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Novel 3,4-seco-3,19-dinor and 5,17-epoxy-19-norspongian diterpenes from the marine sponge *Spongia* sp.

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Contents

Physico-chemical constants of 1-12

Dinorspongian A (1)

Colorless blocks (CH_3OH); mp. 362-363 ℃; $[\alpha]_D^{25}$ -52.7 (*c* 1.25, CH_3OH); HR-ESI-MS *m/z* 334.1662 $[M - H]^-$ (calcd for $C_{18}H_{24}NO_5$: 334.1660); UV λ_{max} (CH_3OH): 216 nm; IR ν_{max}: 3374, 3286, 1694, 1660, 1449, 1046, 668 cm^{-1}.

Dinorspongian B (2)

Colorless oil; $[\alpha]_D^{25}$ -21.0 (*c* 0.78, CH_3OH); HR-ESI-MS *m/z* 372.1422 $[M + Na]^+$ (calcd for $C_{18}H_{23}NO_6Na$: 372.1423); UV λ_{max} (CH_3OH): 215 nm; IR ν_{max}: 3449, 3257, 1697, 1452, 1046, 688 cm^{-1}; CD (CH_3OH): 290 ($\Delta\varepsilon$ +1.89) nm, 240 ($\Delta\varepsilon$ -5.45) nm, 214 ($\Delta\varepsilon$ +3.29) nm.

Dinorspongian C (3)

Colorless oil; $[\alpha]_D^{25}$ -33.2 (*c* 0.98, CH_3OH); HR-ESI-MS *m/z* 334.1666 $[M - H]^-$ (calcd for $C_{18}H_{24}NO_5$: 334.1660); UV λ_{max} (CH_3OH): 217 nm; IR ν_{max}: 3497, 3369, 1713, 1628, 1454, 1043, 681 cm^{-1}; CD (CH_3OH): 285 ($\Delta\varepsilon$ +0.53) nm, 213 ($\Delta\varepsilon$ -5.62) nm.

Dinorspongian D (4)

Colorless oil; $[\alpha]_D^{25}$ -40.2 (*c* 1.02, CH_3OH); HR-ESI-MS *m/z* 350.1965 $[M + H]^+$ (calcd for $C_{19}H_{28}NO_5$: 350.1962); UV λ_{max} (CH_3OH): 216 nm; IR ν_{max}: 3380, 3256, 1660, 1639, 1453, 1044, 653 cm^{-1}; CD (CH_3OH): 291 ($\Delta\varepsilon$ +1.26) nm, 247 ($\Delta\varepsilon$ -0.77) nm, 212 ($\Delta\varepsilon$ -10.59) nm.

Dinorspongian E (5)

Colorless oil; $[\alpha]_D^{25}$ -52.1 (*c* 1.22, CH_3OH); HR-ESI-MS *m/z* 335.1509 $[M - H]^-$ (calcd for $C_{18}H_{23}O_6$: 335.1500); UV λ_{max} (CH_3OH): 214 nm; IR ν_{max}: 3389, 1722, 1694, 1451, 1032, 681 cm^{-1}; CD (CH_3OH): 291 ($\Delta\varepsilon$ +1.50) nm, 246 ($\Delta\varepsilon$ -2.66) nm, 212 ($\Delta\varepsilon$ +2.29) nm.

Dinorspongian F (6)

Colorless oil; $[\alpha]_D^{25}$ -62.5 (*c* 1.65, CH_3OH); HR-ESI-MS *m/z* 353.1600 $[M + H]^+$ (calcd for $C_{18}H_{25}O_7$: 353.1595)； UV λ_{max} (CH_3OH): 215 nm；IR ν_{max}: 3372, 1731, 1688, 1451, 1084, 626 cm^{-1}； CD (CH_3OH): 290 ($\Delta\varepsilon$ +4.90) nm, 230 ($\Delta\varepsilon$ -16.26) nm, 211 ($\Delta\varepsilon$ -2.67) nm.

Epoxynorspongian A (7)

Colorless blocks (CH_3OH); mp. 352-353 ℃; $[\alpha]_D^{25}$ -62.1 (*c* 1.32, CH_3OH); HR-ESI-MS *m/z* 390.1559 $[M + HCOO^-]^-$ (calcd for $C_{20}H_{24}NO_7$: 390.1558)；UV λ_{max} (CH_3OH): 216, 282 nm；IR ν_{max}: 3378, 3294, 1668, 1633, 1387, 1044, 611 cm^{-1}.

Epoxynorspongian B (8)

Colorless oil; $[\alpha]_D^{25}$ -24.8 (*c* 0.58, CH_3OH); HR-ESI-MS *m/z* 330.1696 $[M + H]^+$ (calcd for $C_{19}H_{24}NO_4$: 330.1700); UV λ_{max} (CH_3OH): 216, 285 nm; IR ν_{max}: 3379, 3237, 1666, 1633, 1389, 1051, 633 cm^{-1}; CD (CH_3OH): 319 ($\Delta\varepsilon$ -5.86) nm, 281 ($\Delta\varepsilon$ +29.00) nm, 217 ($\Delta\varepsilon$ -21.70) nm.

Epoxynorspongian C (9)

Colorless oil; $[\alpha]_D^{25}$ -22.1 (*c* 0.73, CH_3OH); HR-ESI-MS *m/z* 342.1347 $[M - H]^-$ (calcd for $C_{19}H_{20}NO_5$: 342.1347); UV λ_{max} (CH_3OH): 216, 285 nm; IR ν_{max}: 3410, 3302, 1717, 1700, 1390, 1078, 574 cm^{-1}; CD (CH_3OH): 313 ($\Delta\varepsilon$ -1.13) nm, 276 ($\Delta\varepsilon$ +5.38) nm.

Epoxynorspongian D (10)

Colorless oil; $[\alpha]_D^{25}$ -43.6 (*c* 0.54, CH_3OH); HR-ESI-MS *m/z* 330.1704 $[M + H]^+$ (calcd for $C_{19}H_{24}NO_4$: 330.1700); UV λ_{max} (CH_3OH): 216, 284 nm; IR ν_{max}: 3390, 3276, 1669, 1642, 1445, 1052, 635 cm^{-1}; CD (CH_3OH): 319 ($\Delta\varepsilon$ -2.52) nm, 280 ($\Delta\varepsilon$ +12.44) nm, 217 ($\Delta\varepsilon$ -9.77) nm.

Epoxynorspongian E (11)

Colorless blocks (CH_3OH); mp. 343-344 ℃; $[\alpha]_D^{25}$ -50.7 (*c* 1.20, CH_3OH); HR-ESI-MS *m/z* 345.1347 $[M - H]^-$ (calcd for $C_{19}H_{21}O_6$: 345.1344); UV λ_{max}(CH_3OH): 216, 283 nm; IR ν_{max}: 3395, 1747, 1667, 164, 1388, 1074, 552 cm^{-1}.

Epoxynorspongian F (12)

Colorless blocks (CH_3OH); mp. 347-348 ℃; $[\alpha]_D^{25}$ -19.2 (*c* 0.74, CH_3OH); HR-ESI-MS *m/z* 345.1344 $[M - H]^-$ (calcd for $C_{19}H_{21}O_6$: 345.1344); UV λ_{max} (CH_3OH): 217, 284 nm；IR ν_{max}: 3395, 1745, 1671, 1644, 1389, 1094, 575 cm^{-1}.

Cytotoxicity Assays

The cytotoxicity assay was performed according to a previous method.[1] The Cell MTT method was used for *in vitro* evaluation of the cytotoxicities of compounds **1**−**12** against cancer cell lines Hela, Huh7, RBL-2H3 and PC3.

References:

1 W. Lai, S. Y. Qin, G. Zou, X. J. Liao, G. D. Chen, H. Zhang, B. X. Zhao and S. H. Xu. Sinulaspirolactam A, a novel *aza*-spirocyclic valerenane sesquiterpenoid from soft coral *Sinularia* sp.. *J. Asian Nat. Prod. Res.*, 2019, **21**, 494-501.

X-ray Crystallographic Analysis of 1

Upon crystallization from CH_3OH using the vapor diffusion method, blocks of **1** were obtained. Data was collected at 100 K on a Rigaku Oxford Diffraction Supernova Dual Source, Cu at Zero equipped with an AtlasS2 CCD using Cu Kα radiation (λ = 1.54184 Å). Data reduction was carried out with the diffractometer's software.[1] Crystal data: $C_{18}H_{25}NO_5$, 2(H_2O), M = 371.42, space group monoclinic, $P2_1$; unit cell dimensions were determined to be a = 6.58016(9) Å, b = 18.0241(2) Å, c = 7.96795(11) Å, α = 90.00 °, β = 94.6953(13) °, γ = 90.00 °, V = 941.84(2) Å^3, Z = 2, Dx = 1.310 g/cm^3, F (000) = 400.0, μ (Cu Kα) = 0.836 mm^{-1}. 6390 reflections were collected (9.814° ≤ 2θ ≤ 147.06°), in which 3201 independent unique reflections (R_{int} = 0.0197, R_{sigma} = 0.0211) were used in all calculations. Using Olex2,[2] the structure was solved by direct methods using the SHELXS program, and refined by the SHELXL program.[3] In the structure refinements, hydrogen atoms were fixed geometrically at the calculated distances and allowed to ride on their parent atoms. The final refinement gave R_1 = 0.0357 (I > 2σ(I)), $_wR_2$ = 0.0947 (all data), and S = 1.043, Flack = -0.09(10), and Hooft = -0.07 (6). Crystallographic data for **1** have been deposited in the Cambridge Crystallographic Data Center as supplementary publication no. CCDC 2022808. Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0)1223-336033, or e-mail: deposit@ccdc.cam.ac. uk).

References:

1. Agilent Technologies, CrysAlisPRO, Version 1.171.36.28, 2013.

2. Dolomanov, O.V., Bourhis, L.J., Gildea, R.J., Howard, J.A.K. Puschmann. H. *J. Appl. Cryst.*, 2009, 42, 339-341.

3. Sheldrick, G.M. *Acta Cryst.* 2015, C71, 3-8.

X-ray Crystallographic Analysis of 7

Upon crystallization from CH_3OH using the vapor diffusion method, blocks of **7** were obtained. Data was collected at 100 K on a Rigaku Oxford Diffraction Supernova Dual Source, Cu at Zero equipped with an AtlasS2 CCD using Cu Kα radiation (λ = 1.54184 Å). Data reduction was carried out with the diffractometer's software.[1] Crystal data: $C_{19}H_{27}O_7N$, M = 381.41, space group orthorhombic, $P2_12_12$; unit cell dimensions were determined to be a = 12.91520(10) Å, b = 18.3839(2) Å, c =7.54850(10) Å, α = 90.00 °, β = 90.00 °, γ = 90.00 °, V = 1792.25(4) (4) Å^3, Z = 4, Dx = 1.414 g/cm^3, F (000) = 816.0, μ (Cu Kα) = 0.899 mm^{-1}. 20012 reflections were collected (8.368° ≤ 2θ ≤ 147.278°), in which 3604 independent unique reflections (R_{int} = 0.0316, R_{sigma} = 0.0166) were used in all calculations. Using Olex2,[2] the structure was solved by direct methods using the SHELXS program, and refined by the SHELXL program. In the structure refinements, hydrogen atoms were fixed geometrically at the calculated distances and allowed to ride on their parent atoms. The final refinement gave R_1 = 0.0397 (I > 2σ(I)), $_wR_2$ = 0.1066 (all data), and S = 1.106, Flack = -0.06 (4), and Hooft = -0.05 (4). Crystallographic data for **7** have been deposited in the Cambridge Crystallographic Data Center as supplementary publication no. CCDC 2022809. Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0)1223-336033, or e-mail: deposit@ccdc.cam.ac. uk).

References:

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2. Dolomanov, O.V., Bourhis, L.J., Gildea, R.J., Howard, J.A.K. Puschmann. H. *J. Appl. Cryst.*, 2009, 42, 339-341.

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X-ray Crystallographic Analysis of 11

Upon crystallization from CH_3OH using the vapor diffusion method, blocks of **11** were obtained. Data was collected at 120 K on a Rigaku Oxford Diffraction Supernova Dual Source, Cu at Zero equipped with an AtlasS2 CCD using Cu Kα radiation (λ = 1.54184 Å). Data reduction was carried out with the diffractometer's software.[1] Crystal data: $C_{19}H_{22}O_6$, M = 346.36, space group orthorhombic, $P2_12_12_1$; unit cell dimensions were determined to be a = 9.28120(10) Å, b = 11.92810(10) Å, c = 14.17700(10) Å, α = 90.00 °, β = 90.00 °, γ = 90.00 °, V = 1569.49(2) Å^3, Z = 4, Dx = 1.466 g/cm^3, F (000) = 736.0, μ (Cu Kα) = 0.904 mm^{-1}. 19454 reflections were collected (9.690≤ 2θ ≤ 147.422), which 3134 independent unique reflections (R_{int} = 0.0346, R_{sigma} = 0.0166) were used in all calculations. Using Olex2,[2] the structure was solved by direct methods using the SHELXS program, and refined by the SHELXL program. In the structure refinements, hydrogen atoms were fixed geometrically at the calculated distances and allowed to ride on their parent atoms. The final refinement gave R_1 = 0.0326 (I > 2σ(I)), $_wR_2$ = 0.0861 (all data), and S = 1.052, Flack = -0.06(5), and Hooft = -0.07 (4). Crystallographic data for **11** have been deposited in the Cambridge Crystallographic Data Center as supplementary publication no. CCDC 2022810. Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0)1223-336033, or e-mail: deposit@ccdc.cam.ac. uk).

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1. Agilent Technologies, CrysAlisPRO, Version 1.171.36.28, 2013.

2. Dolomanov, O.V., Bourhis, L.J., Gildea, R.J., Howard, J.A.K. Puschmann. H. *J. Appl. Cryst.*, 2009, 42, 339-341.

3. Sheldrick, G.M. *Acta Cryst.* 2015, C71, 3-8.

X-ray Crystallographic Analysis of 12

Upon crystallization from CH_3OH using the vapor diffusion method, blocks of **12** were obtained. Data was collected at 120.00(10) K on a Rigaku Oxford Diffraction Supernova Dual Source, Cu at Zero equipped with an AtlasS2 CCD using Cu Kα radiation (λ = 1.54184 Å). Data reduction was carried out with the diffractometer's software.[1] Crystal data: $C_{19}H_{22}O_6$, M = 346.37, space group orthorhombic, $P2_12_12_1$; unit cell dimensions were determined to be a = 10.1810(2) Å, b = 12.4105(2) Å, c = 12.7012(3) Å, α = 90.00 °, β = 90.00 °, γ = 90.00 °, V = 1604.81 (6) Å^3, Z = 4, Dx = 1.434 g/cm^3, F (000) = 736.0, μ (Cu Kα) = 0.884 mm^{-1}. 7990 reflections were collected (9.964° ≤ 2θ ≤ 148.152°), in which 3142 independent unique reflections (R_{int} = 0.0242, R_{sigma} = 0.0252) were used in all calculations. Using Olex2,[2] the structure was solved by direct methods using the SHELXS program, and refined by the SHELXL program. In the structure refinements, hydrogen atoms were fixed geometrically at the calculated distances and allowed to ride on their parent atoms. The final refinement gave R_1 = 0.0513 (I > 2σ(I)), $_wR_2$ = 0.1447 (all data), and S = 1.089, Flack = -0.02 (9), and Hooft = -0.04 (8). Crystallographic data for **12** have been deposited in the Cambridge Crystallographic Data Center as supplementary publication no. CCDC 2022811. Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0)1223-336033, or e-mail: deposit@ccdc.cam.ac. uk).

References:

1. Agilent Technologies, CrysAlisPRO, Version 1.171.36.28, 2013.

2. Dolomanov, O. V., Bourhis, L.J., Gildea, R.J., Howard, J.A.K. Puschmann. H. *J. Appl. Cryst.*, 2009, 42, 339-341.

3. Sheldrick, G.M. *Acta Cryst.* 2015, C71, 3-8.

Quantum chemical ECD calculation of 2

The theoretical calculations of **2** was performed using Gaussian 09.[1] The systematic random conformational analysis of (5*R*, 8*S*, 9*R*, 10*R*)-**2** was performed in the SYBYL 8.1 program by using MMFF94s molecular force field, which afforded 22 conformers for (5*R*, 8*S*, 9*R*, 10*R*)-**2** with an energy cutoff of 10 kcal mol^{-1} to the global minima. All the obtained conformers were further optimized using DFT at the B3LYP/6-31+G(d) level in gas phase by using Gaussian09 software.[1] All of the optimized stable conformers were used for TDDFT computation of the excited stats at the same levels, with the consideration of the first 30 excitations. The overall ECD curves of (5*R*, 8*S*, 9*R*, 10*R*)-**2** was weighted by Boltzmann distribution of each conformer (with a half-bandwidth of 0.33 eV), with a UV correction of 10 nm. The calculated ECD spectra of (5*R*, 8*S*, 9*R*, 10*R*)-**2** was subsequently compared with the experimental one. The ECD spectra were produced by SpecDis 1.6 software.[2,3]

References

1. Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, Scalmani G, Barone V, Mennucci B, Petersson GA, et al. 2010. Gaussian 09, Revision D.01, Gaussian, Inc., Wallingford CT.
2. Bruhn T, Schaumlöffel, A, Hemberger Y, Bringmann G. 2013. SpecDics, Version 1.61 ed. University of Würzburg: Würzburg, Germany.
3. Bruhn T, Schaumlöffel A, Hemberger Y, Bringmann G. 2013. SpecDics: quantifying the comparison of calculated and experimental electronic circular dichroism spectra. Chirality. 25: 243-249.

Quantum chemical ECD calculation of 3

The theoretical calculations of **3** was performed using Gaussian 09.[1] The systematic random conformational analysis of (5*R*, 8*S*, 9*R*, 10*R*)-**3** was performed in the SYBYL 8.1 program by using MMFF94s molecular force field, which afforded 31 conformers for (5*R*, 8*S*, 9*R*, 10*R*)-**3** with an energy cutoff of 10 kcal mol^{-1} to the global minima. All the obtained conformers were further optimized using DFT at the B3LYP/6-31+G(d) level in gas phase by using Gaussian09 software.[1] All of the optimized stable conformers were used for TDDFT computation of the excited stats at the same levels, with the consideration of the first 30 excitations. The overall ECD curves of (5*R*, 8*S*, 9*R*, 10*R*)-**3** was weighted by Boltzmann distribution of each conformer (with a half-bandwidth of 0.33 eV), with a UV correction of 15 nm. The calculated ECD spectra of (5*R*, 8*S*, 9*R*, 10*R*)-**3** was subsequently compared with the experimental one. The ECD spectra were produced by SpecDis 1.6 software.[2,3]

References

1. Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, Scalmani G, Barone V, Mennucci B, Petersson GA, et al. 2010. Gaussian 09, Revision D.01, Gaussian, Inc., Wallingford CT.
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3. Bruhn T, Schaumlöffel A, Hemberger Y, Bringmann G. 2013. SpecDics: quantifying the comparison of calculated and experimental electronic circular dichroism spectra. Chirality. 25: 243-249.

Quantum chemical ECD calculation of 4

The theoretical calculations of **4** was performed using Gaussian 09.[1] The systematic random conformational analysis of (5*R*, 8*S*, 9*R*, 10*R*)-**4** was performed in the SYBYL 8.1 program by using MMFF94s molecular force field, which afforded 29 conformers for (5*R*, 8*S*, 9*R*, 10*R*)-**4** with an energy cutoff of 10 kcal mol^{-1} to the global minima. All the obtained conformers were further optimized using DFT at the B3LYP/6-31+G(d) level in gas phase by using Gaussian09 software.[1] All of the optimized stable conformers were used for TDDFT computation of the excited stats at the same levels, with the consideration of the first 30 excitations. The overall ECD curves of (5*R*, 8*S*, 9*R*, 10*R*)-**4** was weighted by Boltzmann distribution of each conformer (with a half-bandwidth of 0.33 eV), with a UV correction of 10 nm. The calculated ECD spectra of (5*R*, 8*S*, 9*R*, 10*R*)-**4** was subsequently compared with the experimental one. The ECD spectra were produced by SpecDis 1.6 software.[2,3]

References

1. Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, Scalmani G, Barone V, Mennucci B, Petersson GA, et al. 2010. Gaussian 09, Revision D.01, Gaussian, Inc., Wallingford CT.
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3. Bruhn T, Schaumlöffel A, Hemberger Y, Bringmann G. 2013. SpecDics: quantifying the comparison of calculated and experimental electronic circular dichroism spectra. Chirality. 25: 243-249.

Quantum chemical ECD calculation of 5

The theoretical calculations of **5** was performed using Gaussian 09.[1] The systematic random conformational analysis of (5*R*, 8*S*, 9*R*, 10*R*)-**5** was performed in the SYBYL 8.1 program by using MMFF94s molecular force field, which afforded 22 conformers for (5*R*, 8*S*, 9*R*, 10*R*)-**5** with an energy cutoff of 10 kcal mol^{-1} to the global minima. All the obtained conformers were further optimized using DFT at the B3LYP/6-31+G(d) level in gas phase by using Gaussian09 software.[1] All of the optimized stable conformers were used for TDDFT computation of the excited stats at the same levels, with the consideration of the first 30 excitations. The overall ECD curves of (5*R*, 8*S*, 9*R*, 10*R*)-**5** was weighted by Boltzmann distribution of each conformer (with a half-bandwidth of 0.33 eV), with a UV correction of 15 nm. The calculated ECD spectra of (5*R*, 8*S*, 9*R*, 10*R*)-**5** was subsequently compared with the experimental one. The ECD spectra were produced by SpecDis 1.6 software.[2,3]

References

1. Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, Scalmani G, Barone V, Mennucci B, Petersson GA, et al. 2010. Gaussian 09, Revision D.01, Gaussian, Inc., Wallingford CT.
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3. Bruhn T, Schaumlöffel A, Hemberger Y, Bringmann G. 2013. SpecDics: quantifying the comparison of calculated and experimental electronic circular dichroism spectra. Chirality. 25: 243-249.

Quantum chemical ECD calculation of 6

The theoretical calculations of **6** was performed using Gaussian 09.[1] The systematic random conformational analysis of (5*R*, 8*S*, 9*R*, 10*R*, 15*S*)-**6** was performed in the SYBYL 8.1 program by using MMFF94s molecular force field, which afforded 19 conformers for (5*R*, 8*S*, 9*R*, 10*R*, 15*S*)-**6** with an energy cutoff of 10 kcal mol^{-1} to the global minima. All the obtained conformers were further optimized using DFT at the B3LYP/6-31+G(d) level in gas phase by using Gaussian09 software.[1] All of the optimized stable conformers were used for TDDFT computation of the excited stats at the same levels, with the consideration of the first 30 excitations. The overall ECD curves of (5*R*, 8*S*, 9*R*, 10*R*, 15*S*)-**6** was weighted by Boltzmann distribution of each conformer (with a half-bandwidth of 0.33 eV), with a UV correction of 15 nm. The calculated ECD spectra of (5*R*, 8*S*, 9*R*, 10*R*, 15*S*)-**6** was subsequently compared with the experimental one. The ECD spectra were produced by SpecDis 1.6 software.[2,3]

References

1. Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, Scalmani G, Barone V, Mennucci B, Petersson GA, et al. 2010. Gaussian 09, Revision D.01, Gaussian, Inc., Wallingford CT.
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Quantum chemical ECD calculation of 8

The theoretical calculations of **8** was performed using Gaussian 09.[1] The systematic random conformational analysis of (5*R*, 8*S*, 9*S*, 10*R*)-**8** was performed in the SYBYL 8.1 program by using MMFF94s molecular force field, which afforded 1 conformers for (5*R*, 8*S*, 9*S*, 10*R*)-**8** with an energy cutoff of 10 kcal mol^{-1} to the global minima. All the obtained conformers were further optimized using DFT at the B3LYP/6-31+G(d) level in gas phase by using Gaussian09 software.[1] All of the optimized stable conformers were used for TDDFT computation of the excited stats at the same levels, with the consideration of the first 30 excitations. The overall ECD curves of (5*R*, 8*S*, 9*S*, 10*R*)-**8** was weighted by Boltzmann distribution of each conformer (with a half-bandwidth of 0.33 eV), with a UV correction of 15 nm. The calculated ECD spectra of (5*R*, 8*S*, 9*S*, 10*R*)-**8** was subsequently compared with the experimental one. The ECD spectra were produced by SpecDis 1.6 software.[2,3]

References

1. Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, Scalmani G, Barone V, Mennucci B, Petersson GA, et al. 2010. Gaussian 09, Revision D.01, Gaussian, Inc., Wallingford CT.
2. Bruhn T, Schaumlöffel, A, Hemberger Y, Bringmann G. 2013. SpecDics, Version 1.61 ed. University of Würzburg: Würzburg, Germany.
3. Bruhn T, Schaumlöffel A, Hemberger Y, Bringmann G. 2013. SpecDics: quantifying the comparison of calculated and experimental electronic circular dichroism spectra. Chirality. 25: 243-249.

Quantum chemical ECD calculation of 9

The theoretical calculations of **9** was performed using Gaussian 09.[1] The systematic random conformational analysis of (5*R*, 8*S*, 9*S*, 10*R*)-**9** was performed in the SYBYL 8.1 program by using MMFF94s molecular force field, which afforded 1 conformers for (5*R*, 8*S*, 9*S*, 10*R*)-**9** with an energy cutoff of 10 kcal mol^{-1} to the global minima. All the obtained conformers were further optimized using DFT at the B3LYP/6-31+G(d) level in gas phase by using Gaussian09 software.[1] All of the optimized stable conformers were used for TDDFT computation of the excited stats at the same levels, with the consideration of the first 30 excitations. The overall ECD curves of (5*R*, 8*S*, 9*S*, 10*R*)-**9** was weighted by Boltzmann distribution of each conformer (with a half-bandwidth of 0.33 eV), with a UV correction of 10 nm. The calculated ECD spectra of (5*R*, 8*S*, 9*S*, 10*R*)-**9** was subsequently compared with the experimental one. The ECD spectra were produced by SpecDis 1.6 software.[2,3]

References

1. Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, Scalmani G, Barone V, Mennucci B, Petersson GA, et al. 2010. Gaussian 09, Revision D.01, Gaussian, Inc., Wallingford CT.
2. Bruhn T, Schaumlöffel, A, Hemberger Y, Bringmann G. 2013. SpecDics, Version 1.61 ed. University of Würzburg: Würzburg, Germany.
3. Bruhn T, Schaumlöffel A, Hemberger Y, Bringmann G. 2013. SpecDics: quantifying the comparison of calculated and experimental electronic circular dichroism spectra. Chirality. 25: 243-249.

Quantum chemical ECD calculation of 10

The theoretical calculations of **10** was performed using Gaussian 09.[1] The systematic random conformational analysis of (5*R*, 8*S*, 9*S*, 10*R*)-**10** was performed in the SYBYL 8.1 program by using MMFF94s molecular force field, which afforded 1 conformers for (5*R*, 8*S*, 9*S*, 10*R*)-**10** with an energy cutoff of 10 kcal mol^{-1} to the global minima. All the obtained conformers were further optimized using DFT at the B3LYP/6-31+G(d) level in gas phase by using Gaussian09 software.[1] All of the optimized stable conformers were used for TDDFT computation of the excited stats at the same levels, with the consideration of the first 30 excitations. The overall ECD curves of (5*R*, 8*S*, 9*S*, 10*R*)-**10** was weighted by Boltzmann distribution of each conformer (with a half-bandwidth of 0.33 eV), with a UV correction of 18 nm. The calculated ECD spectra of (5*R*, 8*S*, 9*S*, 10*R*)-**10** was subsequently compared with the experimental one. The ECD spectra were produced by SpecDis 1.6 software.[2,3]

References

1. Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, Scalmani G, Barone V, Mennucci B, Petersson GA, et al. 2010. Gaussian 09, Revision D.01, Gaussian, Inc., Wallingford CT.
2. Bruhn T, Schaumlöffel, A, Hemberger Y, Bringmann G. 2013. SpecDics, Version 1.61 ed. University of Würzburg: Würzburg, Germany.
3. Bruhn T, Schaumlöffel A, Hemberger Y, Bringmann G. 2013. SpecDics: quantifying the comparison of calculated and experimental electronic circular dichroism spectra. Chirality. 25: 243-249.

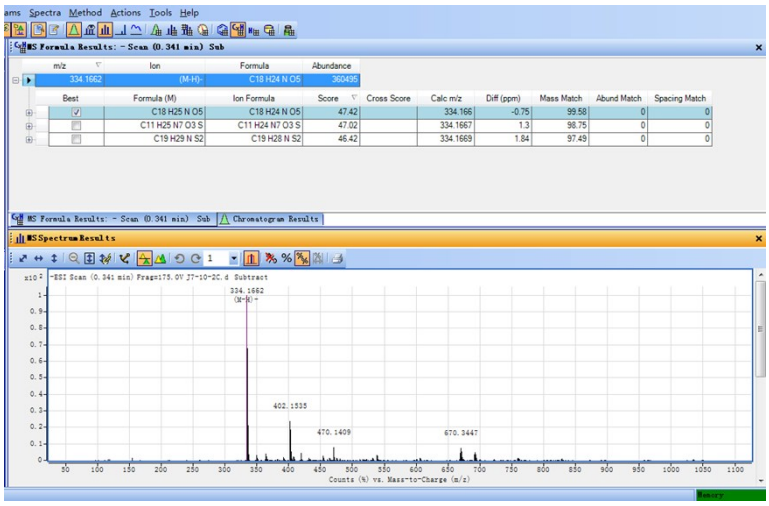

Figure S1. HR-ESI-MS spectrum of **1**

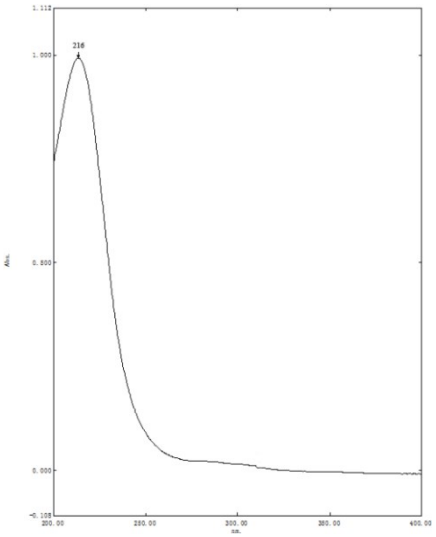

Figure S2. UV spectrum of **1**

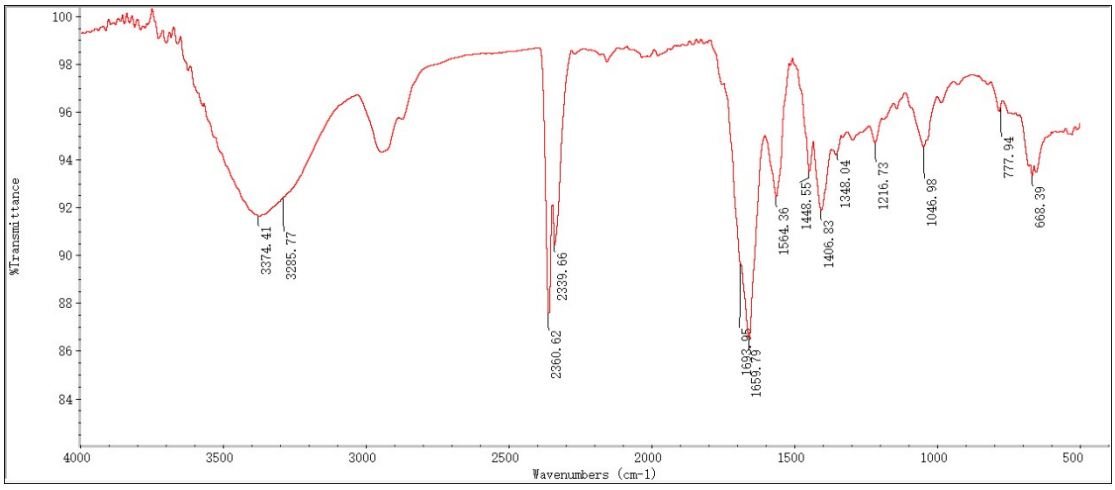

Figure S3. IR spectrum of **1**

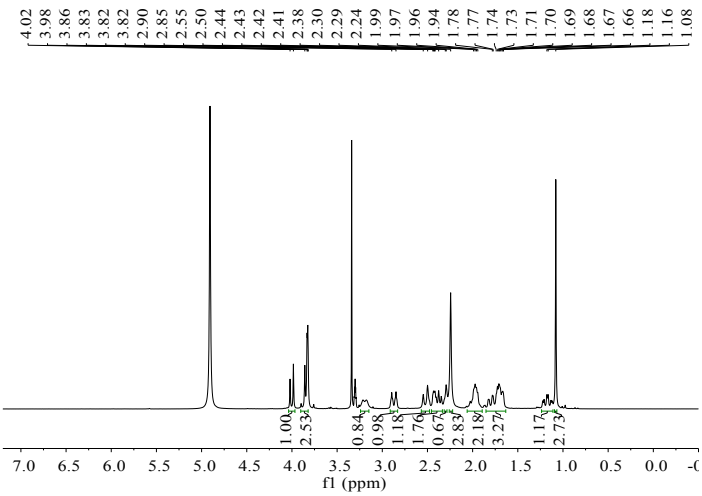

Figure S4. ^{1}H NMR spectrum of **1**

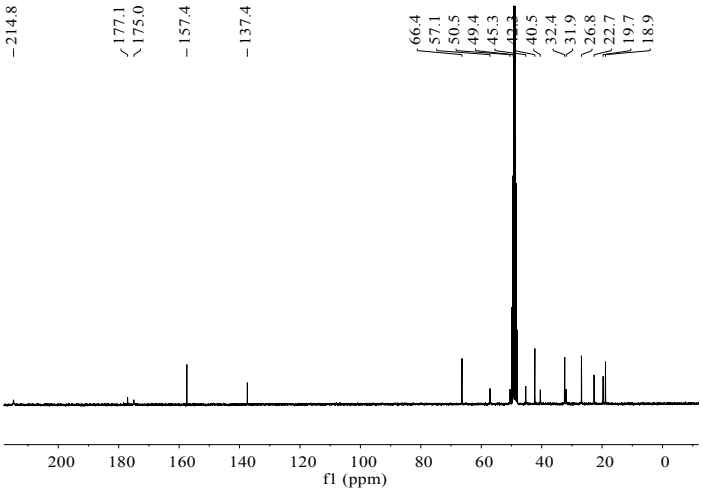

Figure S5. ^{13}C NMR spectrum of **1**

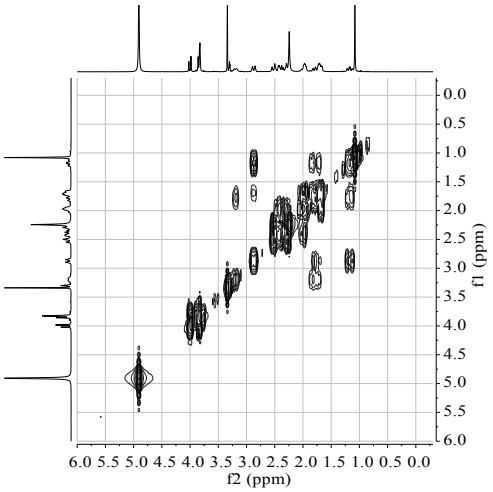

Figure S6. ^{1}H-^{1}H COSY spectrum of **1**

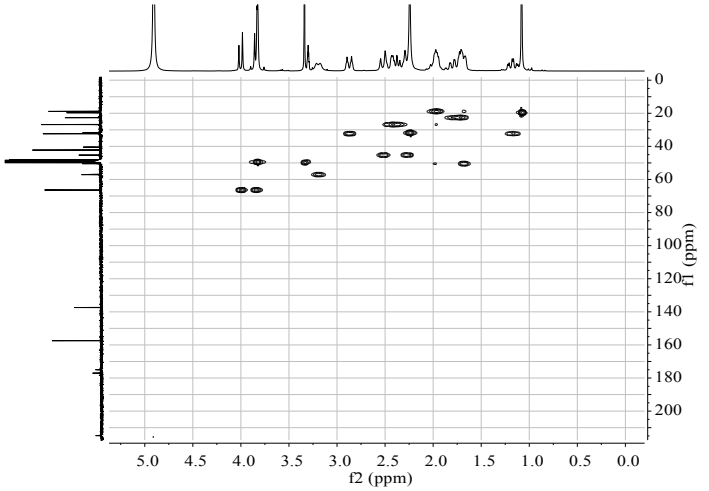

Figure S7. HSQC spectrum of **1**

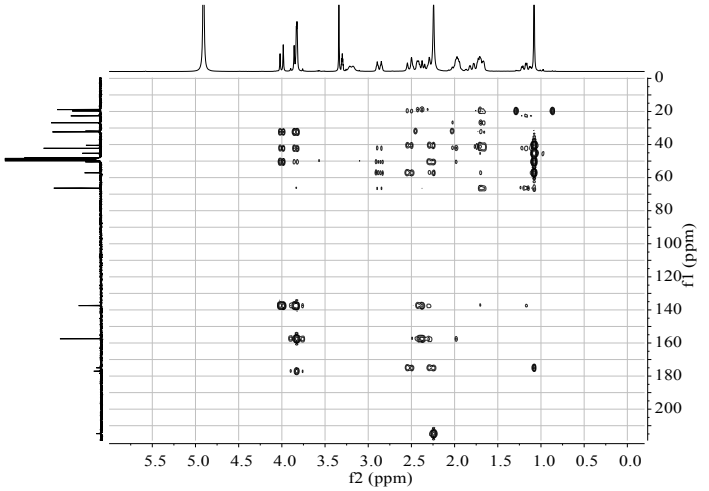

Figure S8. HMBC spectrum of **1**

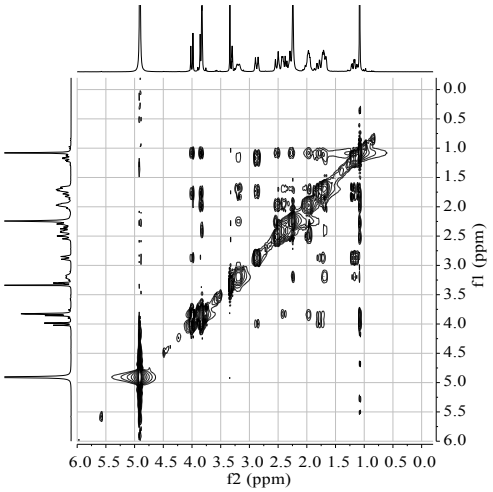

Figure S9. NOESY spectrum of **1**

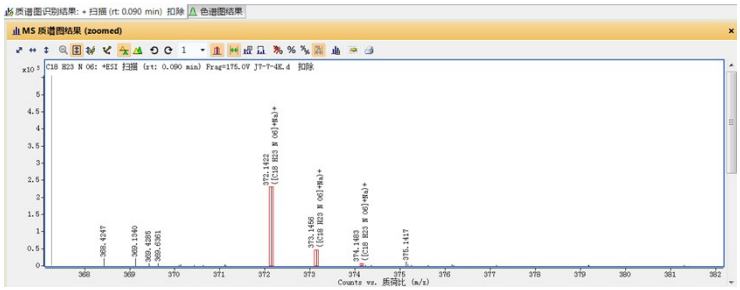

Figure S10. HR-ESI-MS spectrum of **2**

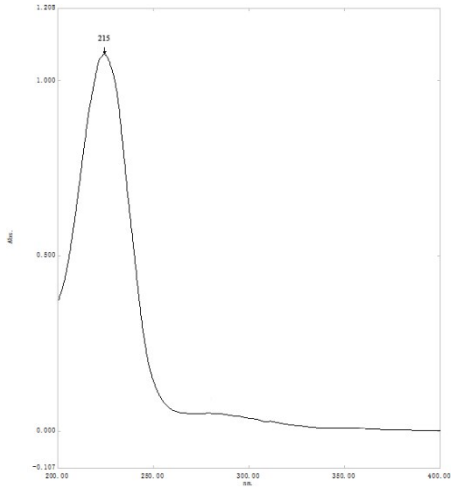

Figure S11. UV spectrum of **2**

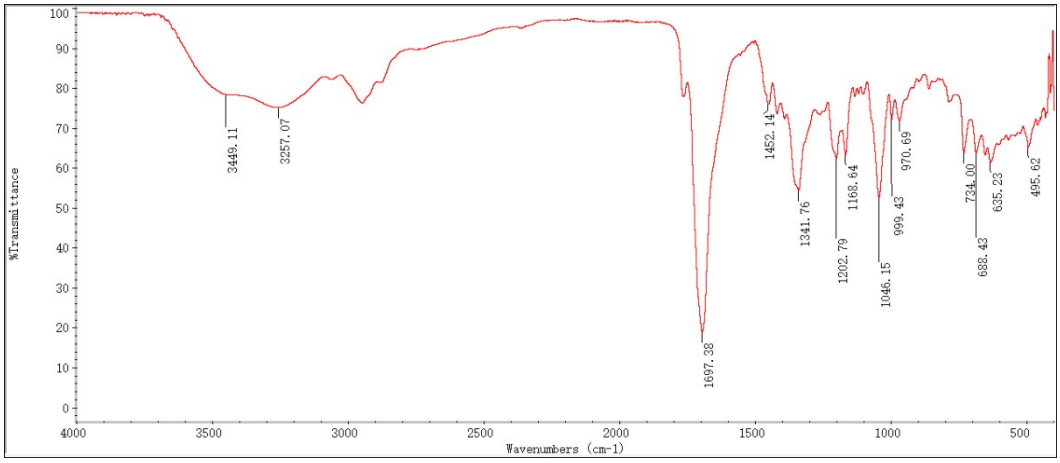

Figure S12. IR spectrum of **2**

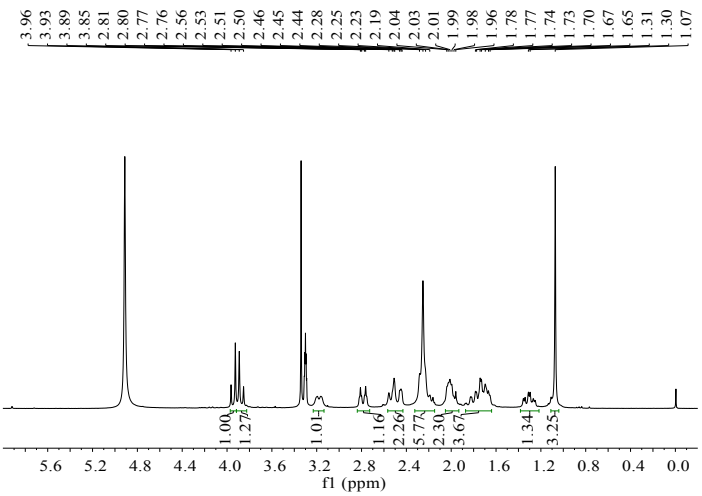

Figure S13. ^{1}H NMR spectrum of **2**

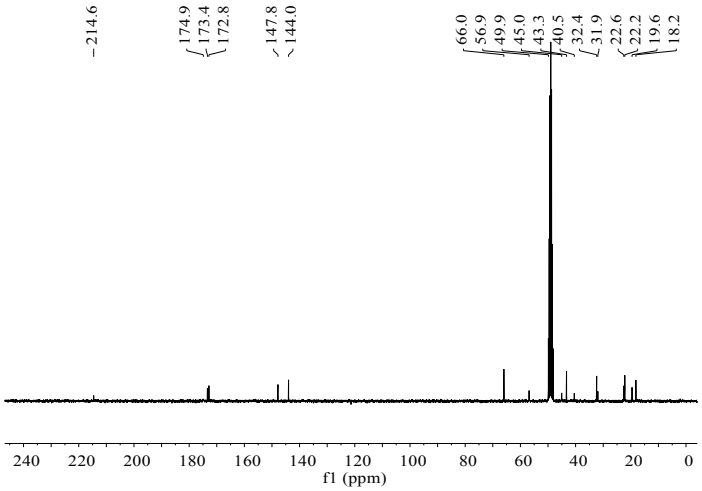

Figure S14. ^{3}C NMR spectrum of **2**

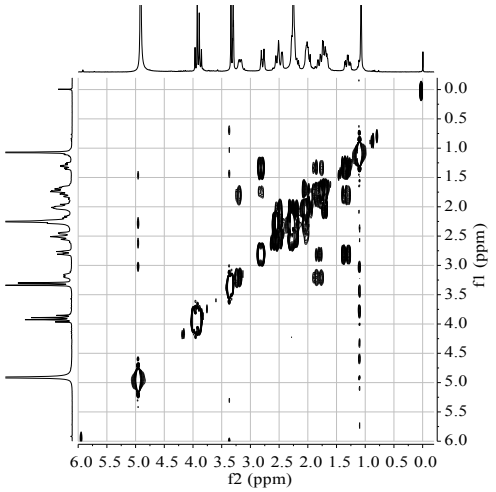

Figure S15. ^{1}H-^{1}H COSY spectrum of **2**

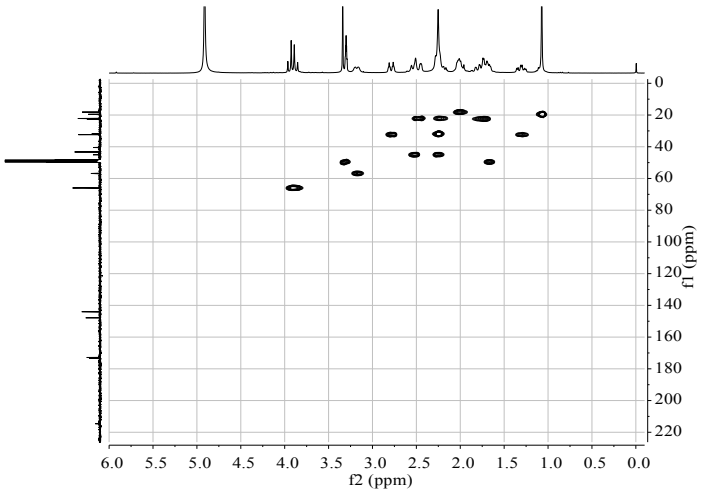

Figure S16. HSQC spectrum of **2**

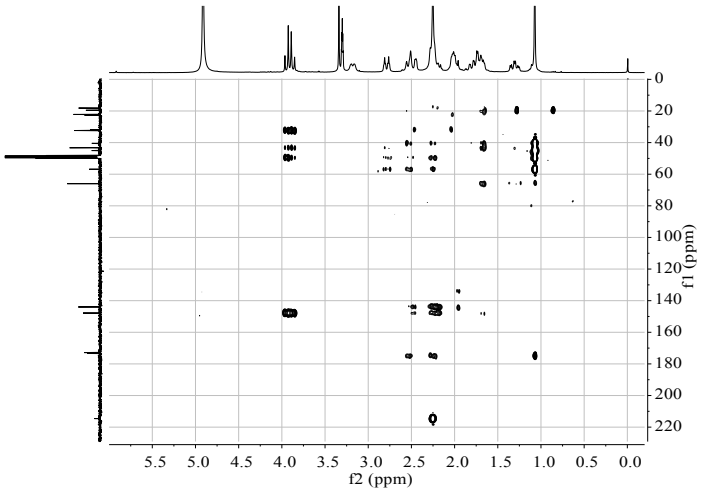

Figure S17. HMBC spectrum of **2**

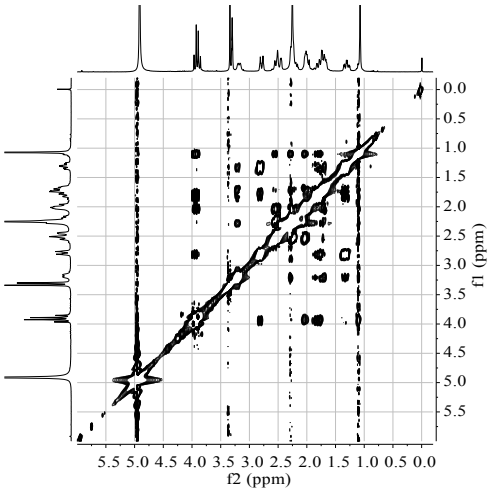

Figure S18. NOESY s spectrum of **2**

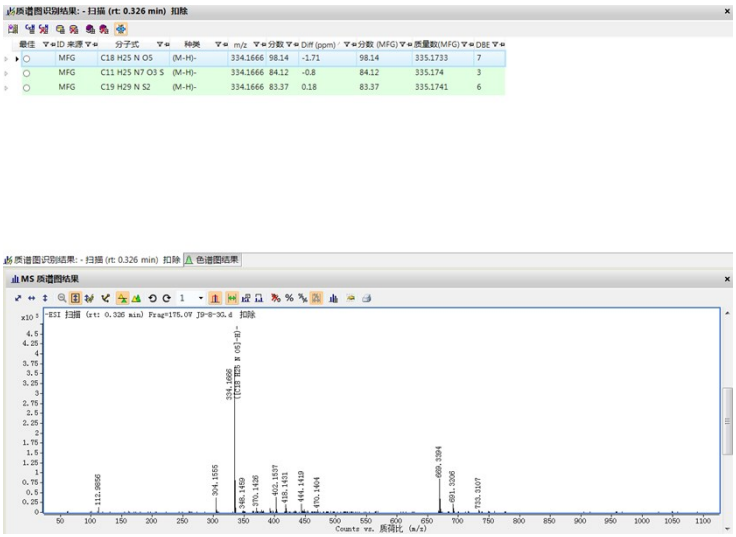

Figure S19. HR-ESI-MS spectrum of **3**

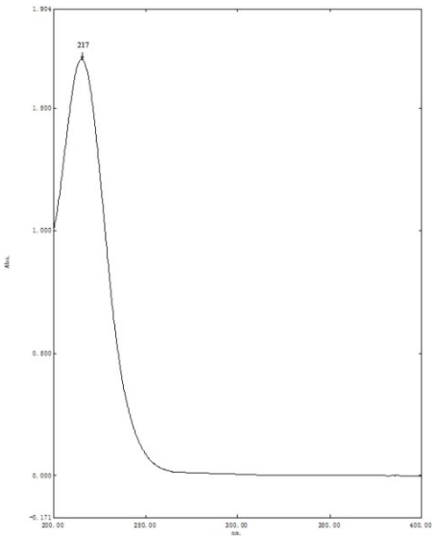

Figure S20. UV spectrum of **3**

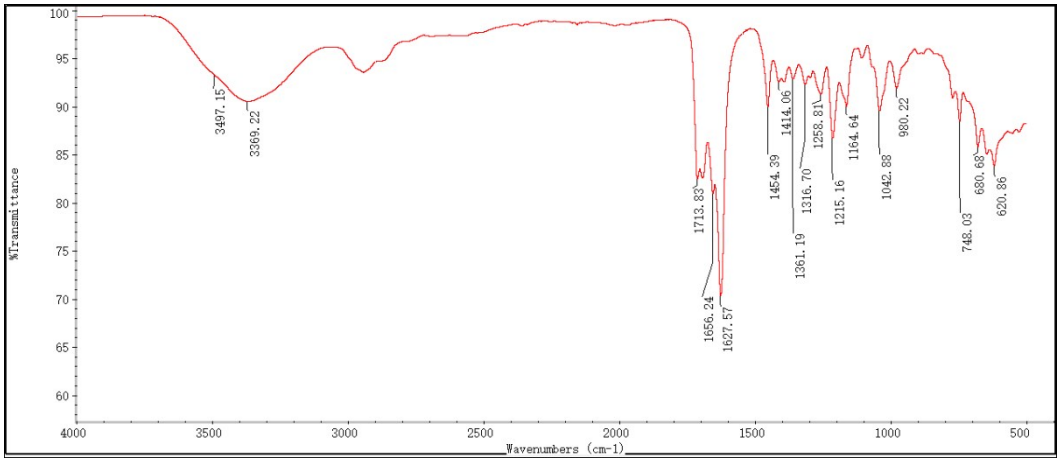

Figure S21. IR spectrum of **3**

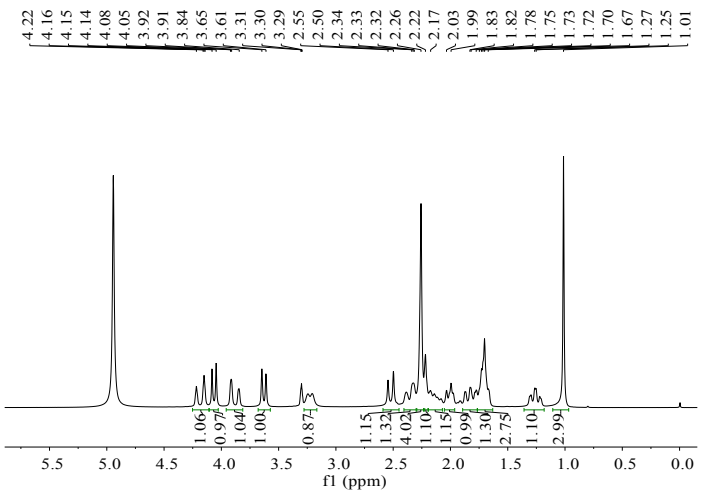

Figure S22. ^{1}H NMR spectrum of **3**

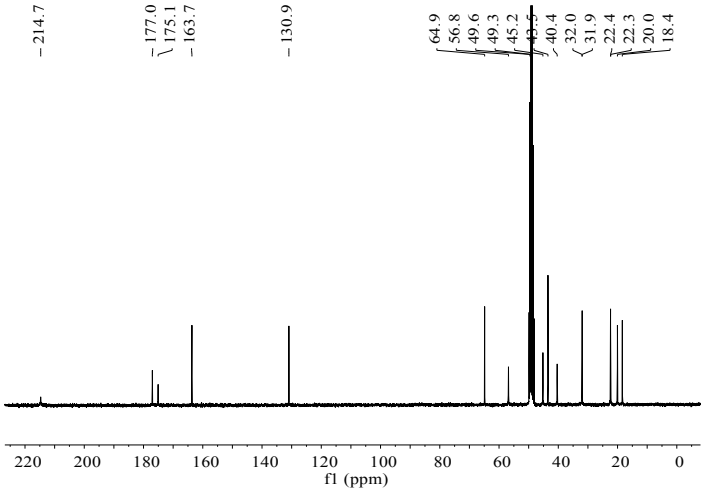

Figure S23. ^{13}C NMR spectrum of **3**

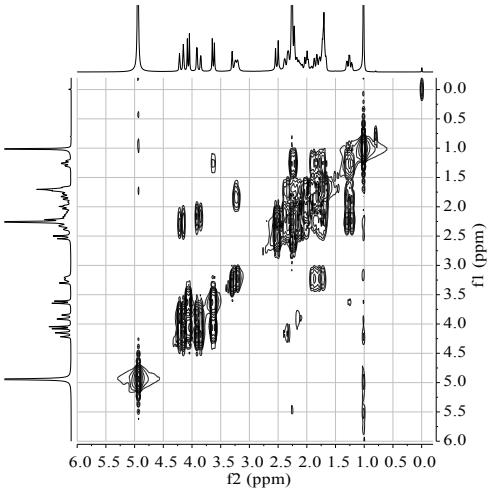

Figure S24. ^{1}H-^{1}H COSY spectrum of **3**

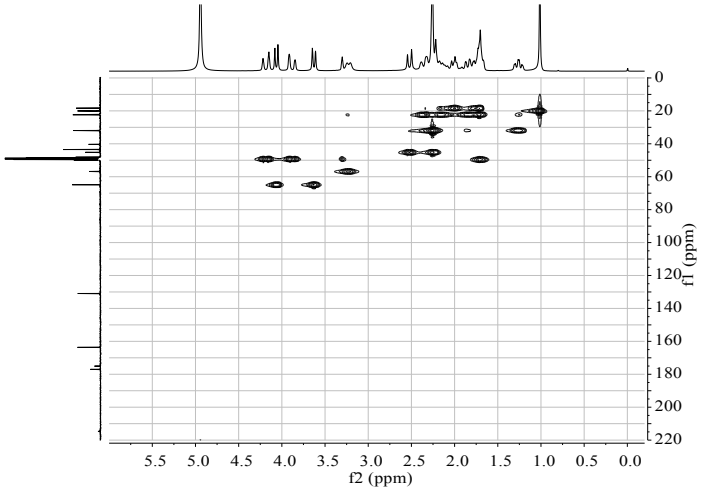

Figure S25. HSQC spectrum of **3**

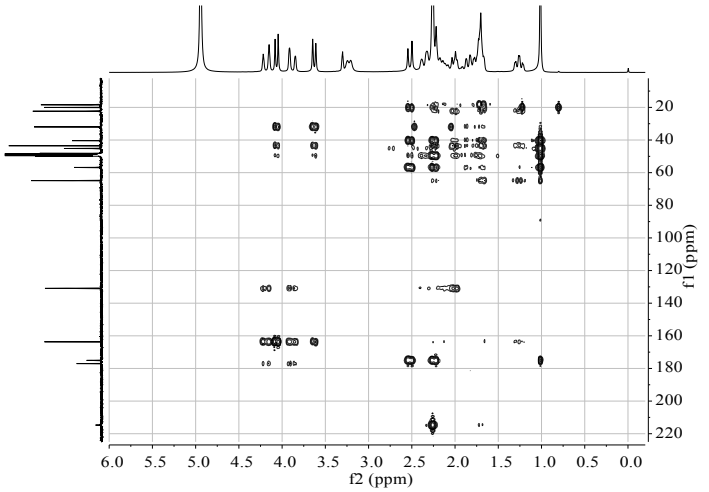

Figure S26. HMBC spectrum of **3**

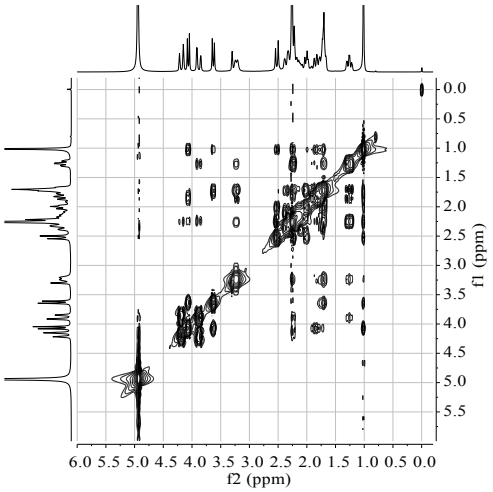

Figure S27. NOESY spectrum of **3**

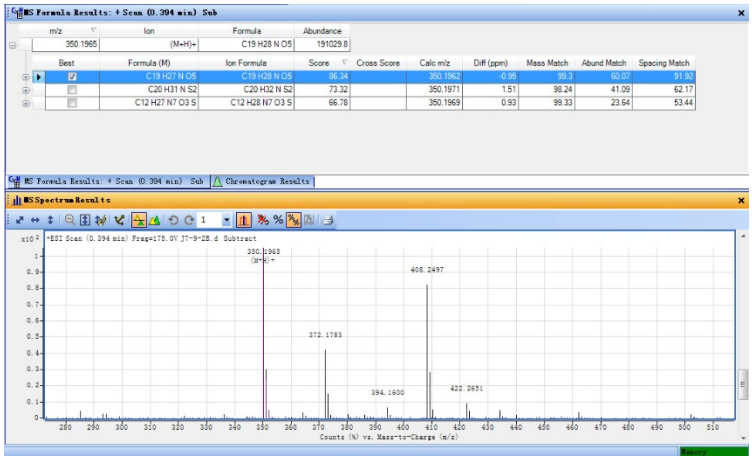

Figure S28. HR-ESI-MS spectrum of **4**

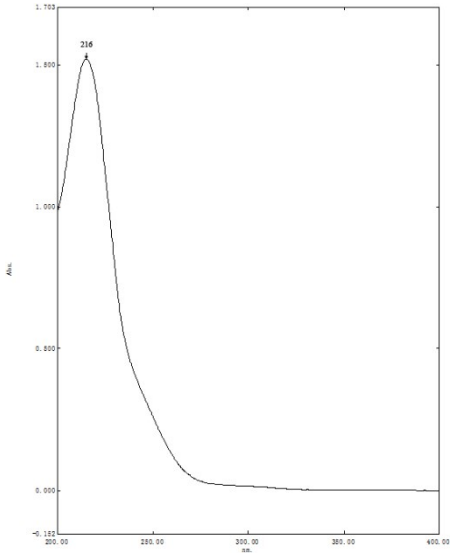

Figure S29. UV spectrum of **4**

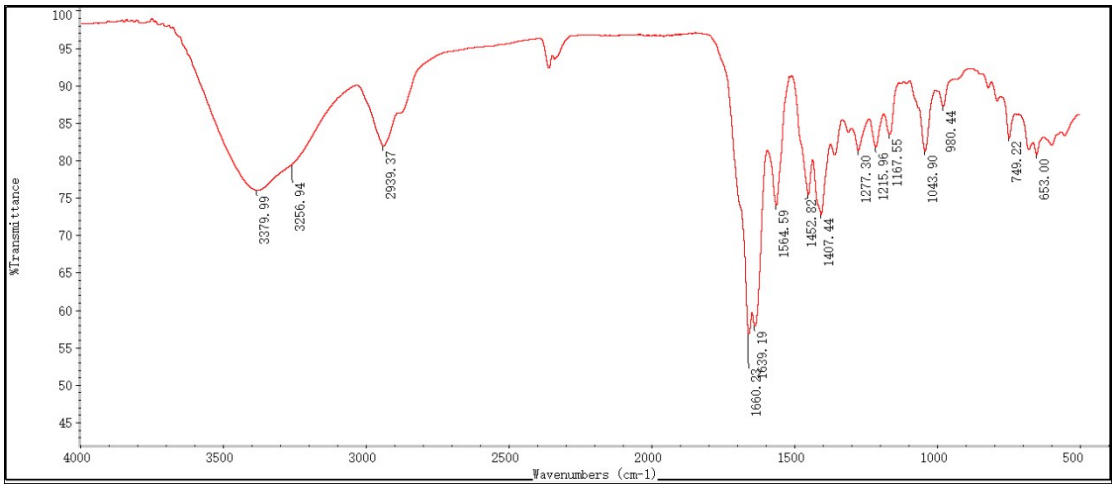

Figure S30. IR spectrum of **4**

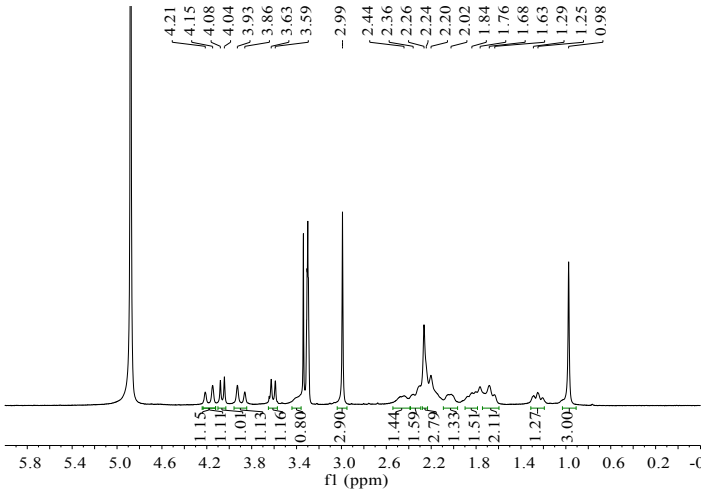

Figure S31. ^{1}H NMR spectrum of **4**

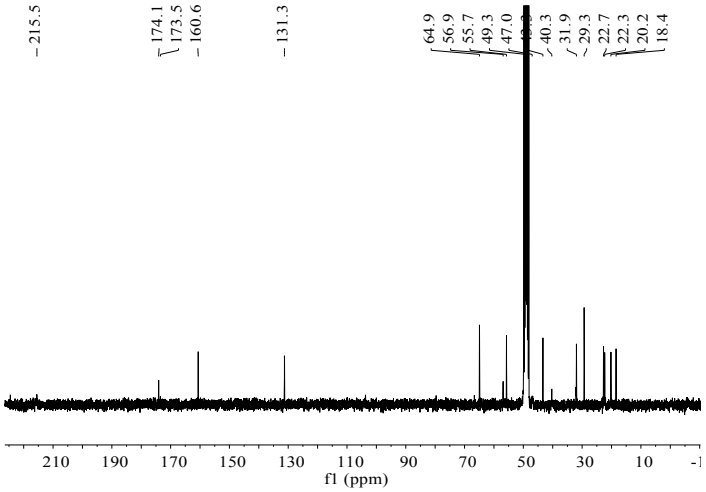

Figure S32. ^{13}C NMR spectrum of **4**

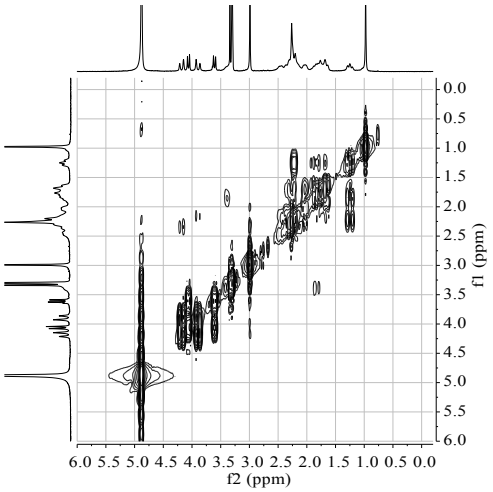

Figure S33. ^{1}H-^{1}H COSY spectrum of **4**

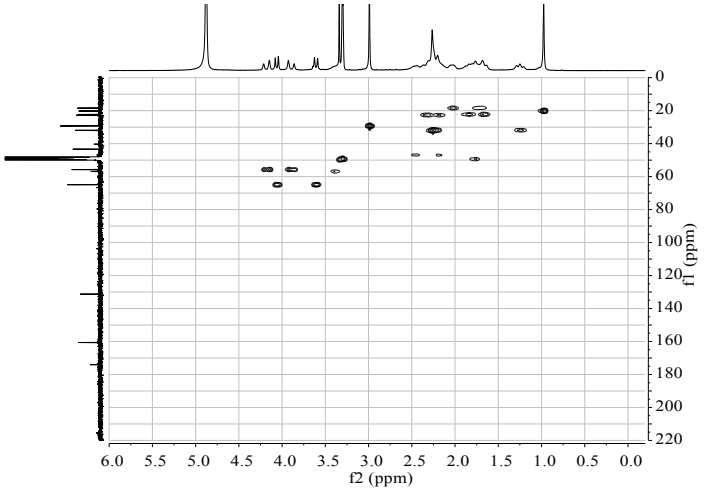

Figure S34. HSQC spectrum of **4**

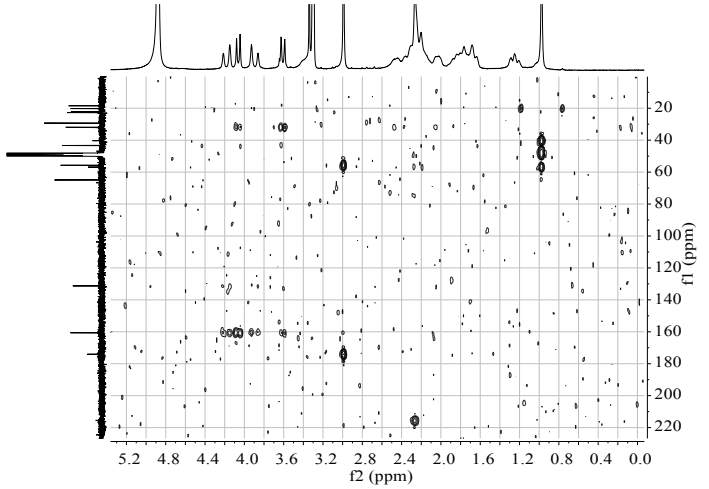

Figure S35. HMBC spectrum of **4**

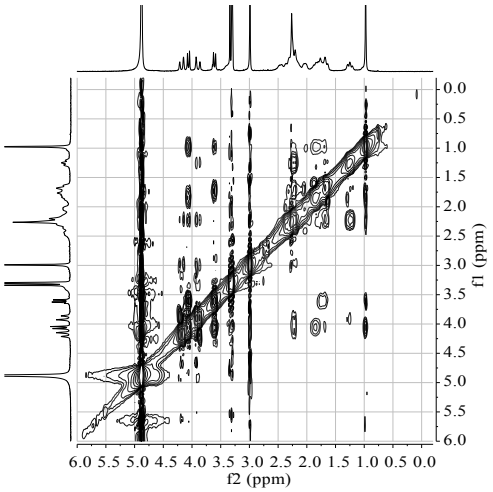

Figure S36. NOESY spectrum of **4**

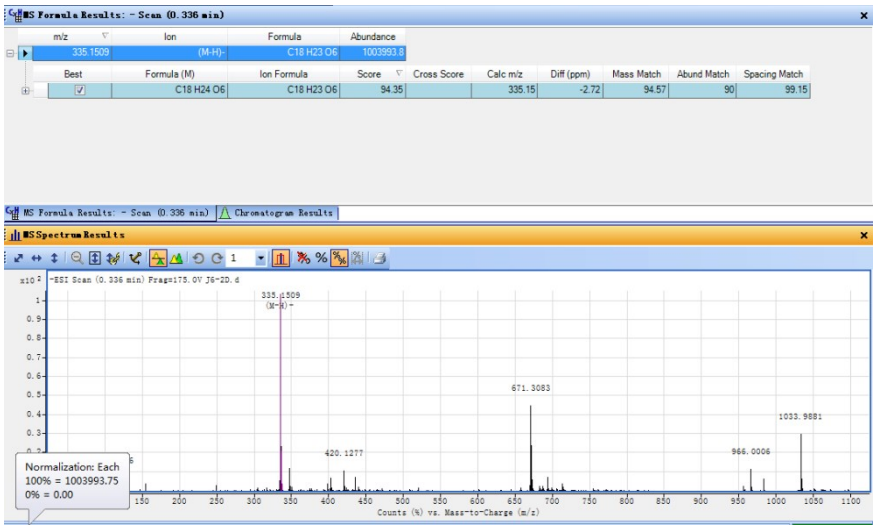

Figure S37. HR-ESI-MS spectrum of **5**

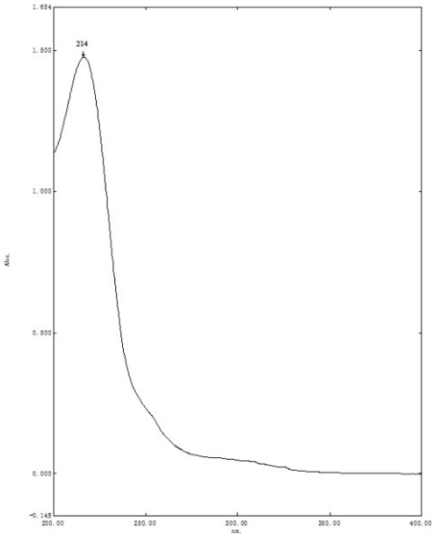

Figure S38. UV spectrum of **5**

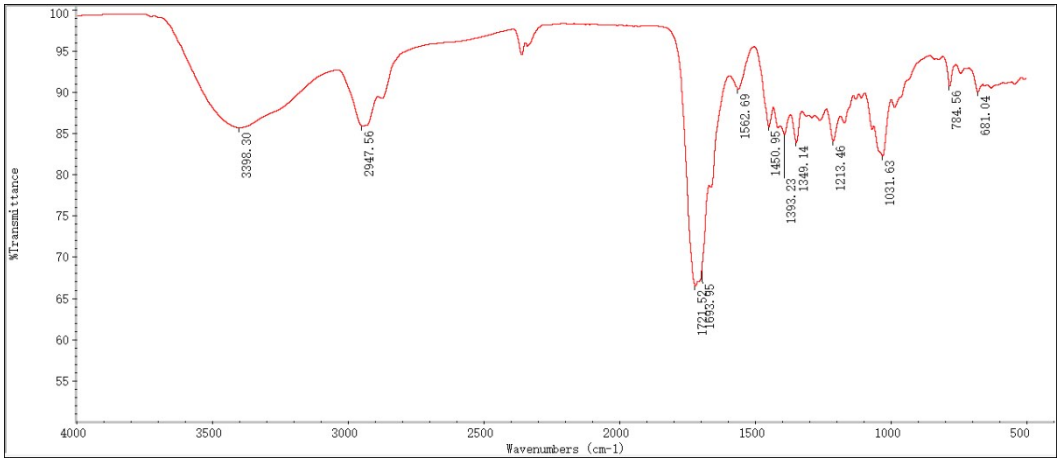

Figure S39. IR spectrum of **5**

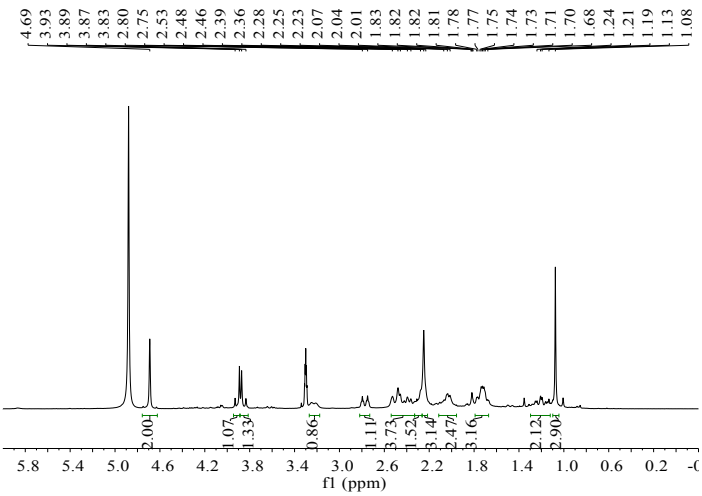

Figure S40. ^{1}H NMR spectrum of **5**

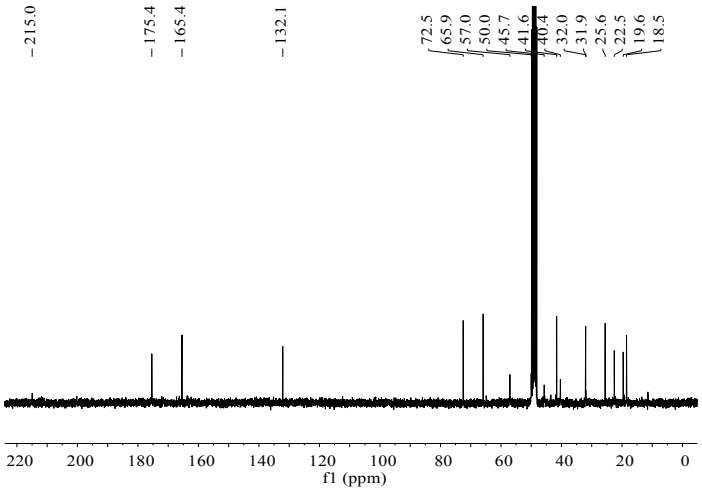

Figure S41. ^{13}C NMR spectrum of **5**

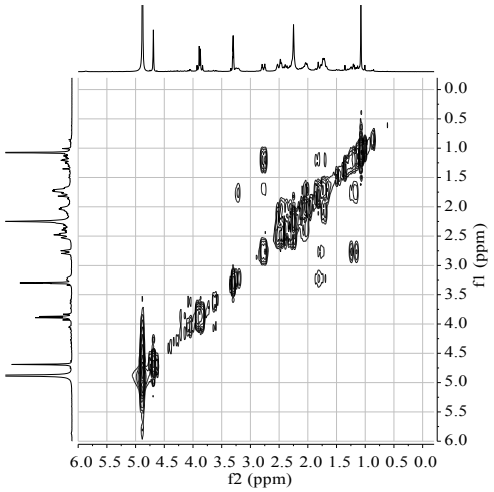

Figure S42. ^{1}H-^{1}H COSY spectrum of **5**

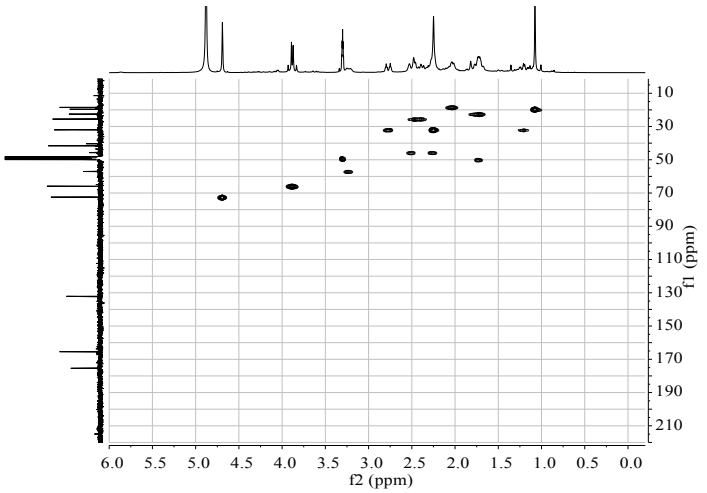

Figure S43. HSQC spectrum of **5**

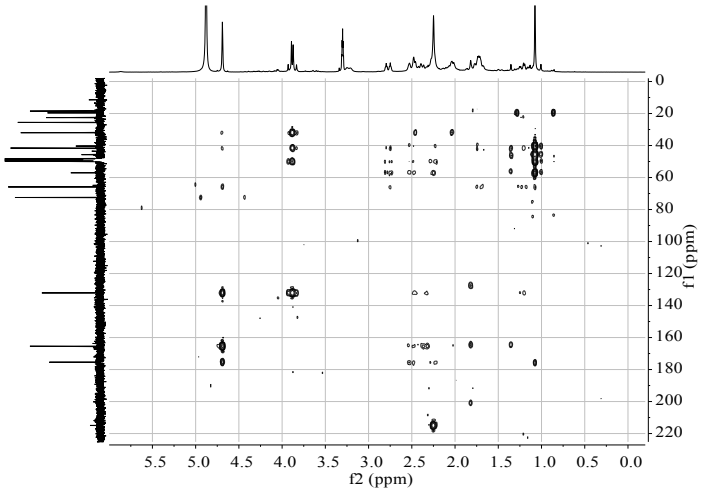

Figure S44. HMBC spectrum of **5**

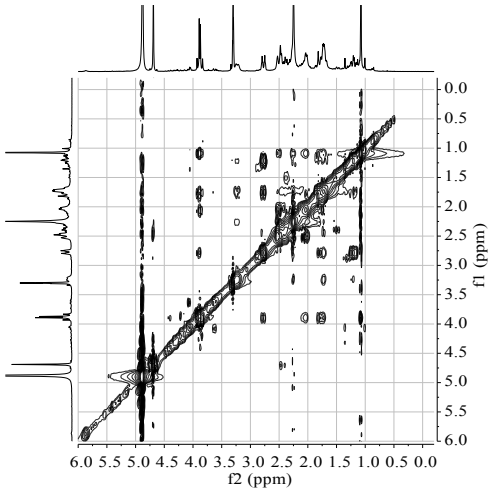

Figure S45. NOESY spectrum of **5**

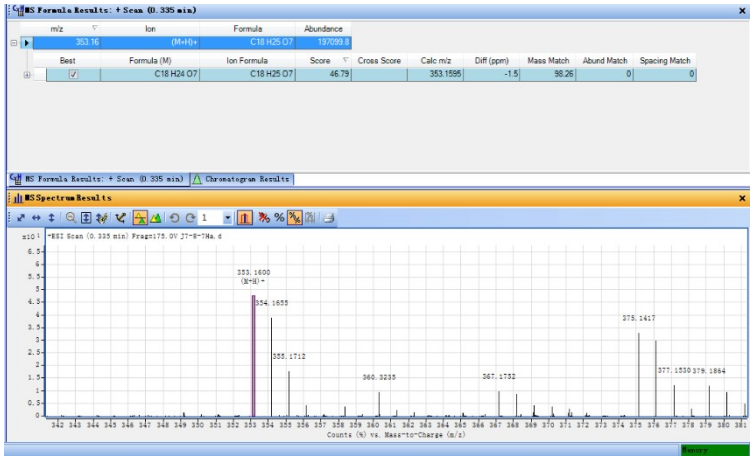

Figure S46. HR-ESI-MS spectrum of **6**

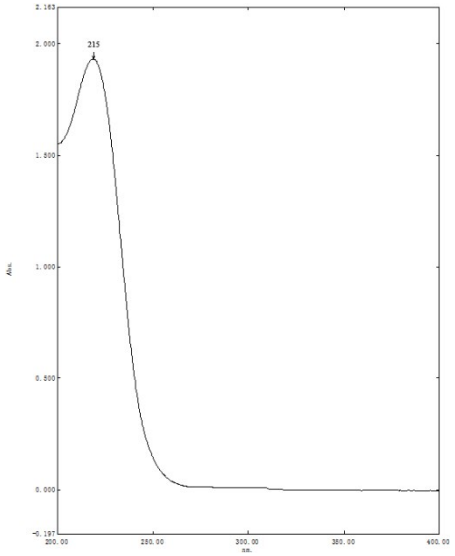

Figure S47. UV spectrum of **6**

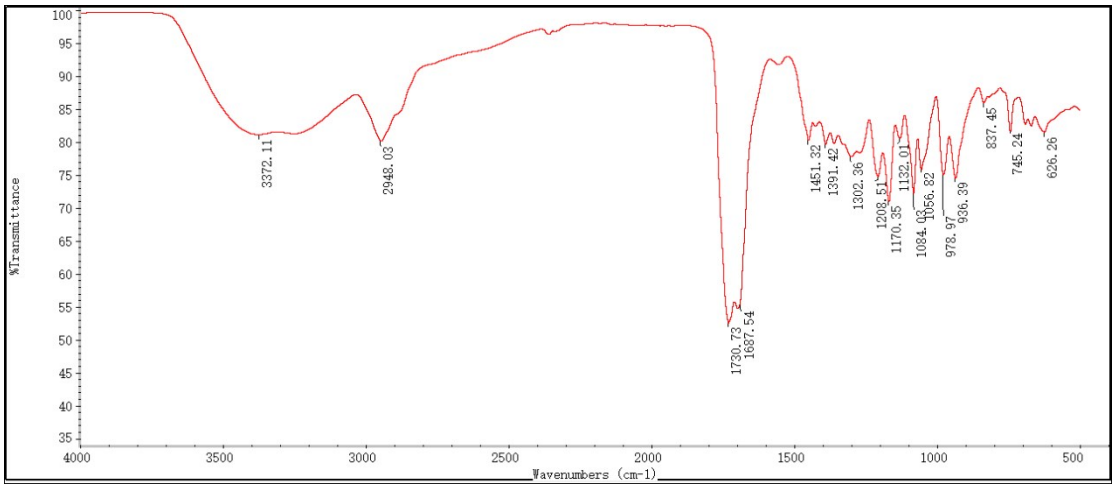

Figure S48. IR spectrum of **6**

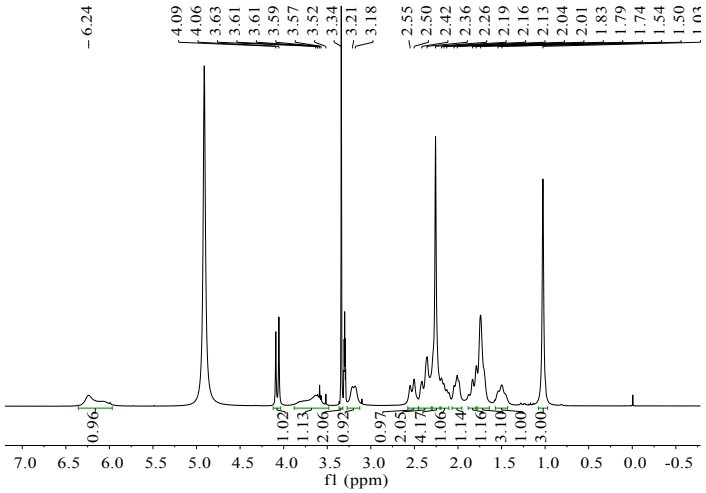

Figure S49. ^{1}H NMR spectrum of **6**

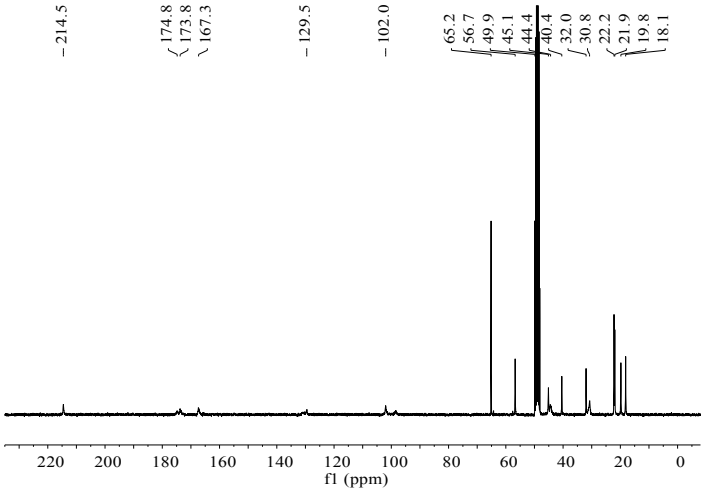

Figure S50. ^{13}C NMR spectrum of **6**

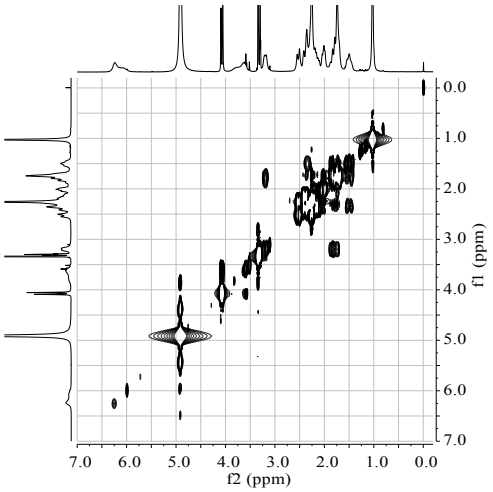

Figure S51. ^{1}H-^{1}H COSY spectrum of **6**

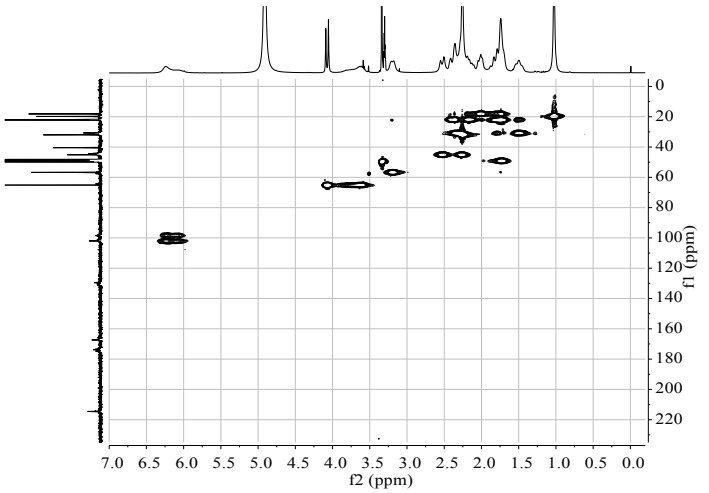

Figure S52. HSQC spectrum of **6**

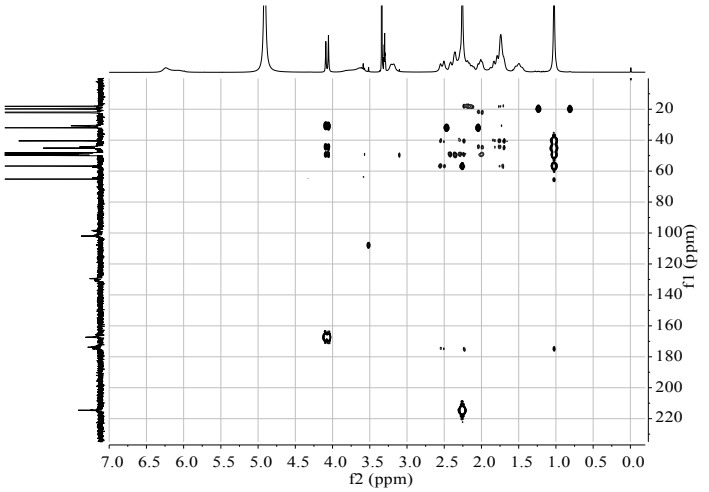

Figure S53. HMBC spectrum of **6**

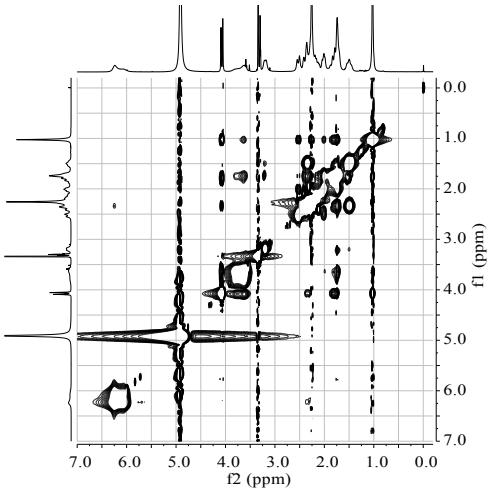

Figure S54. NOESY spectrum of **6**

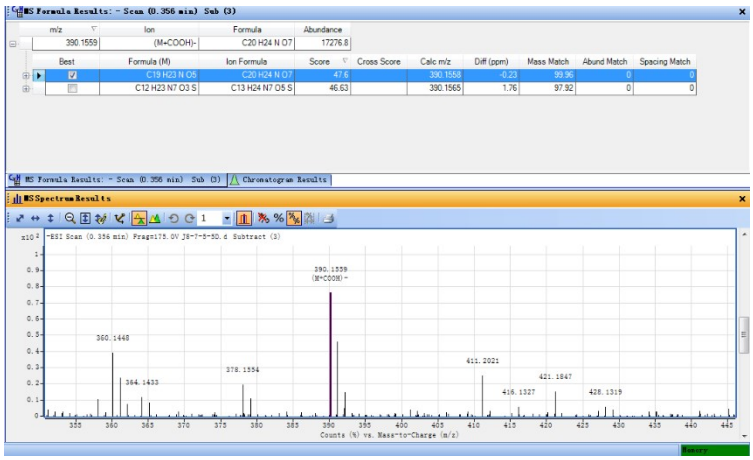

Figure S55. HR-ESI-MS spectrum of **7**

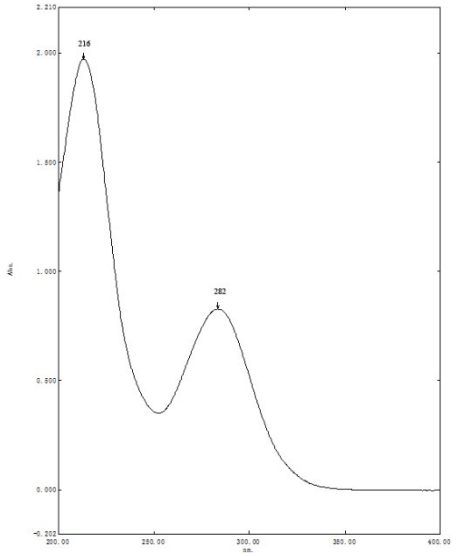

Figure S56. UV spectrum of **7**

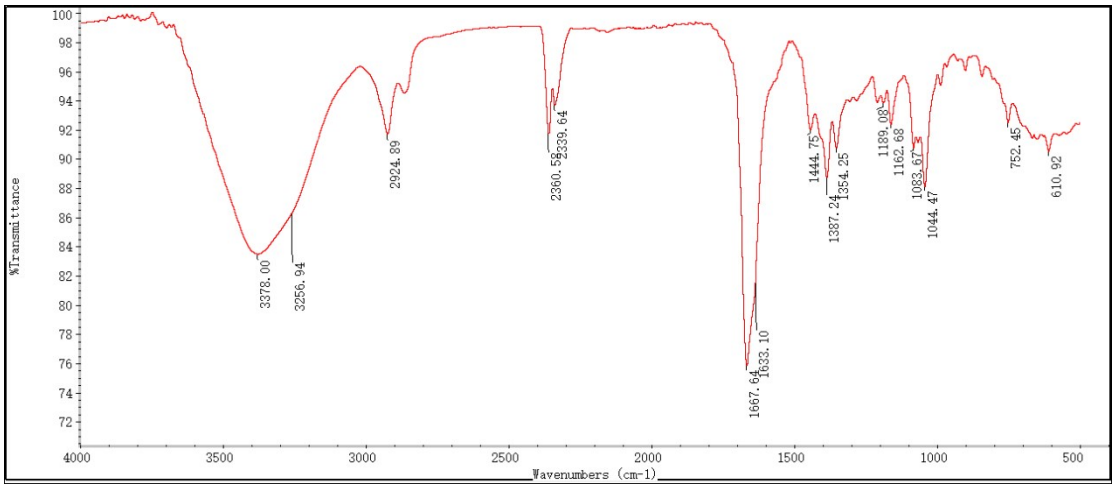

Figure S57. IR spectrum of **7**

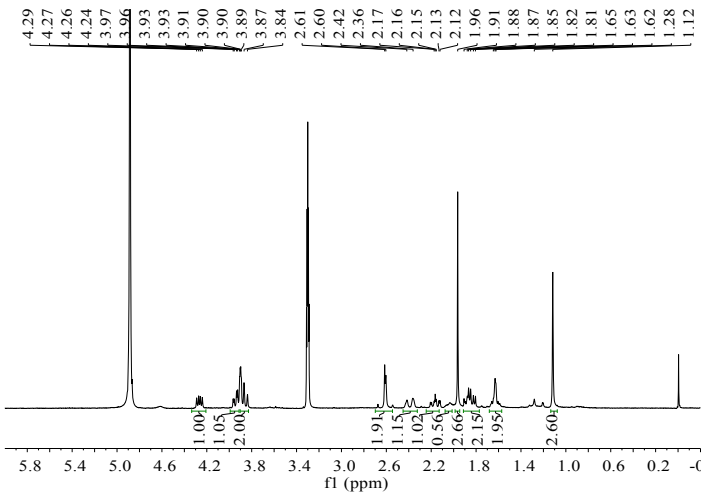

Figure S58. ^{1}H NMR spectrum of **7**

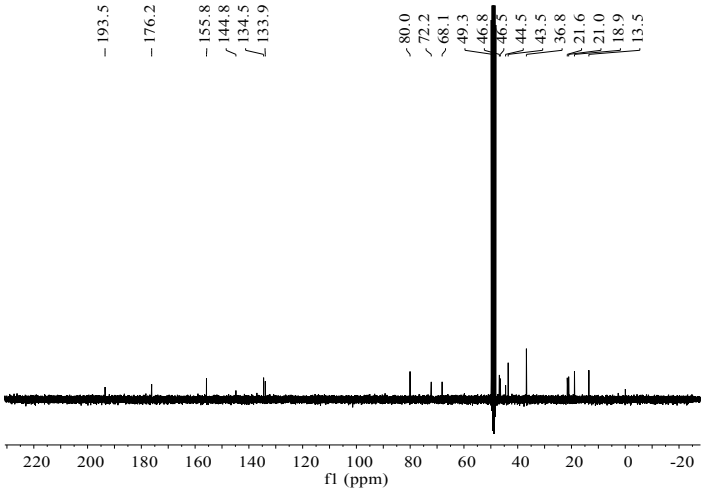

Figure S59. ^{13}C NMR spectrum of **7**

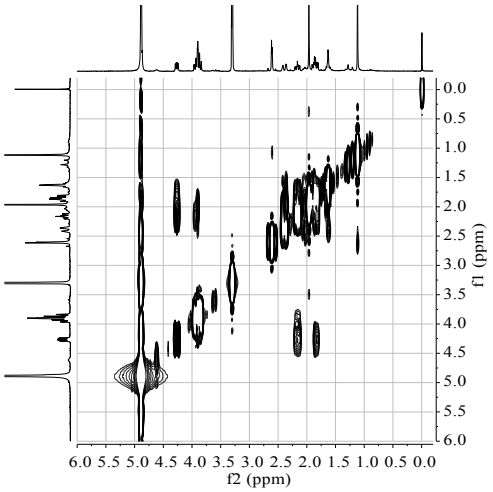

Figure S60. ^{1}H-^{1}H COSY spectrum of **7**

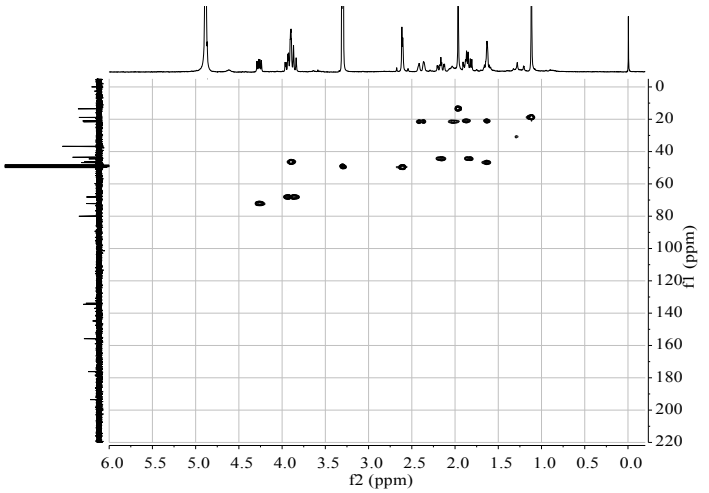

Figure S61. HSQC spectrum of **7**

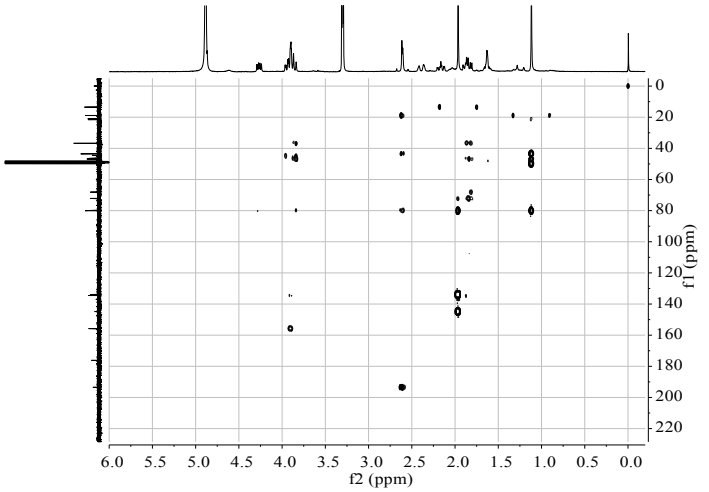

Figure S62. HMBC spectrum of **7**

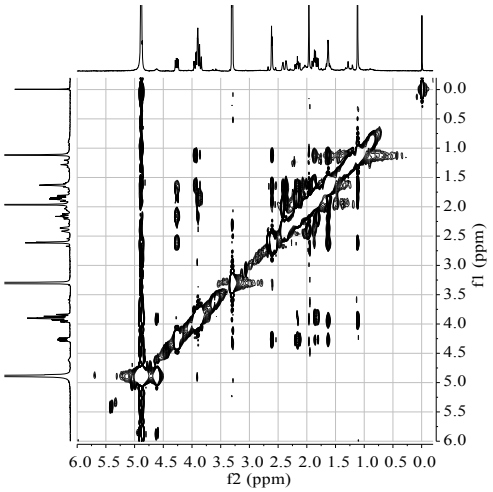

Figure S63. NOESY spectrum of **7**

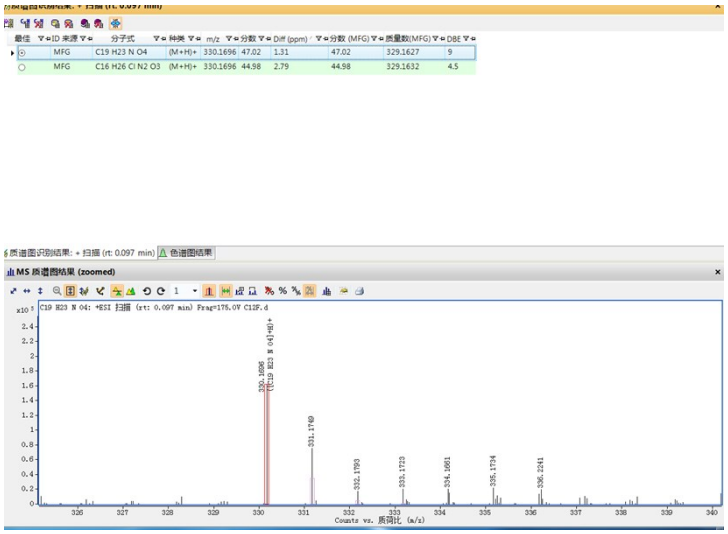

Figure S64. HR-ESI-MS spectrum of **8**

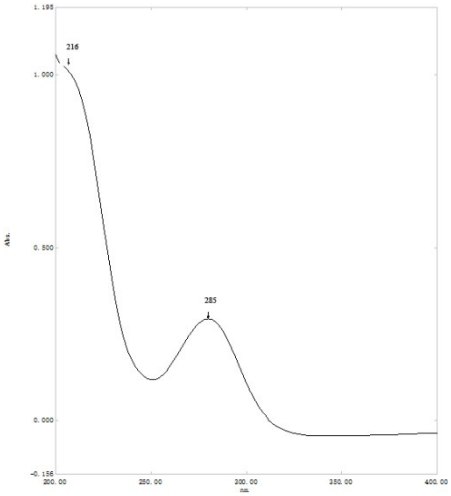

Figure S65. UV spectrum of **8**

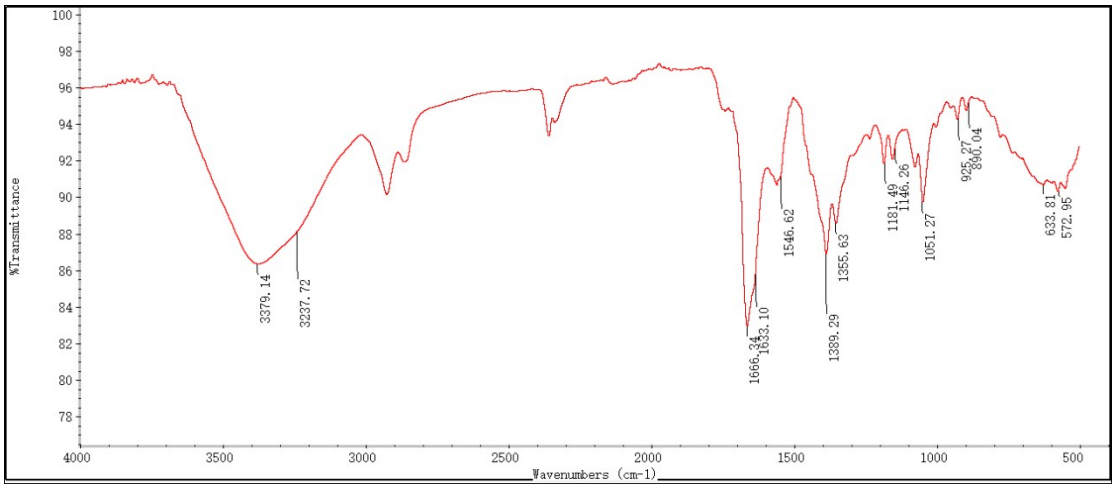

Figure S66. IR spectrum of **8**

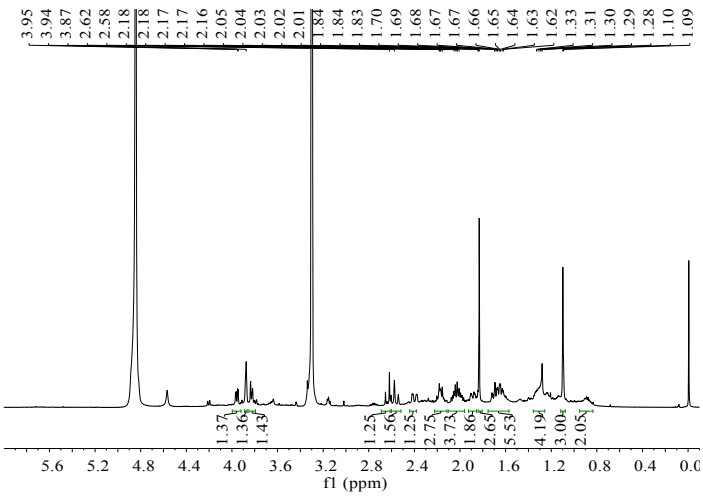

Figure S67. ^{1}H NMR spectrum of **8**

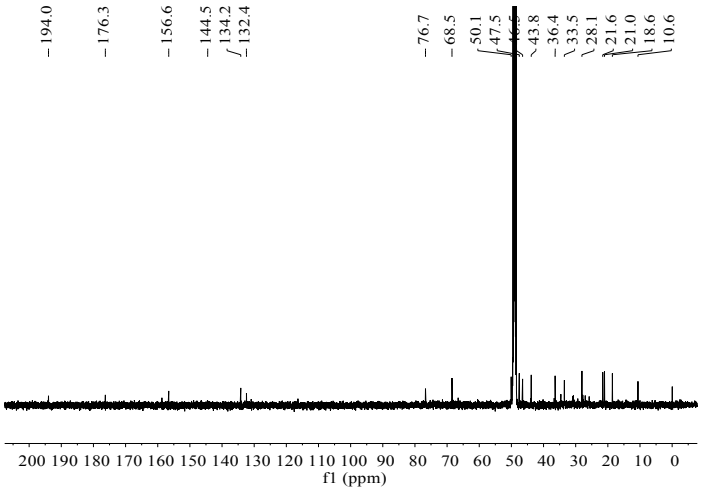

Figure S68. ^{13}C NMR spectrum of **8**

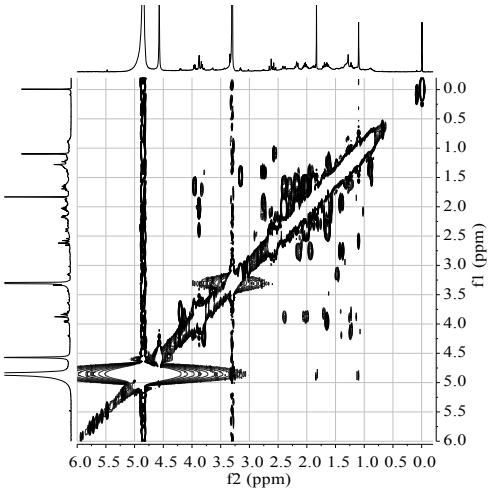

Figure S69. ^{1}H-^{1}H COSY spectrum of **8**

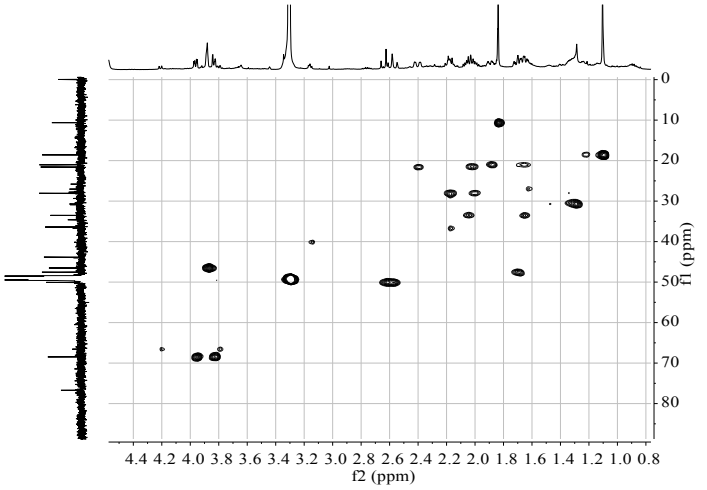

Figure S70. HSQC spectrum of **8**

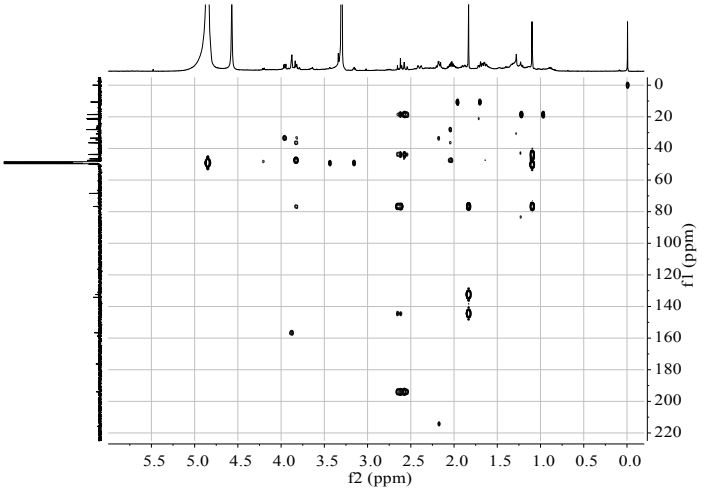

Figure S71. HMBC spectrum of **8**

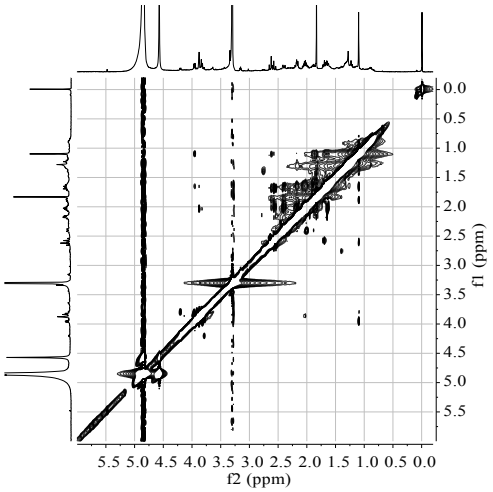

Figure S72. NOESY spectrum of **8**

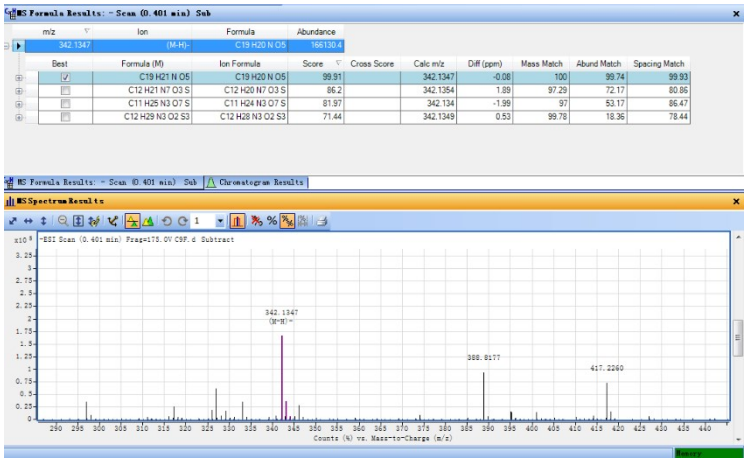

Figure S73. HR-ESI-MS spectrum of **9**

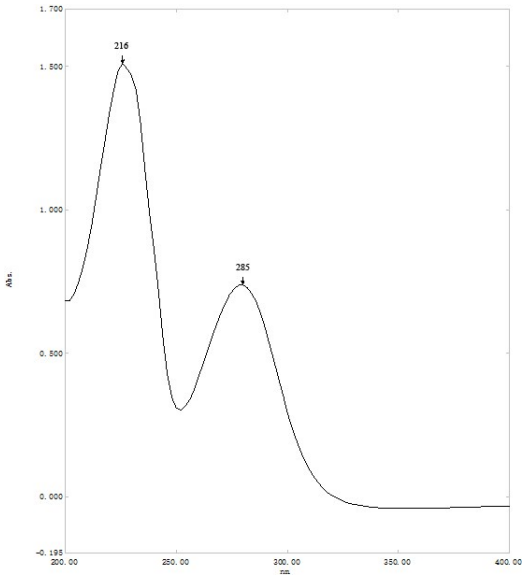

Figure S74. UV spectrum of **9**

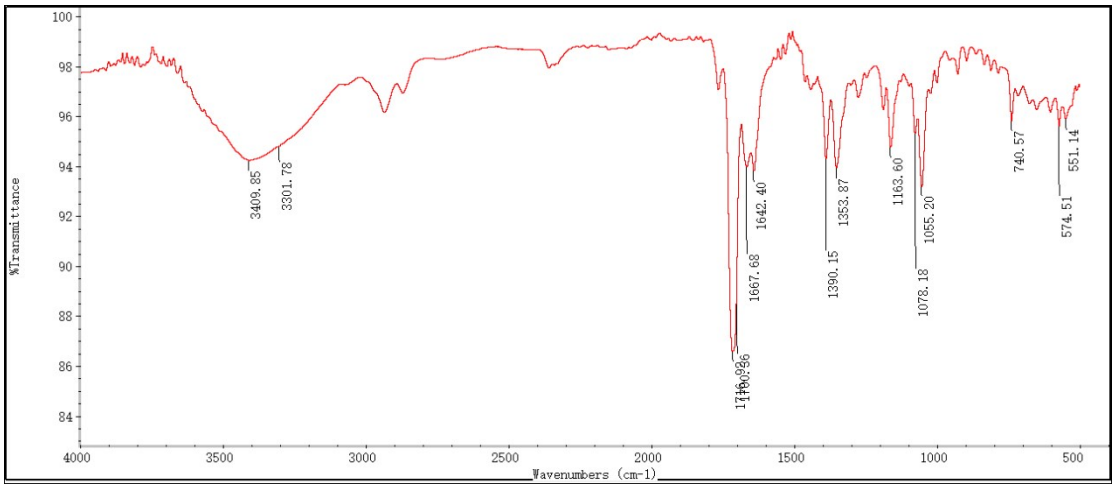

Figure S75. IR spectrum of **9**

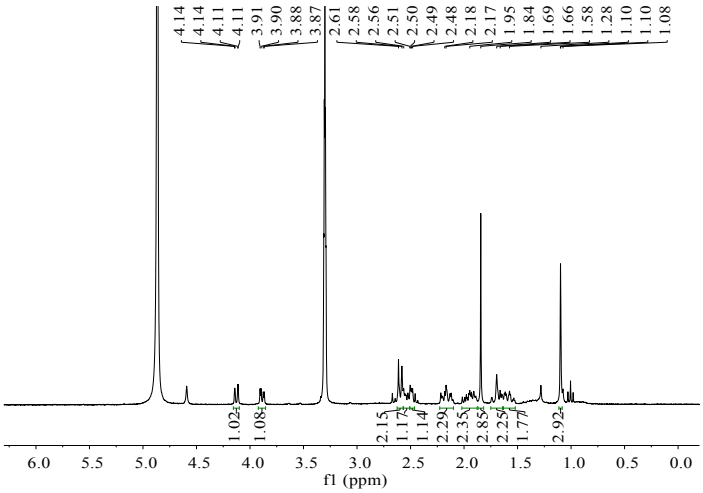

Figure S76. ^{1}H NMR spectrum of **9**

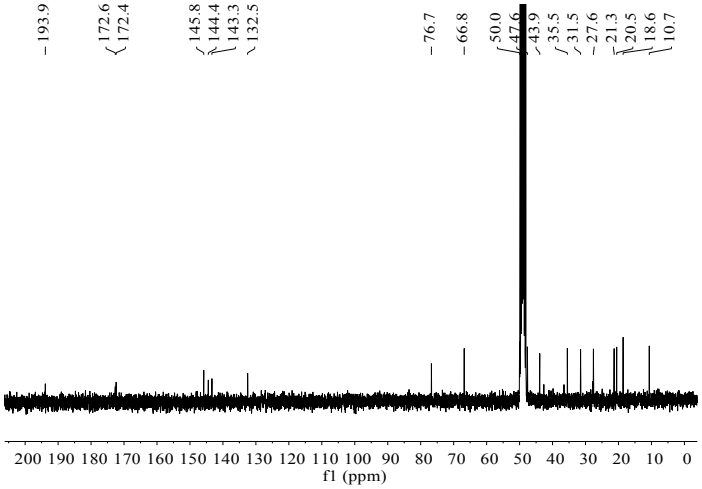

Figure S77. ^{13}C NMR spectrum of **9**

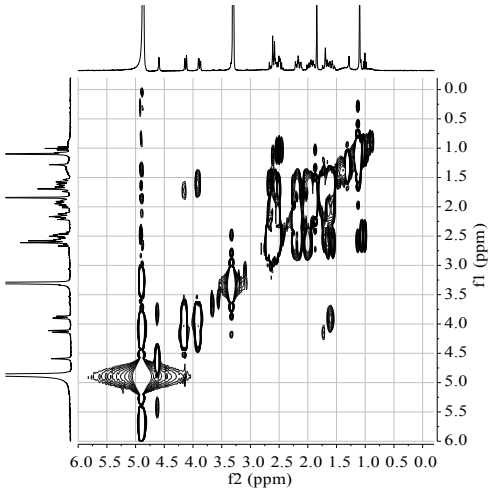

Figure S78. ^{1}H-^{1}H COSY spectrum of **9**

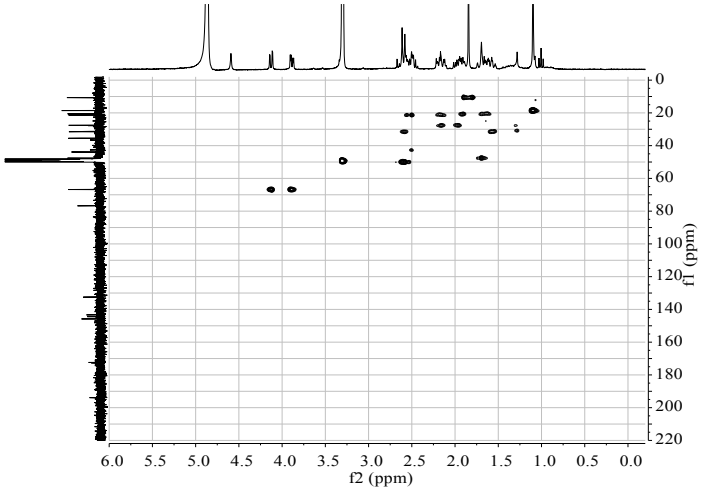

Figure S79. HSQC spectrum of **9**

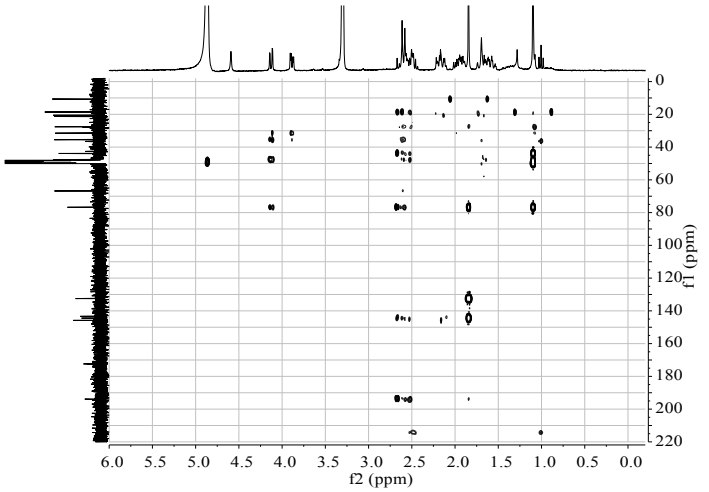

Figure S80. HMBC spectrum of **9**

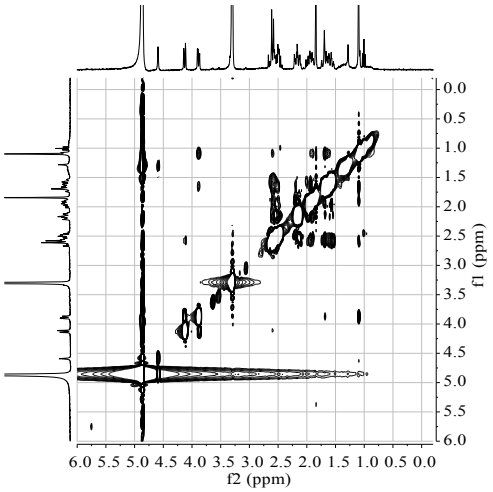

Figure S81. NOESY spectrum of **9**

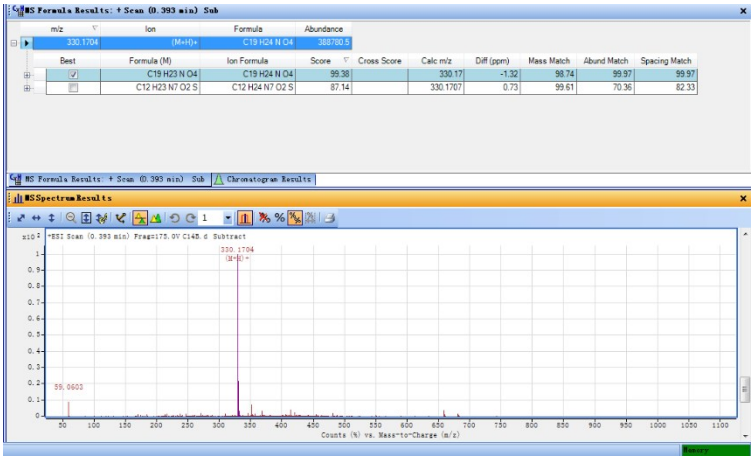

Figure S82. HR-ESI-MS spectrum of **10**

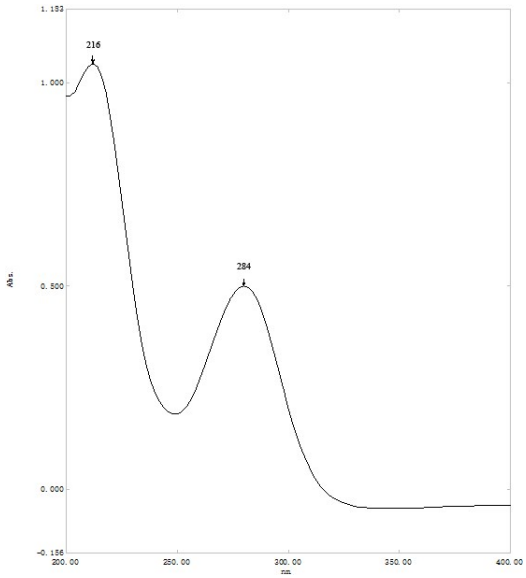

Figure S83. UV spectrum of **10**

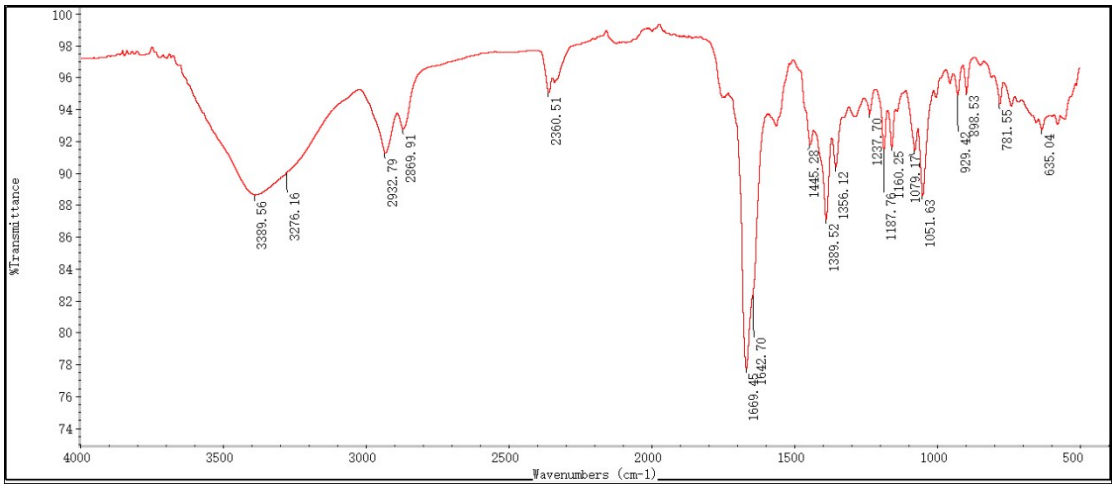

Figure S84. IR spectrum of **10**

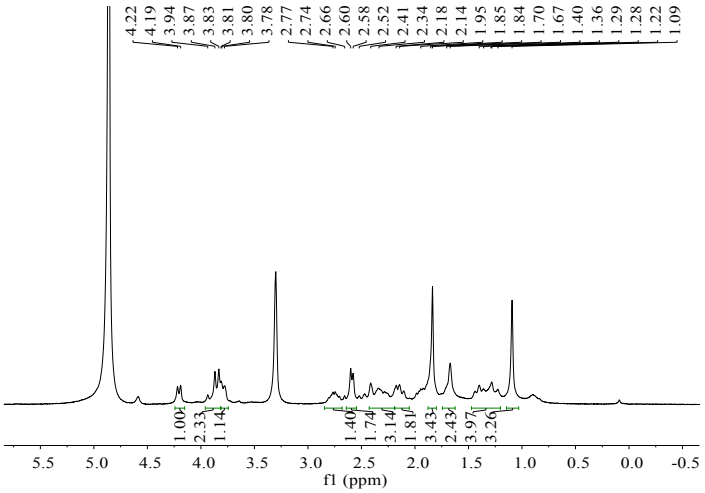

Figure S85. ^{1}H NMR spectrum of **10**

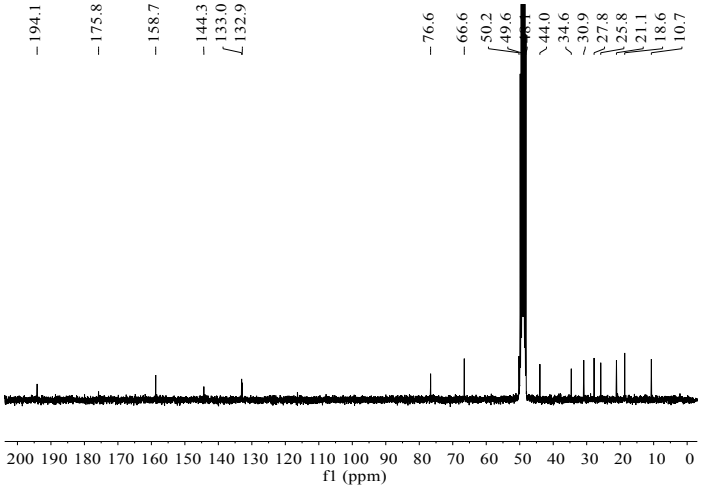

Figure S86. ^{13}C NMR spectrum of **10**

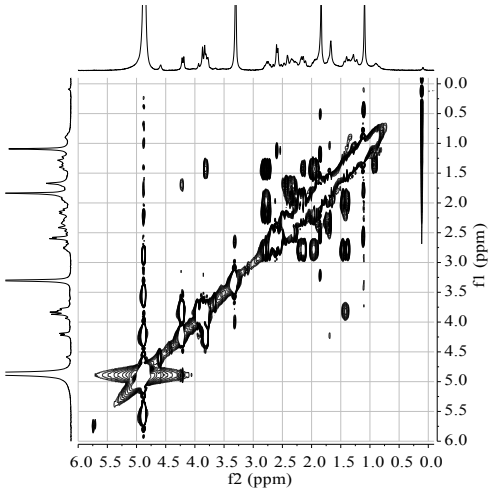

Figure S87. ^{1}H-^{1}H COSY spectrum of **10**

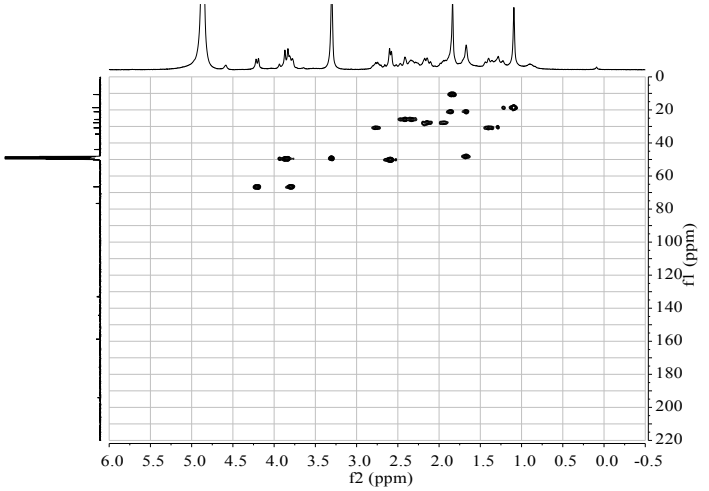

Figure S88. HSQC spectrum of **10**

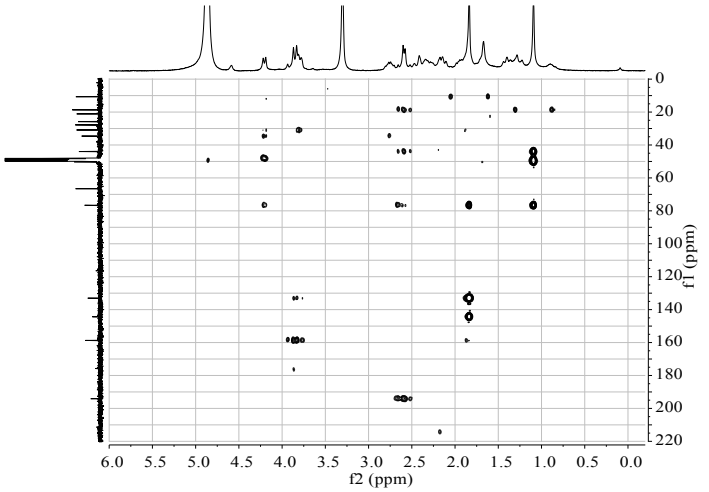

Figure S89. HMBC spectrum of **10**

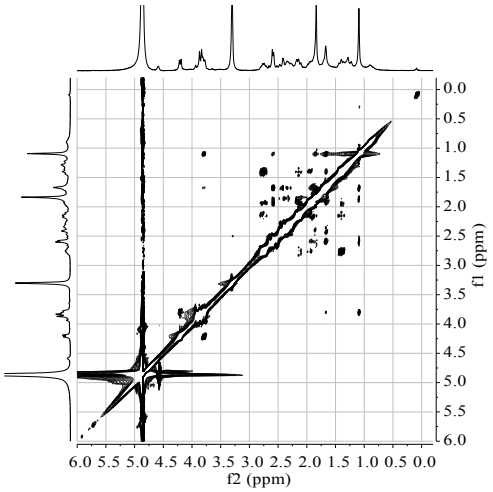

Figure S90. NOESY spectrum of **10**

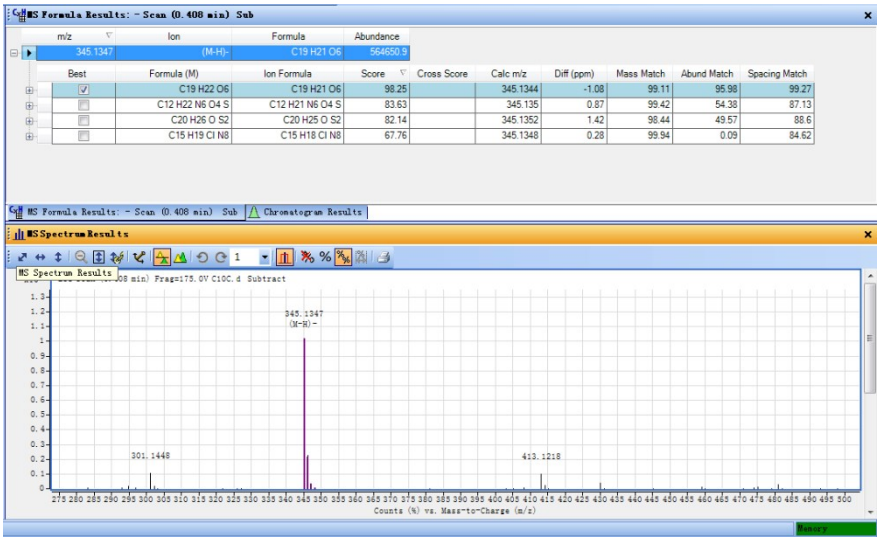

Figure S91. HR-ESI-MS spectrum of **11**

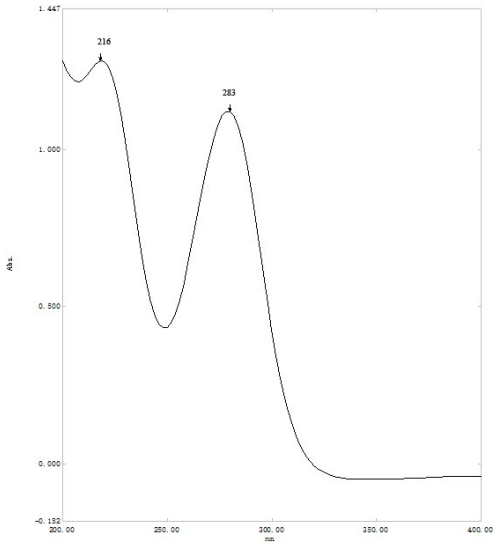

Figure S92. UV spectrum of **11**

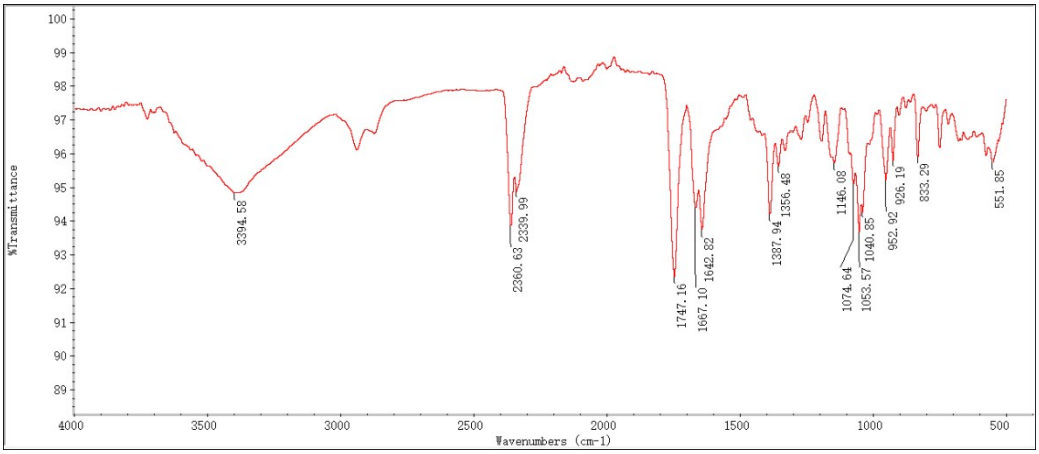

Figure S93. IR spectrum of **11**

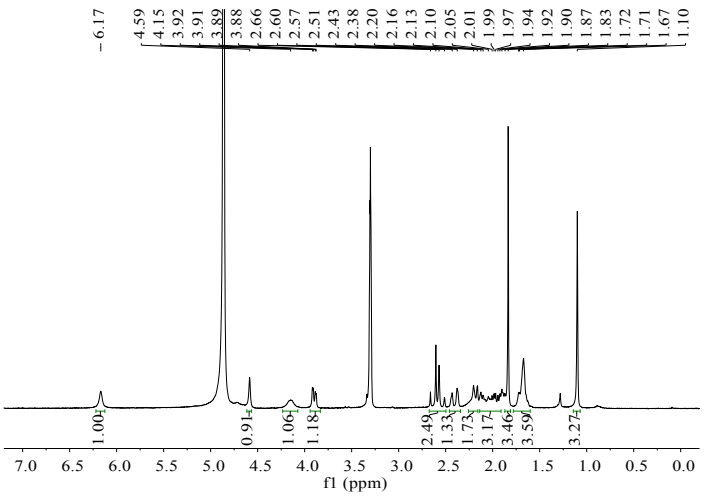

Figure S94. ^{1}H NMR spectrum of **11**

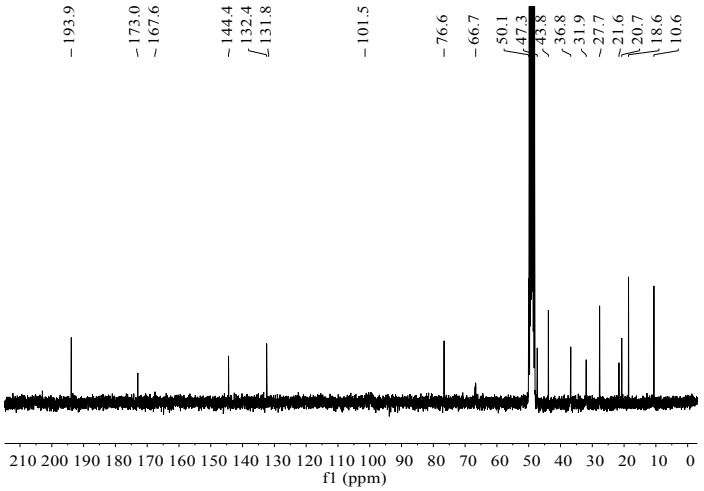

Figure S95. ^{13}C NMR spectrum of **11**

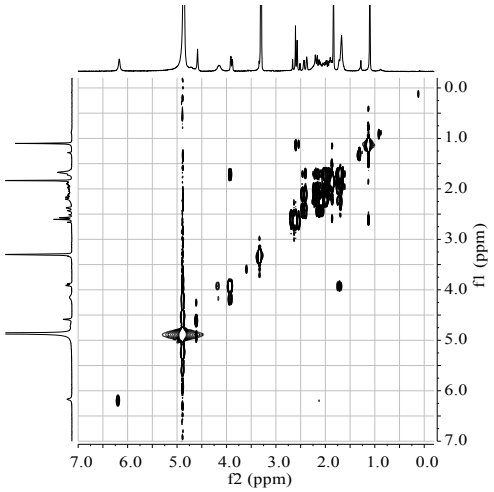

Figure S96. ^{1}H-^{1}H COSY spectrum of **11**

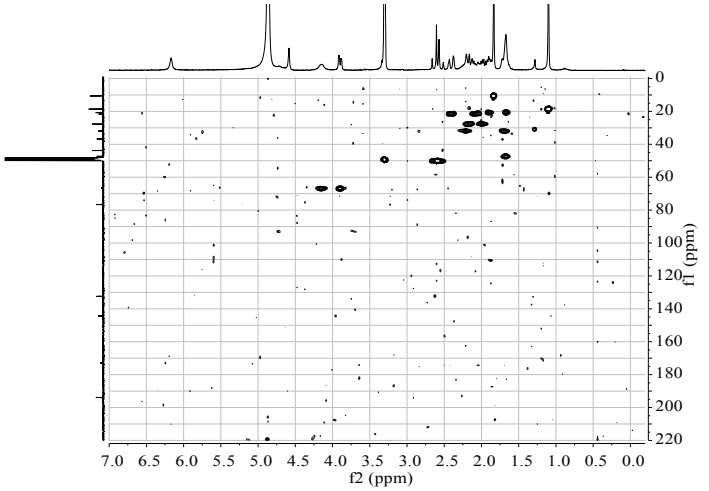

Figure S97. HSQC spectrum of **11**

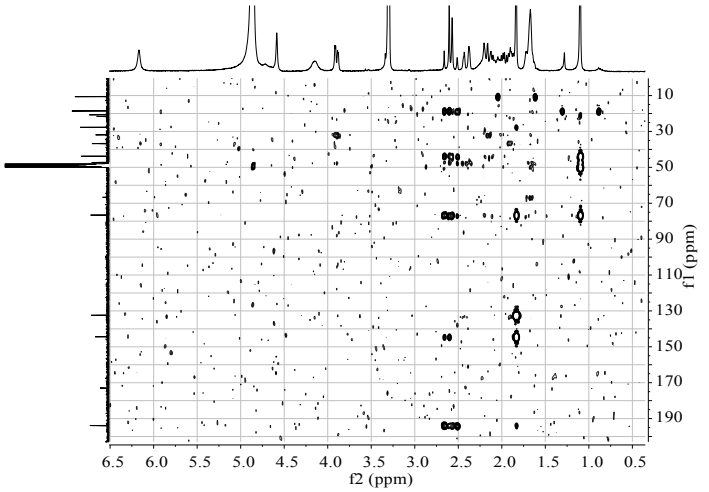

Figure S98. HMBC spectrum of **11**

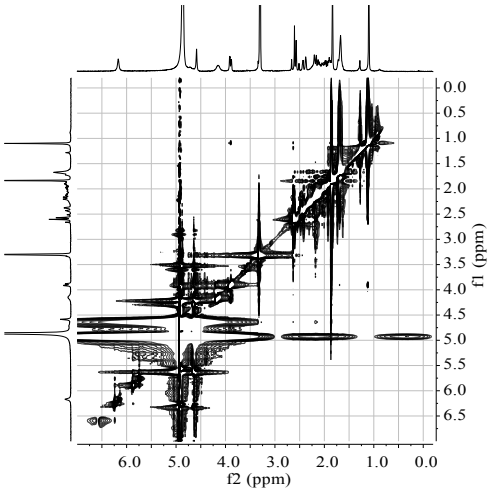

Figure S99. NOESY spectrum of **11**

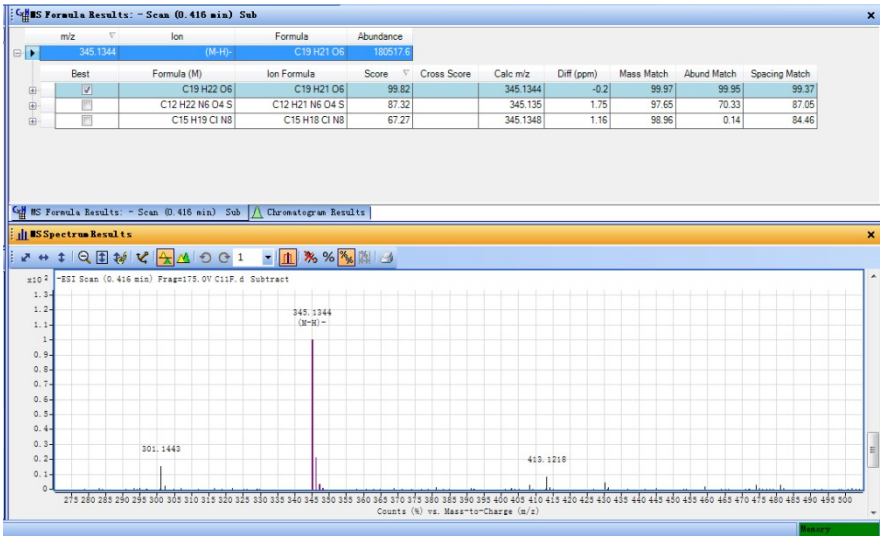

Figure S100. HR-ESI-MS spectrum of **12**

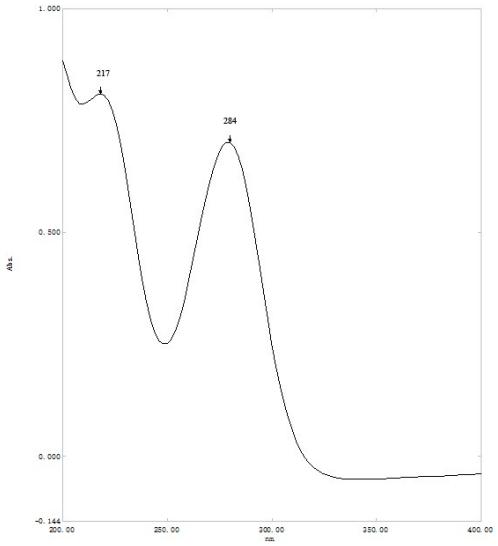

Figure S101. UV spectrum of **12**

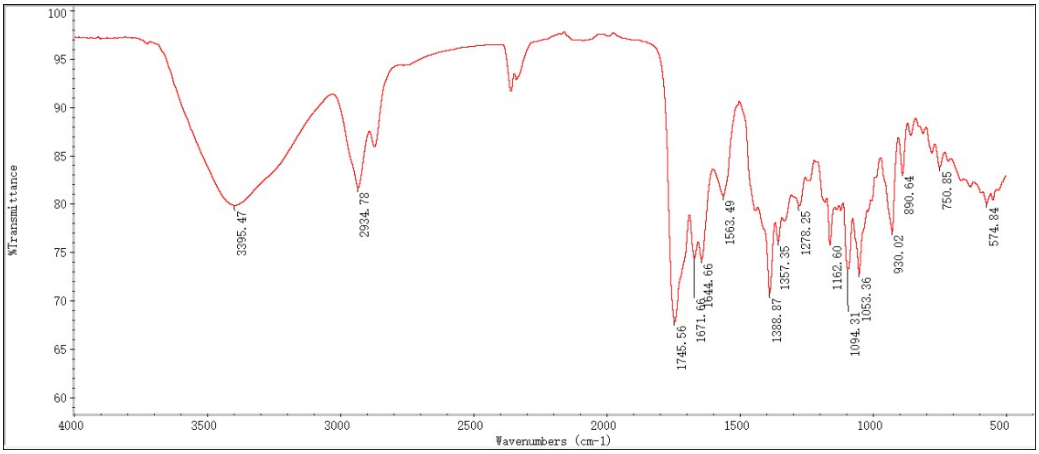

Figure S102. IR spectrum of **12**

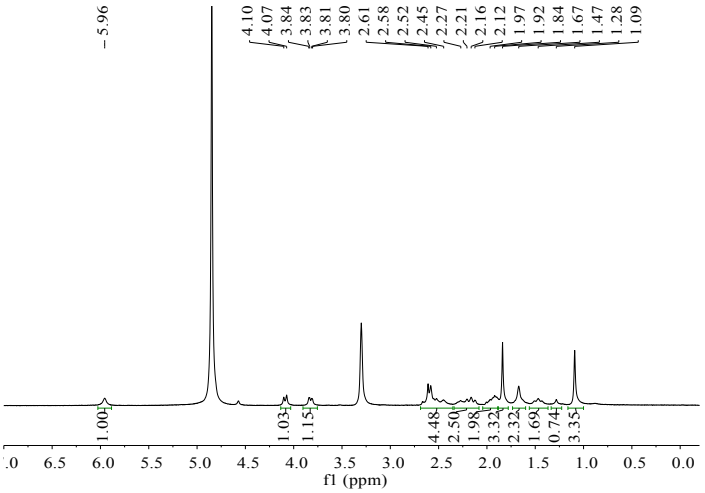

Figure S103. ^{1}H NMR spectrum of **12**

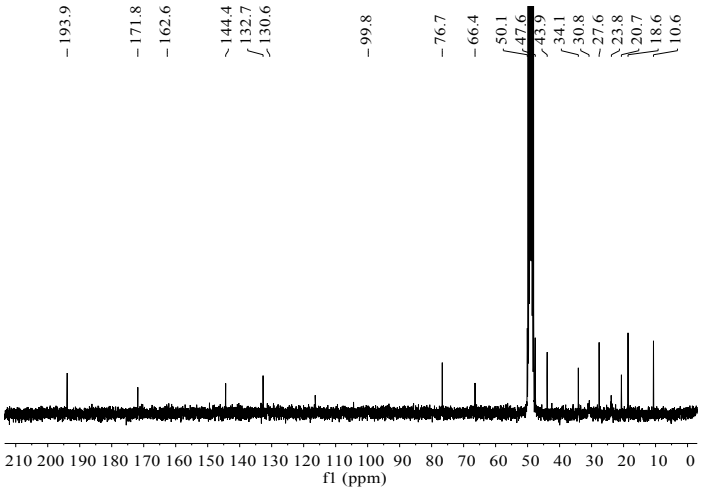

Figure S104. ^{13}C NMR spectrum of **12**

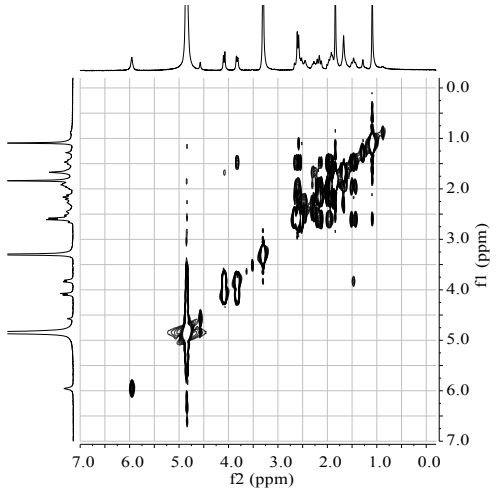

Figure S105. ^{1}H-^{1}H COSY spectrum of **12**

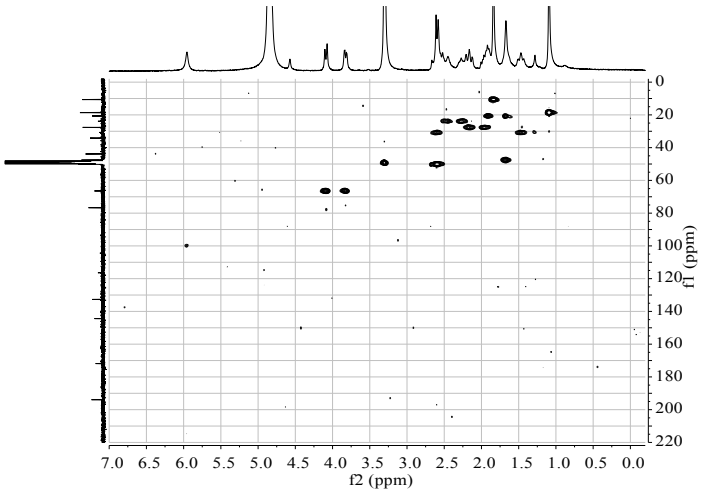

Figure S106. HSQC spectrum of **12**

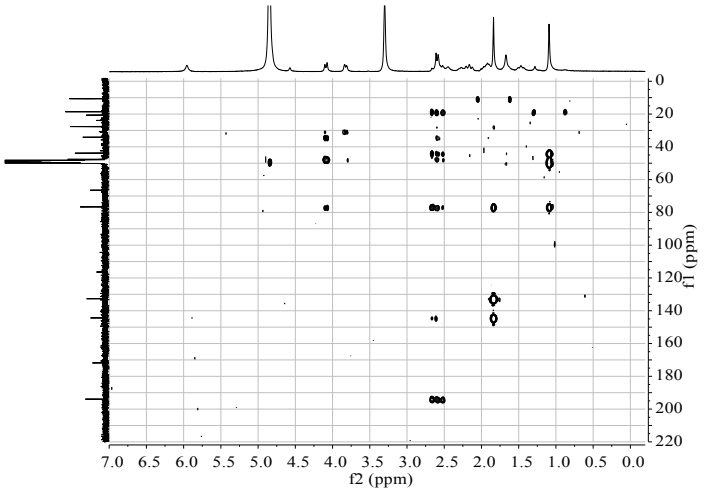

Figure S107. HMBC spectrum of **12**

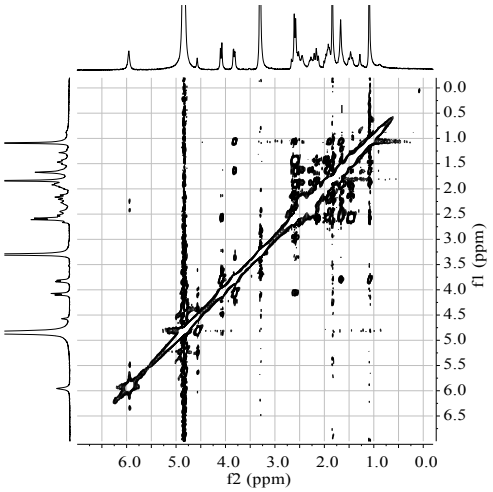

Figure S108. NOESY spectrum of **12**