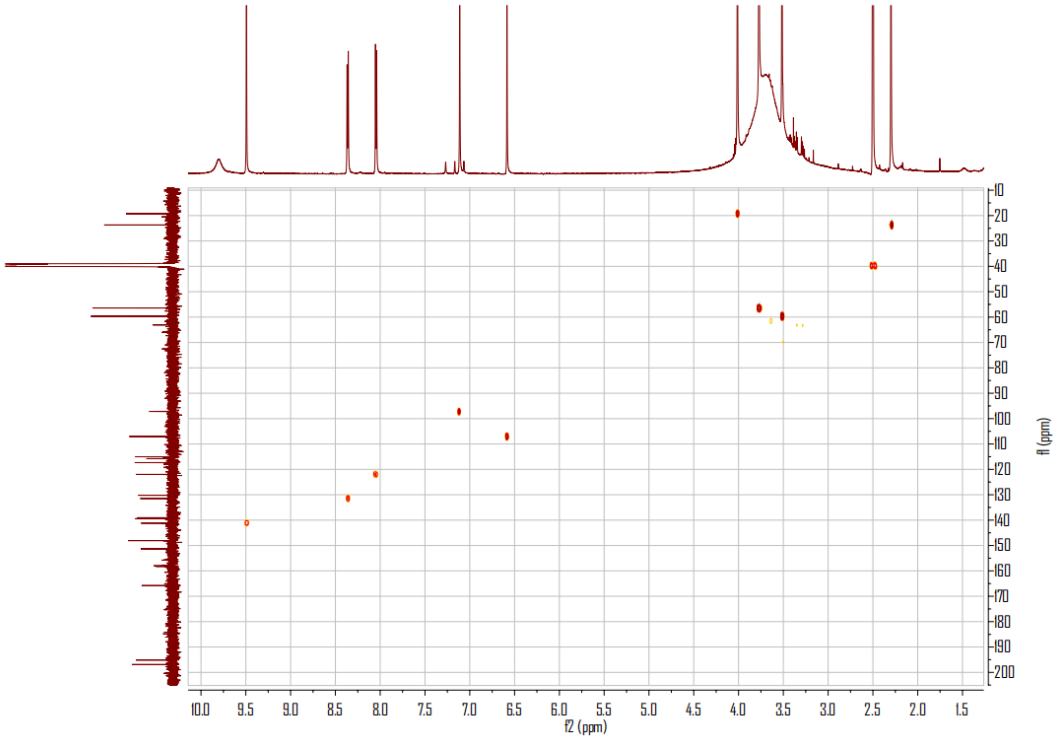



**Figure S60**. HSQC spectrum of **8** in DMSO-$d_6$

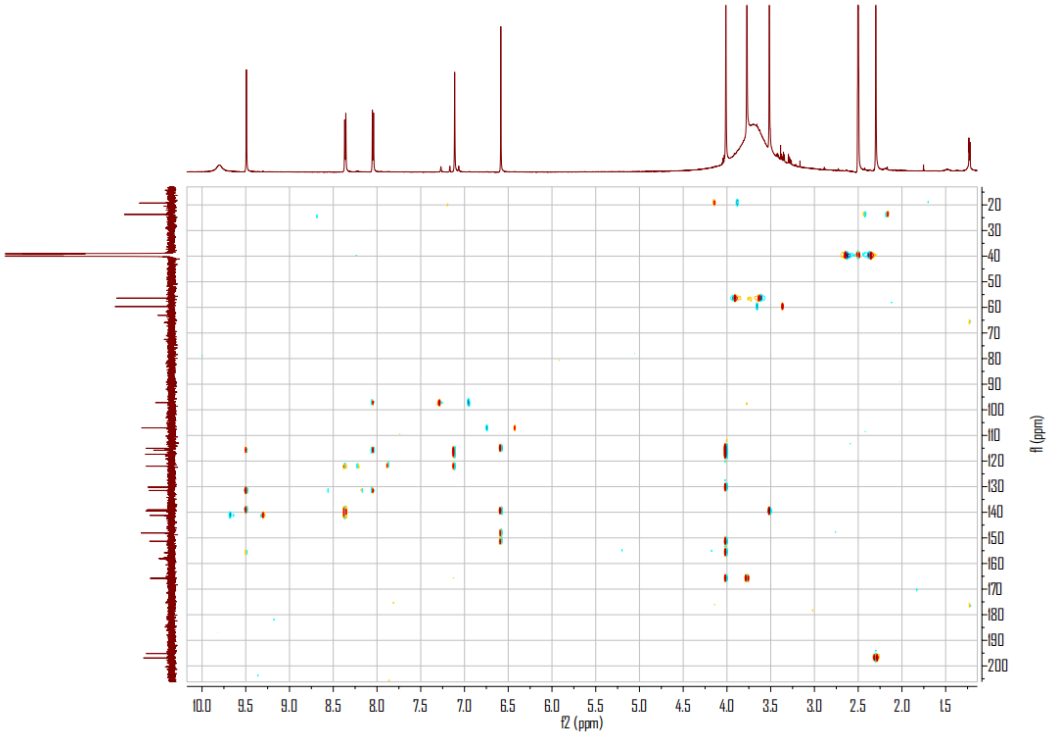



**Figure S61**. HMBC spectrum of **8** in DMSO-$d_6$

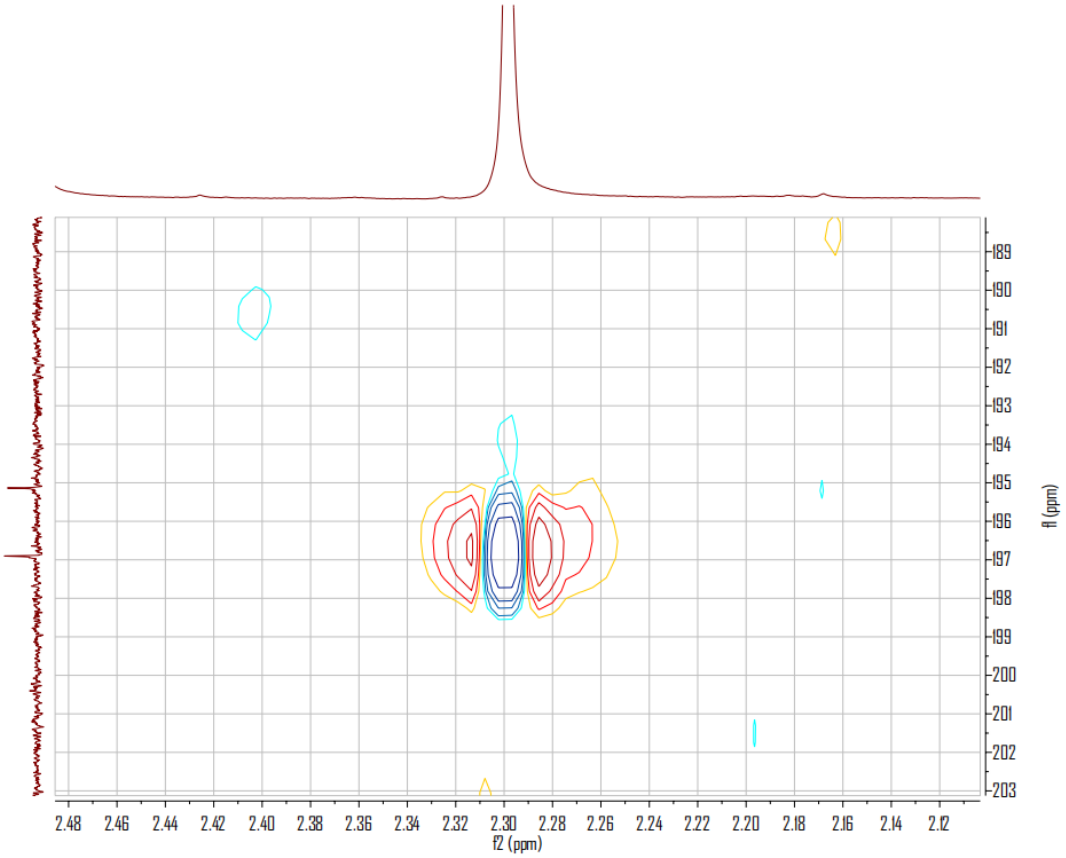



**Figure S62**. Partial HMBC spectrum of **8** in DMSO-$d_6$

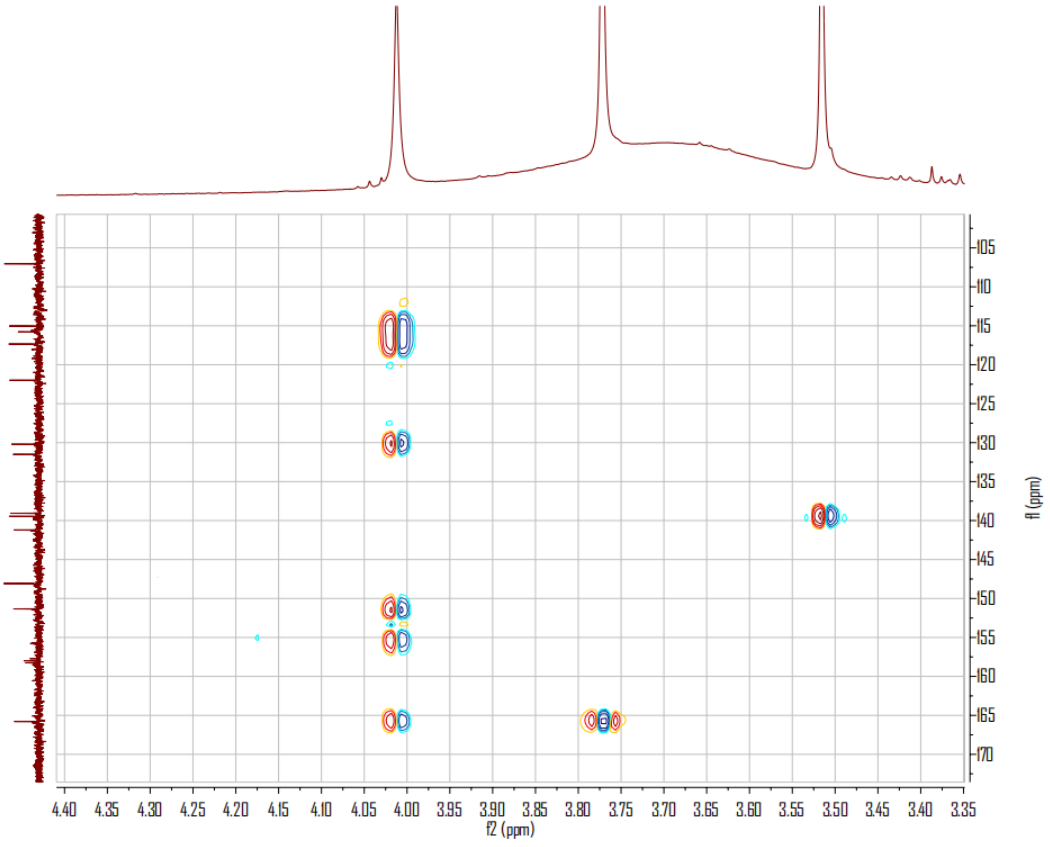



**Figure S63**. Partial HMBC spectrum of **8** in DMSO-$d_6$

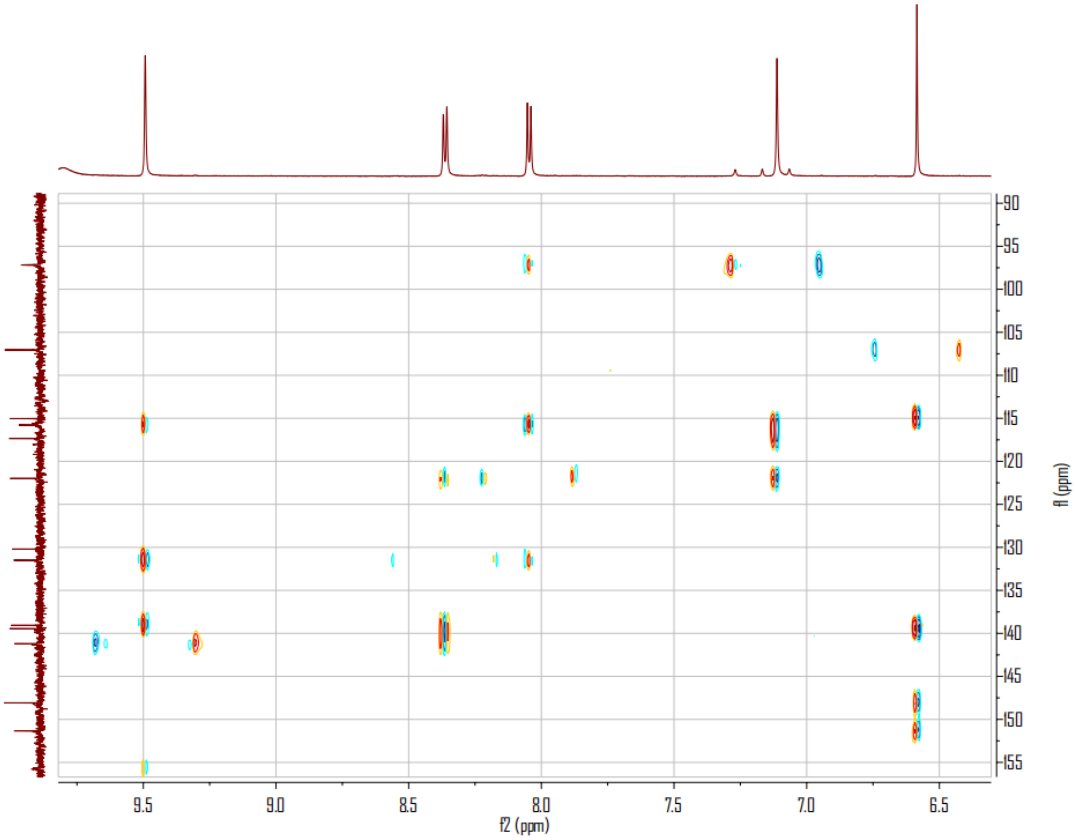



**Figure S64**. Partial HMBC spectrum of **8** in DMSO-$d_6$

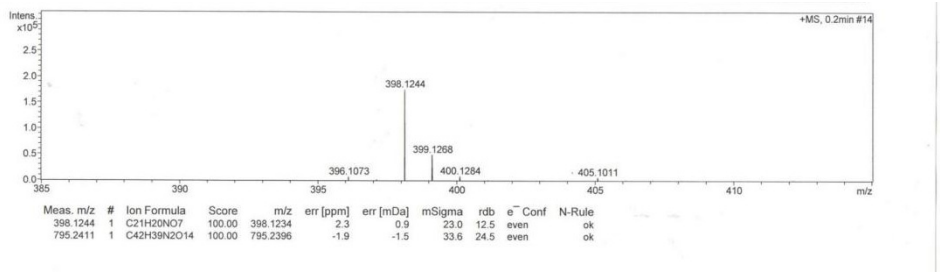



**Figure S65**. HRESIMS spectrum of **8**

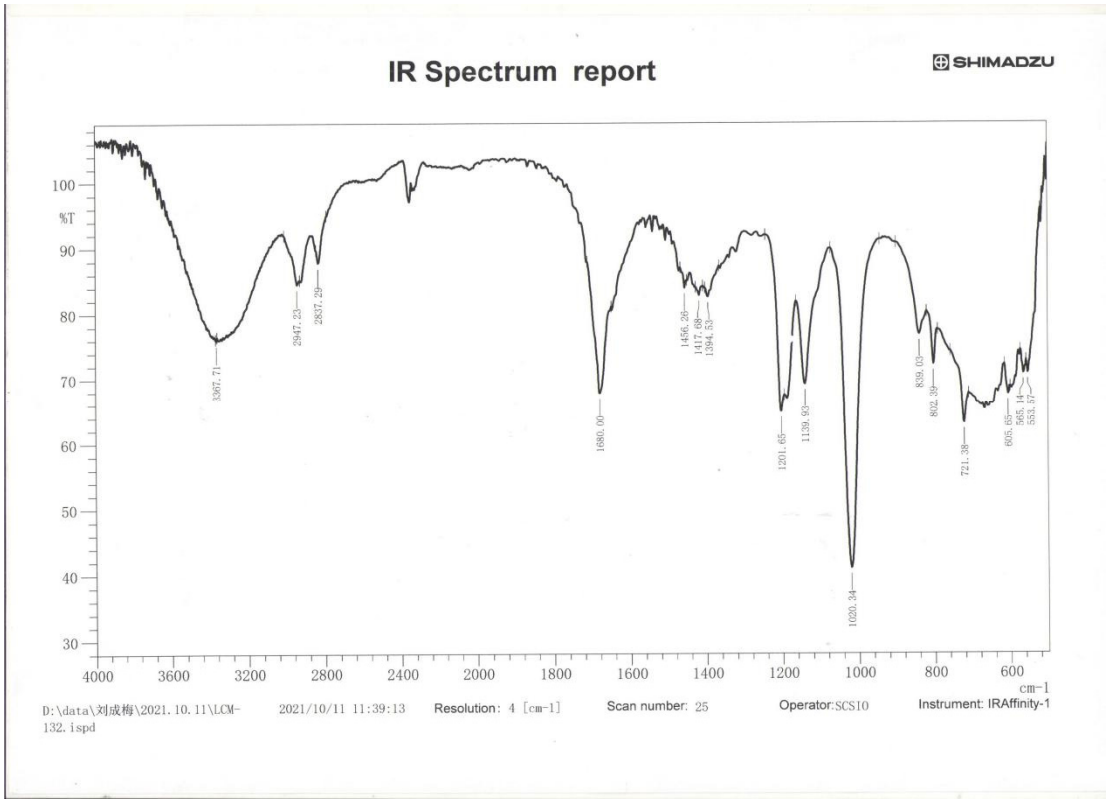



**Figure S66**. IR spectrum of **8**

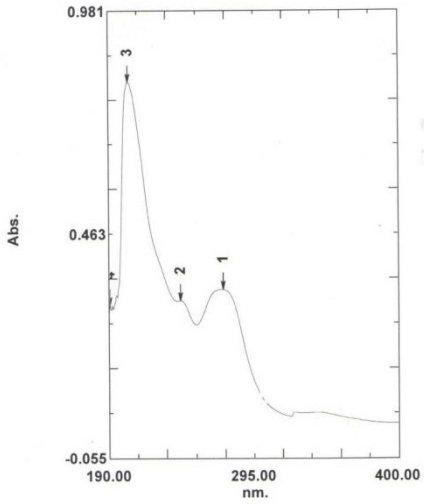



**Figure S67**. UV spectrum of **8**

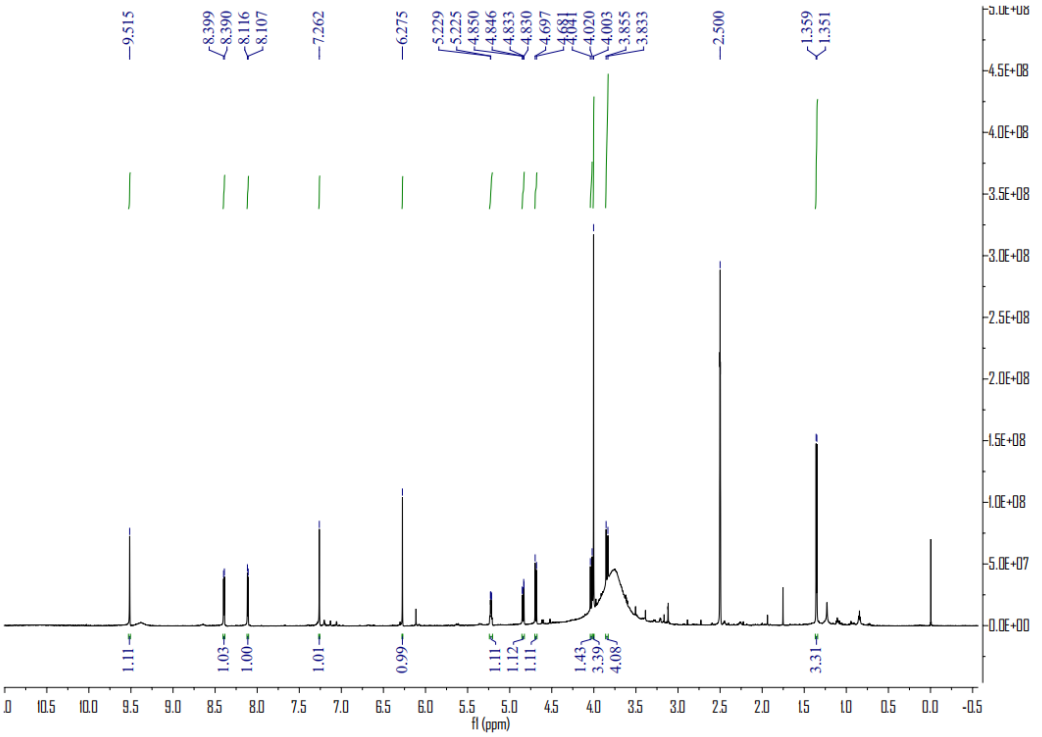



**Figure S68**. $^{1}$H NMR spectrum of **9** in DMSO-$d_6$

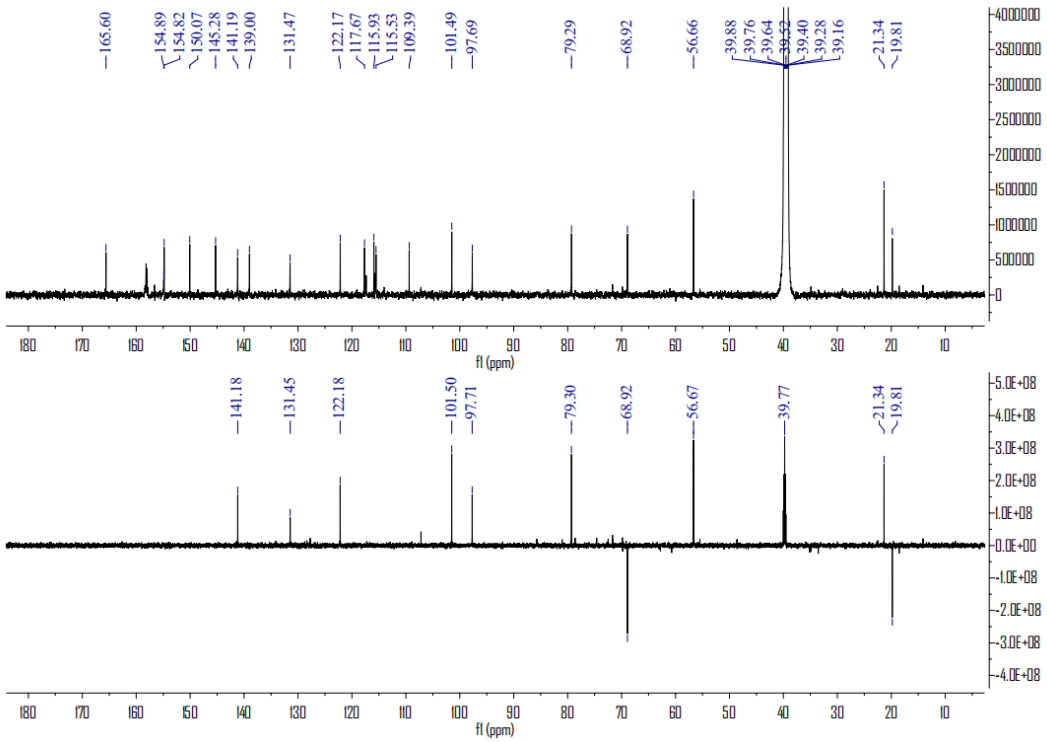



**Figure S69**. $^{13}$C and DEPT135 NMR spectra of **9** in DMSO-$d_6$

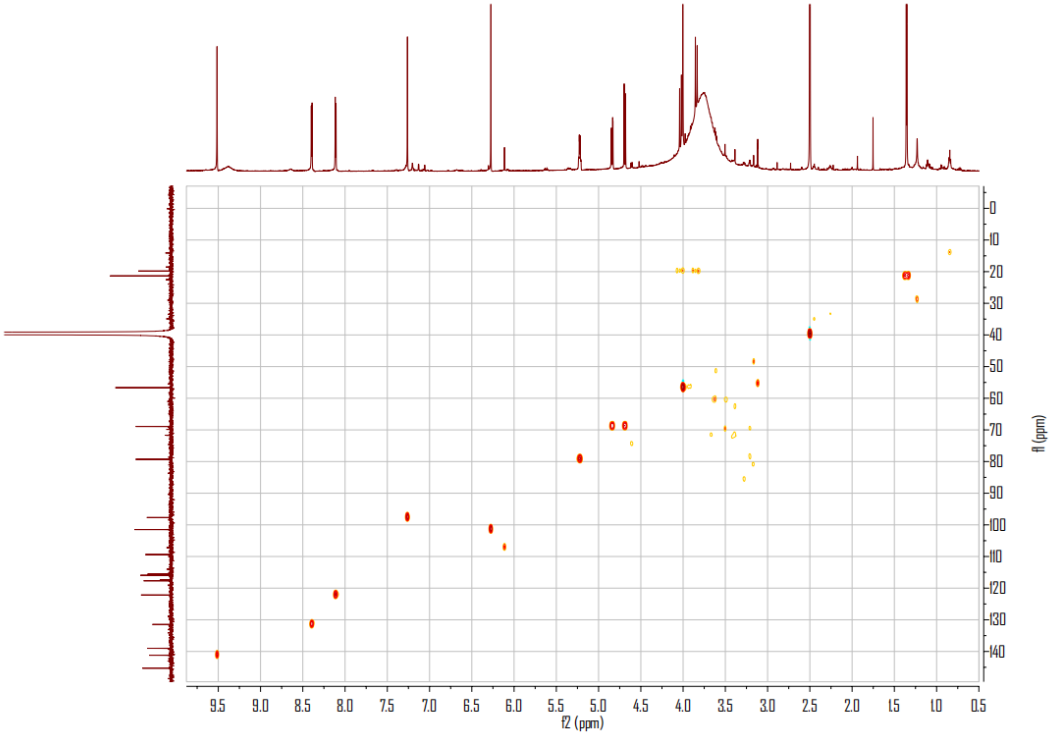



**Figure S70**. HSQC spectrum of **9** in DMSO-$d_6$

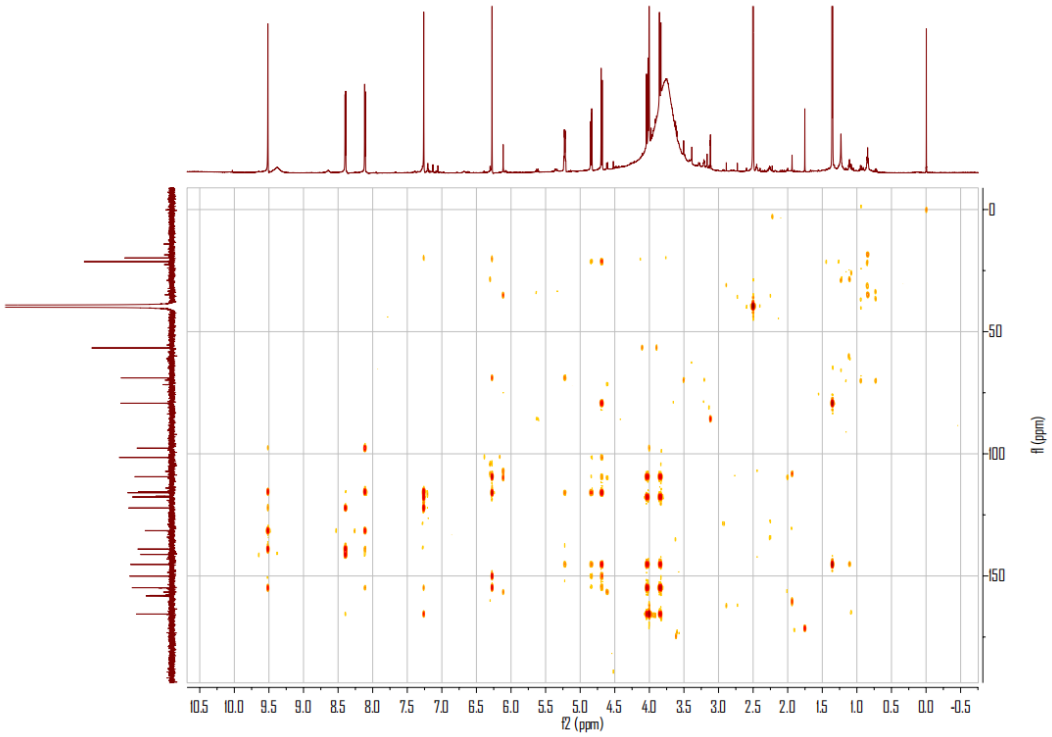



**Figure S71**. HMBC spectrum of **9** in DMSO-$d_6$

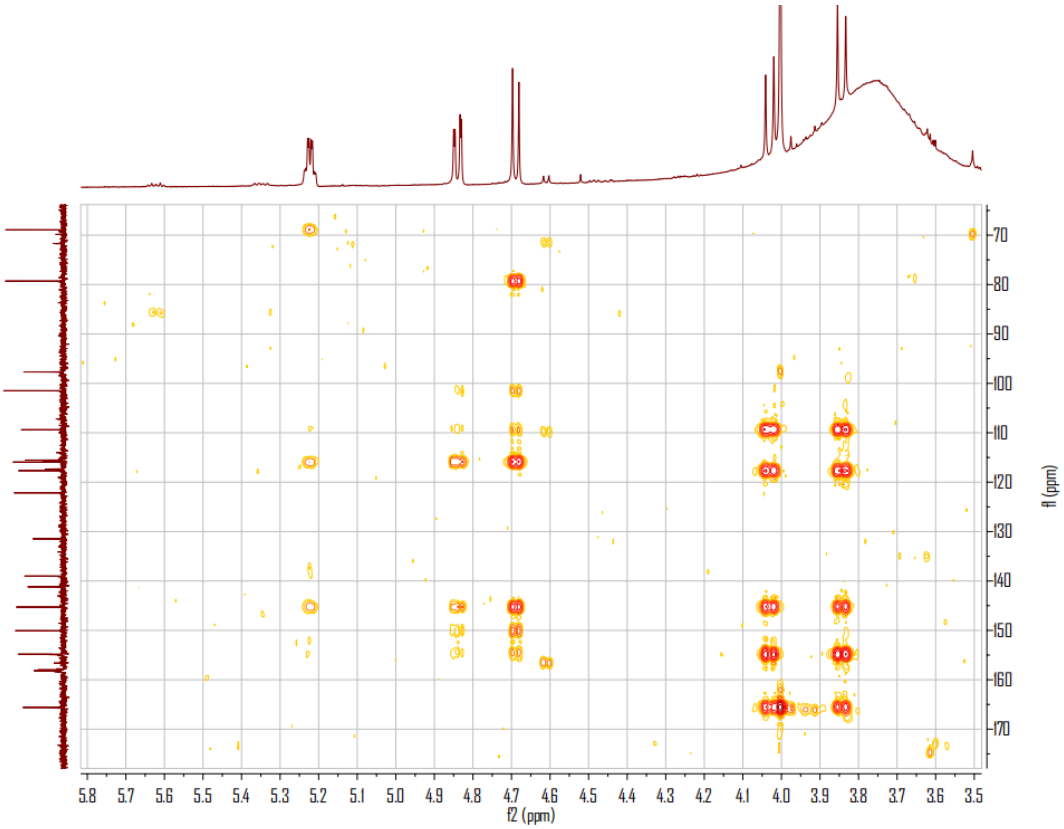



**Figure S72**. Partial HMBC spectrum of **9** in DMSO-$d_6$

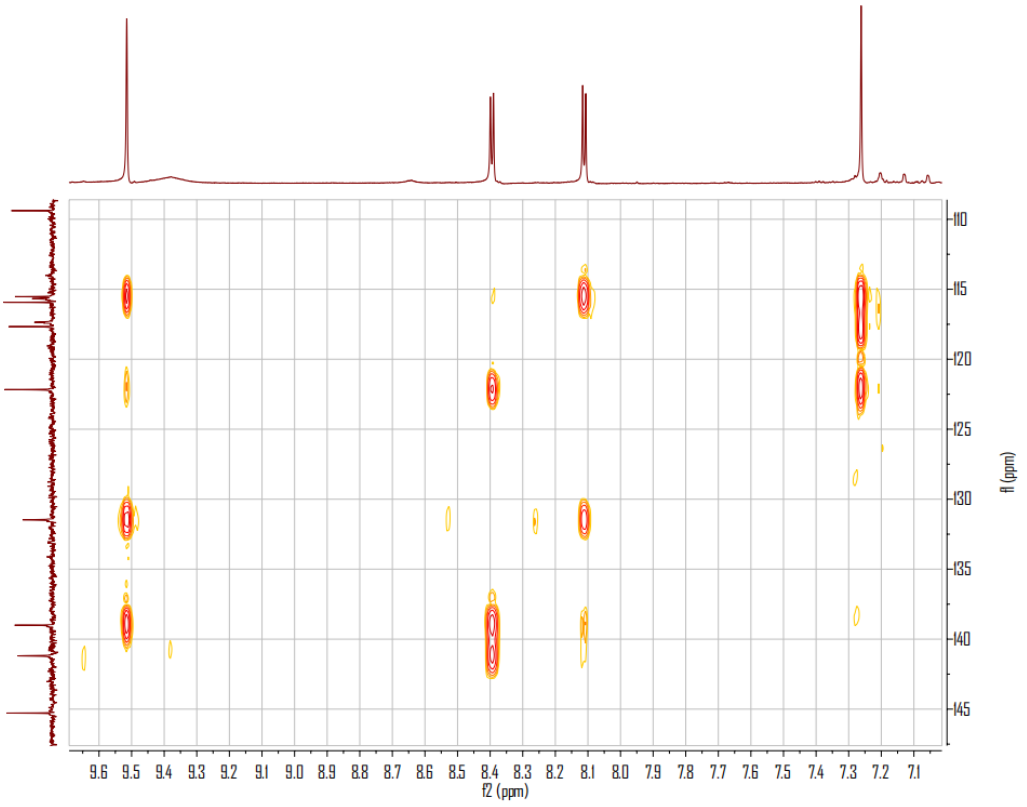



**Figure S73**. Partial HMBC spectrum of **9** in DMSO-$d_6$

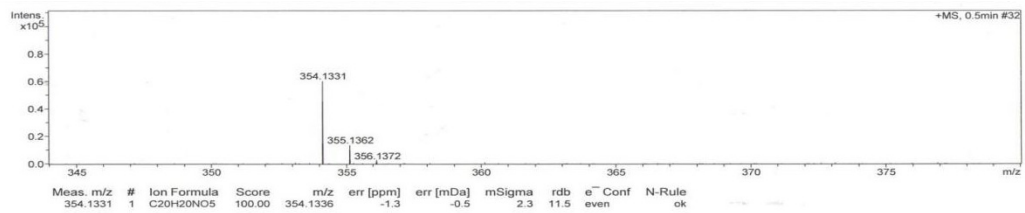



**Figure S74**. HRESIMS spectrum of **9**

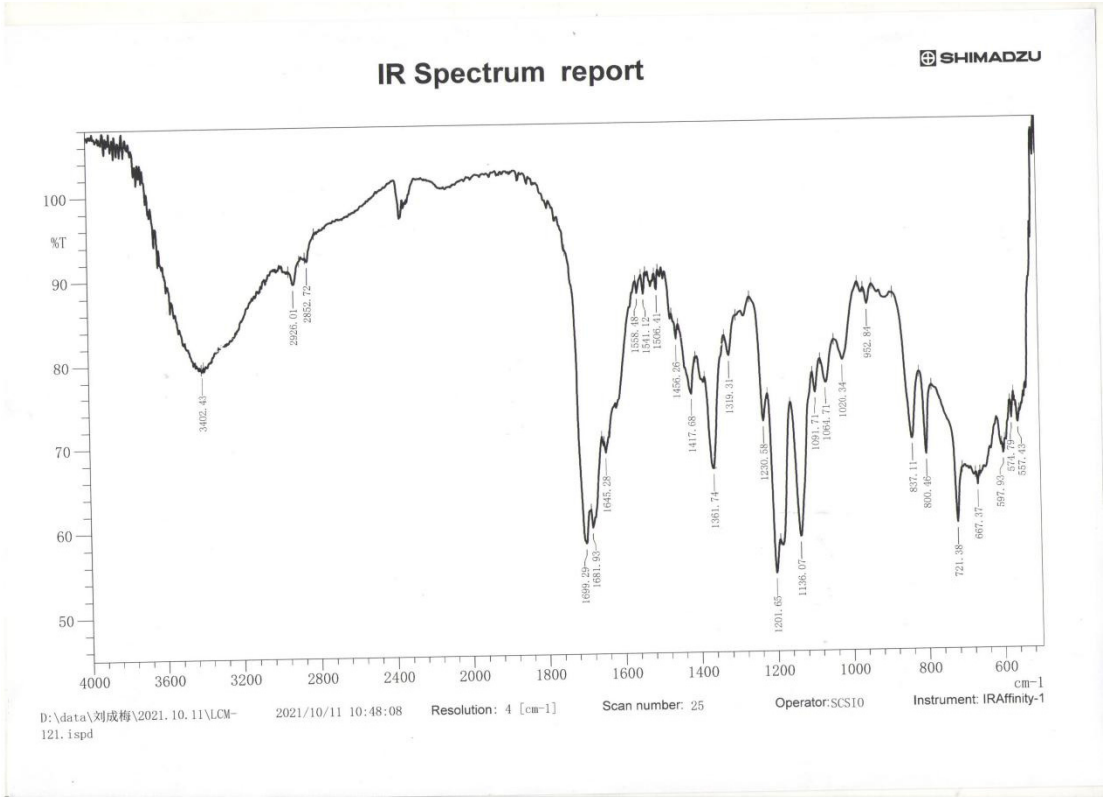



**Figure S75**. IR spectrum of **9**

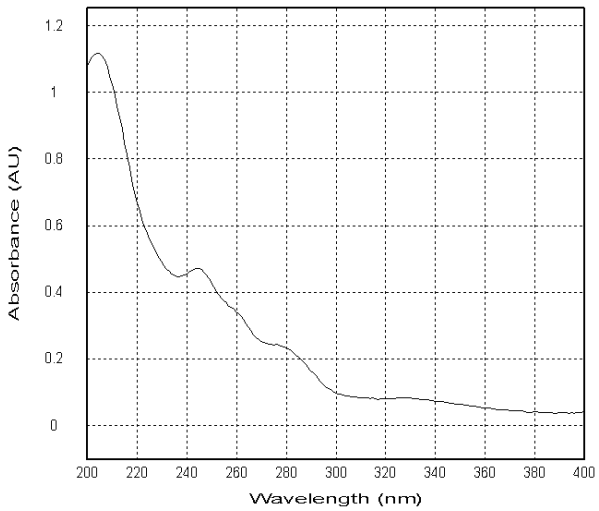



**Figure S76**. UV spectrum of **9**

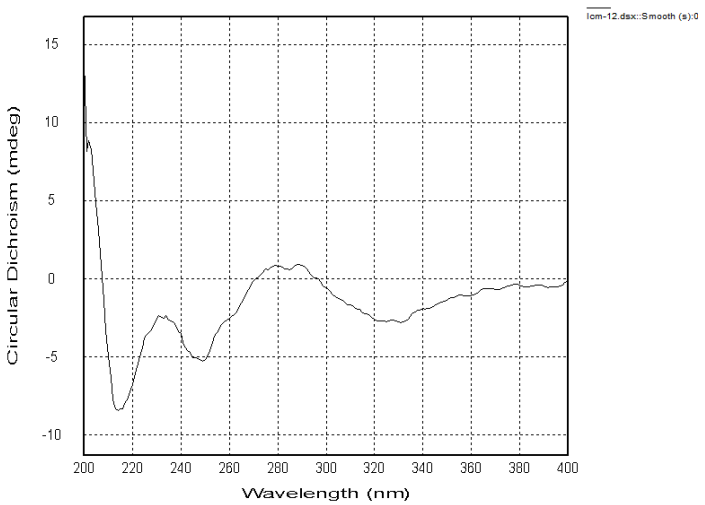



**Figure S77**. CD spectrum of **9** in methanol

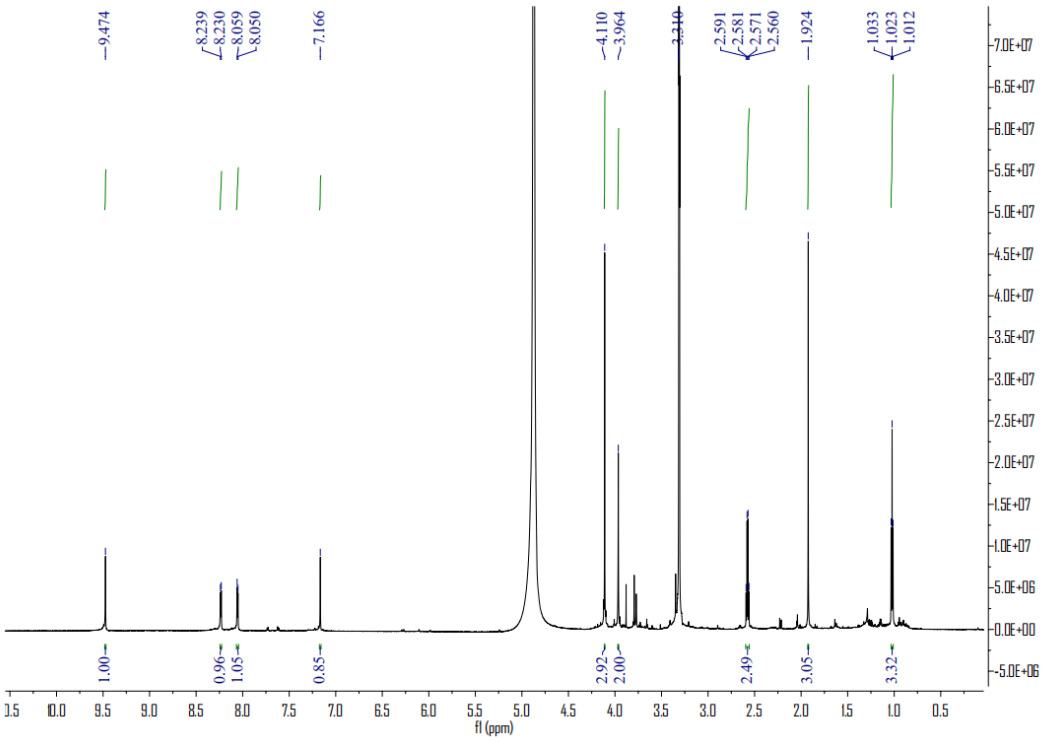



**Figure S78**. $^{1}$H NMR spectrum of **10** in methanol-$d_4$

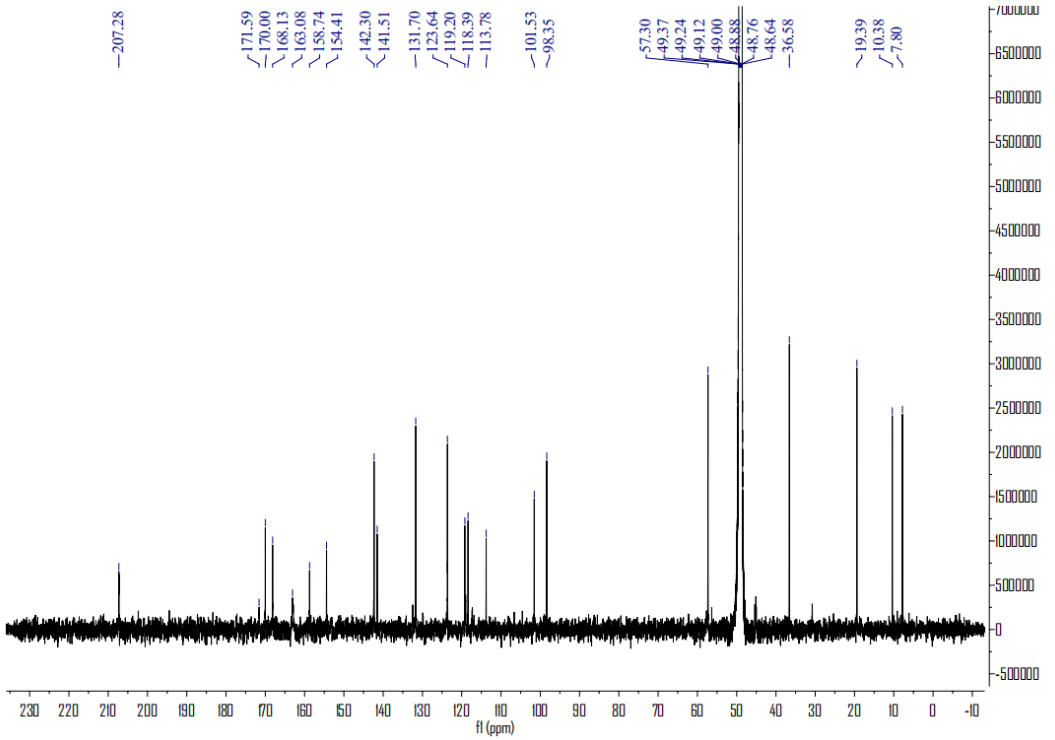



**Figure S79**. $^{13}$C NMR spectrum of **10** in methanol-$d_4$

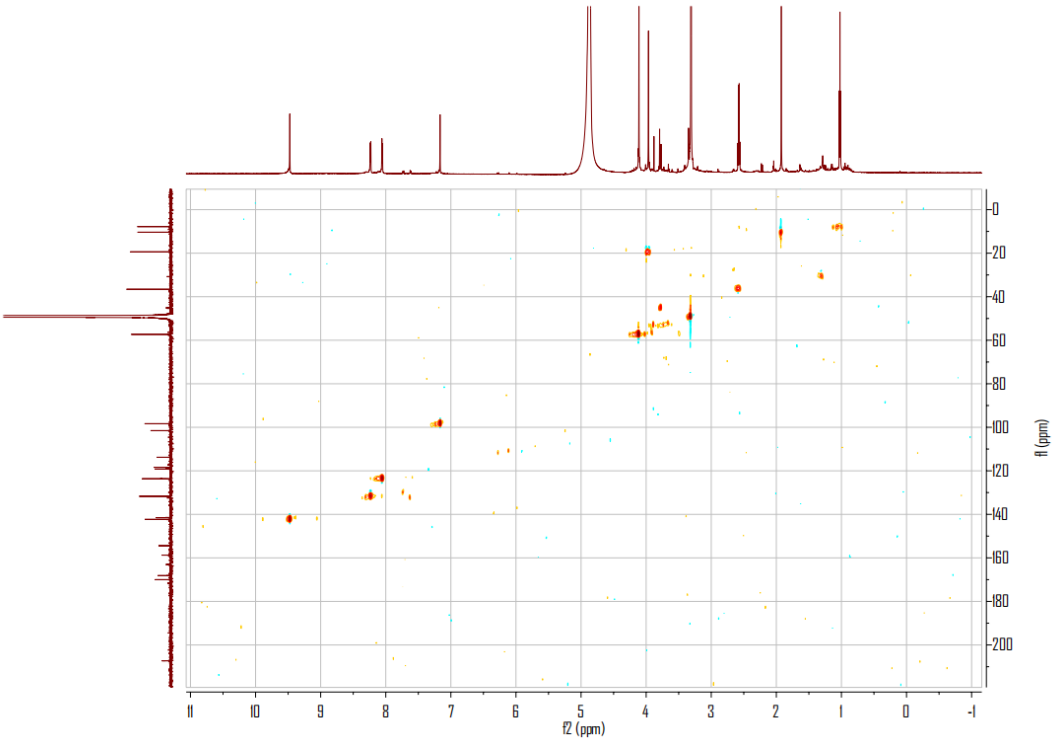



**Figure S80**. HSQC spectrum of **10** in methanol-$d_4$

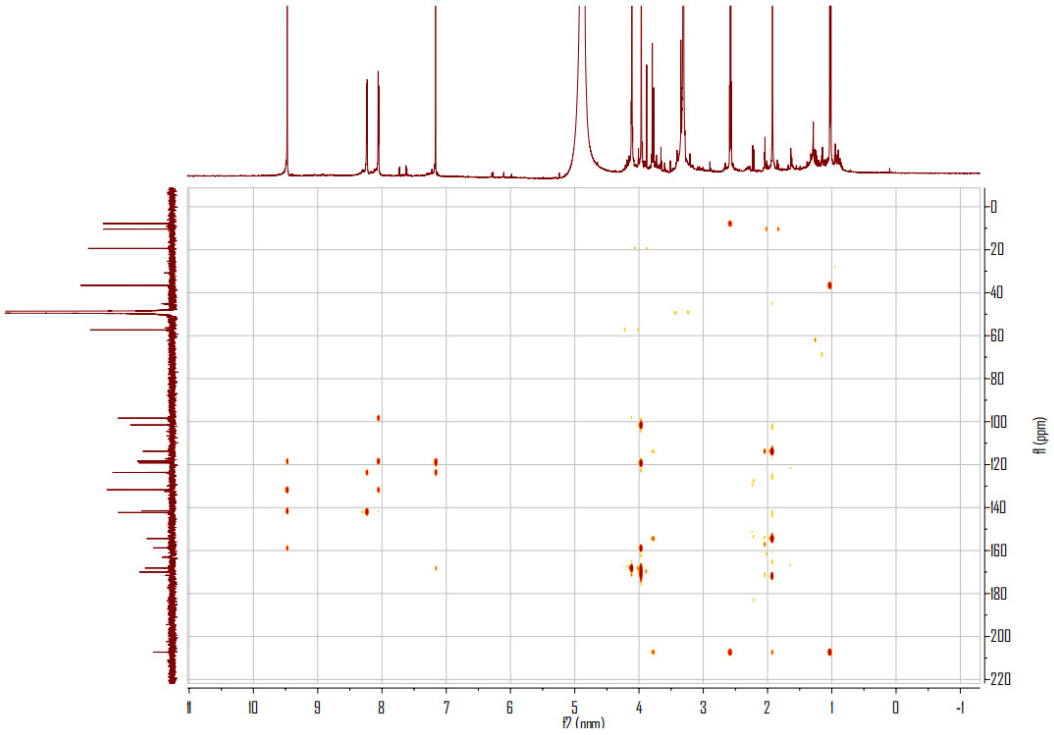



**Figure S81**. HMBC spectrum of **10** in methanol-$d_4$

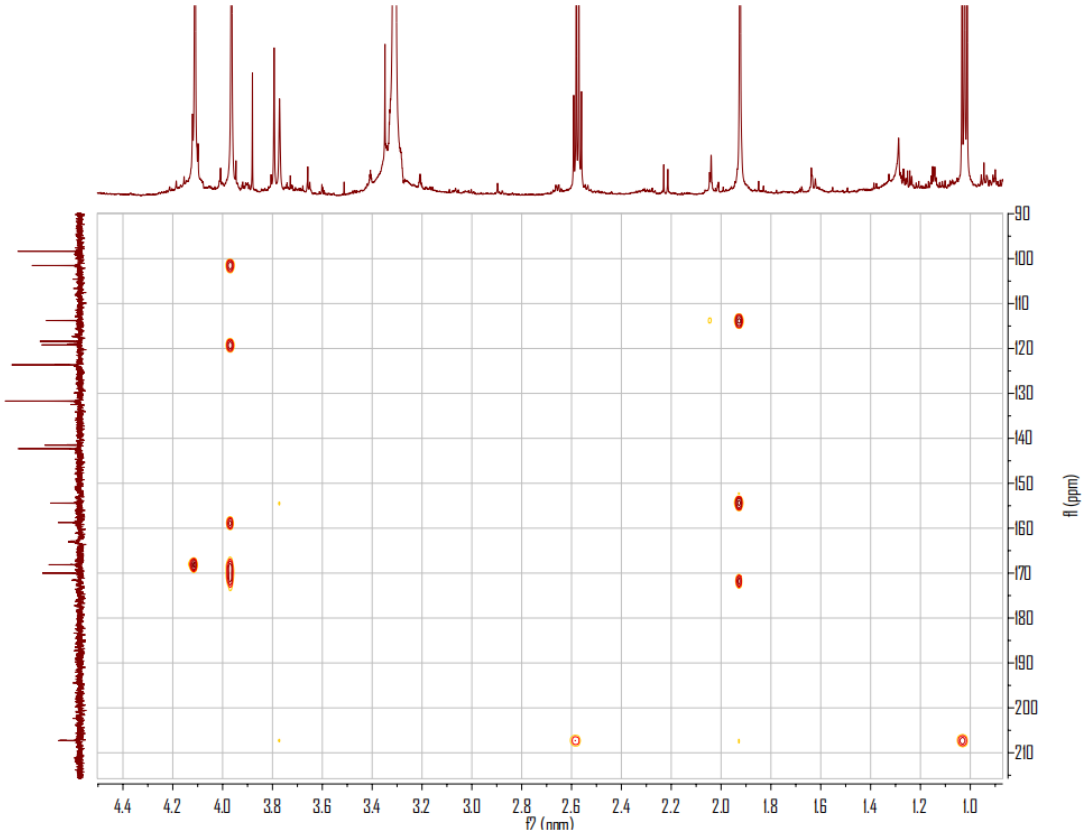



**Figure S82**. Partial HMBC spectrum of **10** in methanol-$d_4$

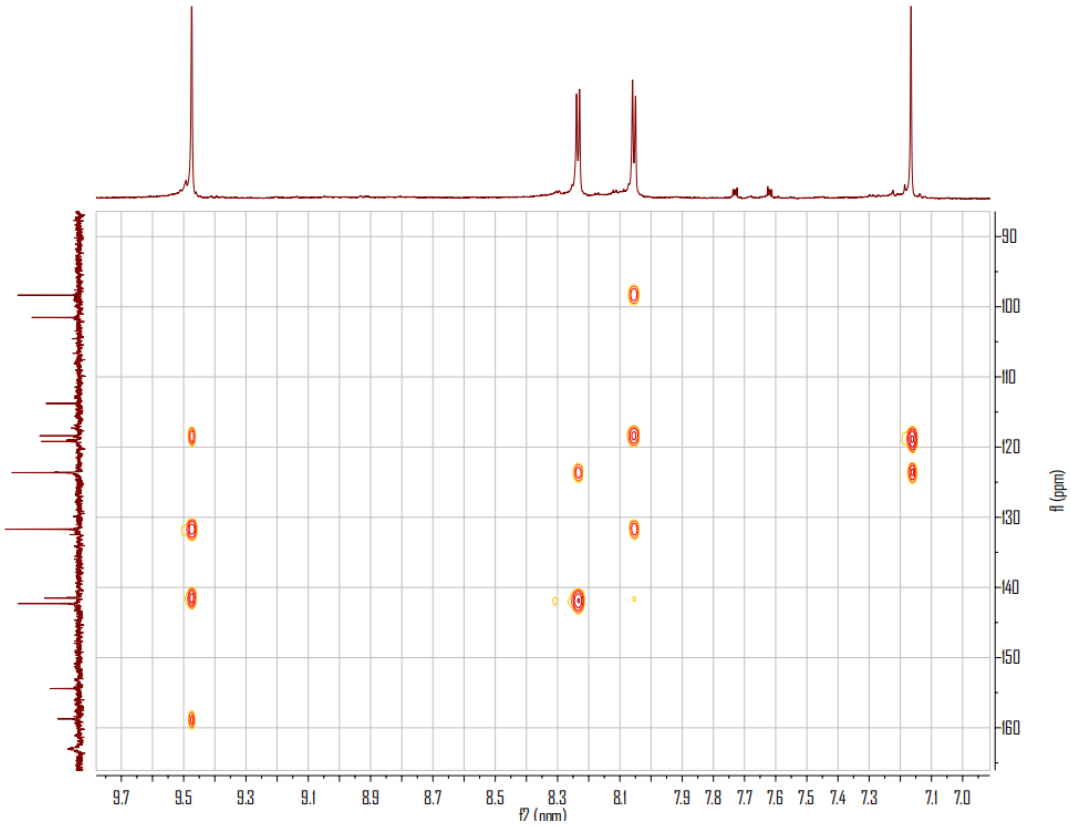



**Figure S83**. Partial HMBC spectrum of **10** in methanol-$d_4$

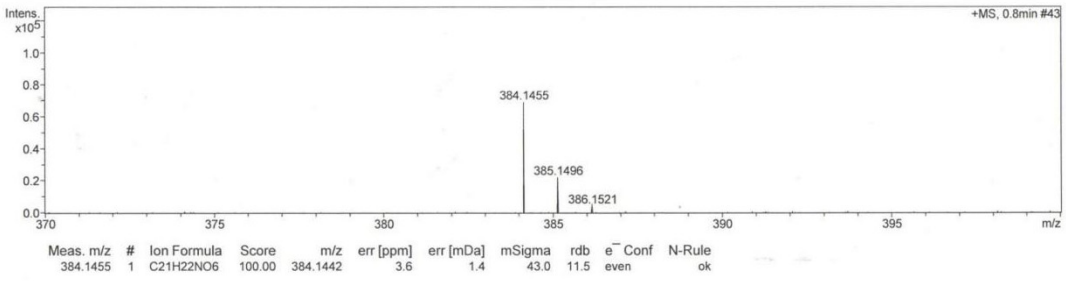



**Figure S84**. HRESIMS spectrum of **10**

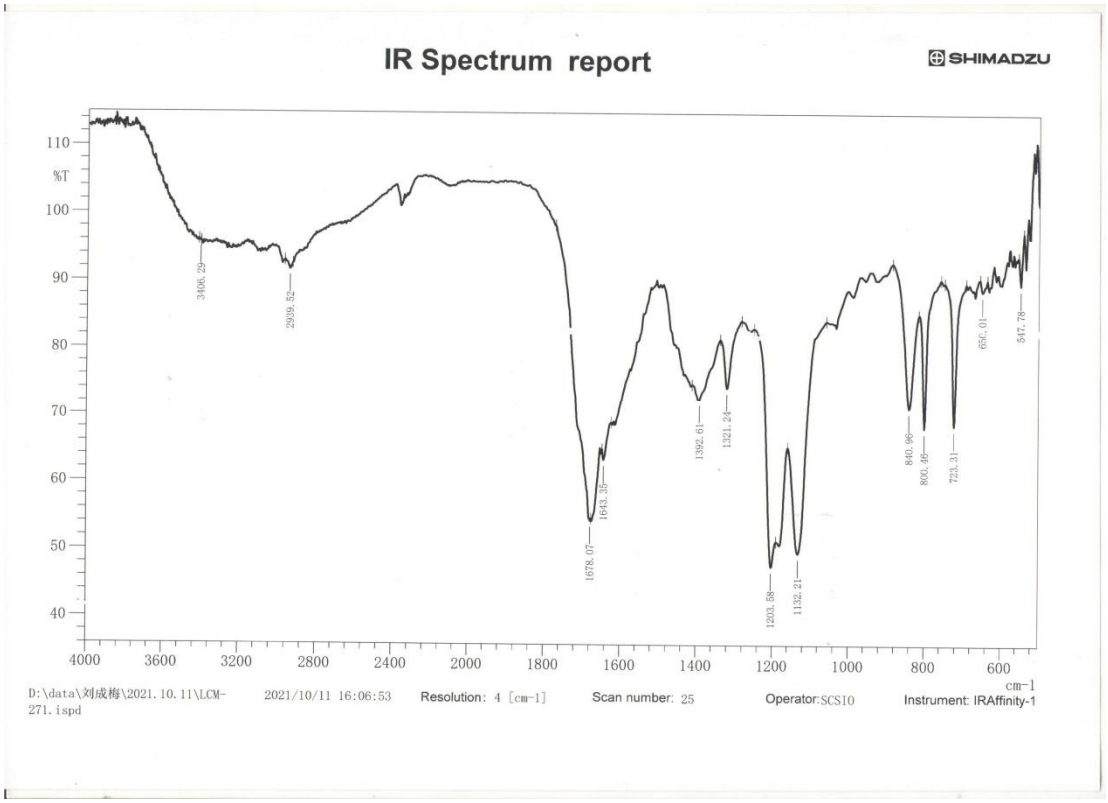



**Figure S85**. IR spectrum of **10**

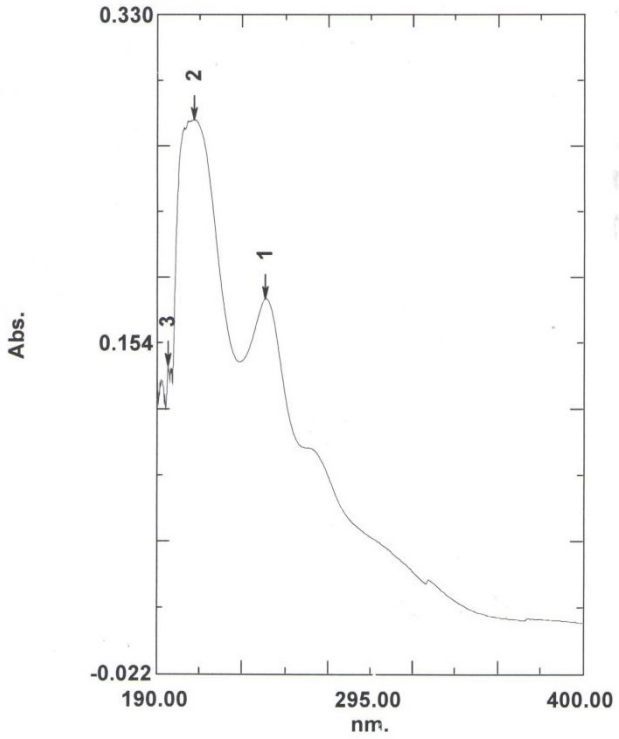



**Figure S86**. UV spectrum of **10**

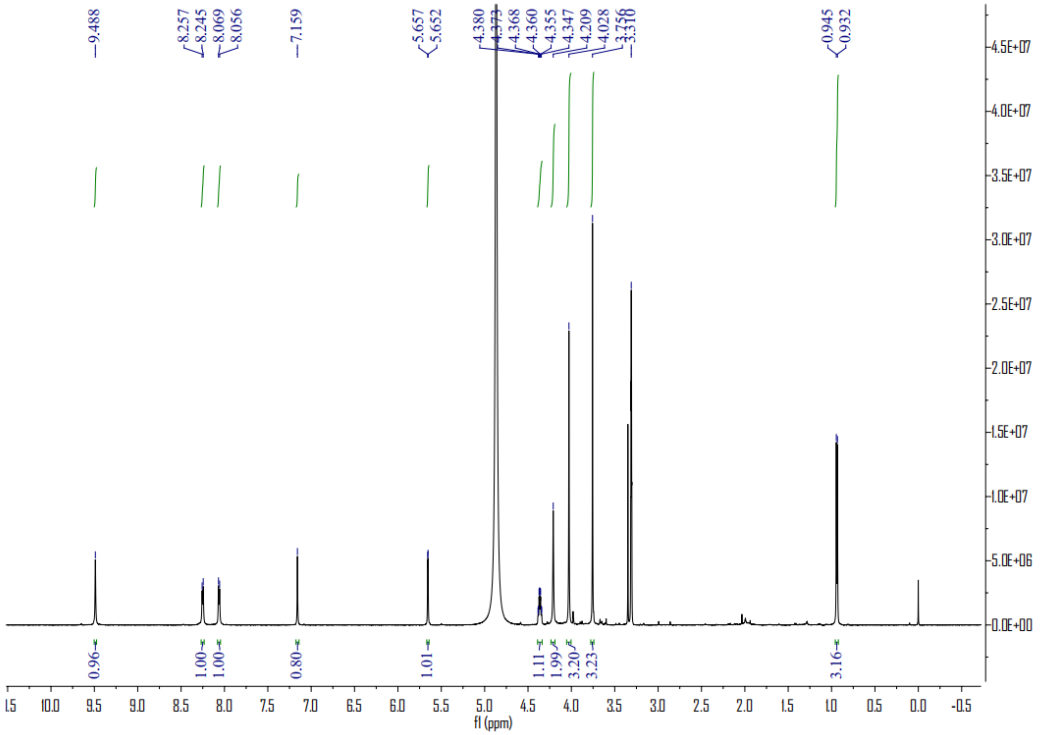



**Figure S87**. $^{1}$H NMR spectrum of **11** in methanol-$d_4$

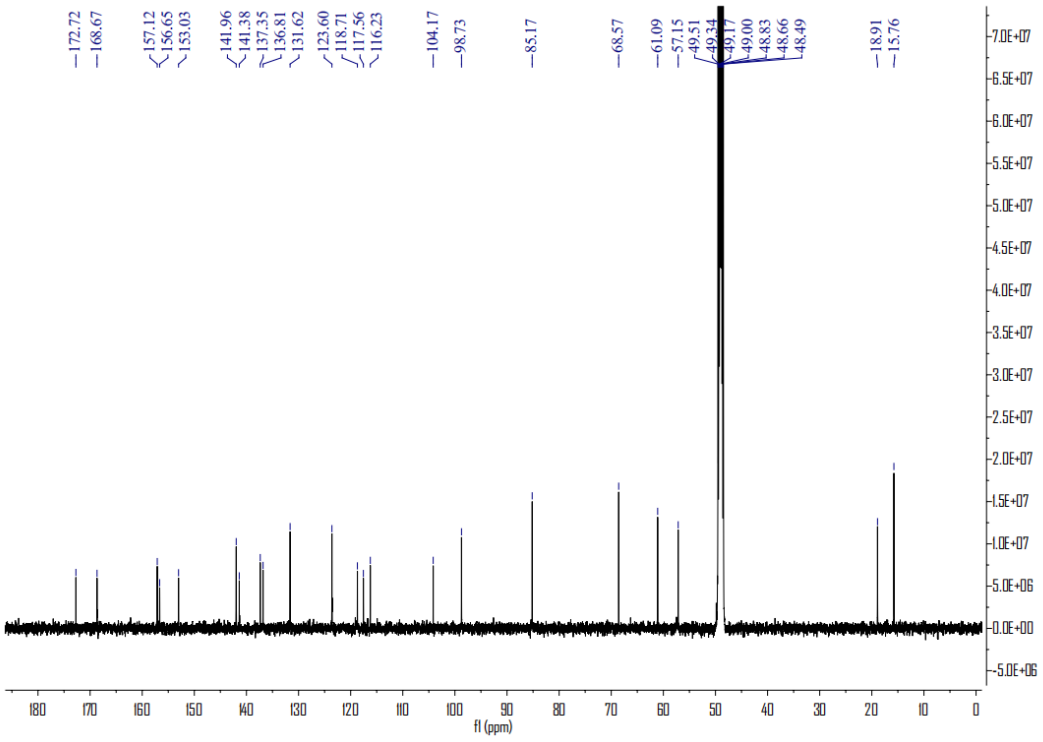



**Figure S88**. $^{13}$C NMR spectrum of **11** in methanol-$d_4$

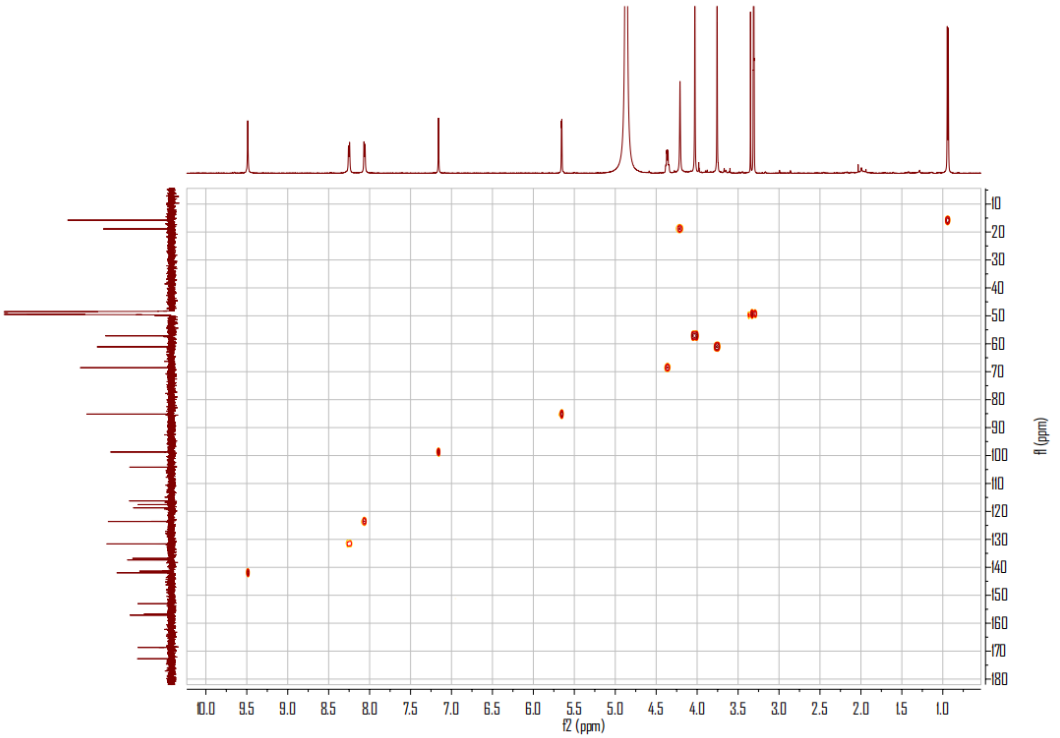



**Figure S89**. HSQC spectrum of **11** in methanol-$d_4$

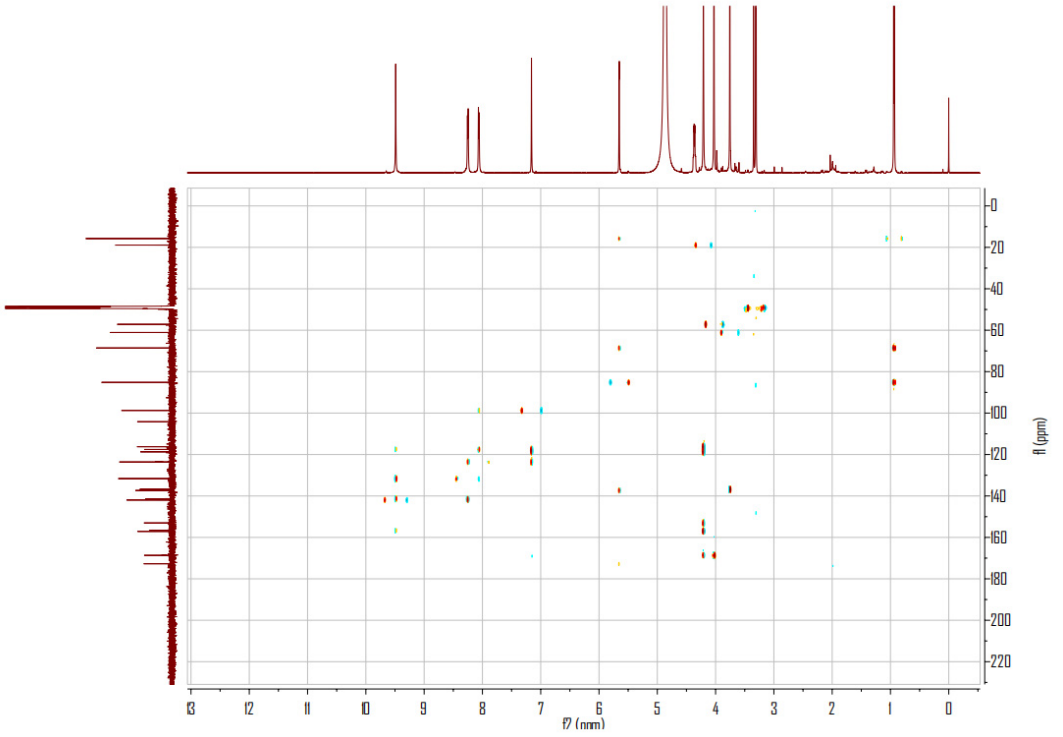



**Figure S90**. HMBC spectrum of **11** in methanol-$d_4$

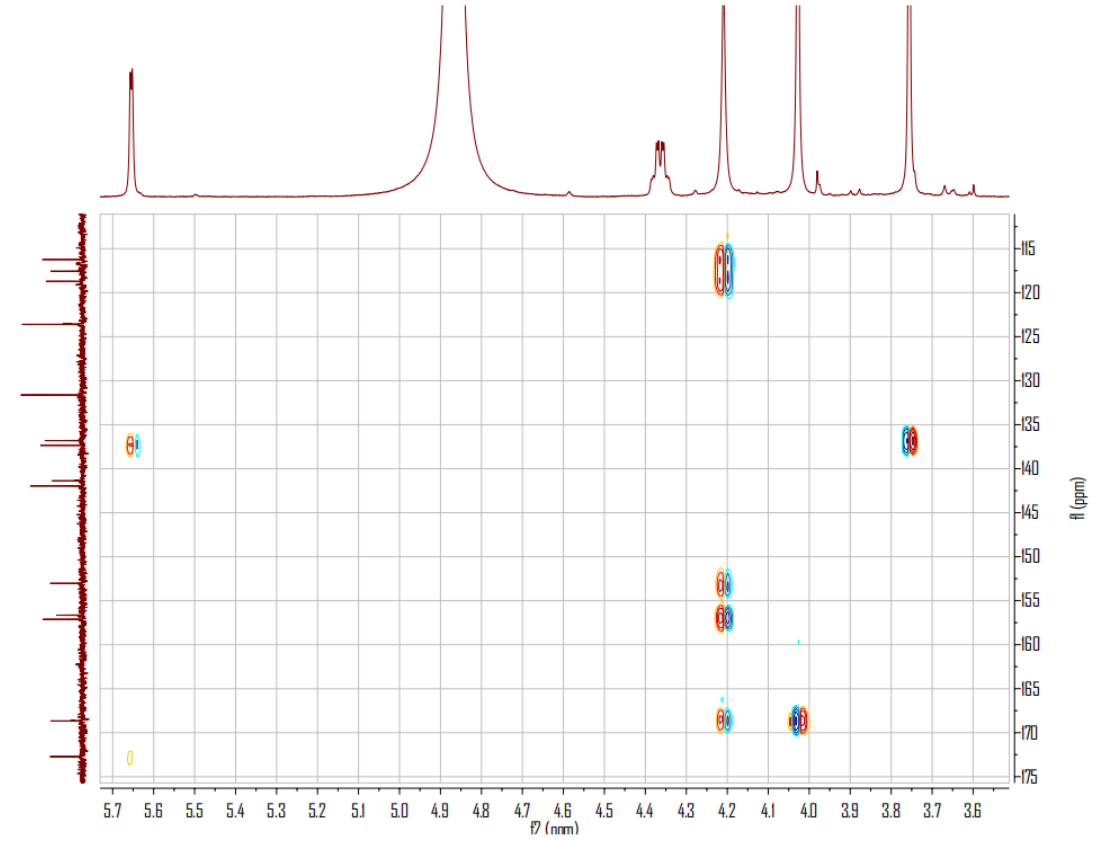



**Figure S91**. Partial HMBC spectrum of **11** in methanol-$d_4$

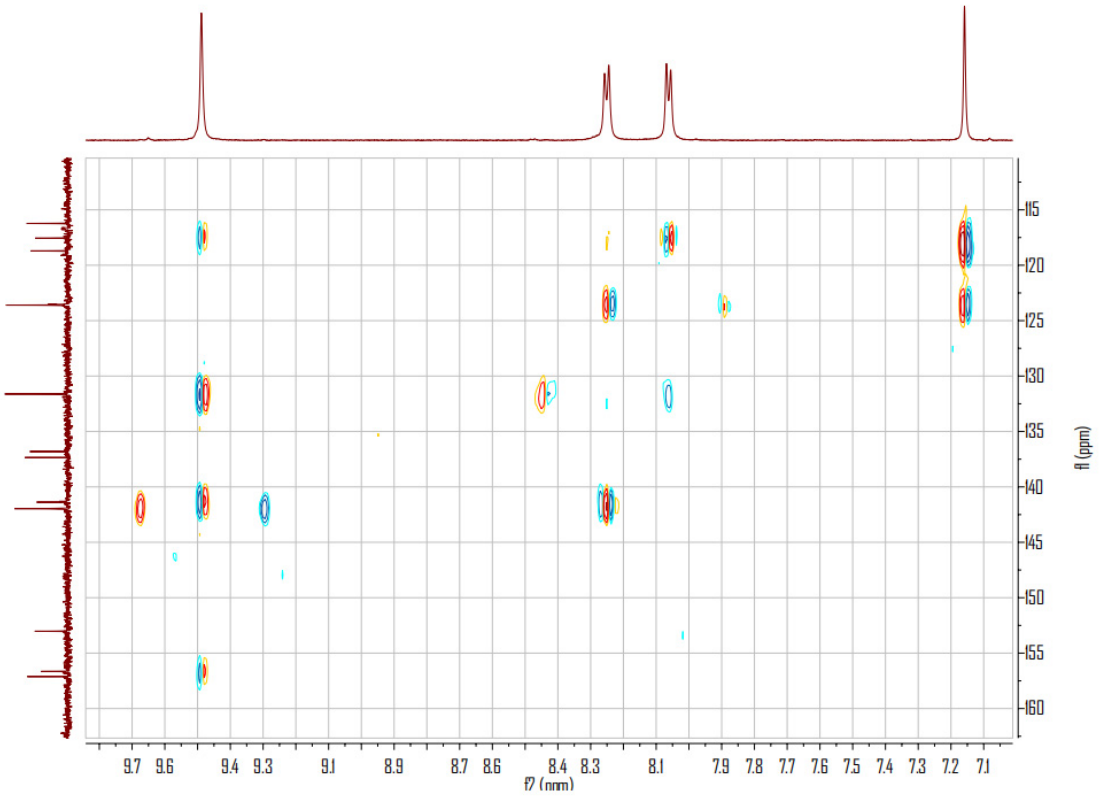



**Figure S92**. Partial HMBC spectrum of **11** in methanol-$d_4$

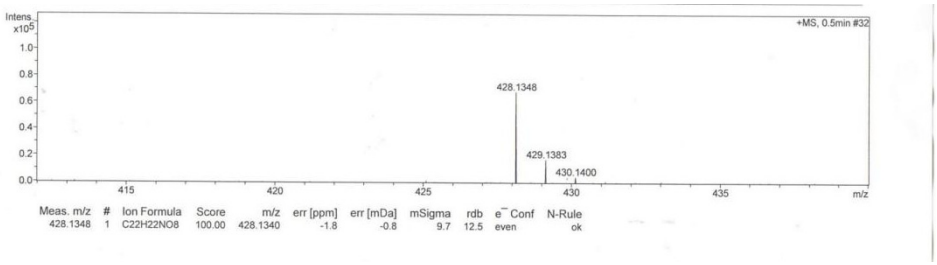



**Figure S93**. HRESIMS spectrum of **11**

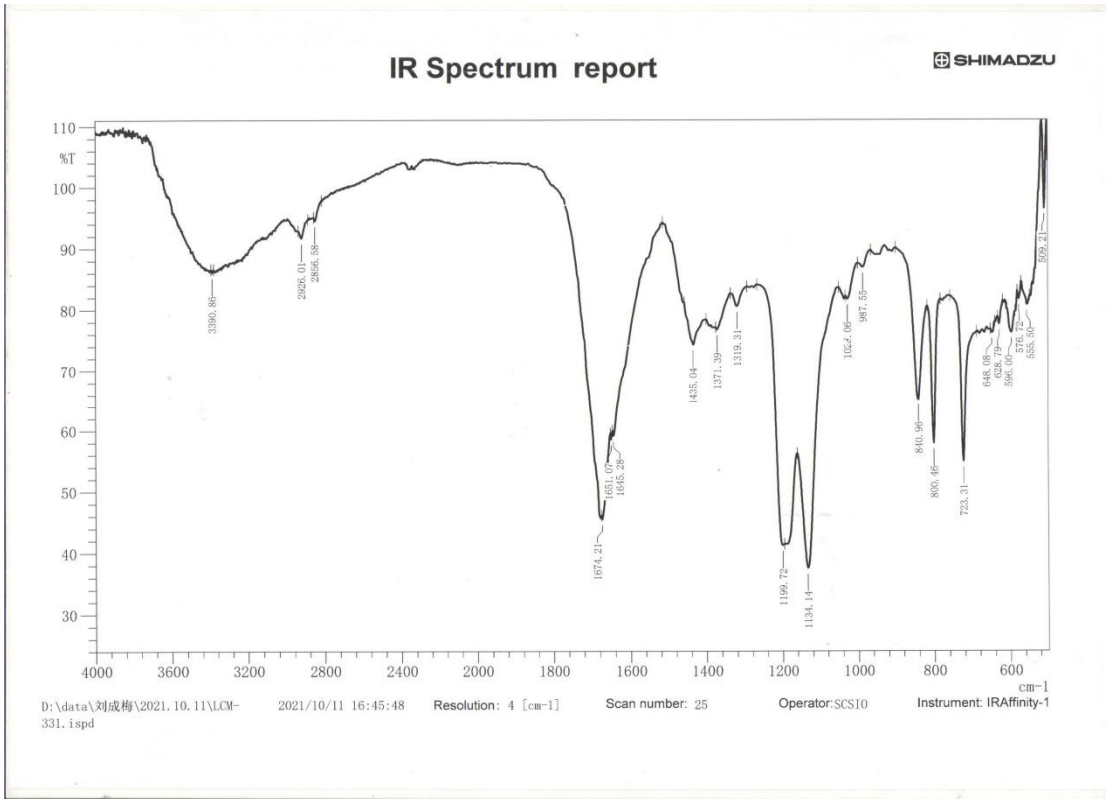



**Figure S94**. IR spectrum of **11**

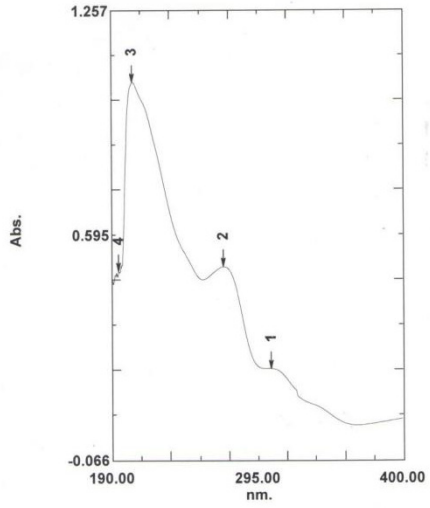



**Figure S95**. UV spectrum of **11**

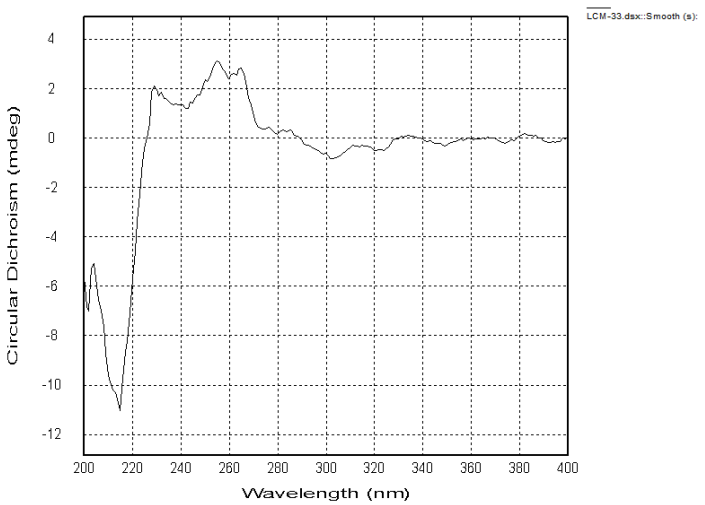



**Figure S96**. CD spectrum of **11** in methanol

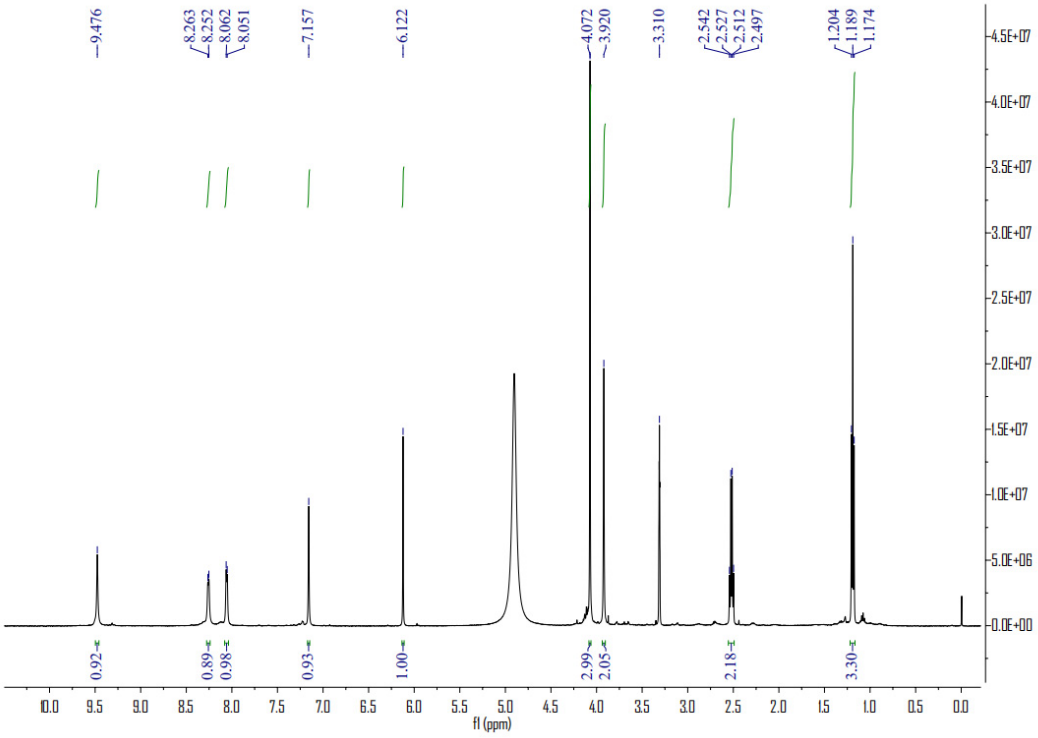



**Figure S97**. $^{1}$H NMR spectrum of **12** in methanol-$d_4$

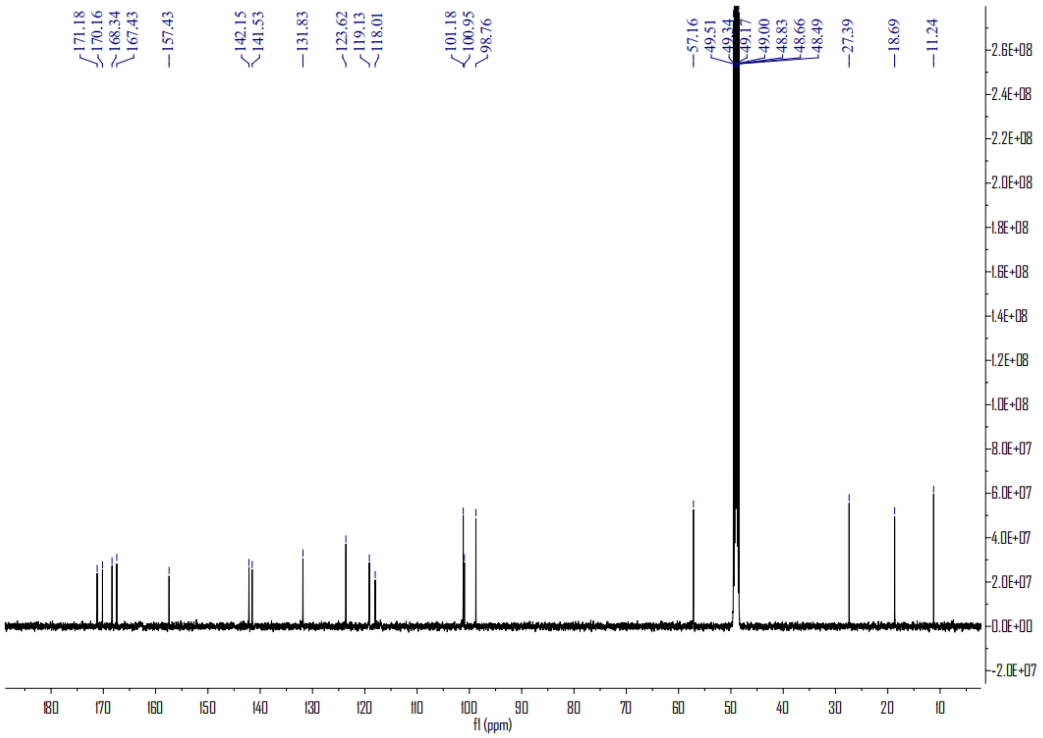



**Figure S98**. $^{13}$C NMR spectrum of **12** in methanol-$d_4$

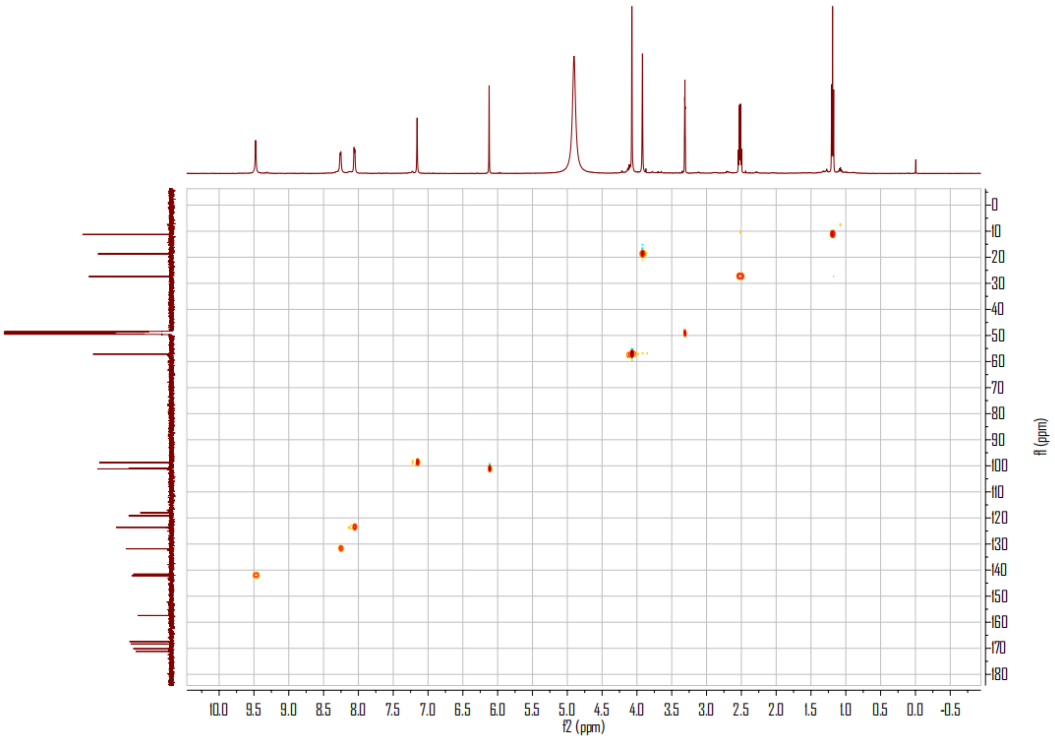



**Figure S99**. HSQC spectrum of **12** in methanol-$d_4$

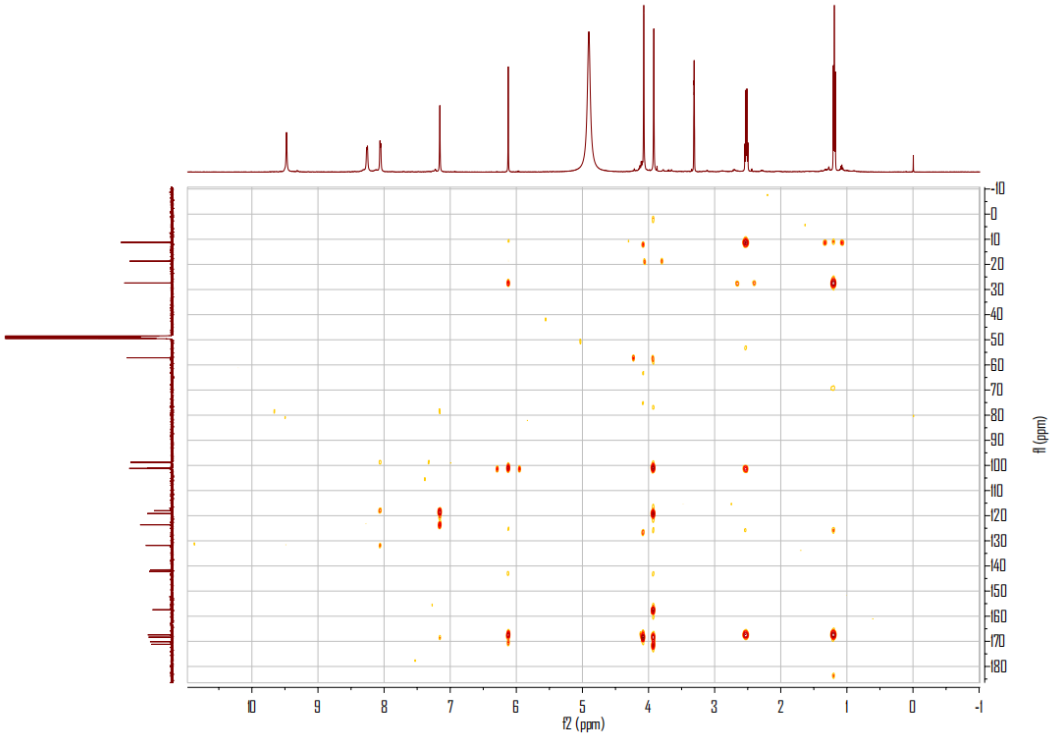



**Figure S100**. HMBC spectrum of **12** in methanol-$d_4$

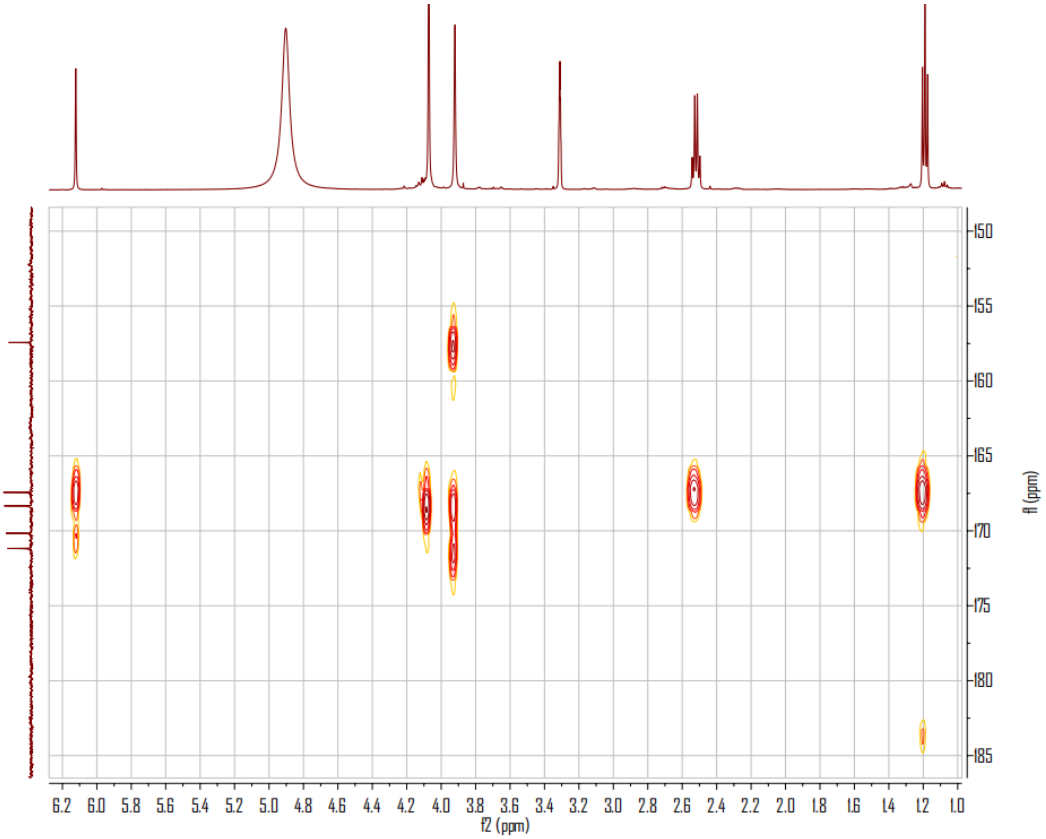



**Figure S101**. Partial HMBC spectrum of **12** in methanol-$d_4$

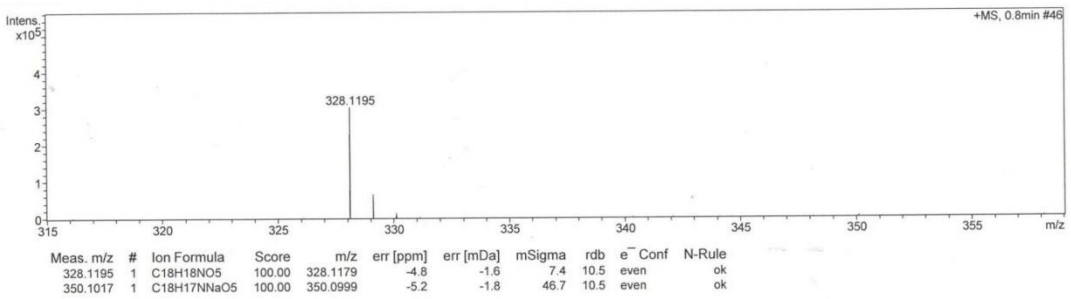



**Figure S102**. HRESIMS spectrum of **12**

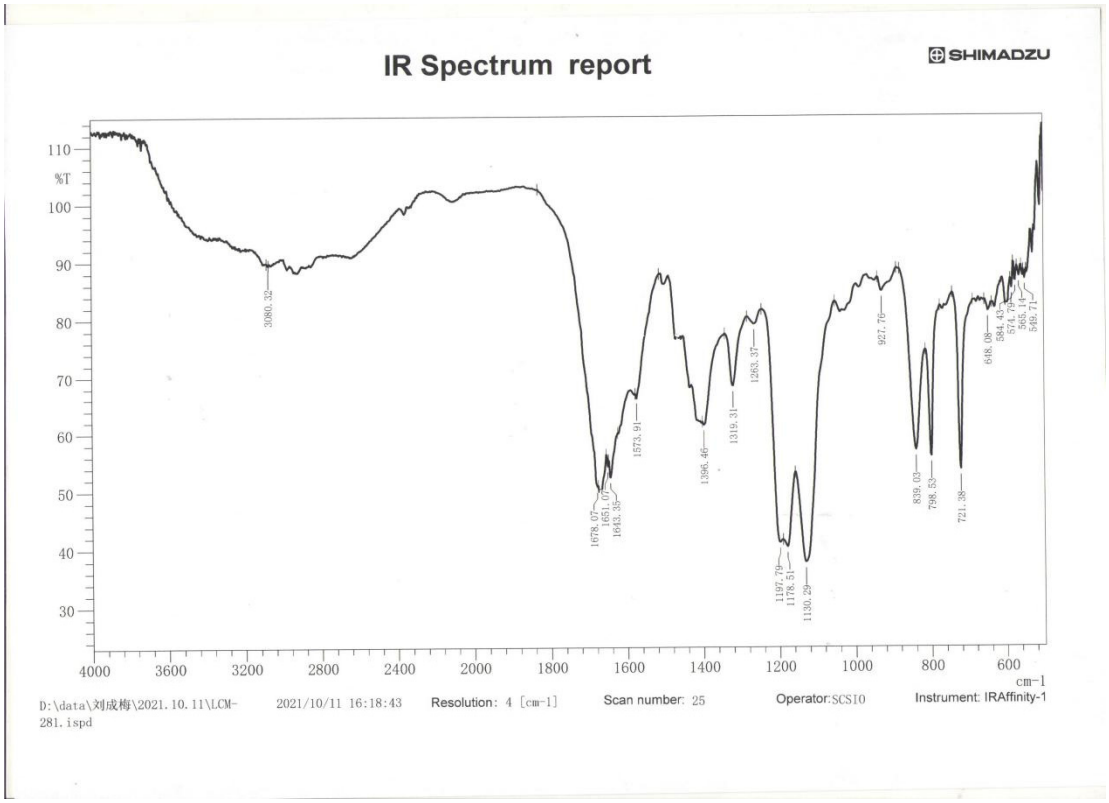



**Figure S103**. IR spectrum of **12**

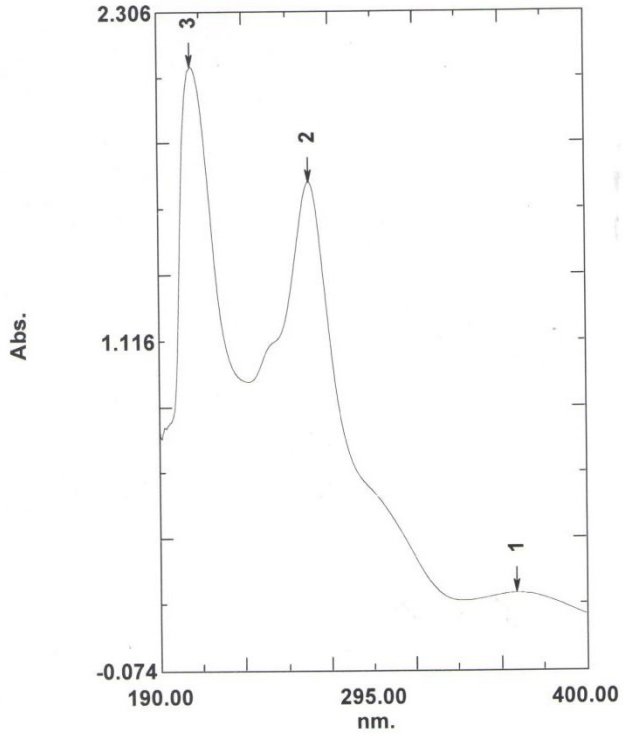



**Figure S104**. UV spectrum of **12**

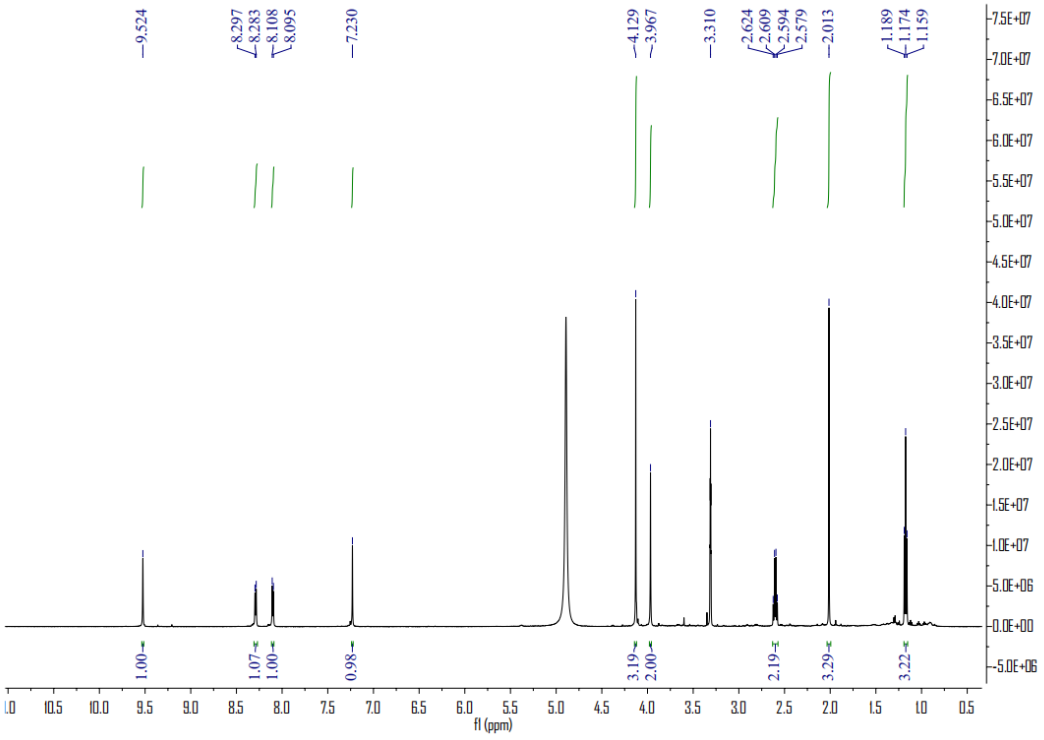



**Figure S105**. $^{1}$H NMR spectrum of **13** in methanol-$d_4$

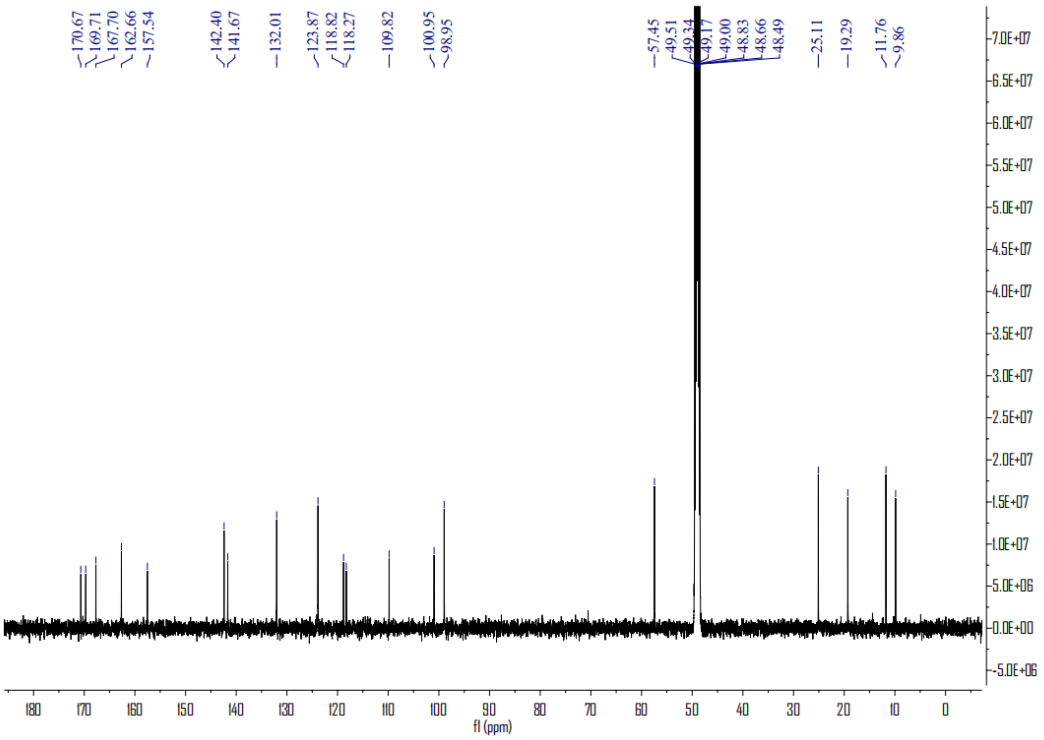



**Figure S106**. $^{13}$C NMR spectrum of **13** in methanol-$d_4$

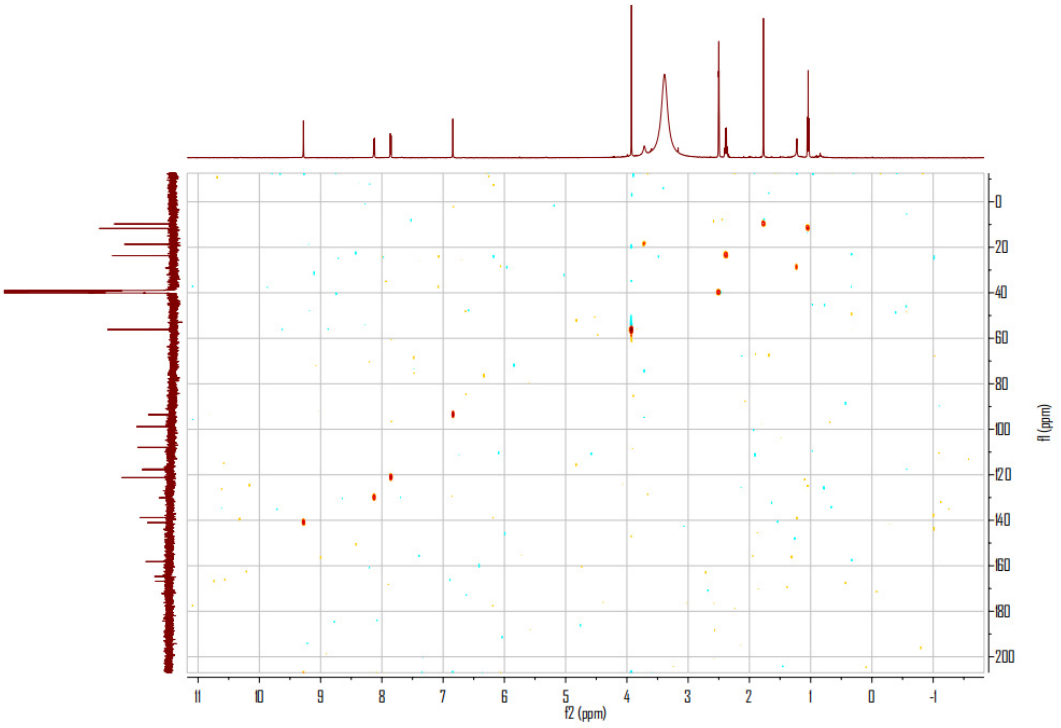



**Figure S107**. HSQC spectrum of **13** in DMSO-$d_6$

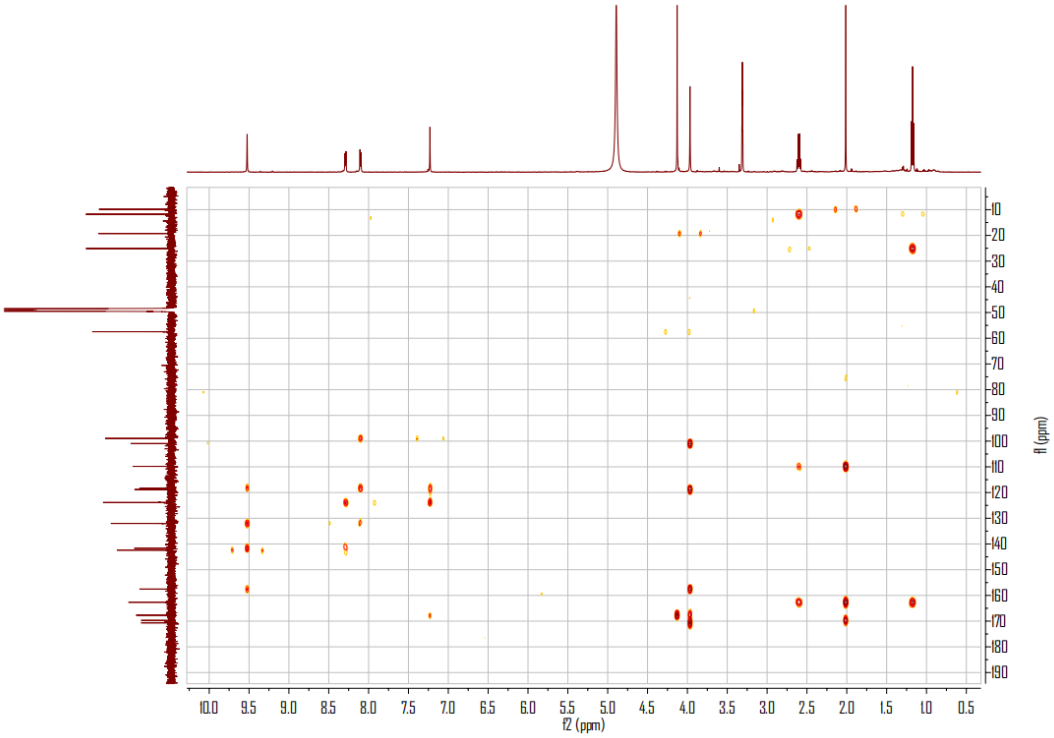



**Figure S108**. HMBC spectrum of **13** in methanol-$d_4$

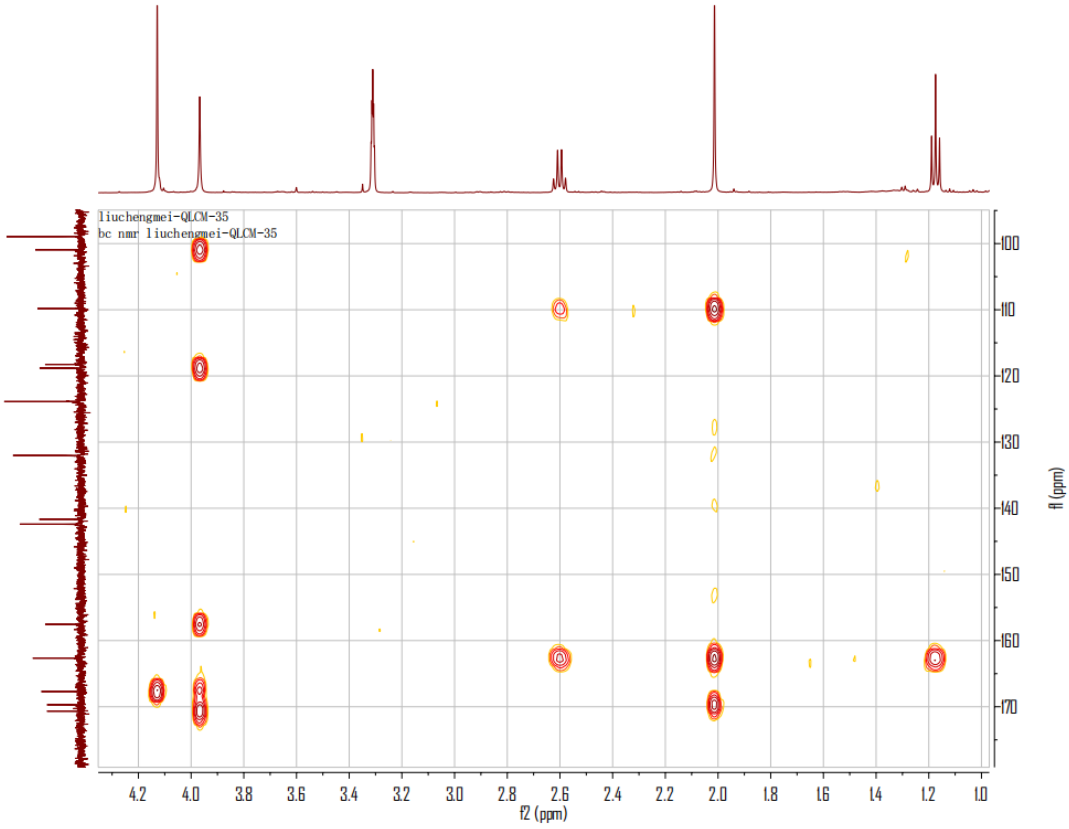



**Figure S109**. Partial HMBC spectrum of **13** in methanol-$d_4$

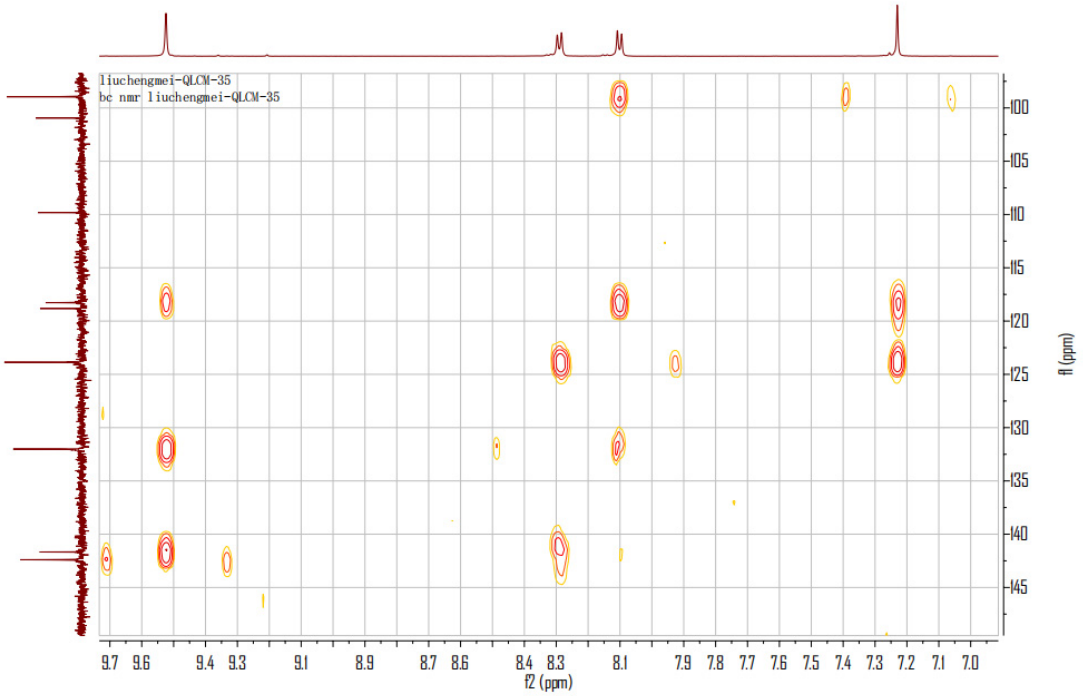



**Figure S110**. Partial HMBC spectrum of **13** in methanol-$d_4$

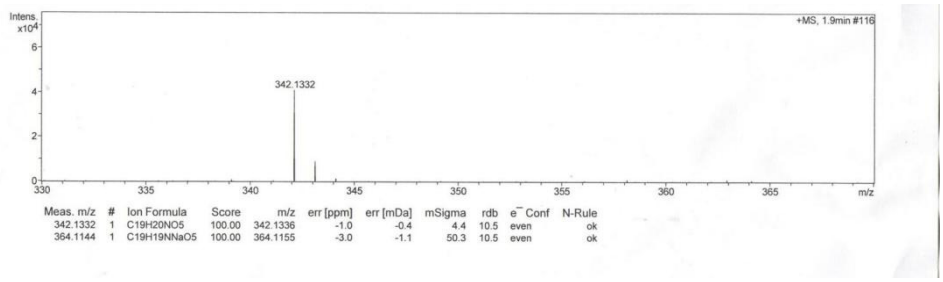



**Figure S111**. HRESIMS spectrum of **13**

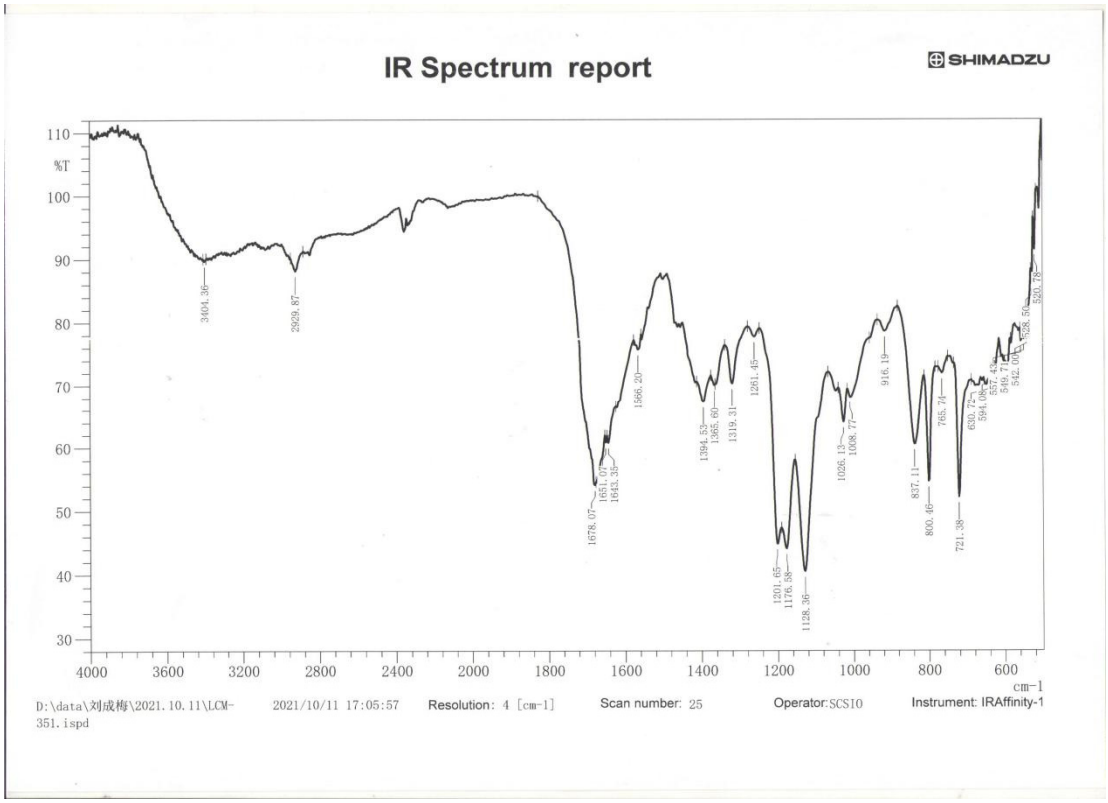



**Figure S112**. IR spectrum of **13**

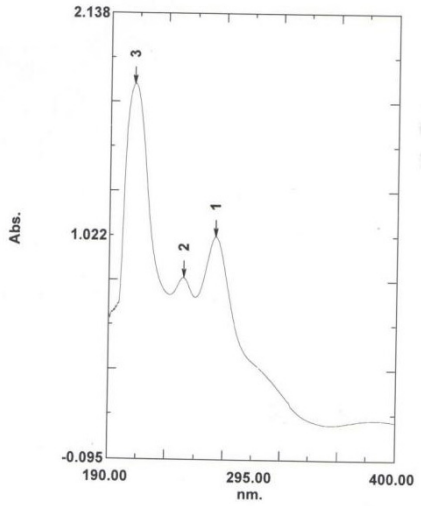



**Figure S113**. UV spectrum of **13.**

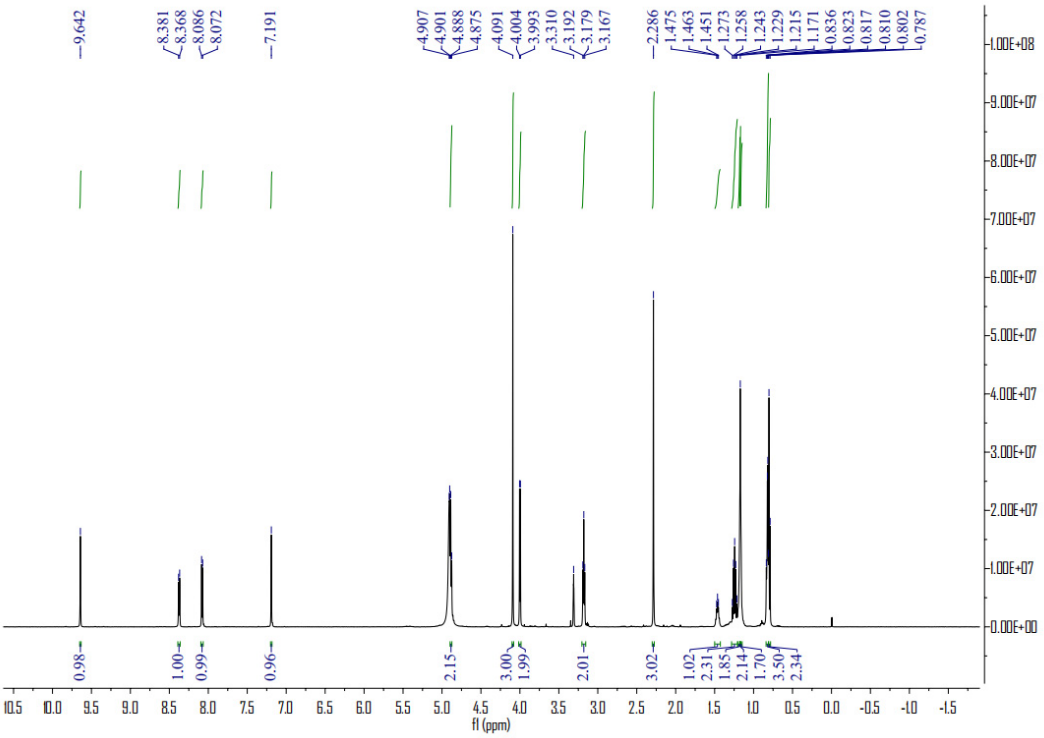



**Figure S114**. $^{1}$H NMR spectrum of **14** in methanol-$d_4$

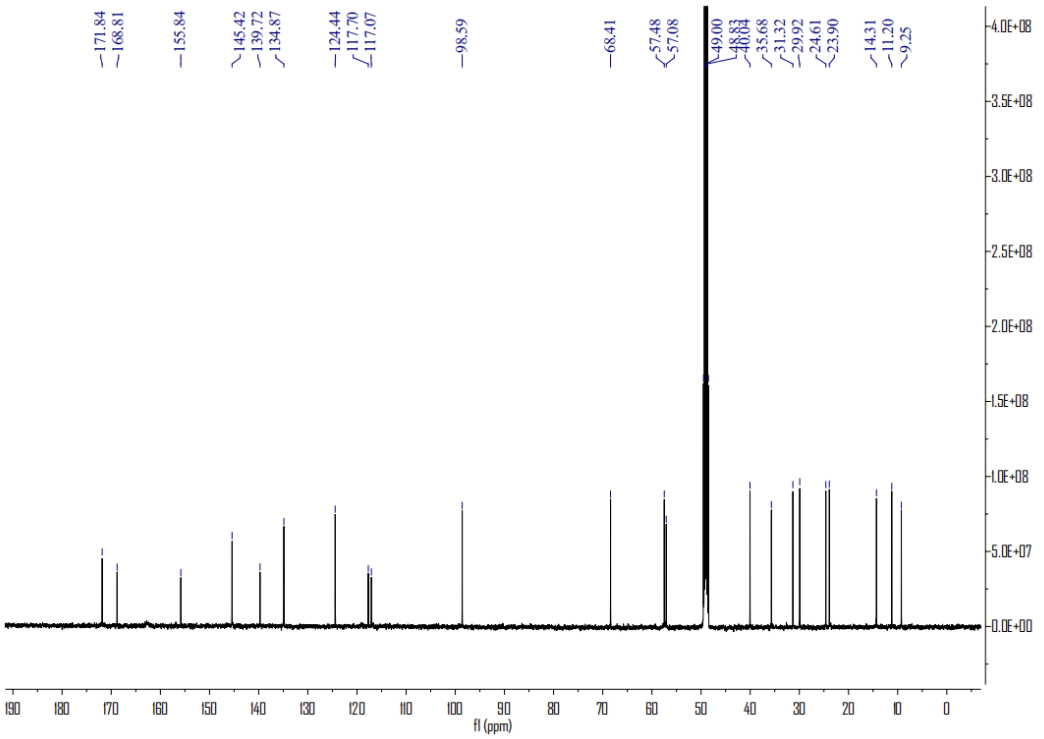



**Figure S115**. $^{13}$C NMR spectrum of **14** in methanol-$d_4$

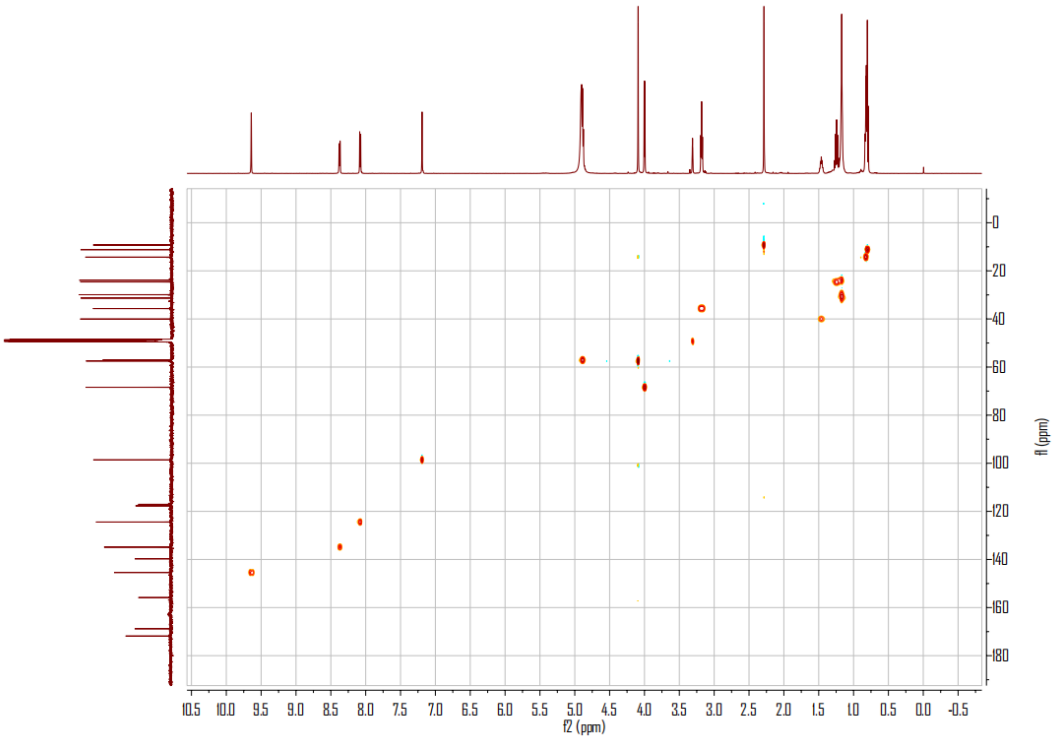



**Figure S116**. HSQC spectrum of **14** in methanol-$d_4$

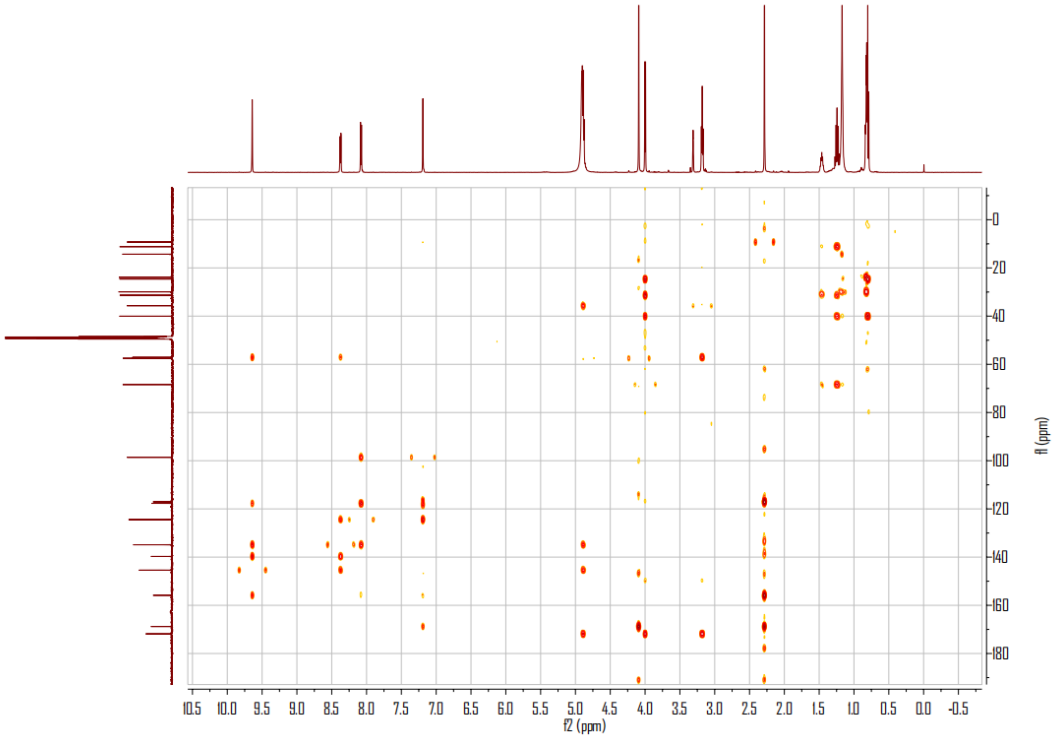



**Figure S117**. HMBC spectrum of **14** in methanol-$d_4$

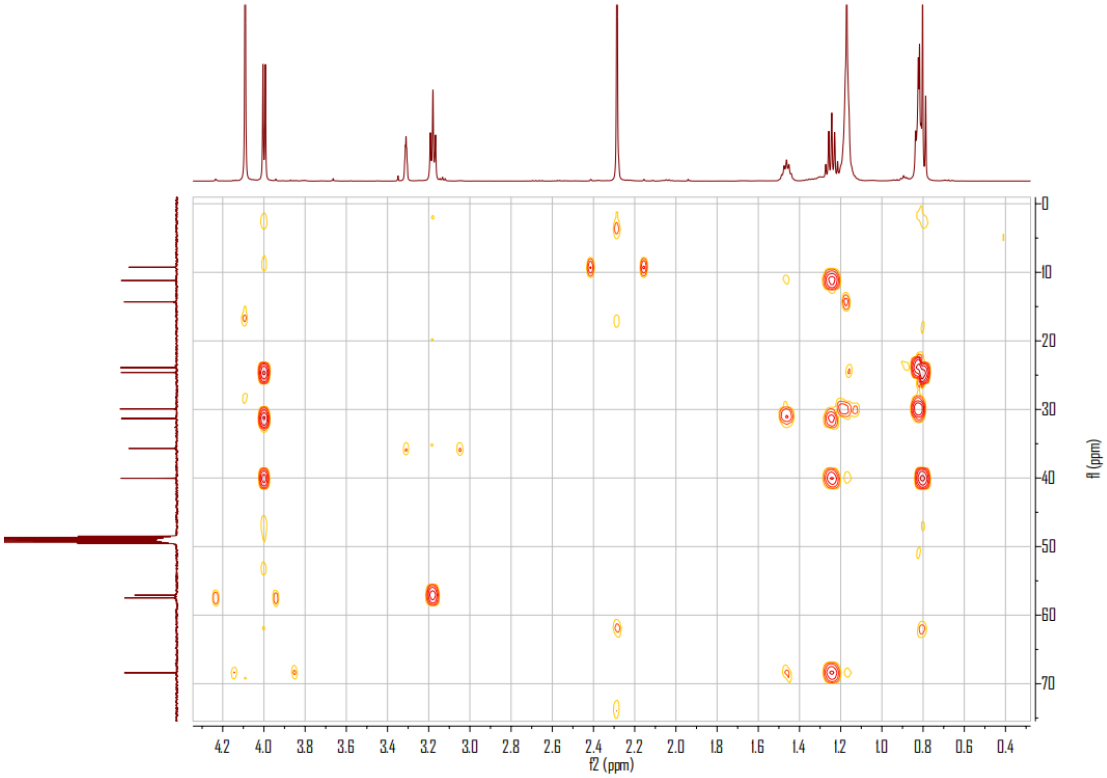



**Figure S118**. Partial HMBC spectrum of **14** in methanol-$d_4$

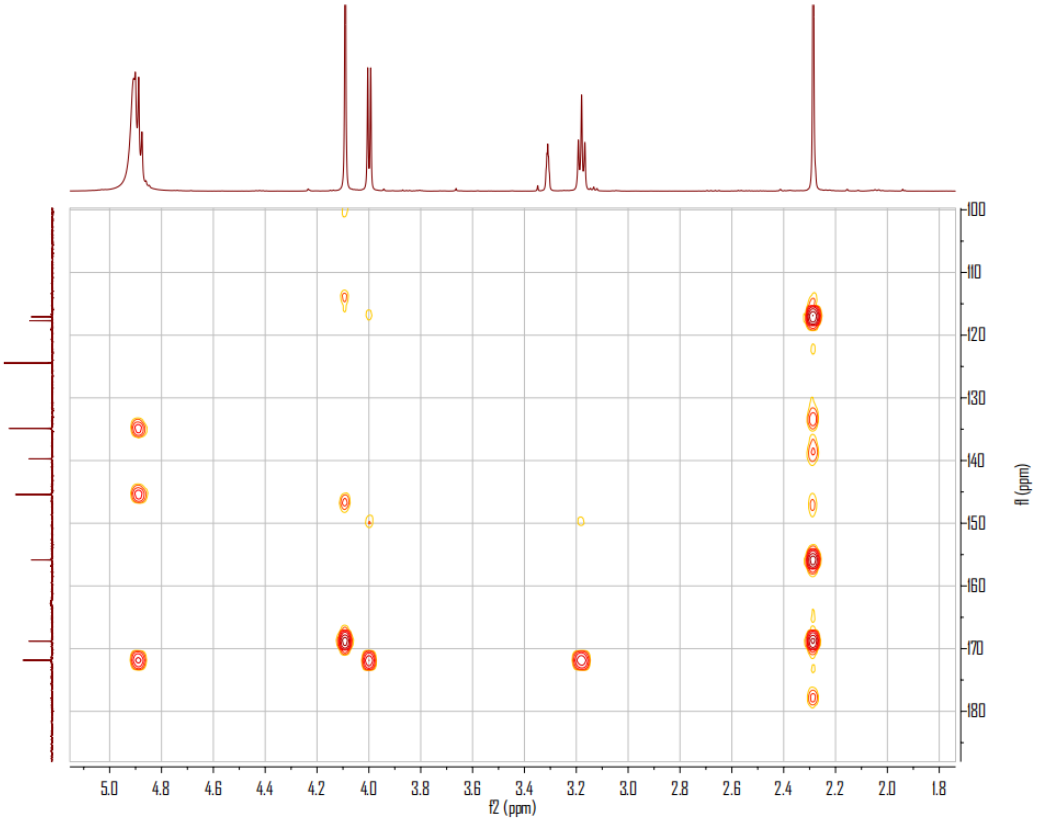



**Figure S119**. Partial HMBC spectrum of **14** in methanol-$d_4$

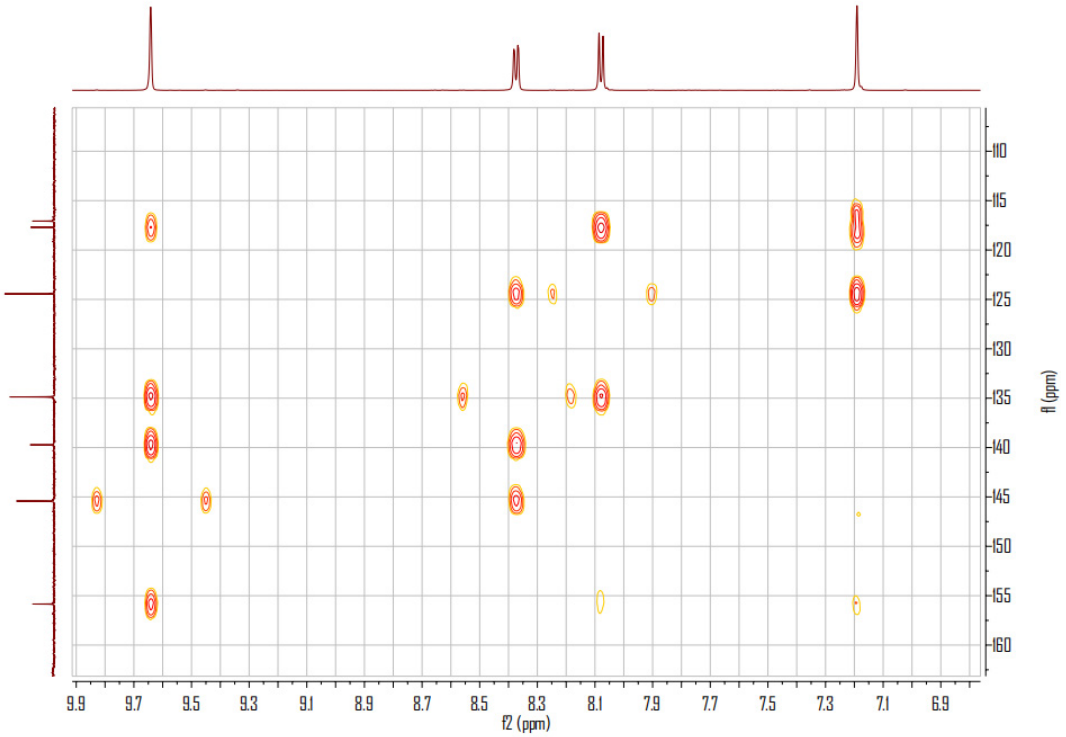



**Figure S120**. Partial HMBC spectrum of **14** in methanol-$d_4$

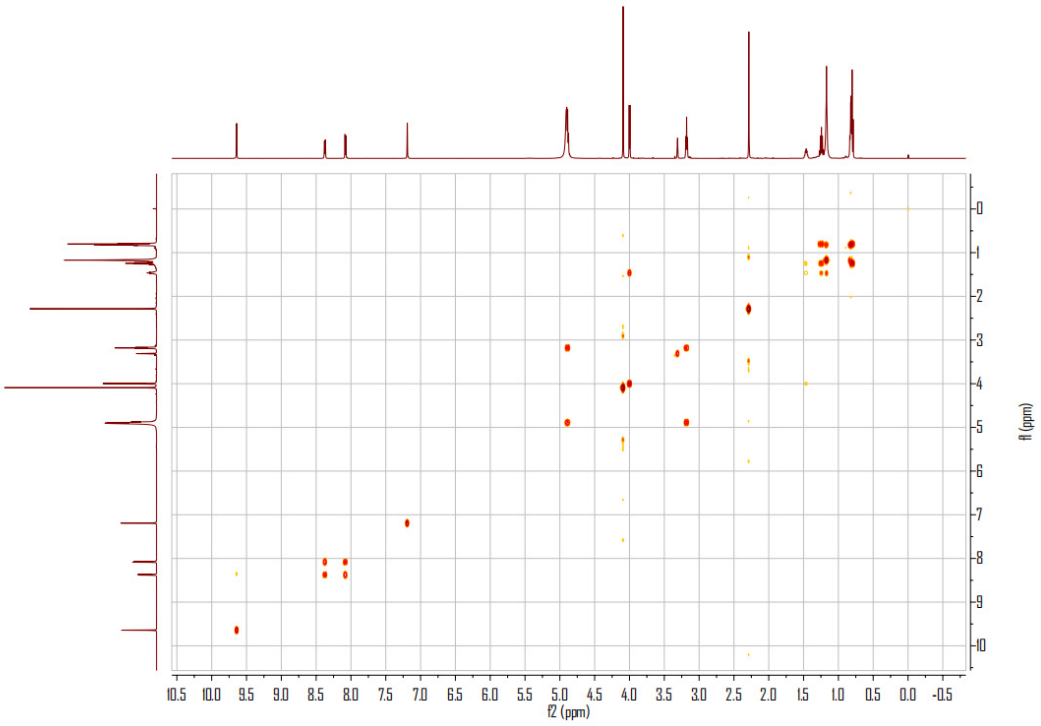



**Figure S121**. COSY spectrum of **14** in methanol-$d_4$

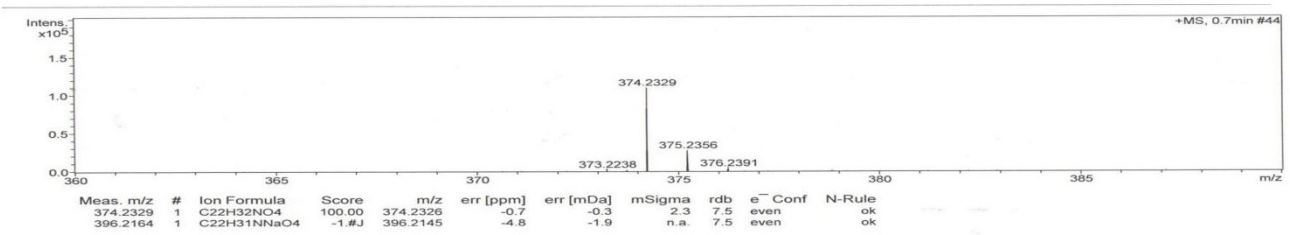



**Figure S122**. HRESIMS spectrum of **14**

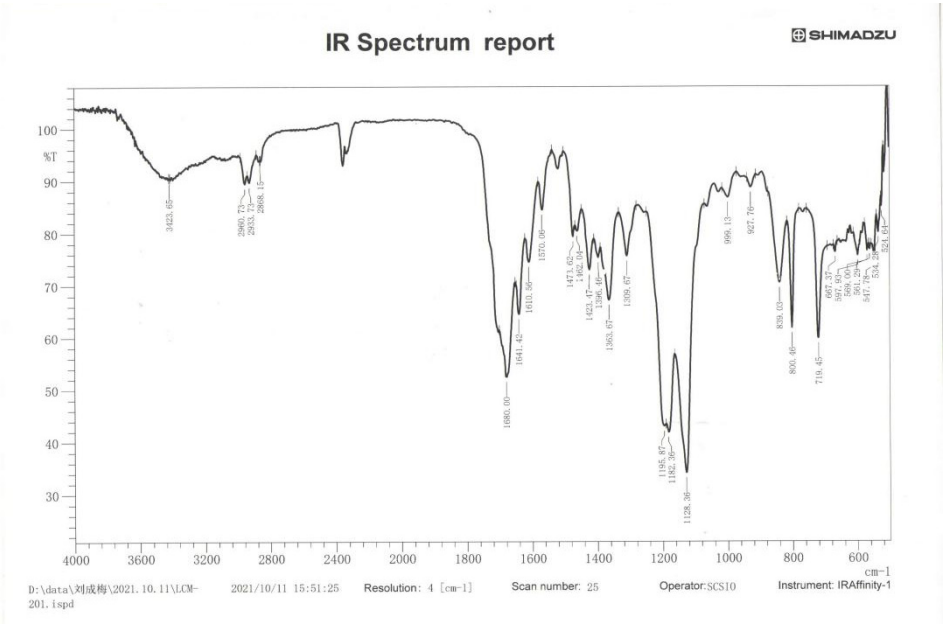



**Figure S123**. IR spectrum of **14**

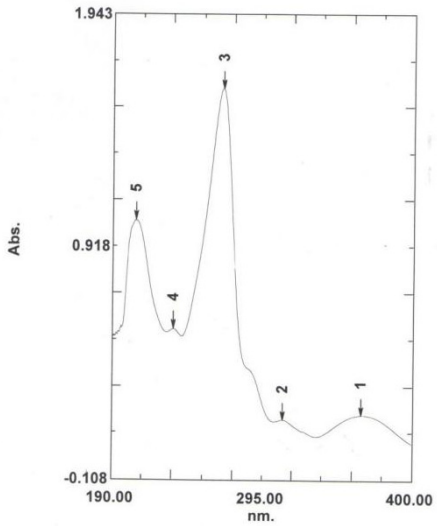



**Figure S124**. UV spectrum of **14**

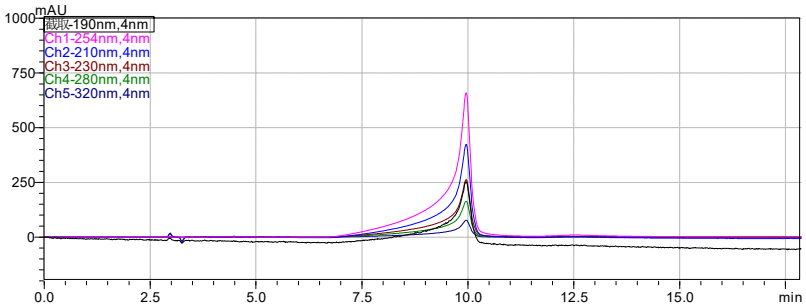



**Figure S125**. Chirality analysis of compound **14** by CHIRALPAK IA

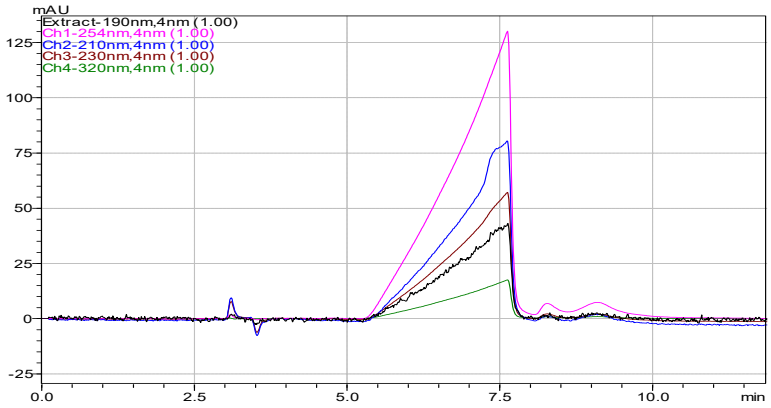
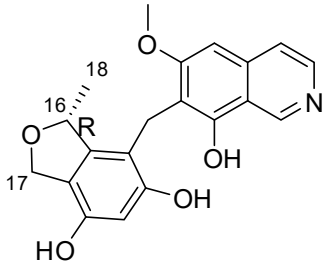
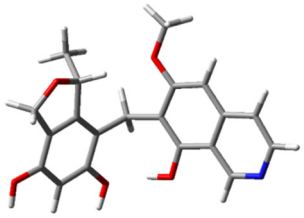
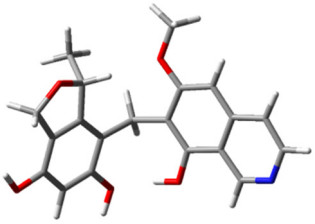
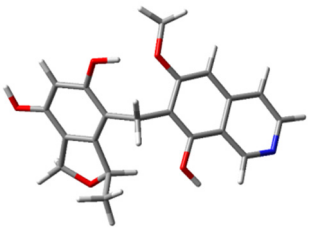
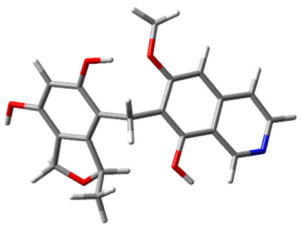
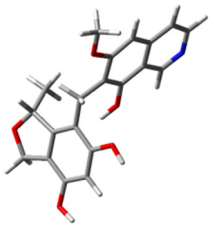



**Figure S126**. Chirality analysis of compound **14** by CHIRALPAK IB

**Table S1**. Stable conformers of compound (16*R*)-**9** used for ECD calculations




(16*R*)-**9**

| Conformer | Conformation |
|---|---|
| **9**-1 |  |
| **9**-2 |  |
| **9**-3 |  |
| **9**-4 |  |
| **9**-5 |  |

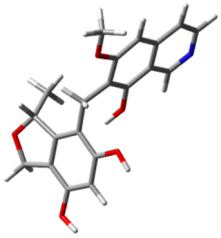
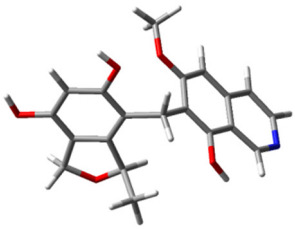
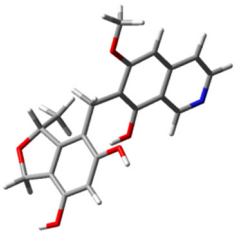
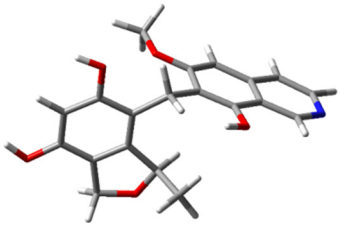
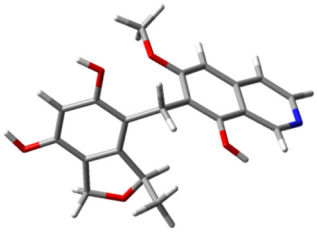
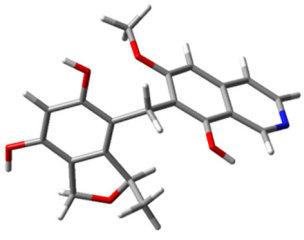
| | |
|---|---|
| **9**-6 |  |
| **9**-7 |  |
| **9**-8 |  |
| **9**-9 |  |
| **9**-10 |  |
| **9**-11 |  |

**Table S2**. Important thermodynamic parameters (a.u.) of (16*R*)-**9** at B3LYP/6-311G (d,p) level in the gas phase

| Conformer | *E(*kcal/mol ) | *H(*kcal/mol ) | *G(*kcal/mol ) | imaginary frequencies |
|---|---|---|---|---|
| **9-**1 | -755574.960 | -755574.367 | -755621.613 | 18.87 |
| **9-**2 | -755574.377 | -755573.784 | -755621.078 | 18.75 |
| **9-**3 | -755572.438 | -755571.846 | -755619.745 | 20.41 |
| **9-**4 | -755571.803 | -755571.211 | -755619.772 | 15.55 |
| **9**-5 | -755572.743 | -755572.150 | -755620.652 | 15.98 |
| **9**-6 | -755572.743 | -755572.150 | -755620.653 | 15.97 |
| **9-**7 | -755572.269 | -755571.677 | -755620.579 | 10.81 |
| **9-**8 | -755572.108 | -755571.516 | -755620.141 | 15.61 |
| **9**-9 | -755571.950 | -755571.357 | -755619.951 | 12.11 |
| **9**-10 | -755572.268 | -755571.675 | -755620.573 | 10.82 |
| **9**-11 | -755571.750 | -755571.157 | -755620.099 | 12.20 |

*E*: total energy; *H*: enthalpy; *G*: Gibbs free energy.

**Table S3.** Relative thermal energies (ΔE), relative free energies (ΔG), and equilibrium populations (P) of low-energy conformers of structures (16*R*)-**9** in methanol.

| Conformer | *ΔE(*kcal/mol )[a] | *ΔG(*kcal/mol )[a] | $P_G$%[b] |
|---|---|---|---|
| **9**-1 | 0.000 | 0.000 | 40.71 |
| **9**-2 | 0.583 | 0.535 | 16.50 |
| **9**-3 | 2.522 | 1.868 | 1.74 |
| **9**-4 | 3.157 | 1.841 | 1.82 |
| **9**-5 | 2.217 | 0.961 | 8.03 |
| **9**-6 | 2.217 | 0.960 | 8.05 |
| **9**-7 | 2.691 | 1.034 | 7.11 |
| **9**-8 | 2.852 | 1.472 | 3.39 |
| **9**-9 | 3.010 | 1.662 | 2.46 |
| **9**-10 | 2.692 | 1.040 | 7.03 |
| **9**-11 | 3.210 | 1.514 | 3.16 |

[a] At the M062X/def2TZVP scrf(SMD) level of theory.
[b] From Δ*G* values at 298.15 K.

**Table S4**. Crystal data and structure refinement for compound **6**

| | |
|---|---|
| Identification code | lcm-16 |
| Empirical formula | $C_{14}H_{14.04}NO_4$ |
| Formula weight | 260.30 |
| Temperature/K | 100.00(10) |
| Crystal system | monoclinic |
| Space group | $P2_1/c$ |
| a/Å | 4.82780(10) |
| b/Å | 13.4963(3) |
| c/Å | 22.6665(7) |
| α/° | 90 |
| β/° | 96.025(3) |
| γ/° | 90 |
| Volume/Å$^3$ | 1468.73(6) |
| Z | 4 |
| $\rho_{calc}$g/cm$^3$ | 1.177 |
| μ/mm$^{-1}$ | 0.724 |
| F(000) | 548.0 |
| Crystal size/mm$^3$ | 0.15 × 0.12 × 0.1 |
| Radiation | Cu Kα (λ = 1.54184) |
| 2Θ range for data collection/° | 7.634 to 147.79 |
| Index ranges | $-5 \leq h \leq 5$, $-16 \leq k \leq 9$, $-27 \leq l \leq 26$ |
| Reflections collected | 7185 |
| Independent reflections | 2852 [$R_{int}$ = 0.0197, $R_{sigma}$ = 0.0255] |
| Data/restraints/parameters | 2852/1/212 |
| Goodness-of-fit on F$^2$ | 1.073 |
| Final R indexes [I>=2σ (I)] | $R_1$ = 0.0487, $wR_2$ = 0.1366 |
| Final R indexes [all data] | $R_1$ = 0.0545, $wR_2$ = 0.1406 |
| Largest diff. peak/hole / e Å$^{-3}$ | 0.48/-0.26 |

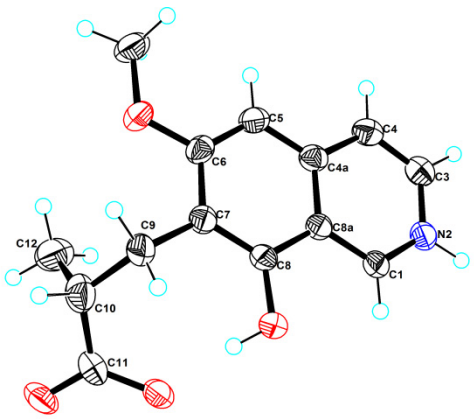


**Table S5.** Crystal data and structure refinement for compound **12**

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| | |
|---|---|
| Identification code | LCM-28 |
| Empirical formula | $C_{18}H_{17}NO_5$ |
| Formula weight | 327.32 |
| Temperature/K | 100.00(10) |
| Crystal system | triclinic |
| Space group | P-1 |
| a/Å | 7.6037(4) |
| b/Å | 9.9253(5) |
| c/Å | 10.5261(6) |
| α/° | 70.543(5) |
| β/° | 85.628(4) |
| γ/° | 81.605(4) |
| Volume/Å$^3$ | 740.68(7) |
| Z | 2 |
| $\rho_{calc}$g/cm$^3$ | 1.468 |
| μ/mm$^{-1}$ | 0.897 |
| F(000) | 344.0 |
| Crystal size/mm$^3$ | 0.13 × 0.12 × 0.1 |
| Radiation | Cu Kα (λ = 1.54184) |
| 2Θ range for data collection/° | 8.914 to 148.202 |
| Index ranges | -9 ≤ h ≤ 9, -7 ≤ k ≤ 12, -11 ≤ l ≤ 13 |
| Reflections collected | 7019 |
| Independent reflections | 2880 [$R_{int}$ = 0.0259, $R_{sigma}$ = 0.0317] |
| Data/restraints/parameters | 2880/0/220 |
| Goodness-of-fit on F$^2$ | 1.082 |
| Final R indexes [I>=2σ (I)] | $R_1$ = 0.0419, w$R_2$ = 0.1114 |
| Final R indexes [all data] | $R_1$ = 0.0523, w$R_2$ = 0.1150 |
| Largest diff. peak/hole / e Å$^{-3}$ | 0.21/-0.27 |