Characteristic *α*-Acid Derivatives from *Humulus lupulus* with Antineuroinflammatory Activities

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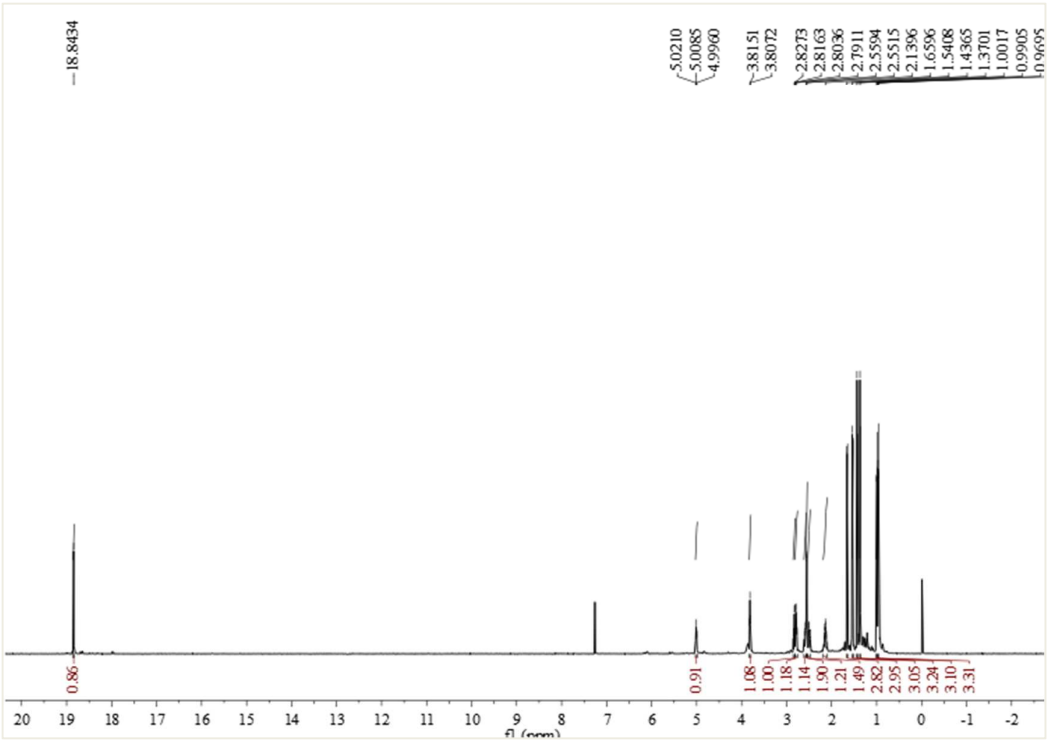
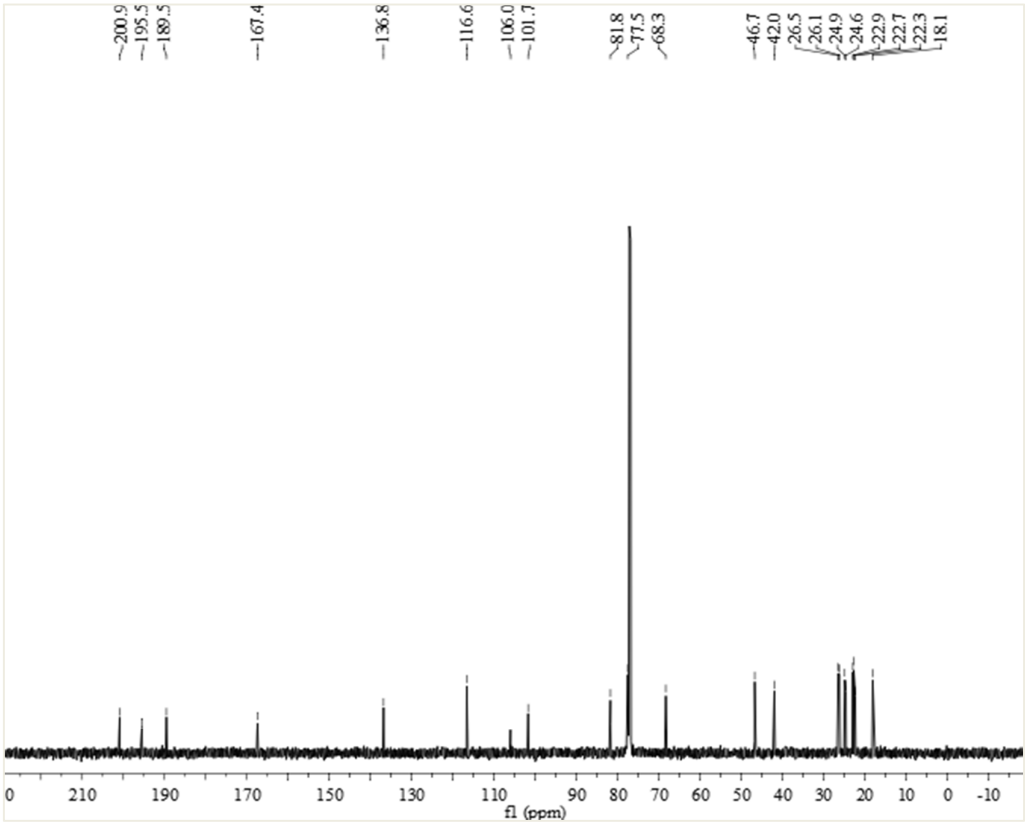
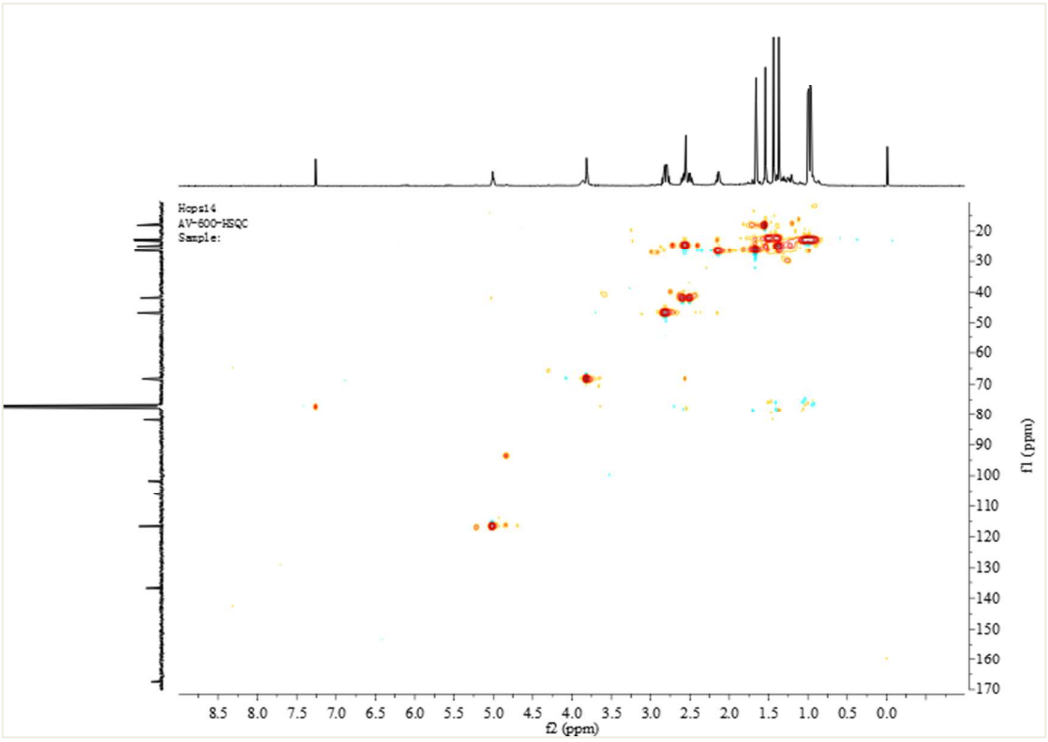
S1. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of (3*R*, 8*S*)-humulone A (**1**).



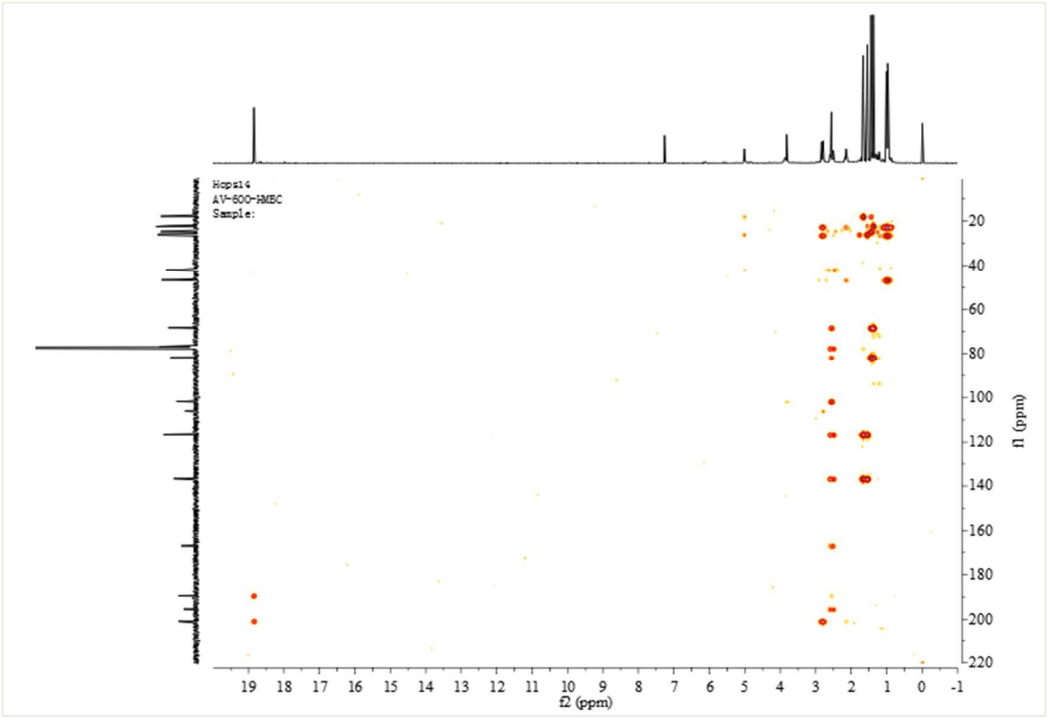
S2. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of (3*R*, 8*S*)-humulone A (**1**).



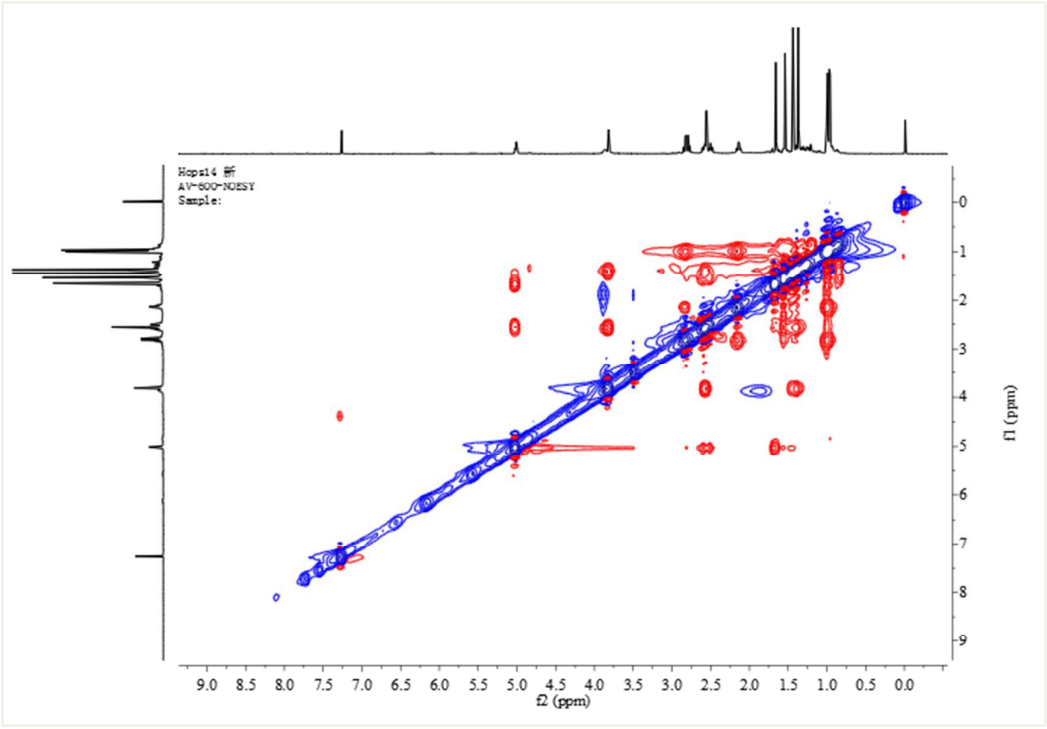
S3. HSQC (600 MHz, $CDCl_3$) spectrum of (3*R*, 8*S*)-humulone A (**1**).



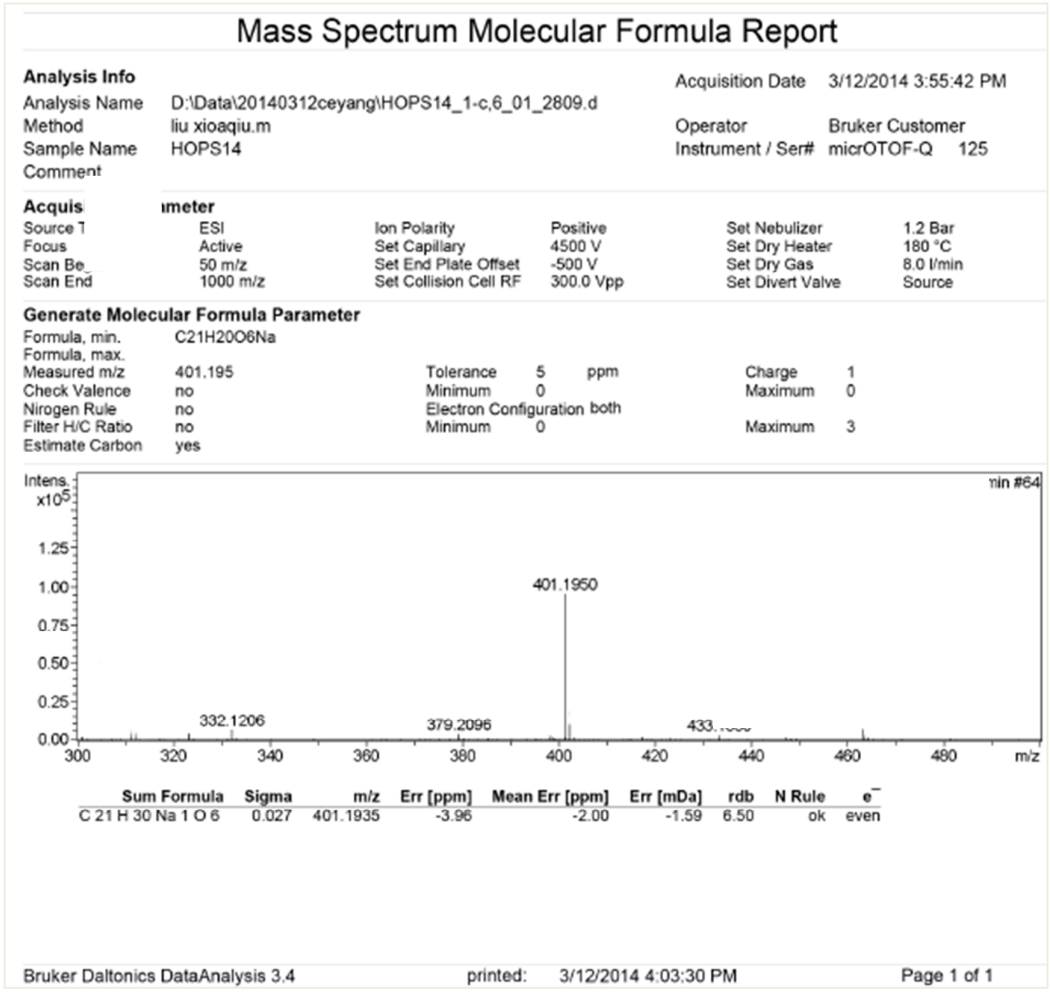
S4. HMBC (600 MHz, $CDCl_3$) spectrum of (3*R*, 8*S*)-humulone A (**1**).



S5. NOESY (600 MHz, $CDCl_3$) spectrum of (3*R*, 8*S*)-humulone A (**1**).



S6. HRESIMS spectrum of (3*R*, 8*S*)-humulone A (**1**).



Mass Spectrum Molecular Formula Report

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Comment			

Acquis ımeter

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Focus	Active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Be_	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	1000 m/z	Set Collision Cell RF	300.0 Vpp	Set Divert Valve	Source

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Formula, max.							
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Filter H/C Ratio	no	Minimum	0		Maximum	3	
Estimate Carbon	yes						

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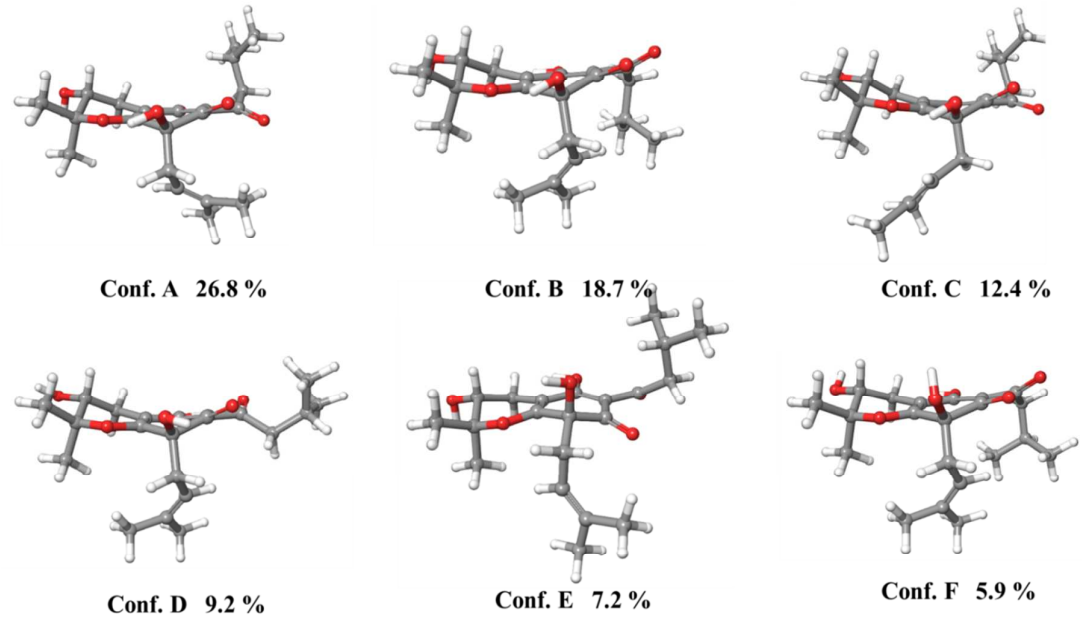
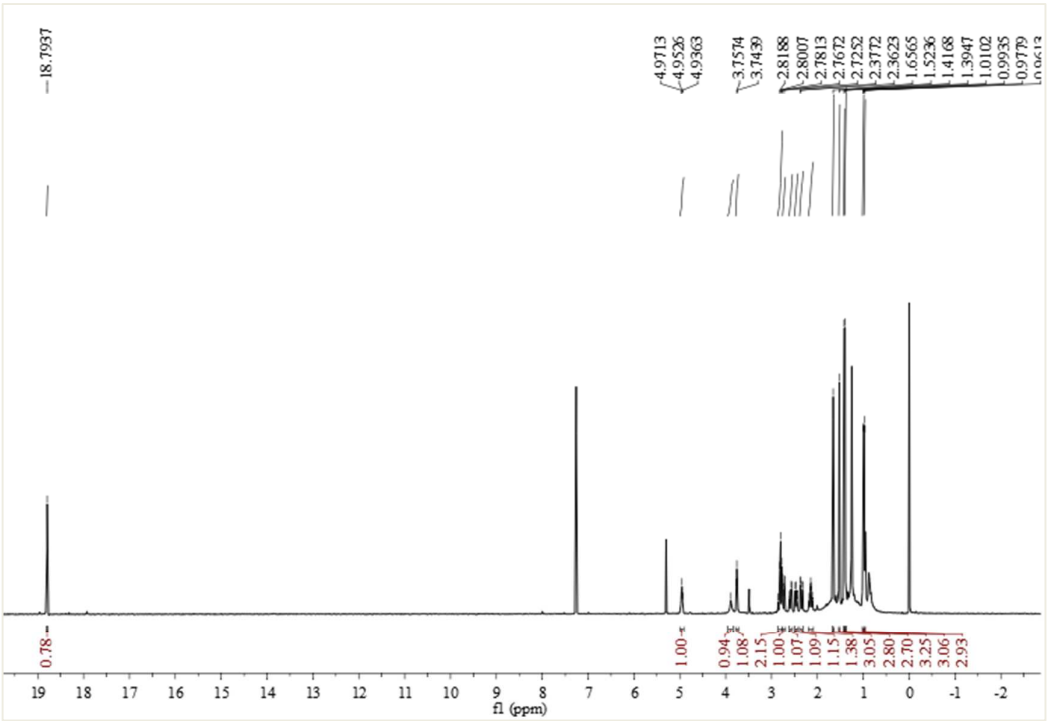
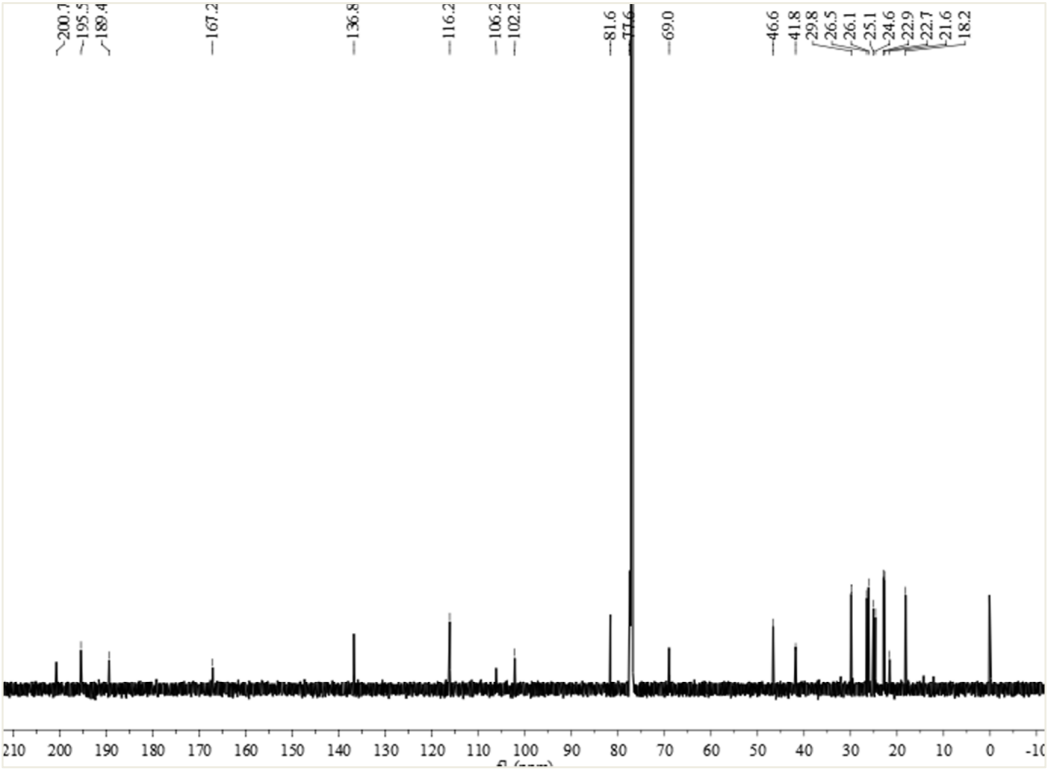
S7. Selected structures and population of the low-energy B3LYP/6-31G (d) in vacuo conformers of (3*R*, 8*S*)-**1** based on experimental NOE correlations.



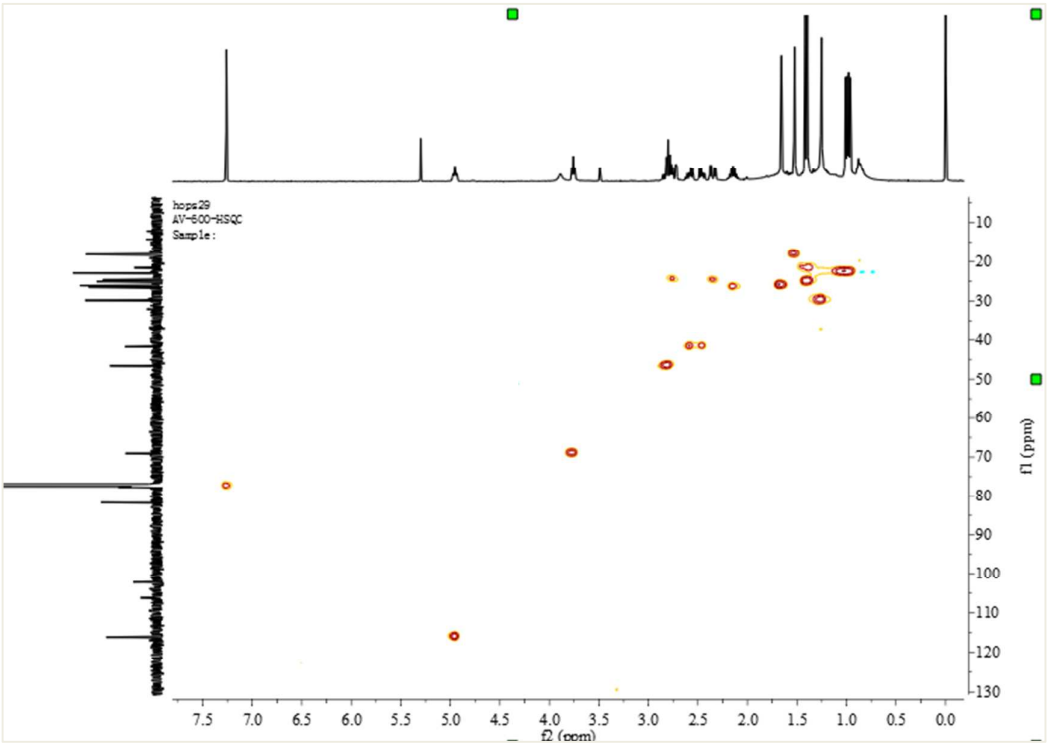
S8. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of (3*S*, 8*S*)-humulone A (**2**).



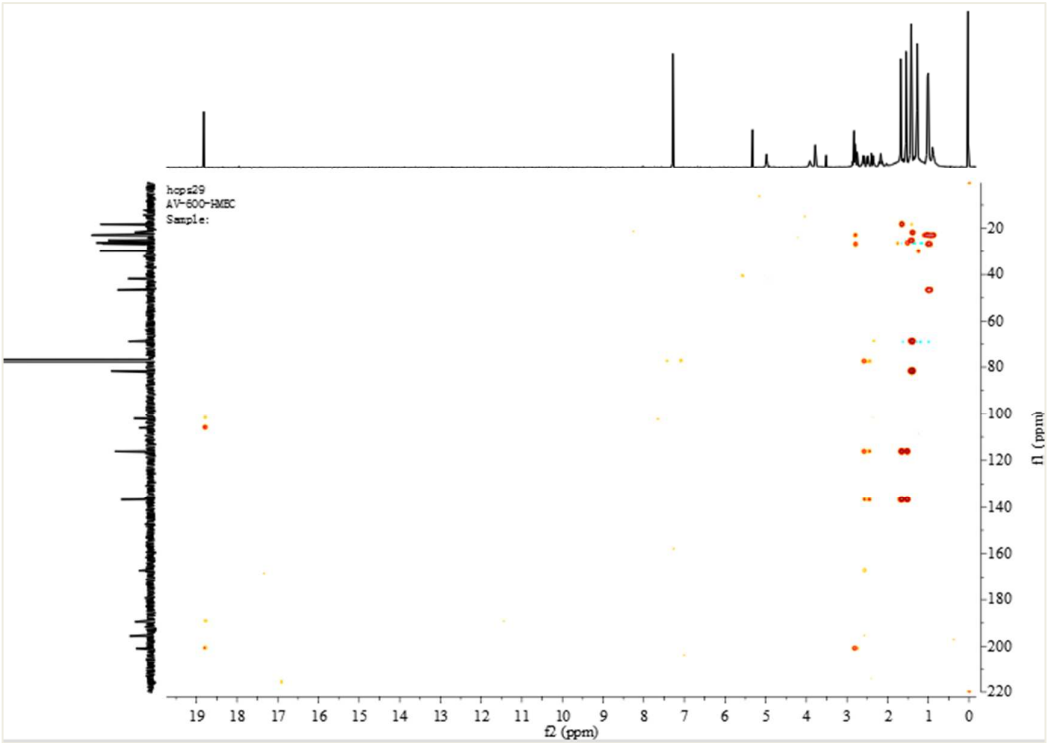
S9. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of (3*S*, 8*S*)-humulone A (**2**).



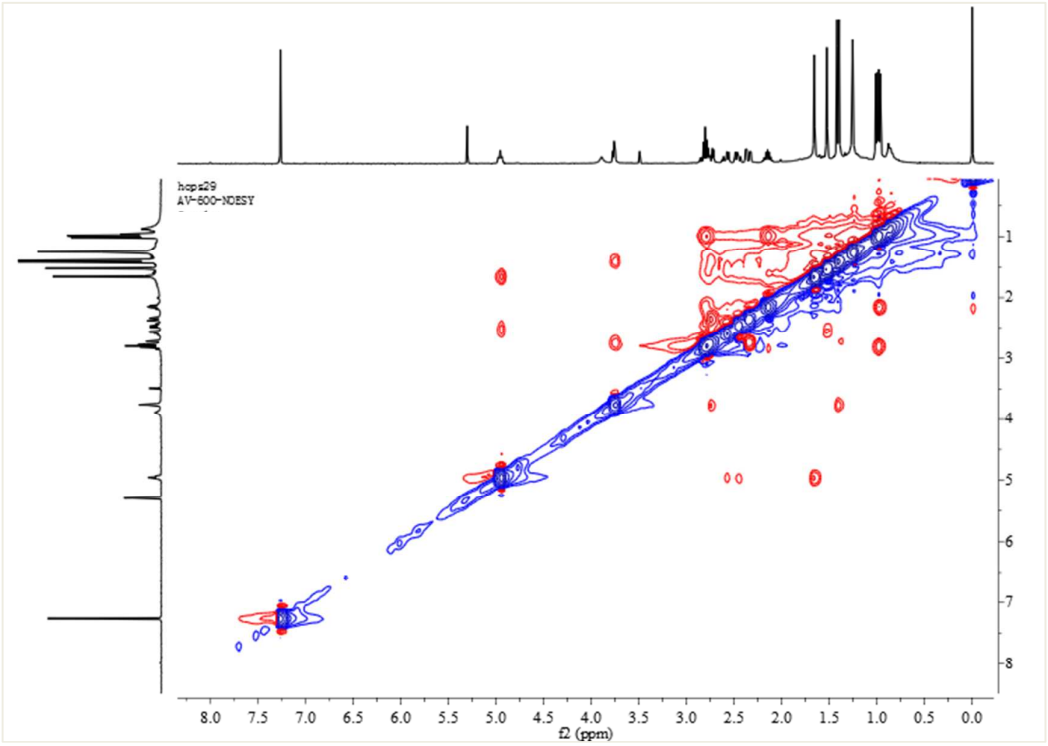
S10. HSQC (600 MHz, $CDCl_3$) spectrum of (3*S*, 8*S*)-humulone A (**2**).



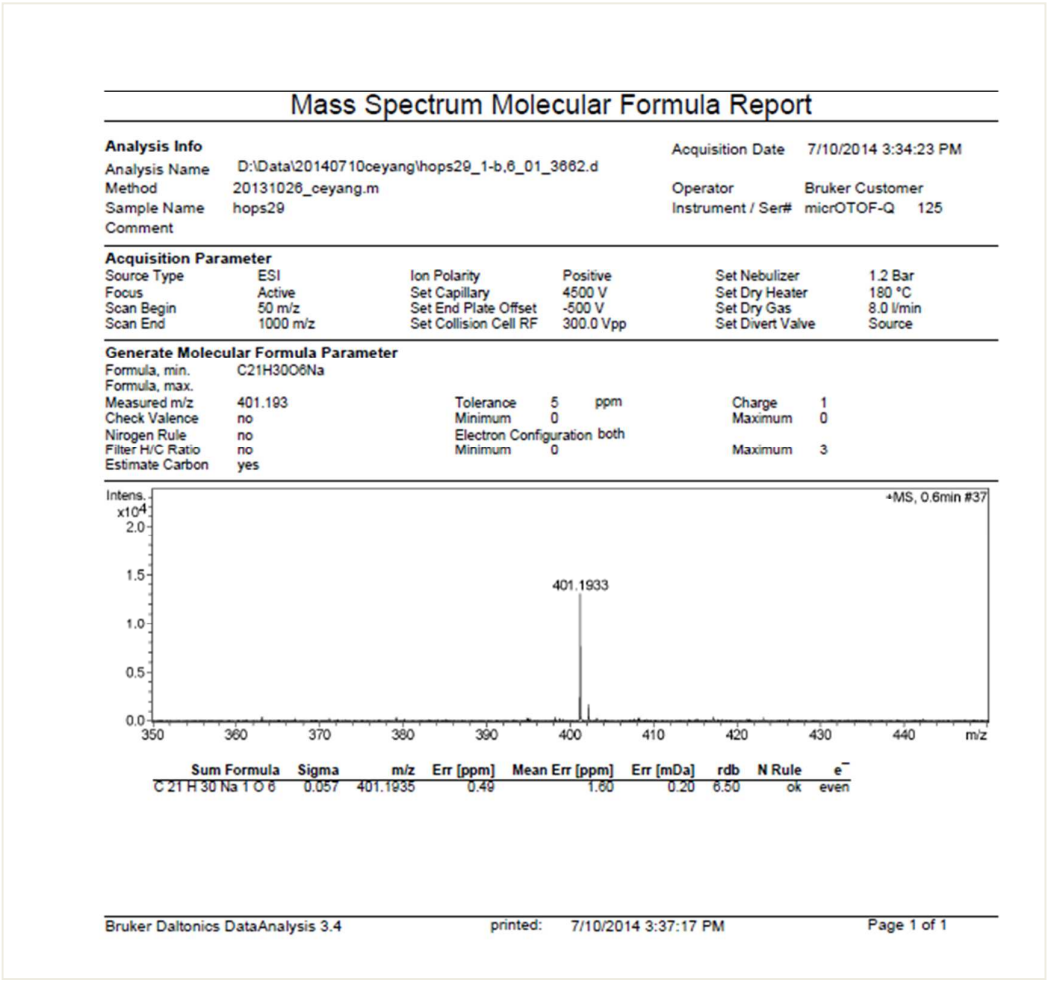
S11. HMBC (600 MHz, $CDCl_3$) spectrum of (3*S*, 8*S*)-humulone A (**2**).



S12. NOESY (600 MHz, $CDCl_3$) spectrum of (3*S*, 8*S*)-humulone A (**2**).



S13. HRESIMS spectrum of (3*S*, 8*S*)-humulone A (**2**).



Mass Spectrum Molecular Formula Report

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Comment			

Acquisition Parameter

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Scan End	1000 m/z	Set Collision Cell RF	300.0 Vpp	Set Divert Valve	Source

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Formula, max.					
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Check Valence	no	Minimum	0	Maximum	0
Nirogen Rule	no	Electron Configuration	both		
Filter H/C Ratio	no	Minimum	0	Maximum	3
Estimate Carbon	yes				

Sum Formula	Sigma	m/z	Err [ppm]	Mean Err [ppm]	Err [mDa]	rdb	N Rule	e⁻
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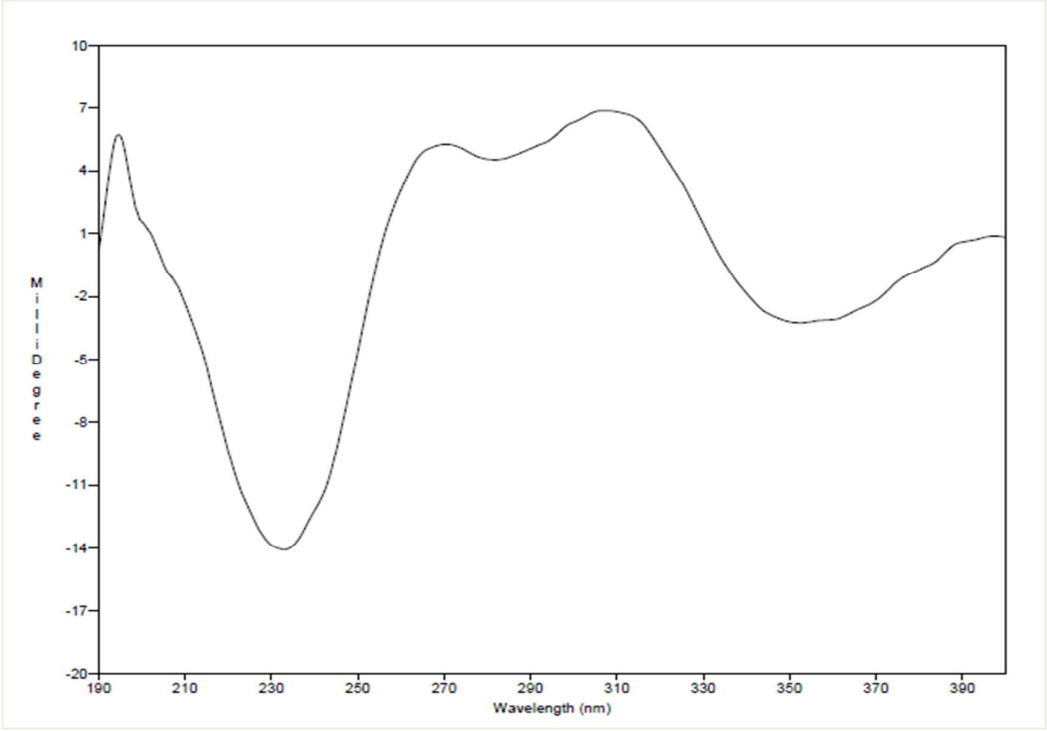
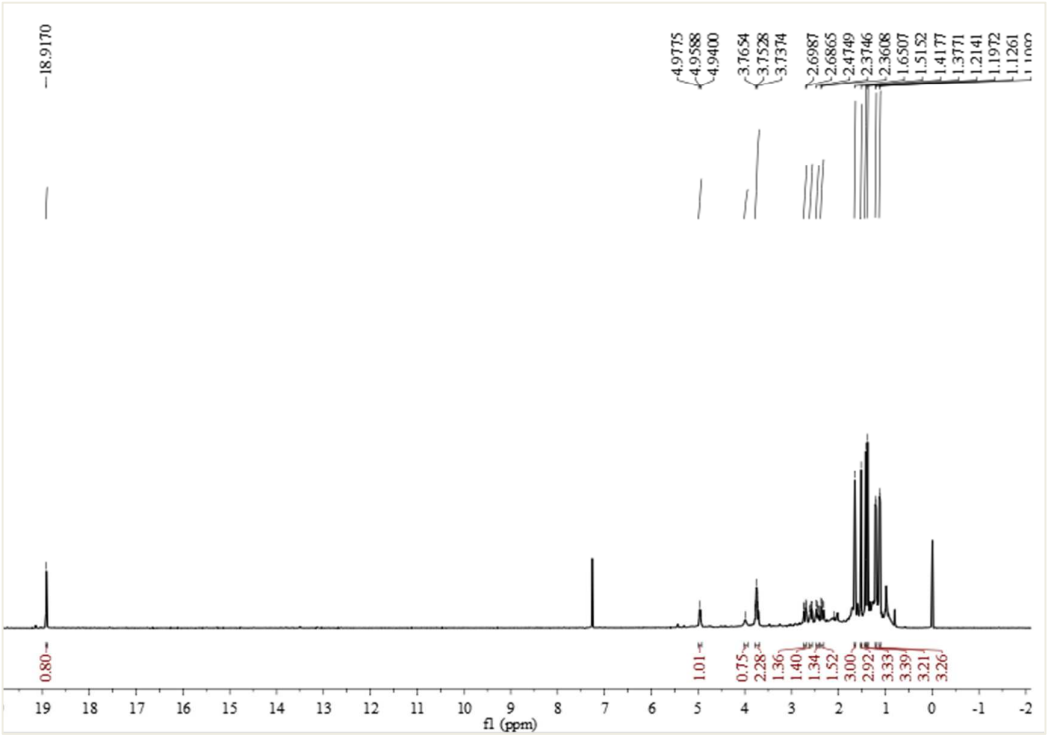
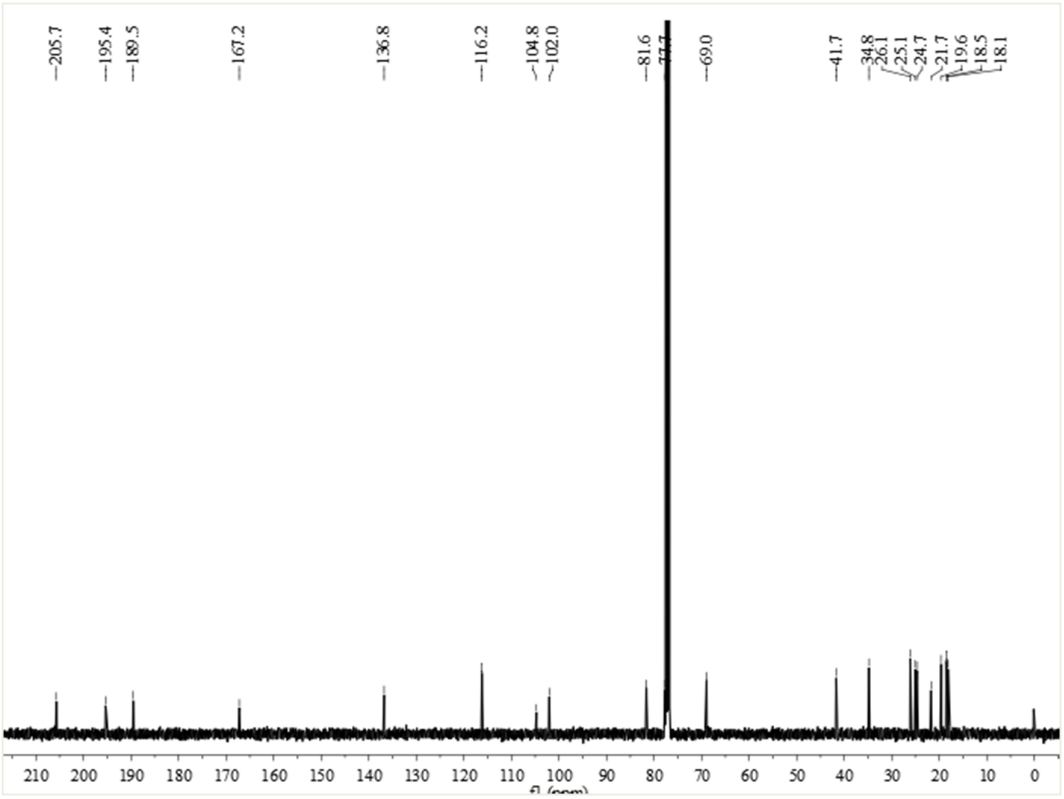
S14. Experimental CD spectrum of (3*S*, 8*S*)-humulone A (**2**).



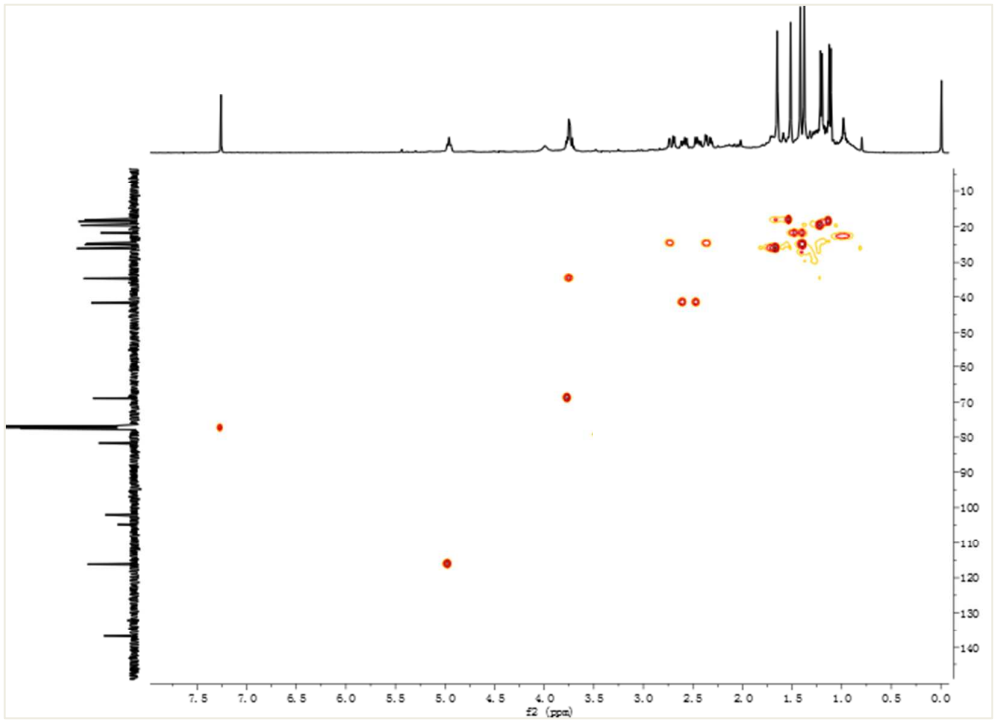
S15. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of (3*S*, 8*S*)-cohumulone A (**3**).



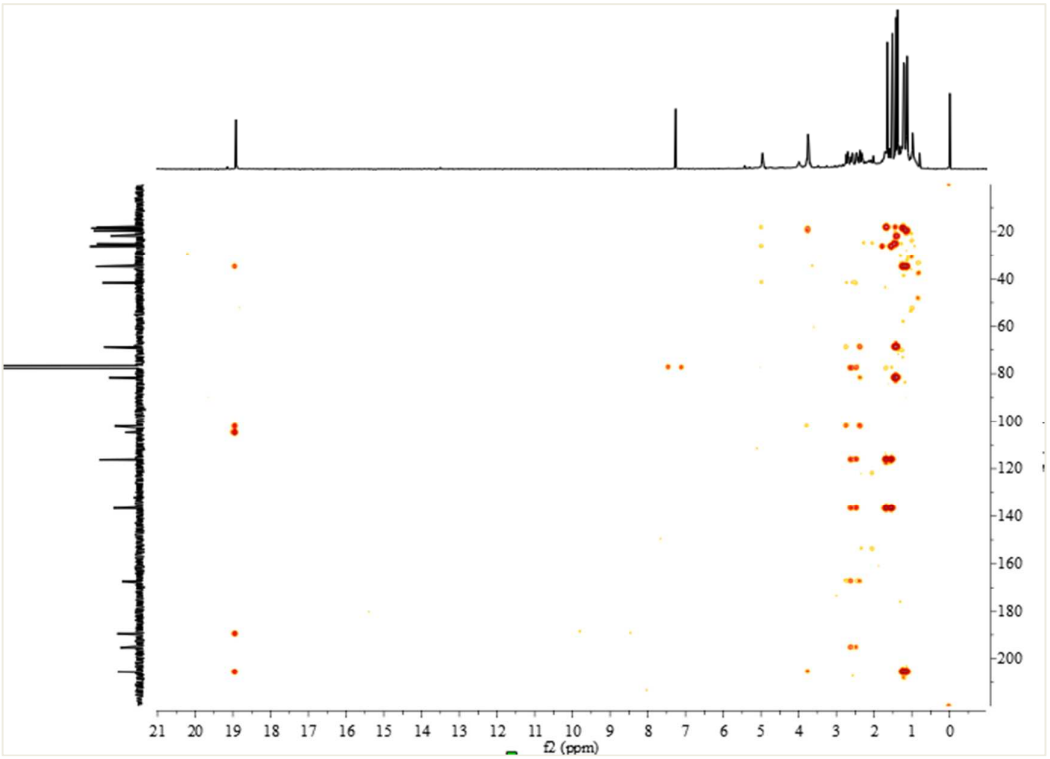
S16. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of (3*S*, 8*S*)-cohumulone A (**3**).



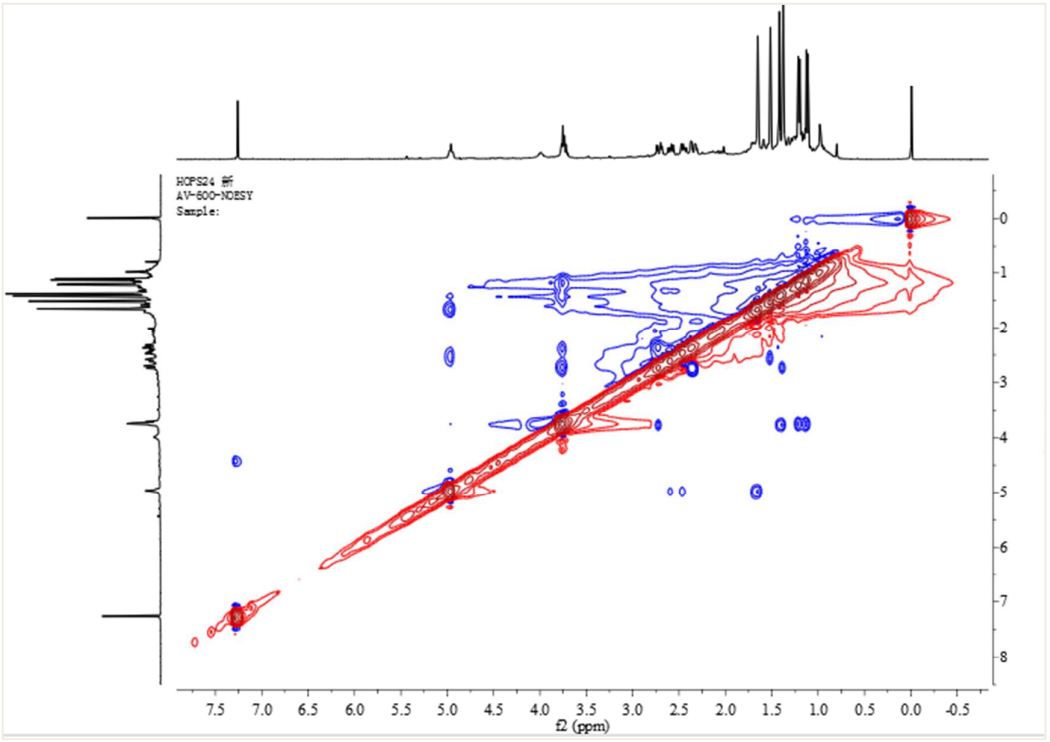
S17. HSQC (600 MHz, $CDCl_3$) spectrum of (3*S*, 8*S*)-cohumulone A (**3**).



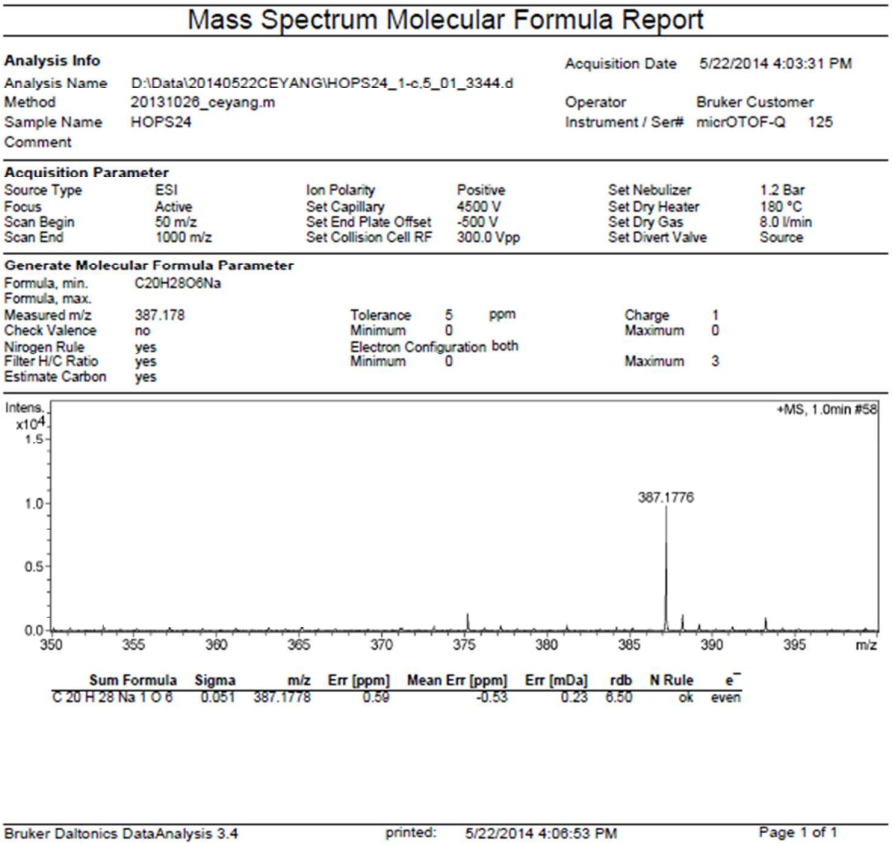
S18. HMBC (600 MHz, $CDCl_3$) spectrum of (3*S*, 8*S*)-cohumulone A (**3**).



S19. NOESY (600 MHz, $CDCl_3$) spectrum of (3*S*, 8*S*)-cohumulone A (**3**).



S20. HRESIMS spectrum of (3*S*, 8*S*)-cohumulone A (**3**).



Mass Spectrum Molecular Formula Report

Analysis Info

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Sample Name	HOPS24	Instrument / Ser#	micrOTOF-Q 125
Comment			

Acquisition Parameter

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Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	1000 m/z	Set Collision Cell RF	300.0 Vpp	Set Divert Valve	Source

Generate Molecular Formula Parameter

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Formula, max.							
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Filter H/C Ratio	yes	Minimum	0		Maximum	3	
Estimate Carbon	yes						

Sum Formula	Sigma	m/z	Err [ppm]	Mean Err [ppm]	Err [mDa]	rdb	N Rule	e⁻
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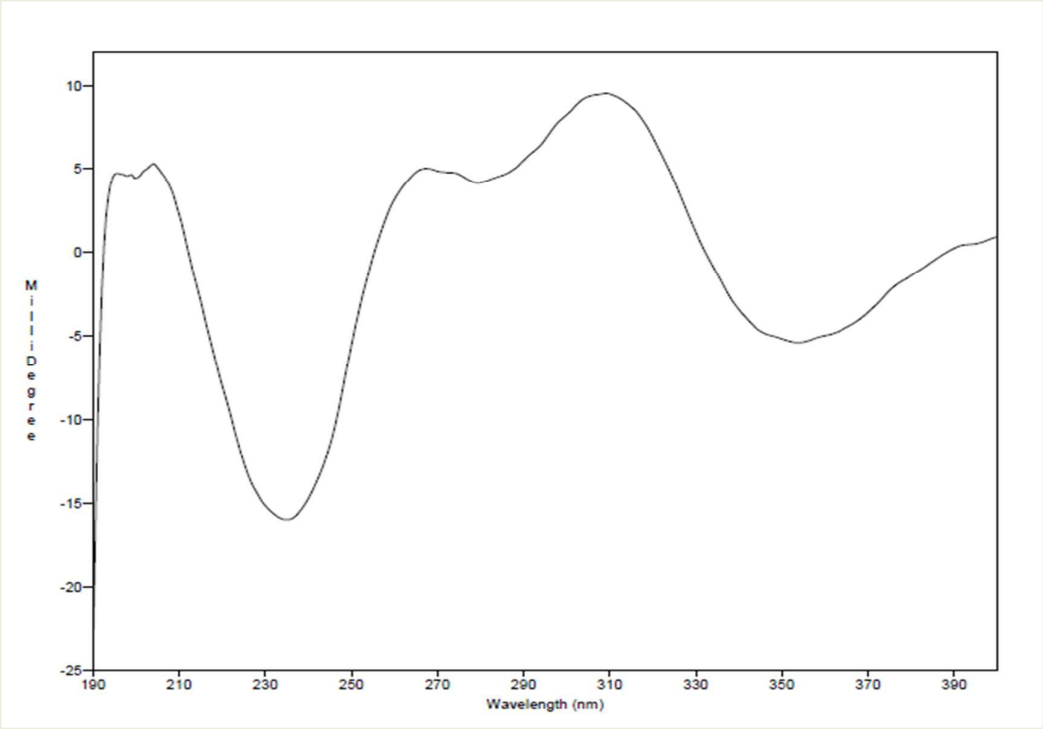
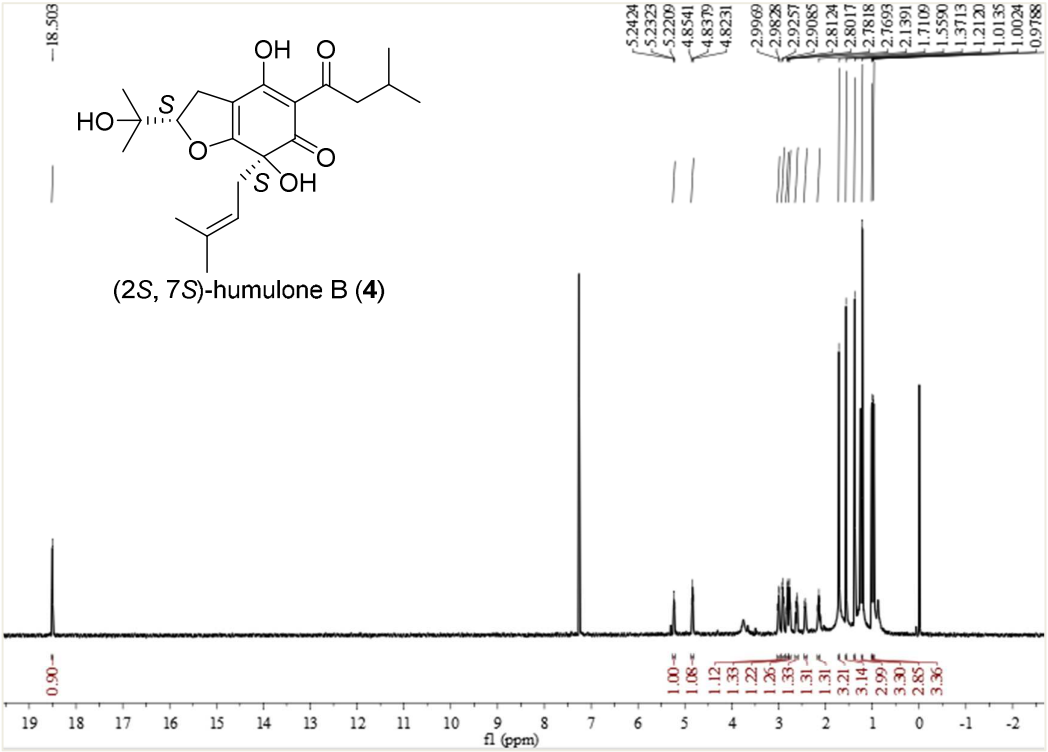
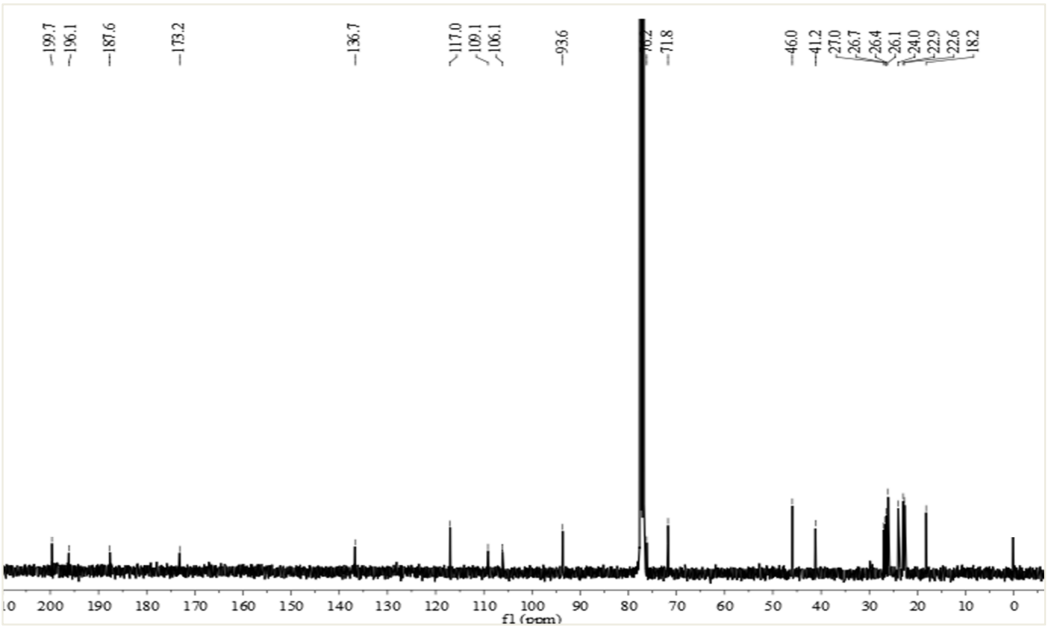
S21. Experimental CD spectrum of (3*S*, 8*S*)-cohumulone A (**3**).



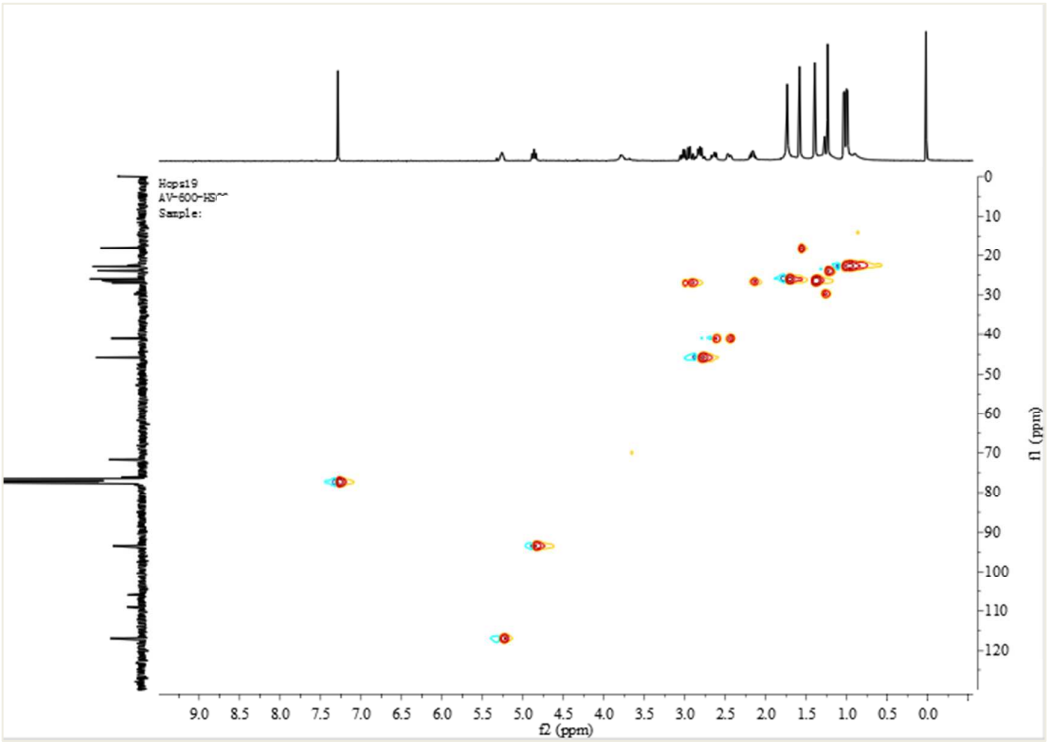
S22. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of (2*S*, 7*S*)-humulone B (**4**).



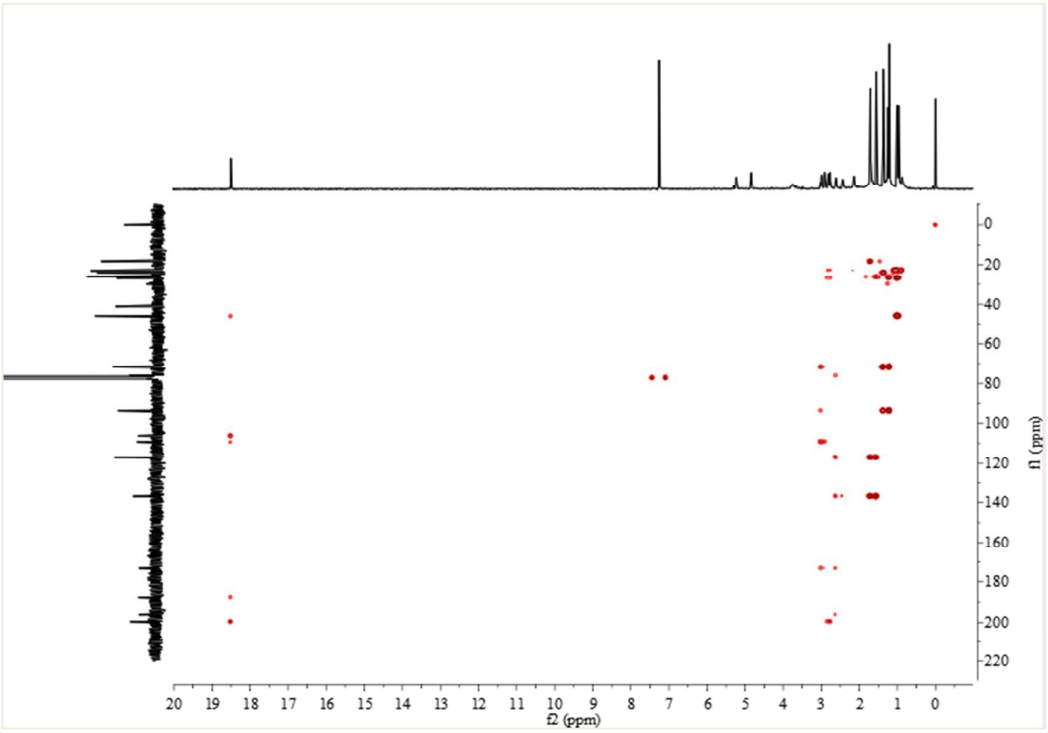
S23. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of (2*S*, 7*S*)-humulone B (**4**).



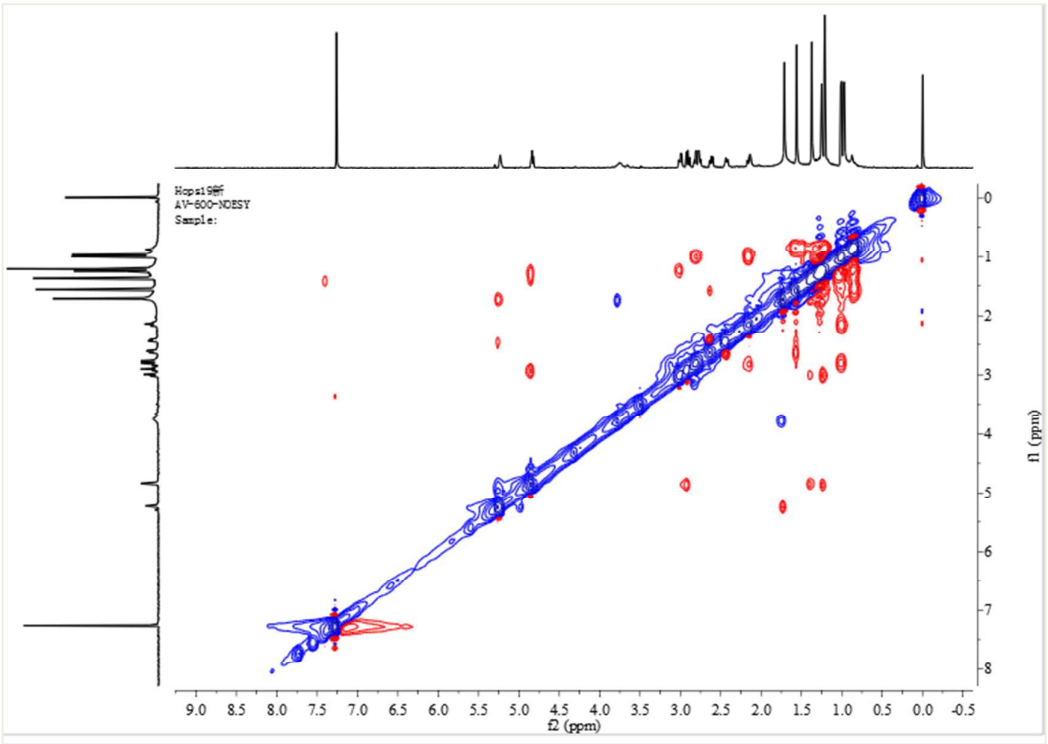
S24. HSQC (600 MHz, $CDCl_3$) spectrum of (2*S*, 7*S*)-humulone B (**4**).



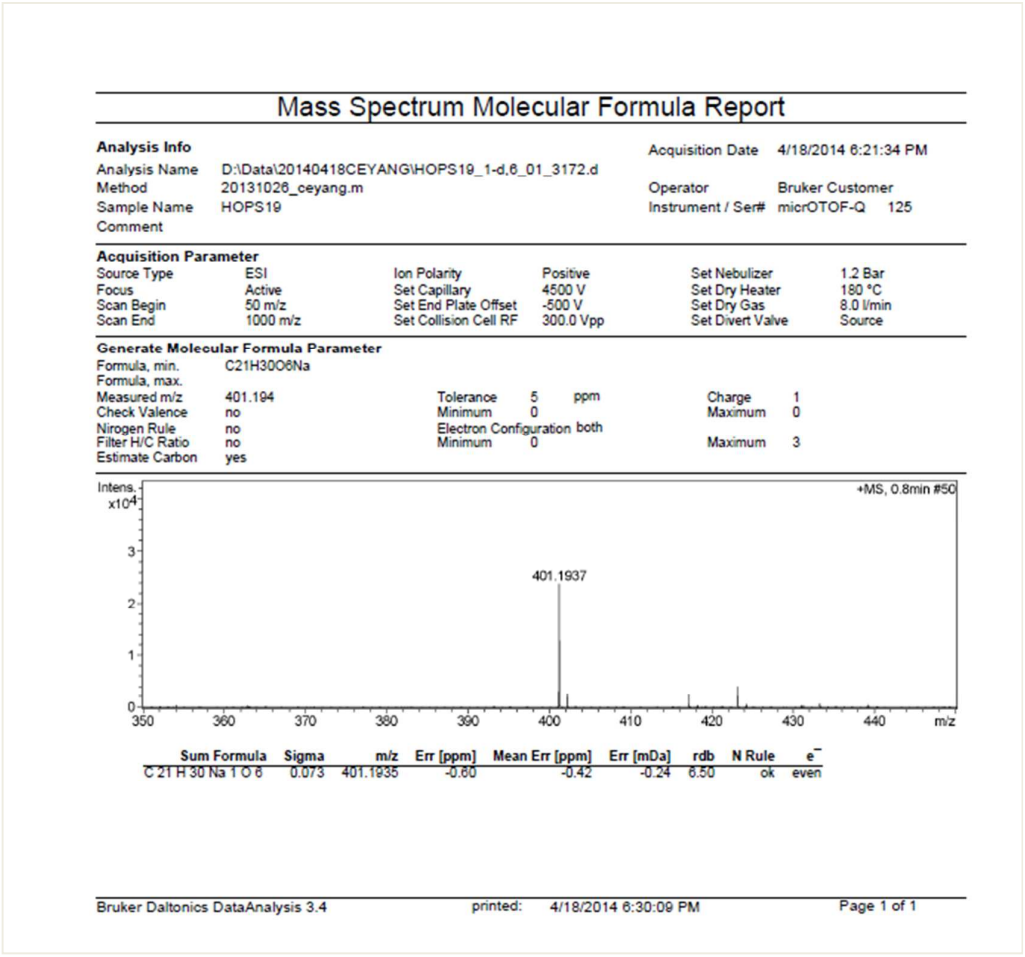
S25. HMBC (600 MHz, $CDCl_3$) spectrum of (2*S*, 7*S*)-humulone B (**4**).



S26. NOESY (600 MHz, $CDCl_3$) spectrum of (2*S*, 7*S*)-humulone B (**4**).



S27. HRESIMS spectrum of (2*S*, 7*S*)-humulone B (**4**).



Mass Spectrum Molecular Formula Report

Analysis Info

Analysis Name	D:\Data\20140418CEYANG\HOPS19_1-d,6_01_3172.d	Acquisition Date	4/18/2014 6:21:34 PM
Method	20131026_ceyang.m	Operator	Bruker Customer
Sample Name	HOPS19	Instrument / Ser#	micrOTOF-Q 125
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.2 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	1000 m/z	Set Collision Cell RF	300.0 Vpp	Set Divert Valve	Source

Generate Molecular Formula Parameter

Formula, min.	C21H30O6Na				
Formula, max.					
Measured m/z	401.194	Tolerance	5 ppm	Charge	1
Check Valence	no	Minimum	0	Maximum	0
Nirogen Rule	no	Electron Configuration	both		
Filter H/C Ratio	no	Minimum	0	Maximum	3
Estimate Carbon	yes				

Sum Formula	Sigma	m/z	Err [ppm]	Mean Err [ppm]	Err [mDa]	rdb	N Rule	e⁻
C 21 H 30 Na 1 O 6	0.073	401.1935	-0.60	-0.42	-0.24	6.50	ok	even

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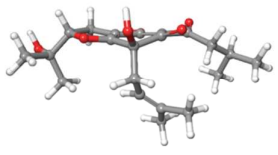
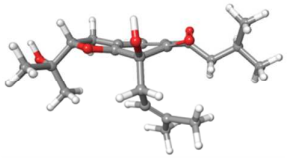
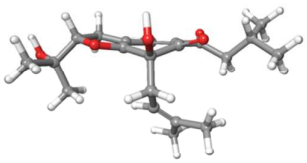
S28. Selected structures and population of the low-energy B3LYP/6-31G (d) in *vacuo* conformers of (2*S*, 7*S*)-**4** based on experimental NOE correlations.



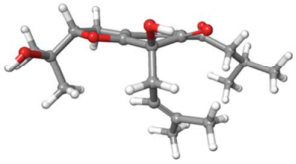
Conf. A 28.9 %



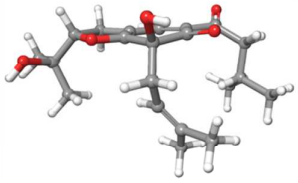
Conf. B 18.0 %



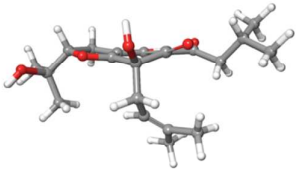
Conf. C 11.2 %



Conf. D 7.6 %

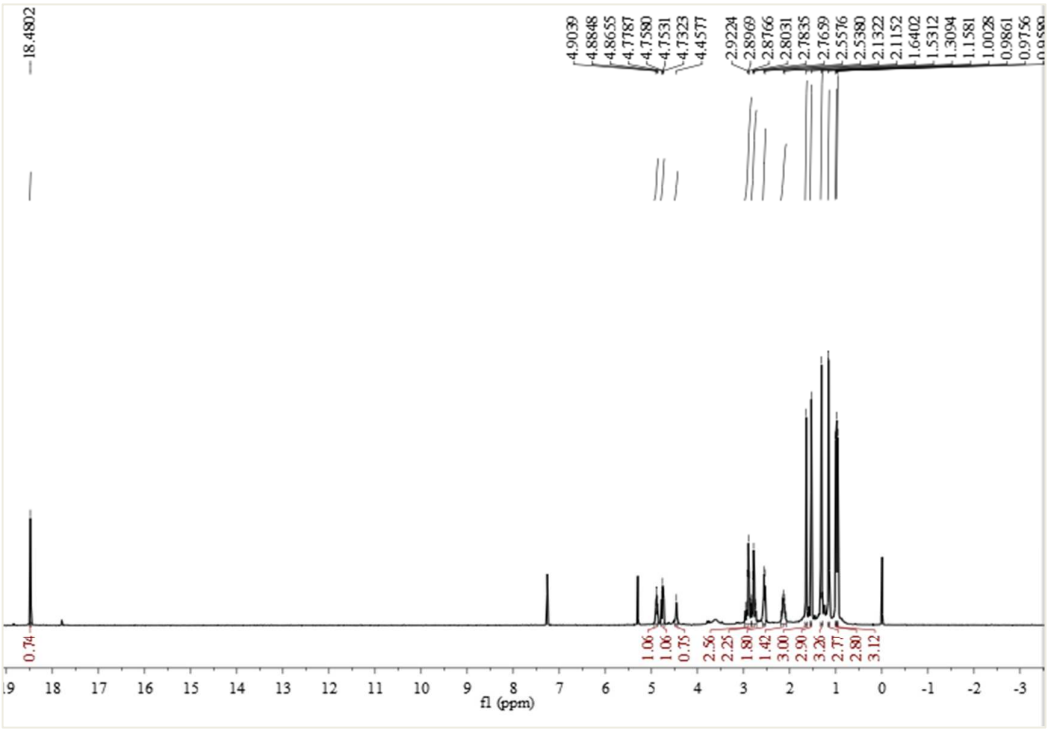


Conf. E 5.2 %

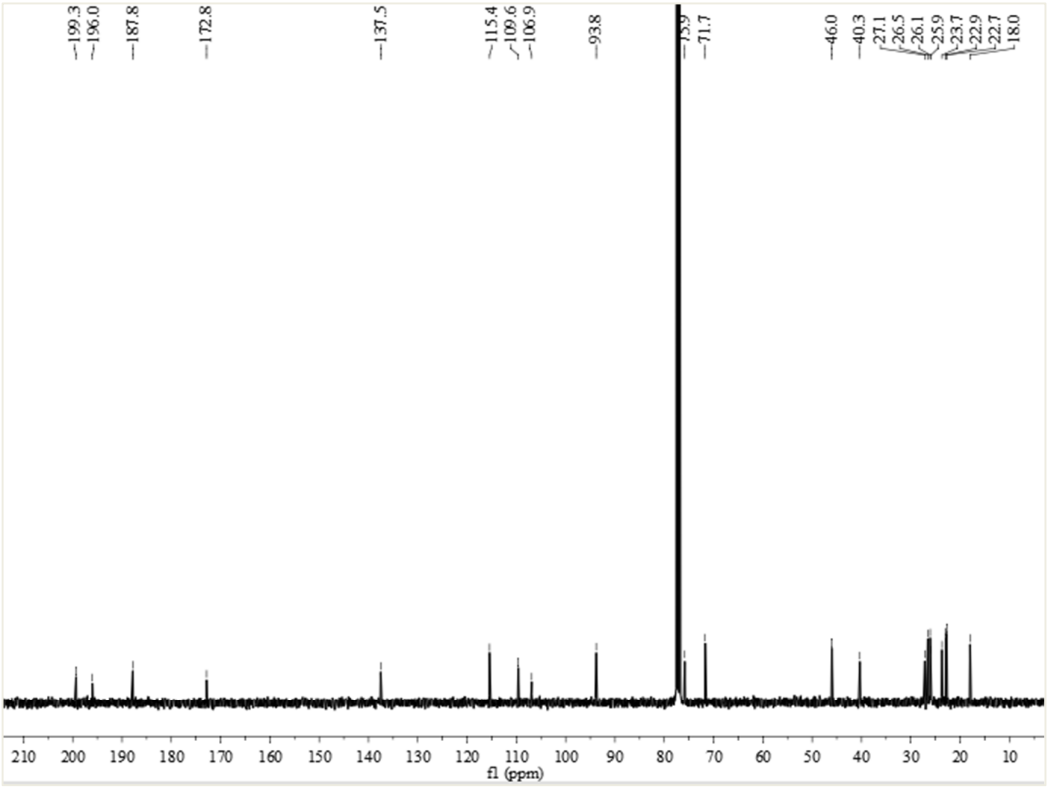


Conf. F 4.1%

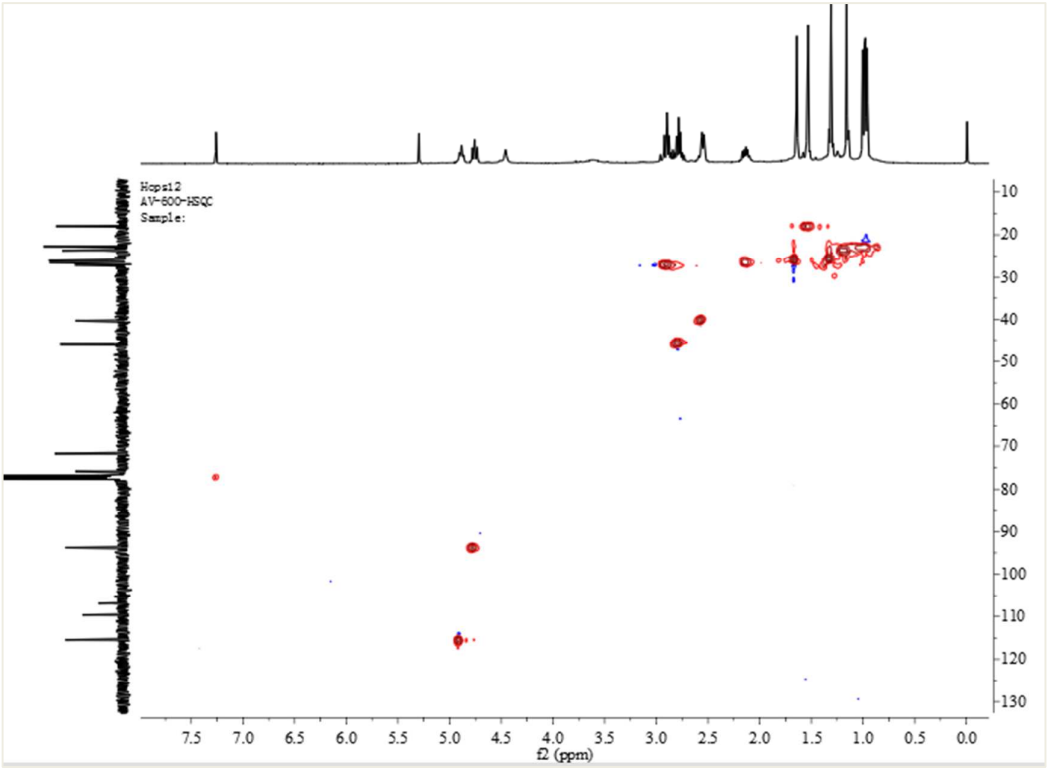
S29. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of (2*R*, 7*S*)-humulone B (**5**).



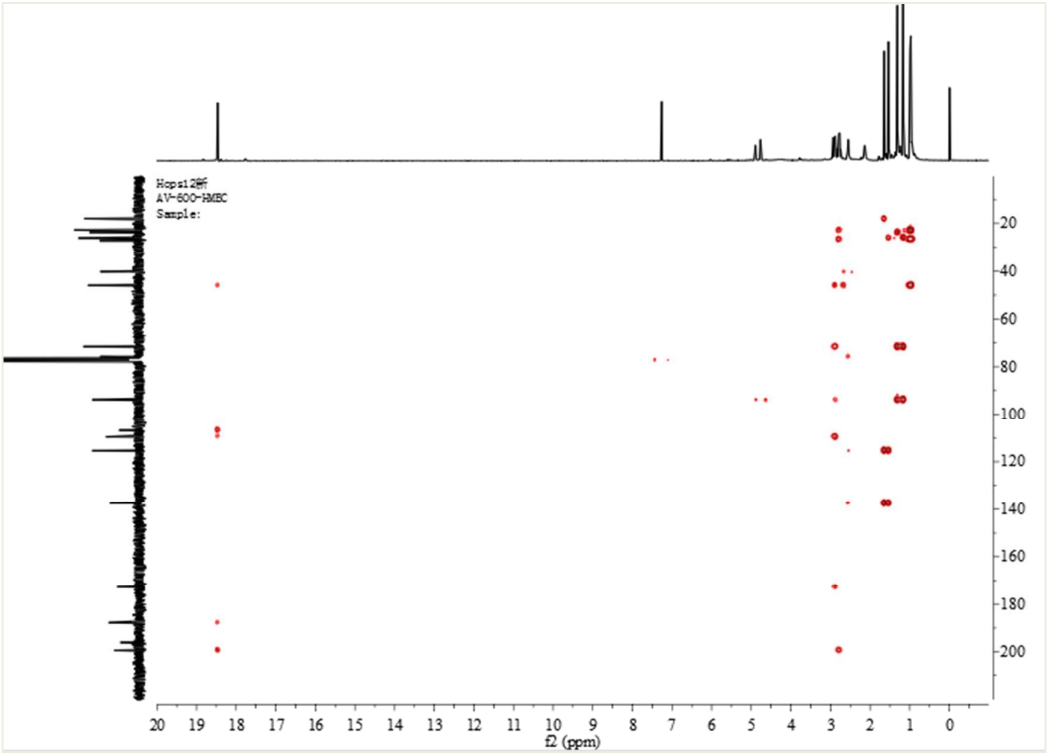
S30. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of (2*R*, 7*S*)-humulone B (**5**).



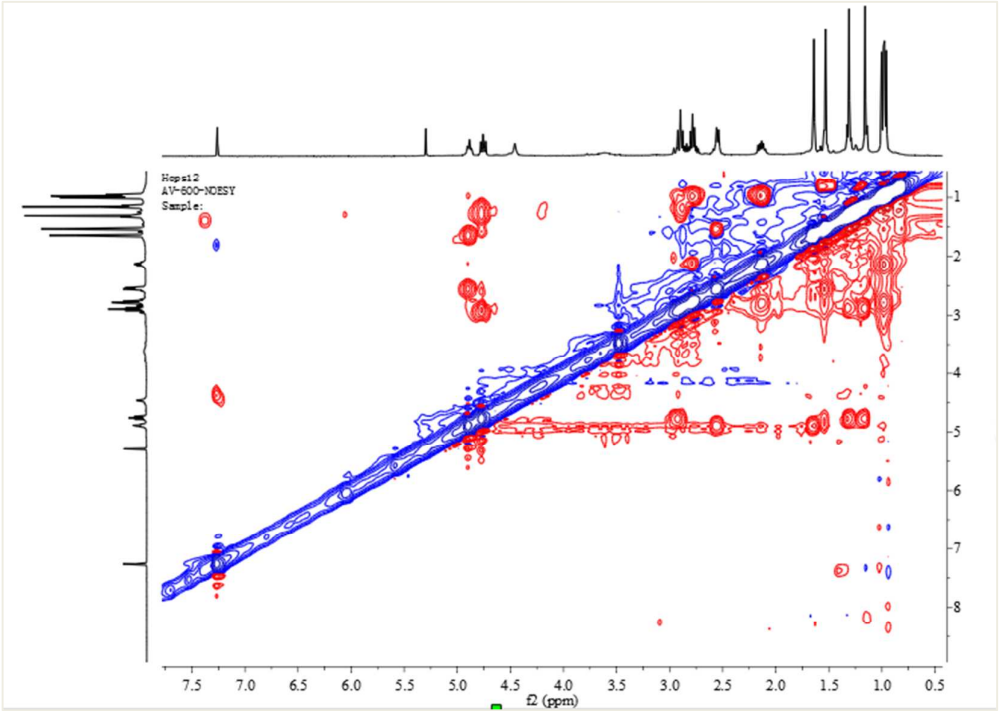
S31. HSQC (600 MHz, $CDCl_3$) spectrum of (2*R*, 7*S*)-humulone B (**5**).



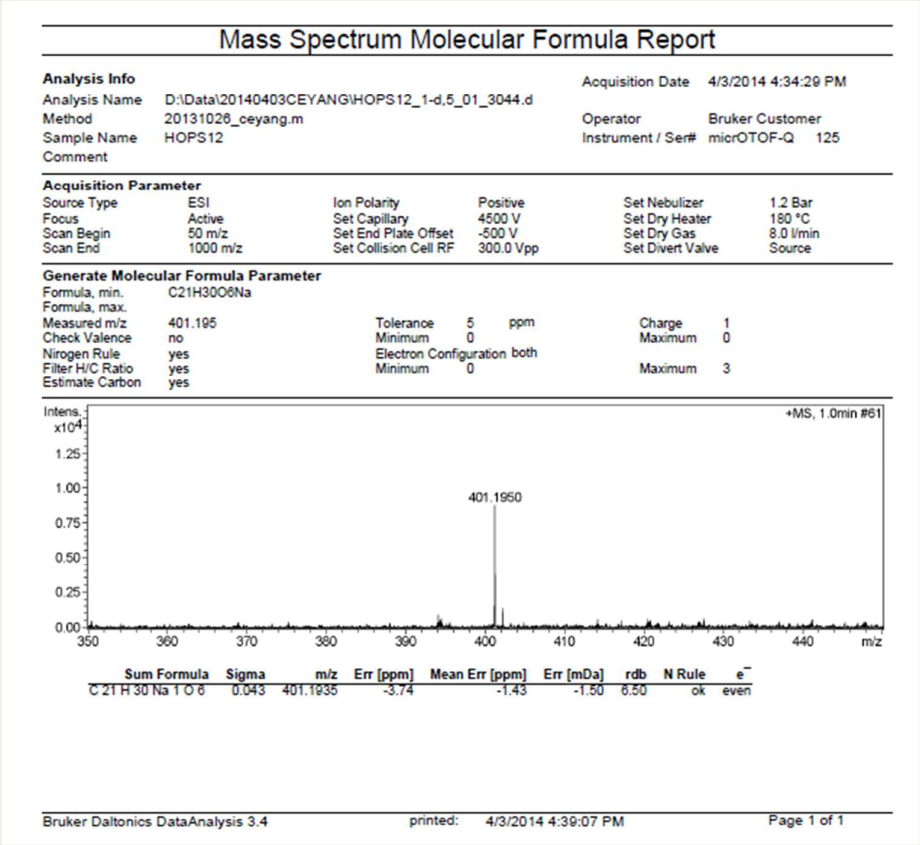
S32. HMBC (600 MHz, $CDCl_3$) spectrum of (2*R*, 7*S*)-humulone B (**5**).



S33. NOESY (600 MHz, $CDCl_3$) spectrum of (2*R*, 7*S*)-humulone B (**5**).



S34. HRESIMS spectrum of (2*R*, 7*S*)-humulone B (**5**).



Mass Spectrum Molecular Formula Report

Analysis Info

Analysis Name	D:\Data\20140403CEYANG\HOPS12_1-d,5_01_3044.d	Acquisition Date	4/3/2014 4:34:29 PM
Method	20131026_ceyang.m	Operator	Bruker Customer
Sample Name	HOPS12	Instrument / Ser#	micrOTOF-Q 125
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.2 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	1000 m/z	Set Collision Cell RF	300.0 Vpp	Set Divert Valve	Source

Generate Molecular Formula Parameter

Formula, min.	C21H30O6Na				
Formula, max.					
Measured m/z	401.195	Tolerance	5 ppm	Charge	1
Check Valence	no	Minimum	0	Maximum	0
Nirogen Rule	yes	Electron Configuration	both		
Filter H/C Ratio	yes	Minimum	0	Maximum	3
Estimate Carbon	yes				

Sum Formula	Sigma	m/z	Err [ppm]	Mean Err [ppm]	Err [mDa]	rdb	N Rule	e⁻
C 21 H 30 Na 1 O 6	0.043	401.1935	-3.74	-1.43	-1.50	6.50	ok	even

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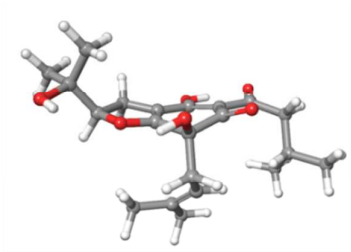
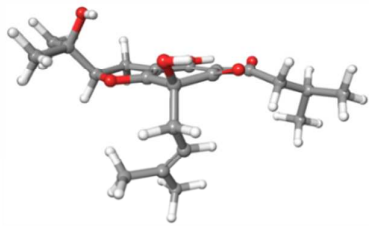
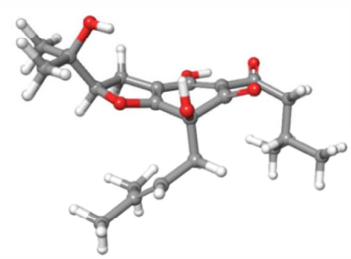
S35. Selected structures and population of the low-energy B3LYP/6-31G (d) in *vacuo* conformers of (2*R*,7*S*)-**5** based on experimental NOE correlations.



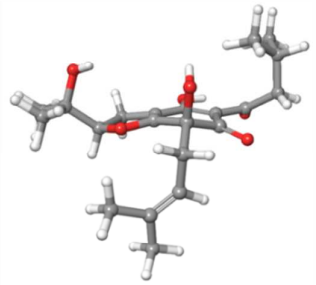
Conf. A 28.4 %



Conf. B 21.6 %

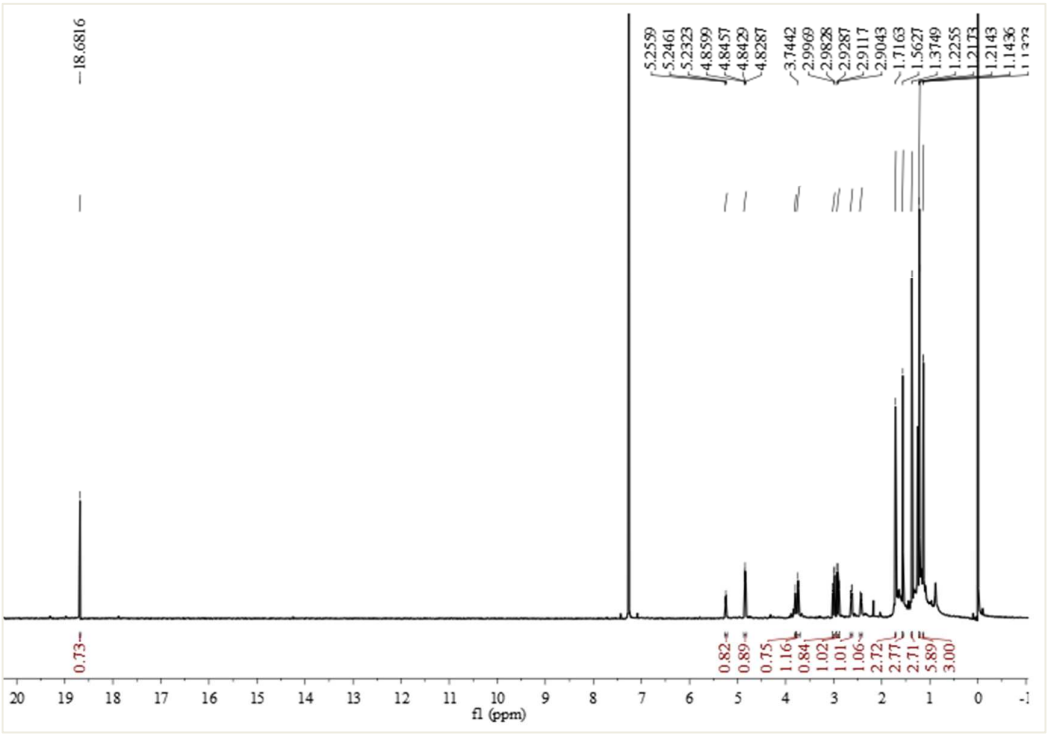


Conf. C 17.8 %

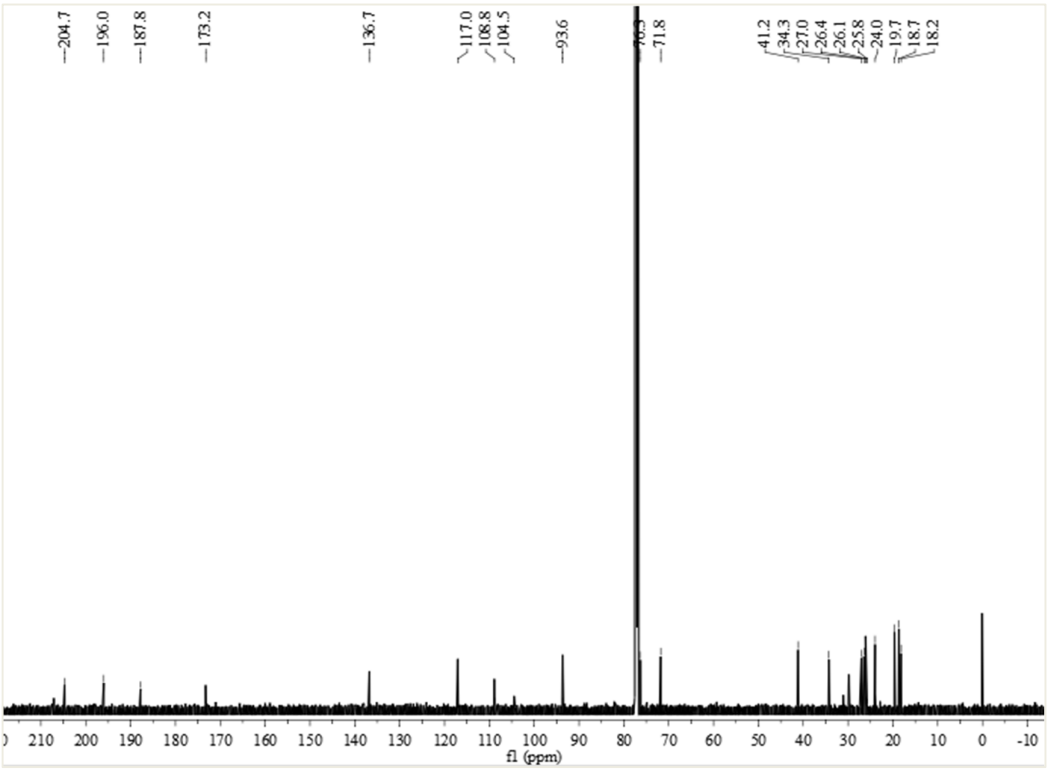


Conf. D 8.0 %

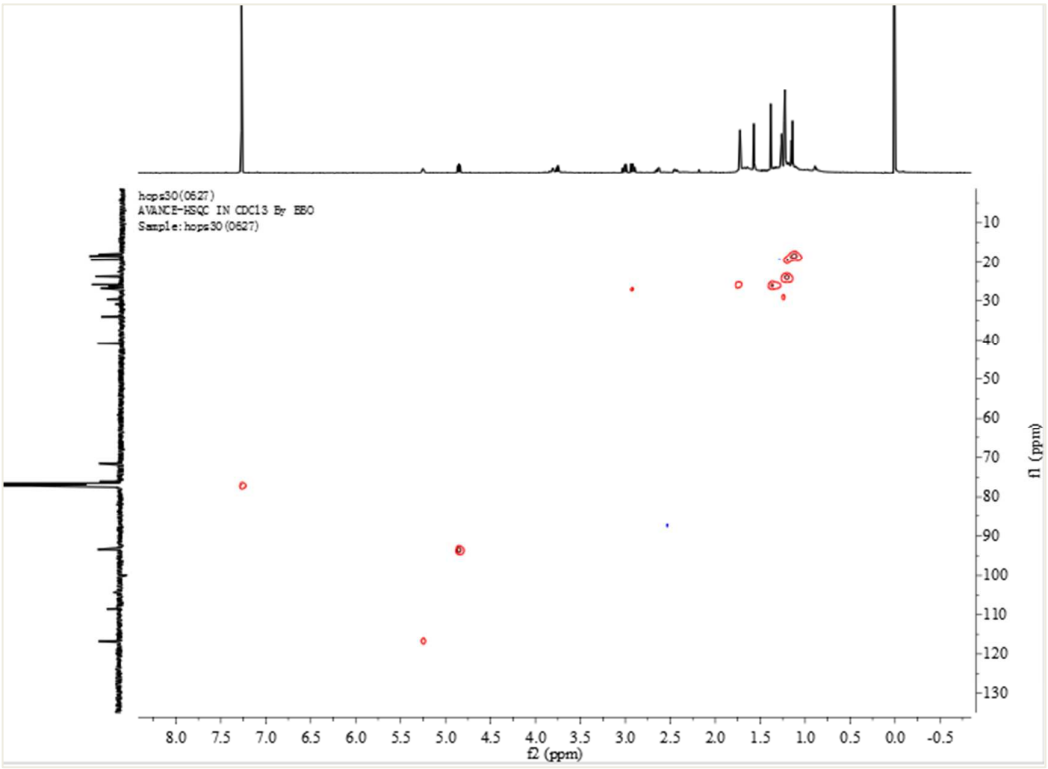
S36. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of (2*S*, 7*S*)-cohumulone B (**6**).



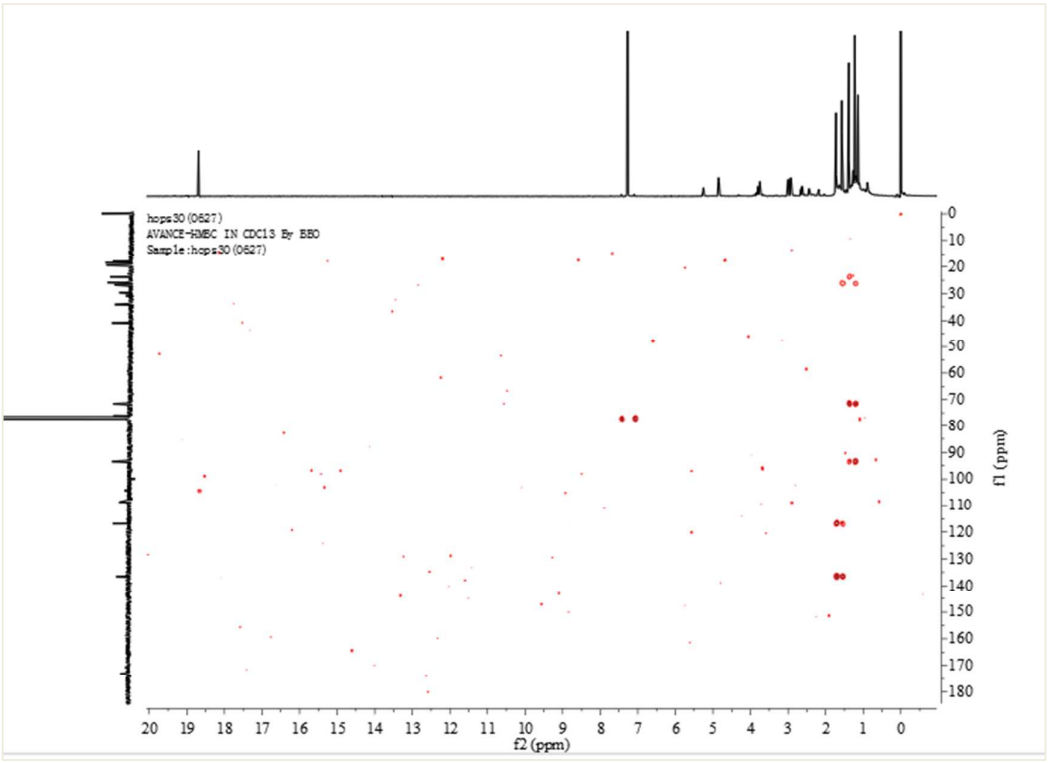
S37. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of (2*S*, 7*S*)-cohumulone B (**6**).



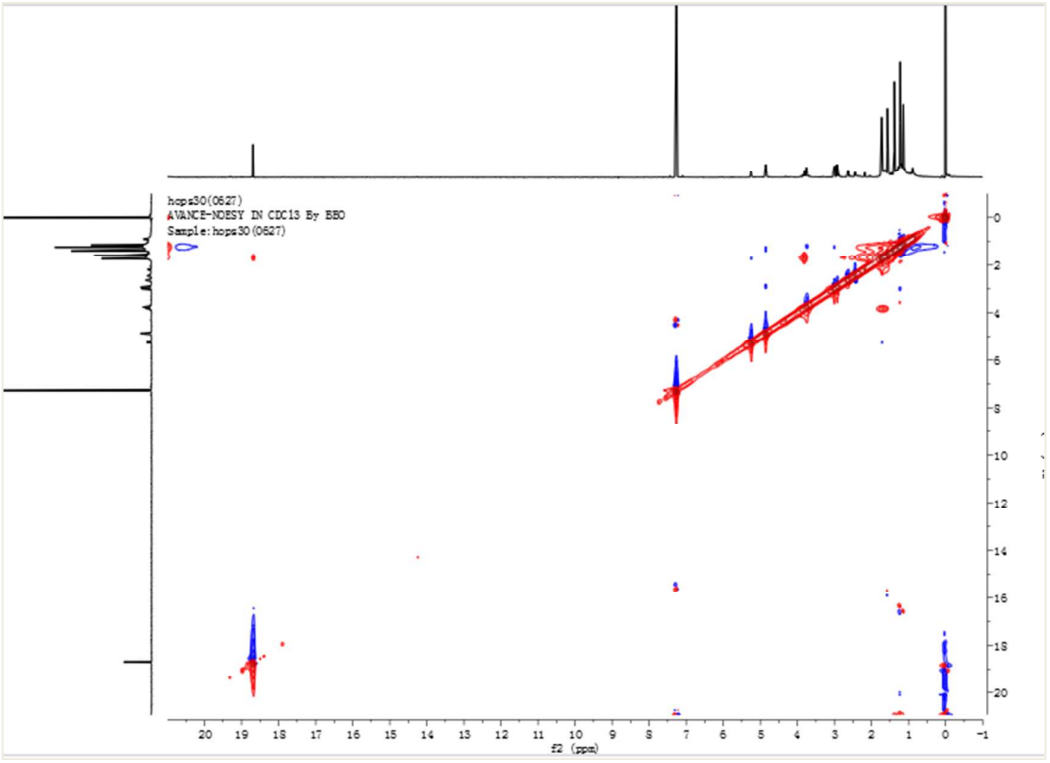
S38. HSQC (600 MHz, $CDCl_3$) spectrum of (2*S*, 7*S*)-cohumulone B (**6**).



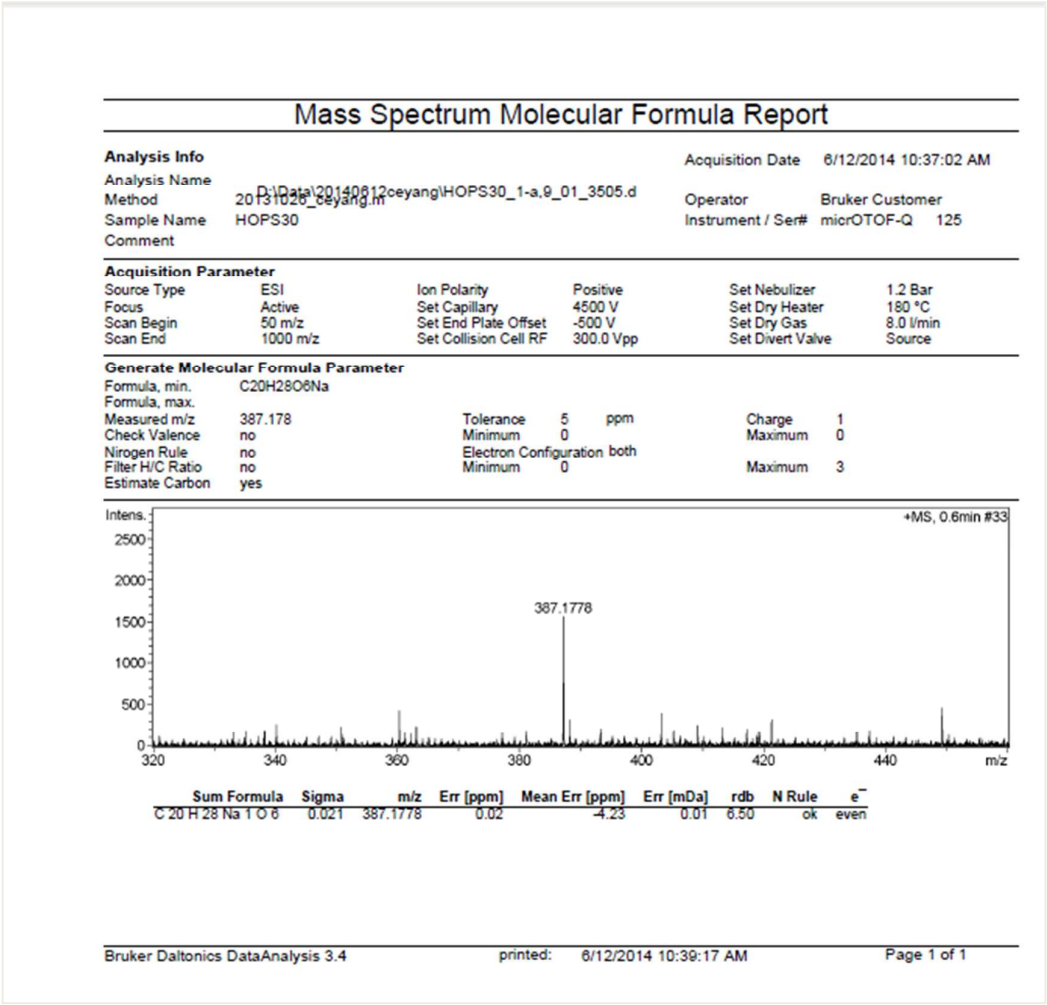
S39. HMBC (600 MHz, $CDCl_3$) spectrum of (2*S*, 7*S*)-cohumulone B (**6**).



S40. NOESY (600 MHz, $CDCl_3$) spectrum of (2*S*, 7*S*)-cohumulone B (**6**)



S41. HRESIMS spectrum of (2*S*, 7*S*)-cohumulone B (**6**).



Mass Spectrum Molecular Formula Report

Analysis Info

Analysis Name	D:\Data\20140612ceyang\HOPS30_1-a,9_01_3505.d	Acquisition Date	6/12/2014 10:37:02 AM
Method	20131026_ceyang.m	Operator	Bruker Customer
Sample Name	HOPS30	Instrument / Ser#	micrOTOF-Q 125
Comment			

Acquisition Parameter

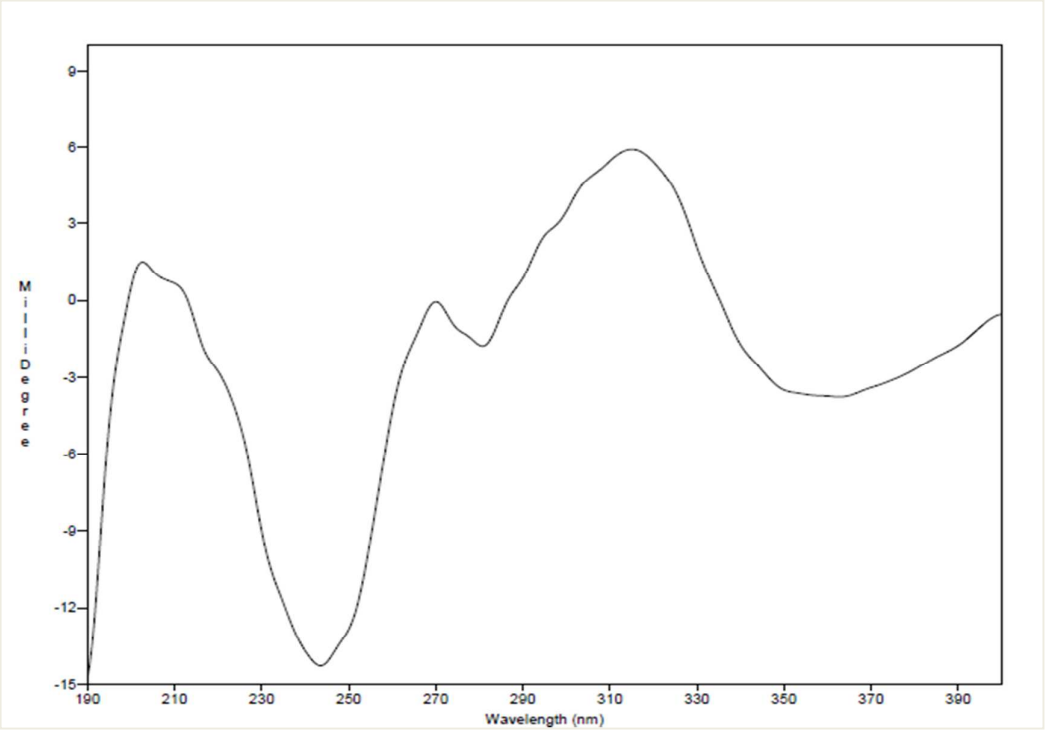
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.2 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	1000 m/z	Set Collision Cell RF	300.0 Vpp	Set Divert Valve	Source

Generate Molecular Formula Parameter

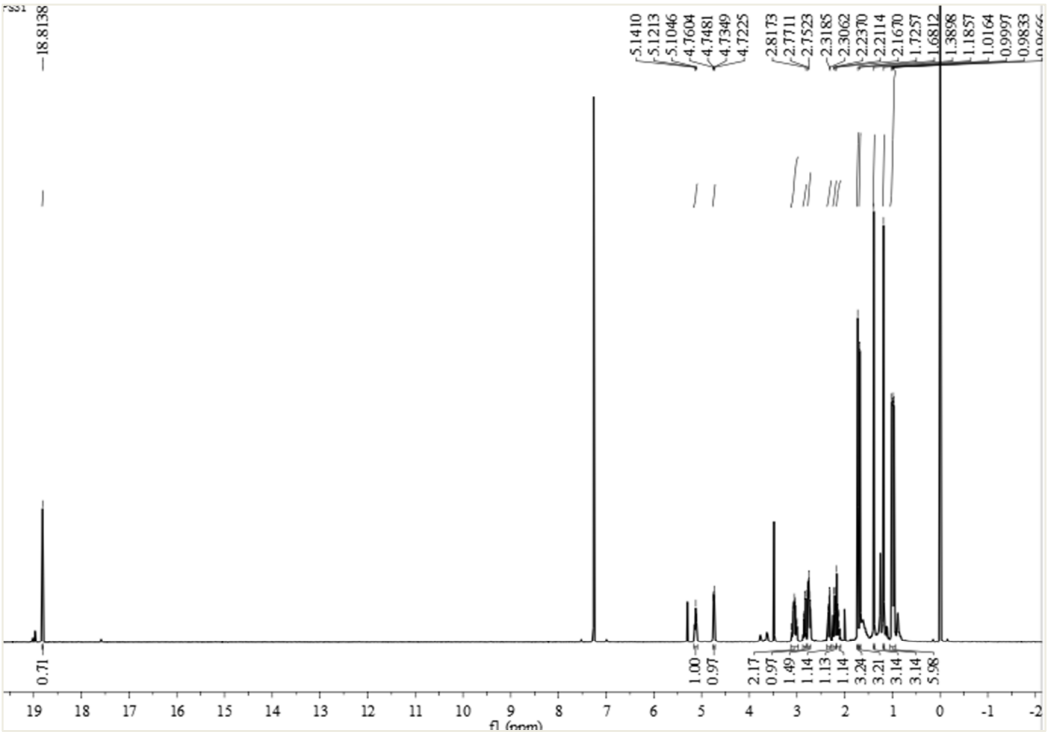
Formula, min.	C20H28O6Na				
Formula, max.					
Measured m/z	387.178	Tolerance	5 ppm	Charge	1
Check Valence	no	Minimum	0	Maximum	0
Nirogen Rule	no	Electron Configuration	both		
Filter H/C Ratio	no	Minimum	0	Maximum	3
Estimate Carbon	yes				

Sum Formula	Sigma	m/z	Err [ppm]	Mean Err [ppm]	Err [mDa]	rdb	N Rule	e⁻
C 20 H 28 Na 1 O 6	0.021	387.1778	0.02	-4.23	0.01	6.50	ok	even

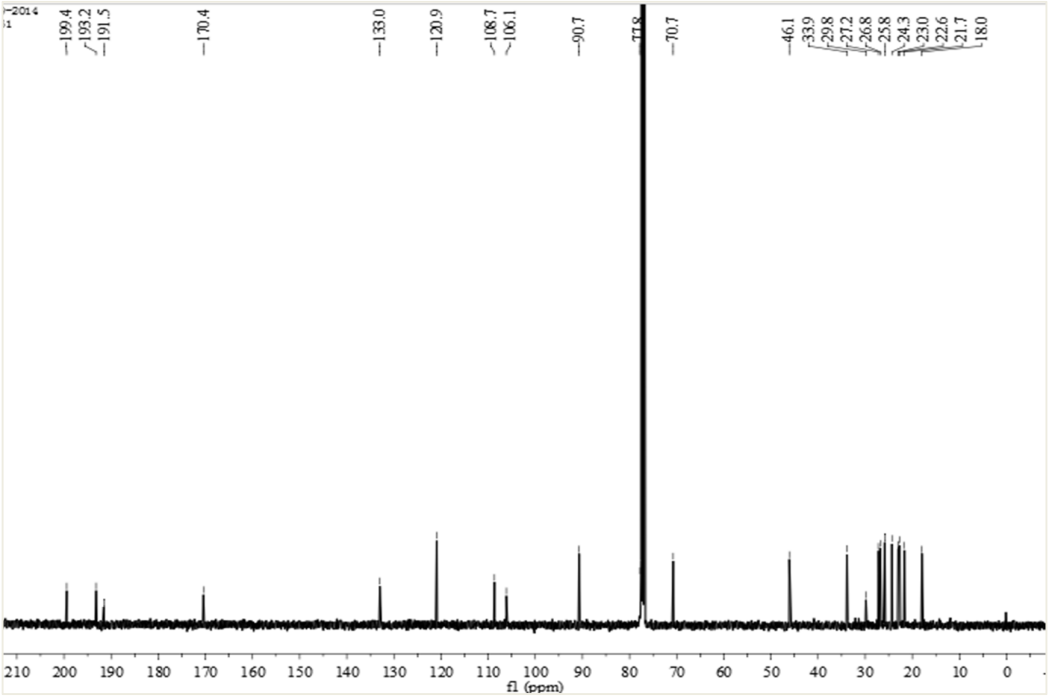
S42. Experimental CD spectrum of (2*S*, 7*S*)-cohumulone B (**6**).



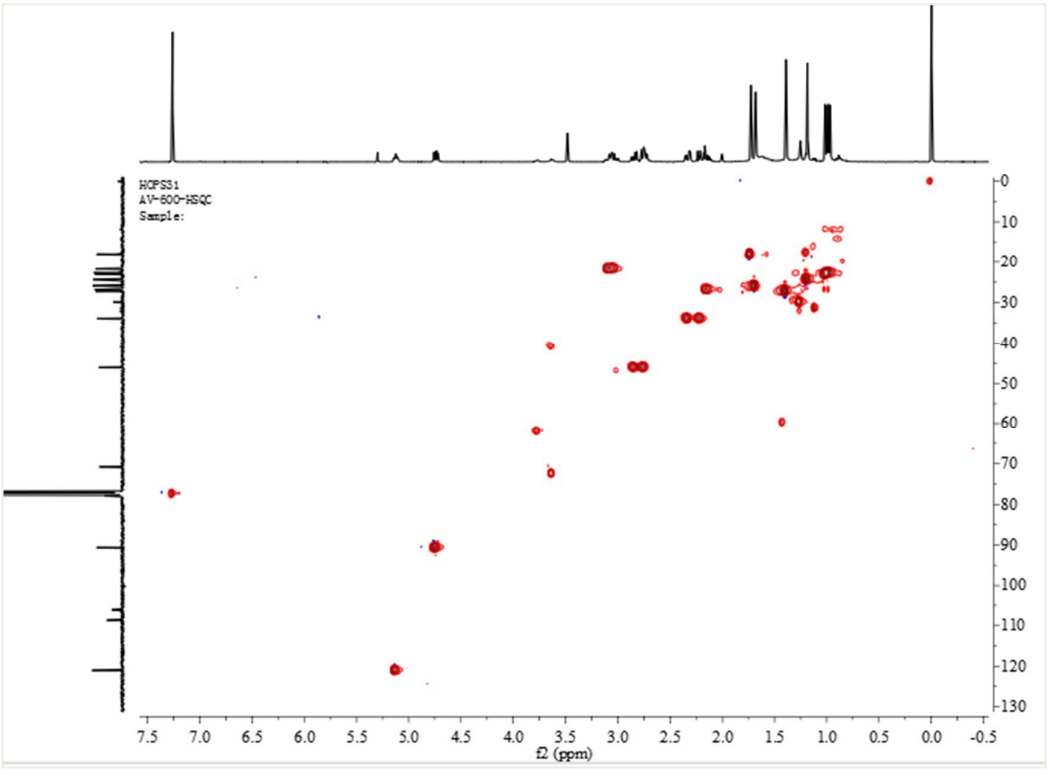
S43. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of (2*S*, 3a*S*)-humulone C (**7**).



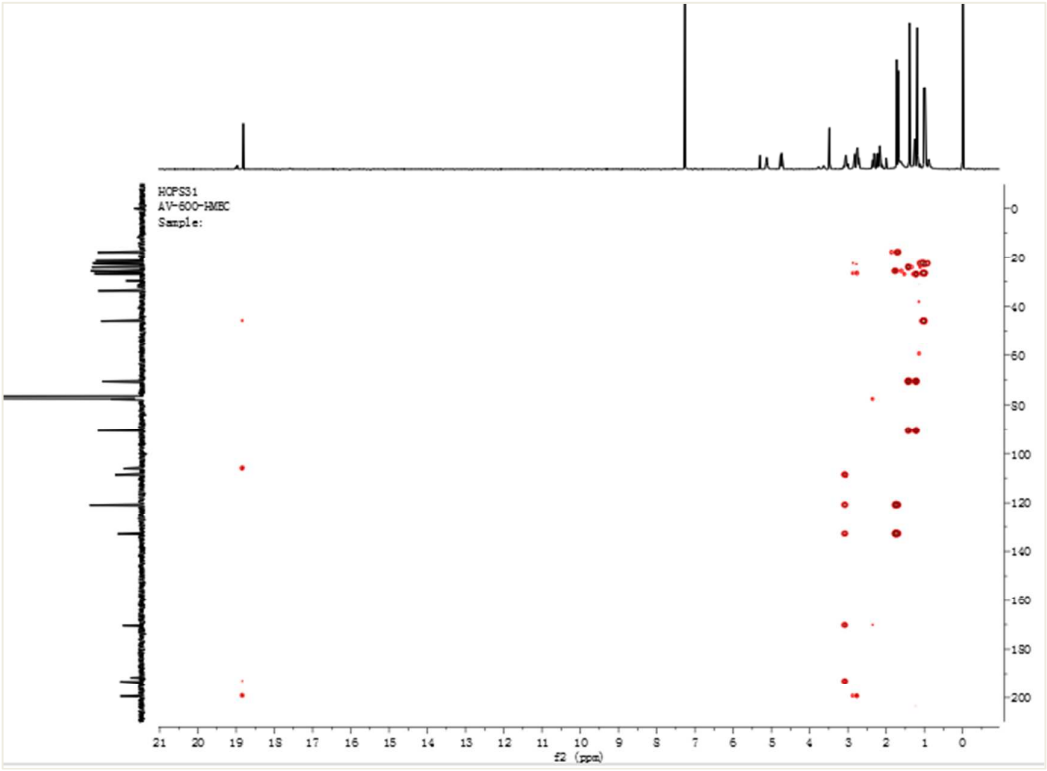
S44. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of (2*S*, 3a*S*)-humulone C (**7**).



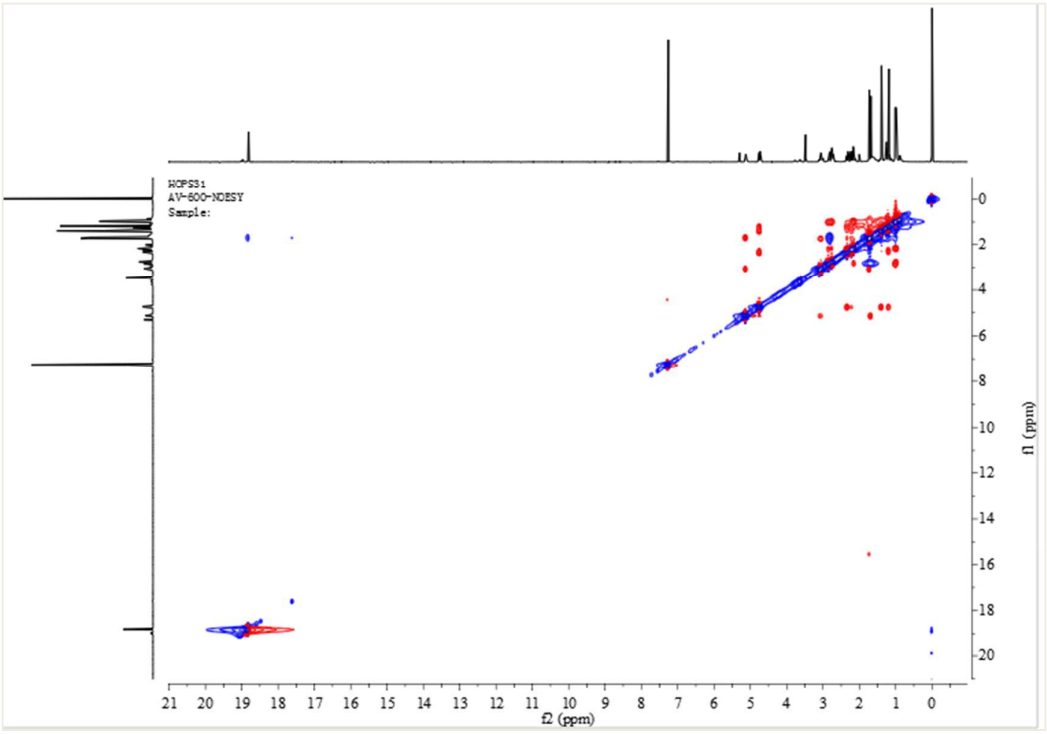
S45. HSQC (600 MHz, $CDCl_3$) spectrum of (2*S*, 3a*S*)-humulone C (**7**).



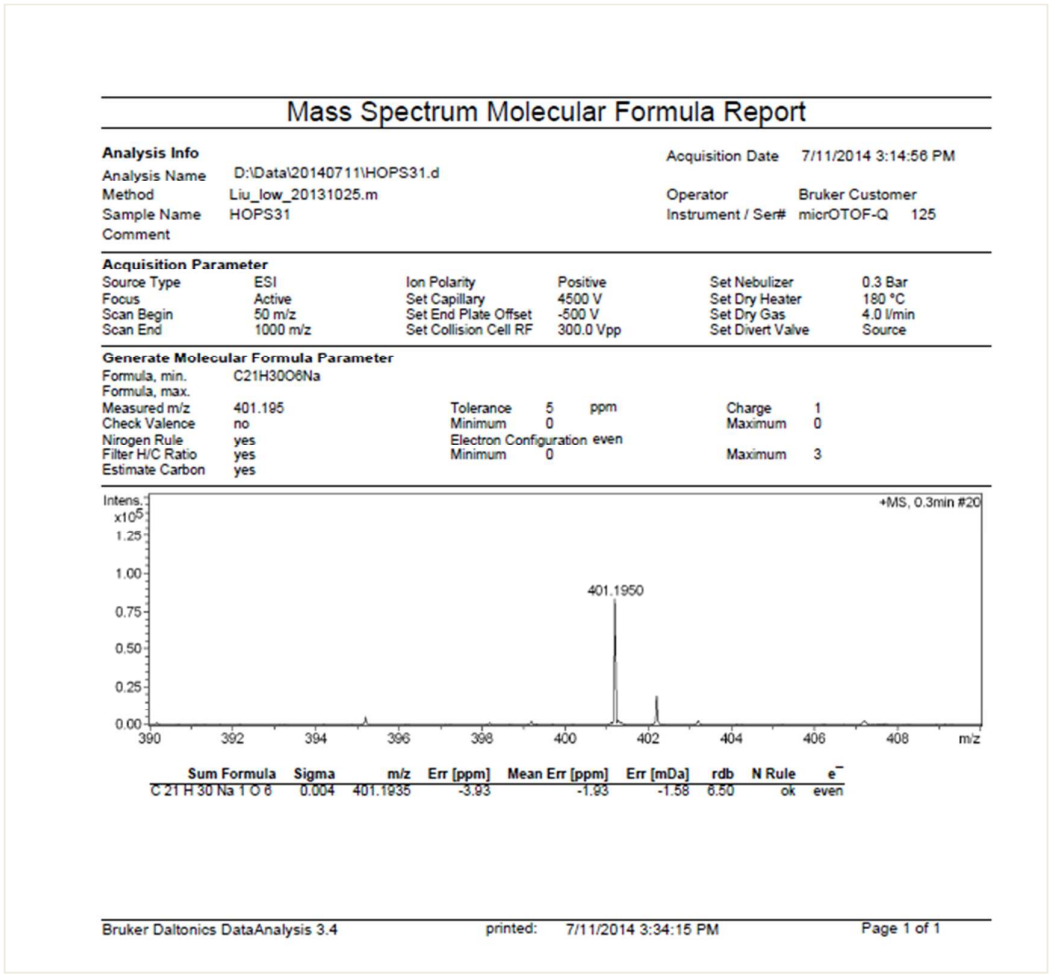
S46. HMBC (600 MHz, $CDCl_3$) spectrum of (2*S*, 3a*S*)-humulone C (**7**).



S47. NOESY(600 MHz, $CDCl_3$) spectrum of (2*S*, 3a*S*)-humulone C (**7**).



S48. HRESIMS spectrum of (2*S*, 3a*S*)-humulone C (**7**).



Mass Spectrum Molecular Formula Report

Analysis Info

Analysis Name	D:\Data\20140711\HOPS31.d	Acquisition Date	7/11/2014 3:14:56 PM
Method	Liu_low_20131025.m	Operator	Bruker Customer
Sample Name	HOPS31	Instrument / Ser#	micrOTOF-Q 125
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1000 m/z	Set Collision Cell RF	300.0 Vpp	Set Divert Valve	Source

Generate Molecular Formula Parameter

Formula, min.	C21H30O6Na				
Formula, max.					
Measured m/z	401.195	Tolerance	5 ppm	Charge	1
Check Valence	no	Minimum	0	Maximum	0
Nirogen Rule	yes	Electron Configuration	even		
Filter H/C Ratio	yes	Minimum	0	Maximum	3
Estimate Carbon	yes				

Sum Formula	Sigma	m/z	Err [ppm]	Mean Err [ppm]	Err [mDa]	rdb	N Rule	e⁻
C 21 H 30 Na 1 O 6	0.004	401.1935	-3.93	-1.93	-1.58	6.50	ok	even

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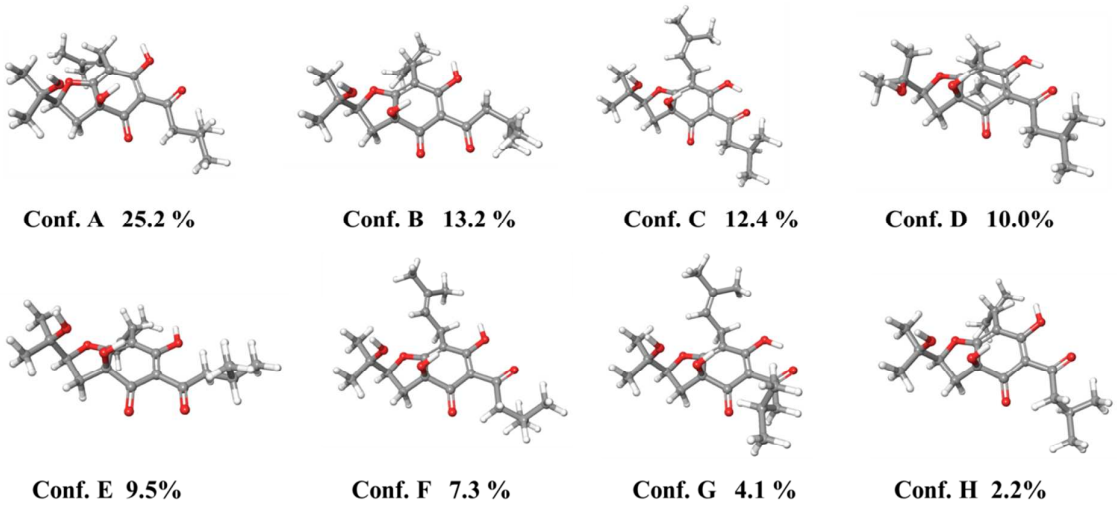
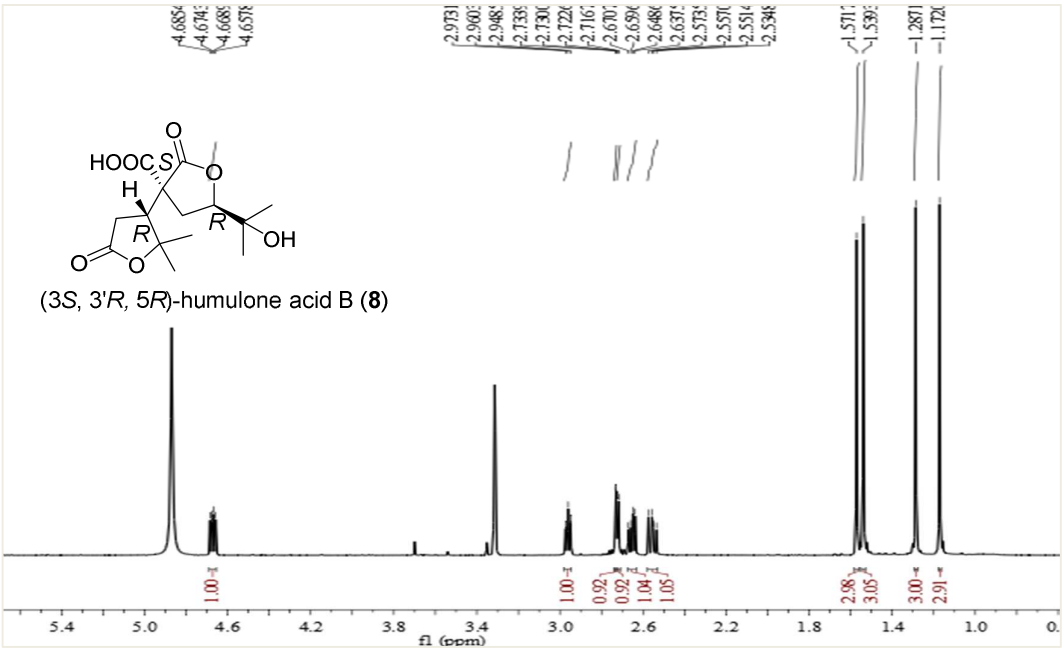
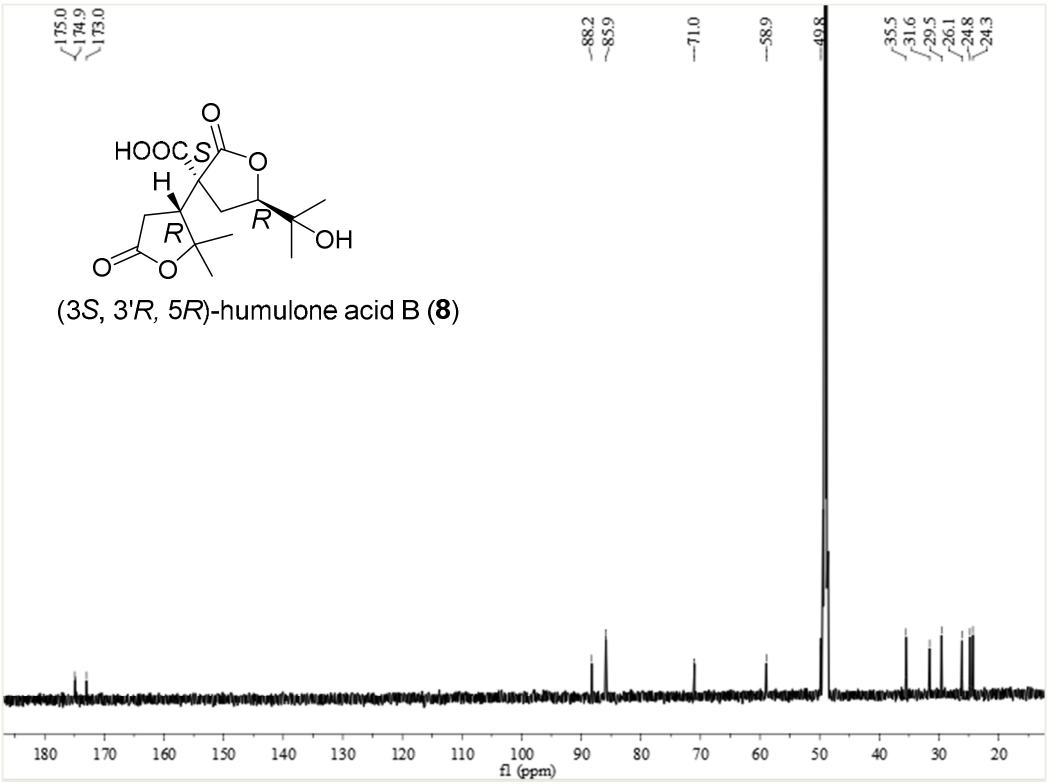
S49. Structures and populations of the low-energy B3LYP/6-31G (d) in *vacuo* conformers (>2%) of (2*S*, 3a*S*)-**7**.



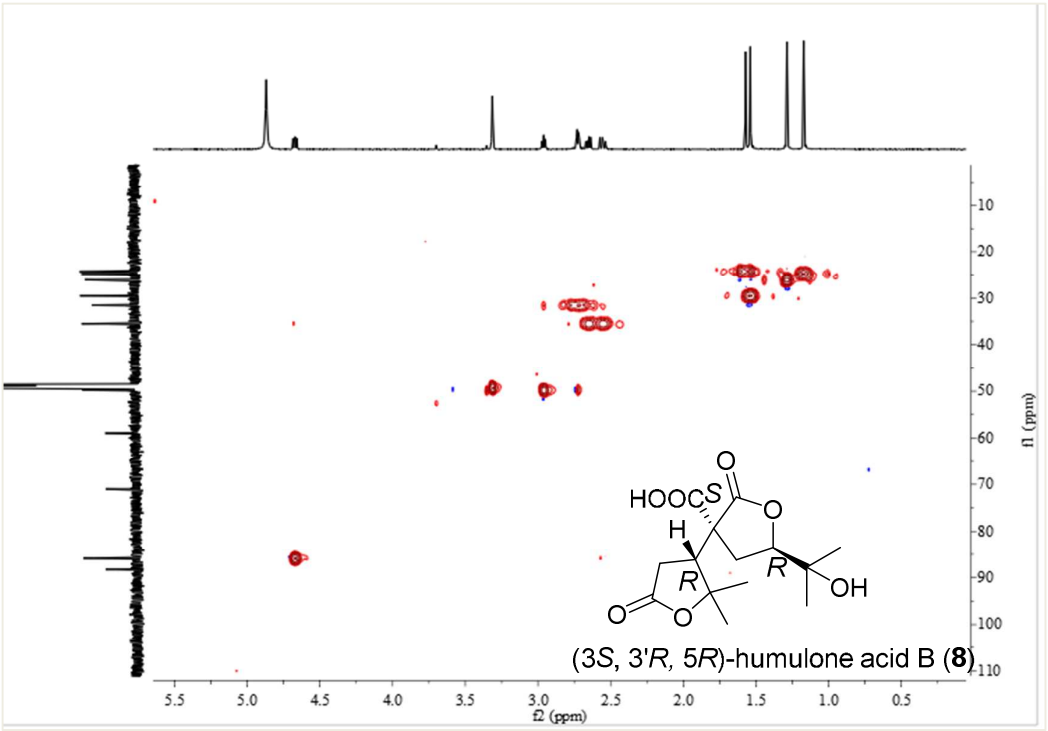
S50. ^{1}H NMR (600 MHz, CD_3OD) spectrum of (3*S*, 3'*R*, 5*R*)-humulone acid B (**8**).



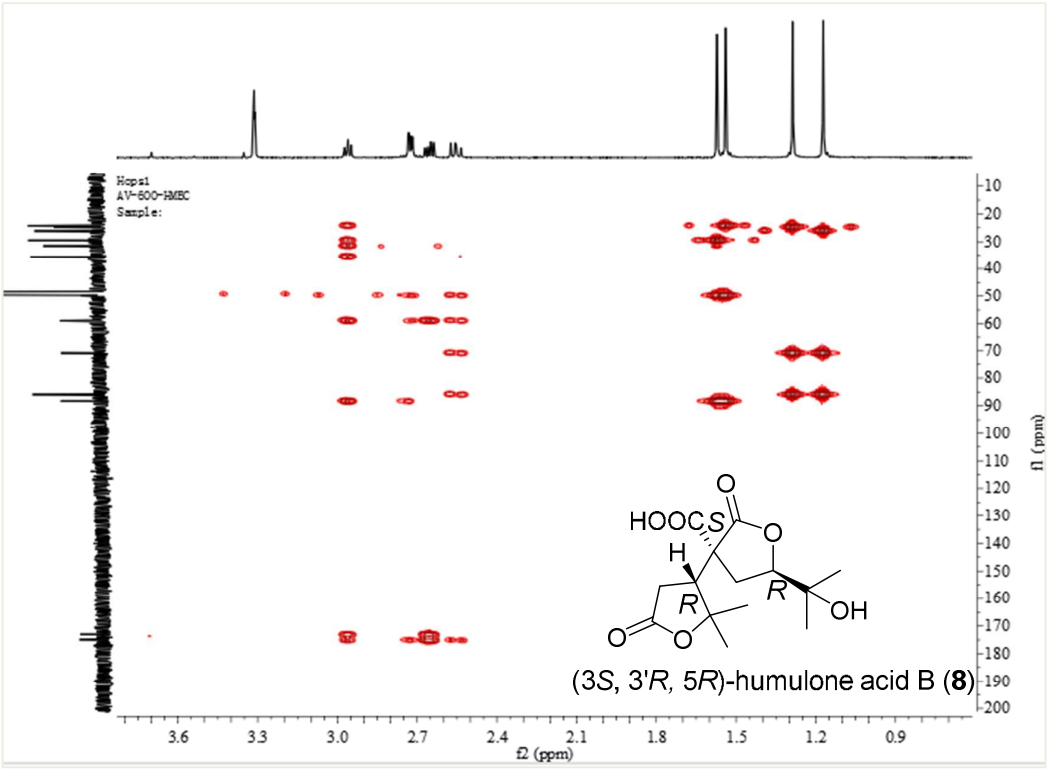
S51. ^{13}C NMR (150 MHz, CD_3OD) spectrum of (3*S*, 3'*R*, 5*R*)-humulone acid B (**8**).



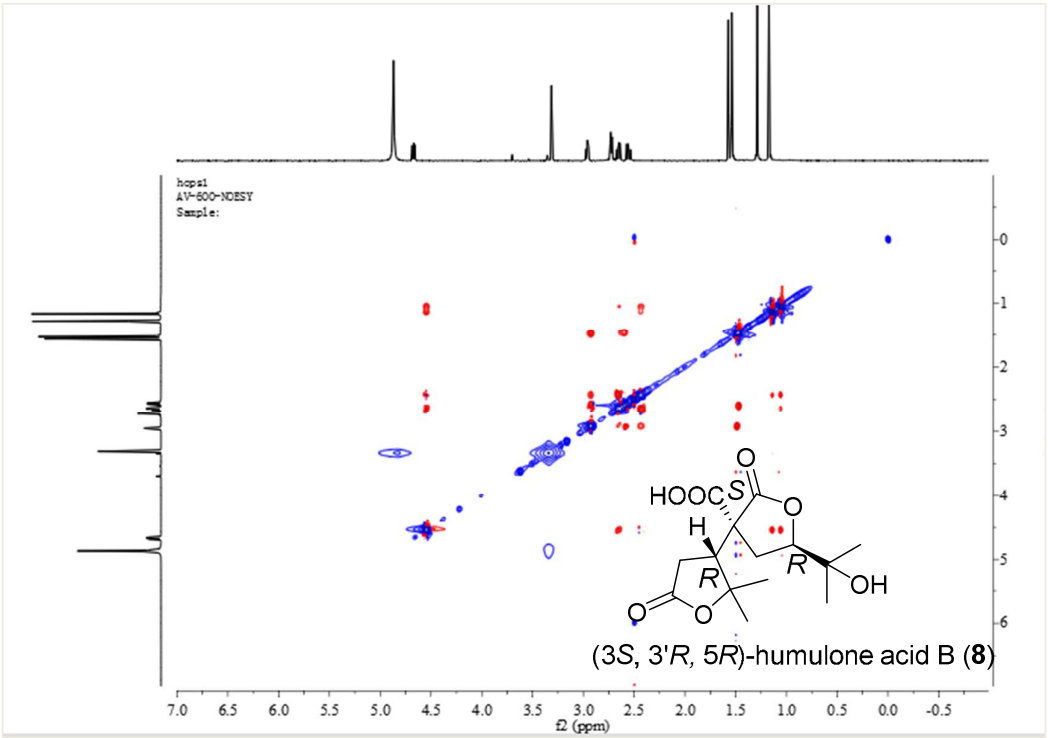
S52. HSQC (600 MHz, CD_3OD) spectrum of (3*S*, 3'*R*, 5*R*)-humulone acid B (**8**).



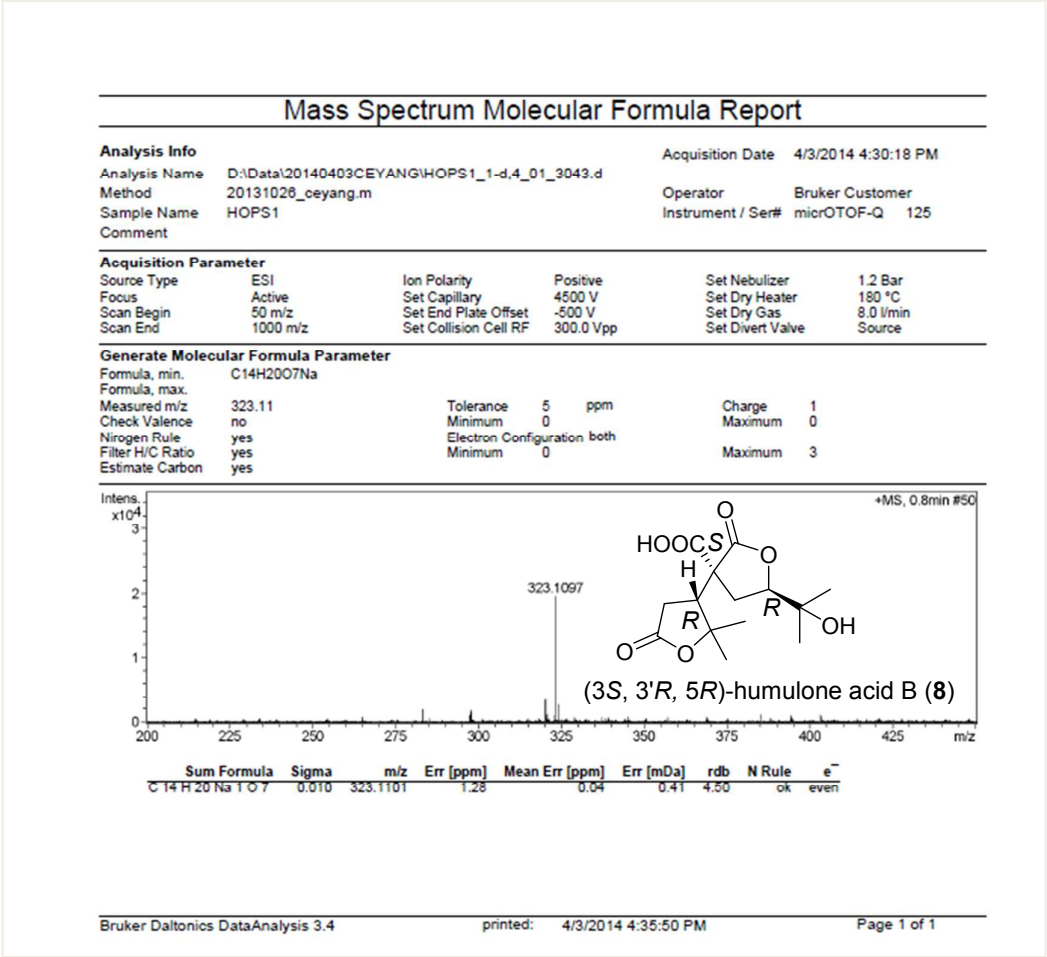
S53. HMBC (600 MHz, CD_3OD) spectrum of (3*S*, 3'*R*, 5*R*)-humulone acid B (**8**).



S54. NOESY (600 MHz, CD_3OD) spectrum of (3*S*, 3'*R*, 5*R*)-humulone acid B (**8**).



S55. HRESIMS spectrum of (3*S*, 3'*R*, 5*R*)-humulone acid B (**8**).



Mass Spectrum Molecular Formula Report

Analysis Info

Analysis Name	D:\Data\20140403CEYANG\HOPS1_1-d,4_01_3043.d	Acquisition Date	4/3/2014 4:30:18 PM
Method	20131026_ceyang.m	Operator	Bruker Customer
Sample Name	HOPS1	Instrument / Ser#	micrOTOF-Q 125
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.2 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	1000 m/z	Set Collision Cell RF	300.0 Vpp	Set Divert Valve	Source

Generate Molecular Formula Parameter

Formula, min.	C14H20O7Na				
Formula, max.					
Measured m/z	323.11	Tolerance	5 ppm	Charge	1
Check Valence	no	Minimum	0	Maximum	0
Nirogen Rule	yes	Electron Configuration	both		
Filter H/C Ratio	yes	Minimum	0	Maximum	3
Estimate Carbon	yes				

Sum Formula	Sigma	m/z	Err [ppm]	Mean Err [ppm]	Err [mDa]	rdb	N Rule	e⁻
C 14 H 20 Na 1 O 7	0.010	323.1101	1.28	0.04	0.41	4.50	ok	even

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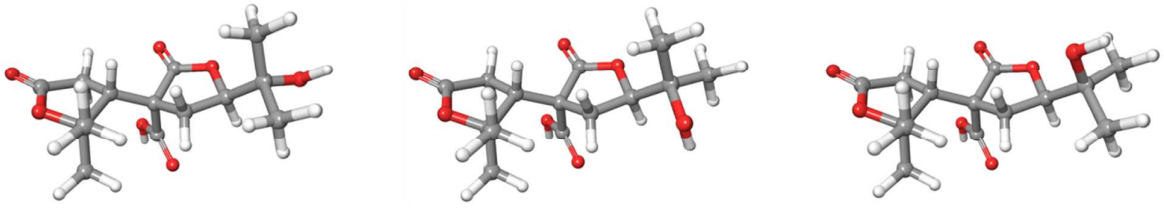
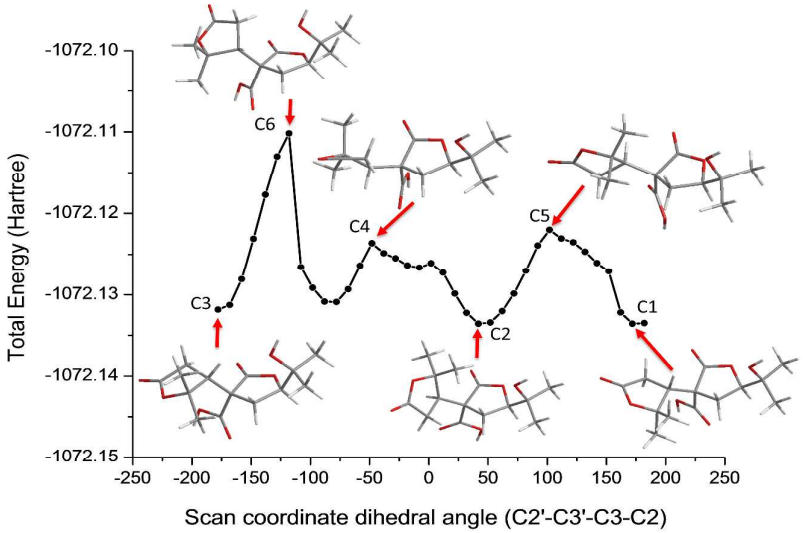
S56. Selected structures and population of the low-energy B3LYP/6-31G (d) in *vacuo* conformers of (3*S*, 3′*R*)-**8** based on experimental NOE correlations.

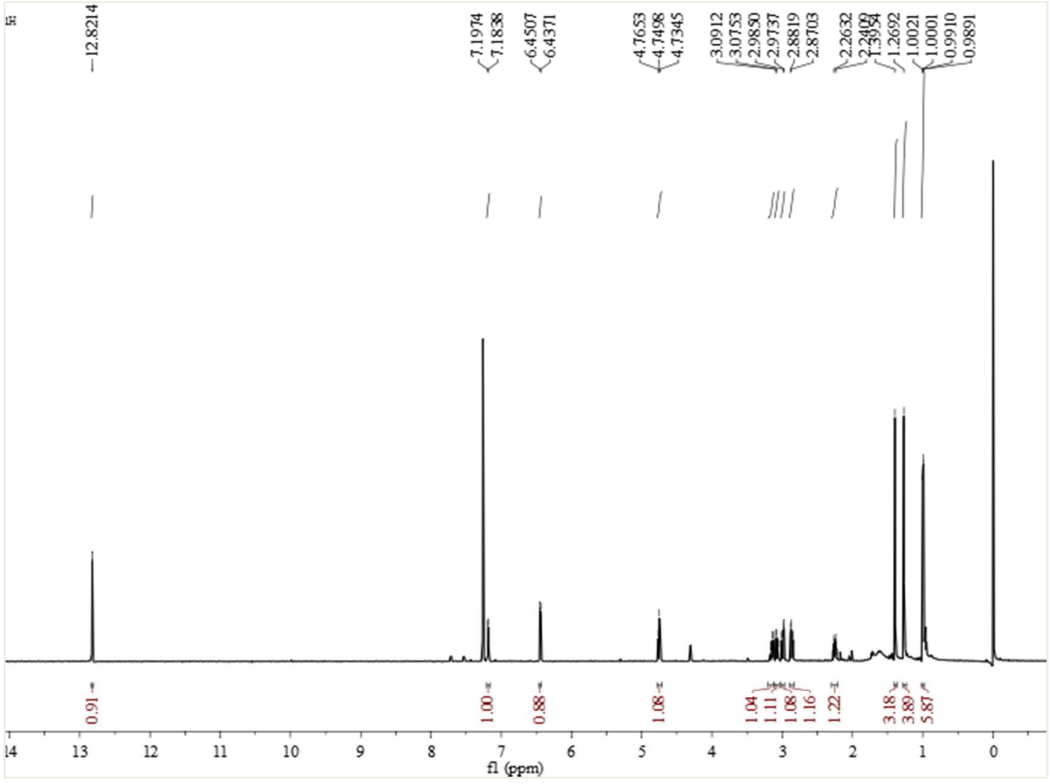


Conf. A 30.1 % **Conf. B 21.1 %** **Conf. C 10.5 %**

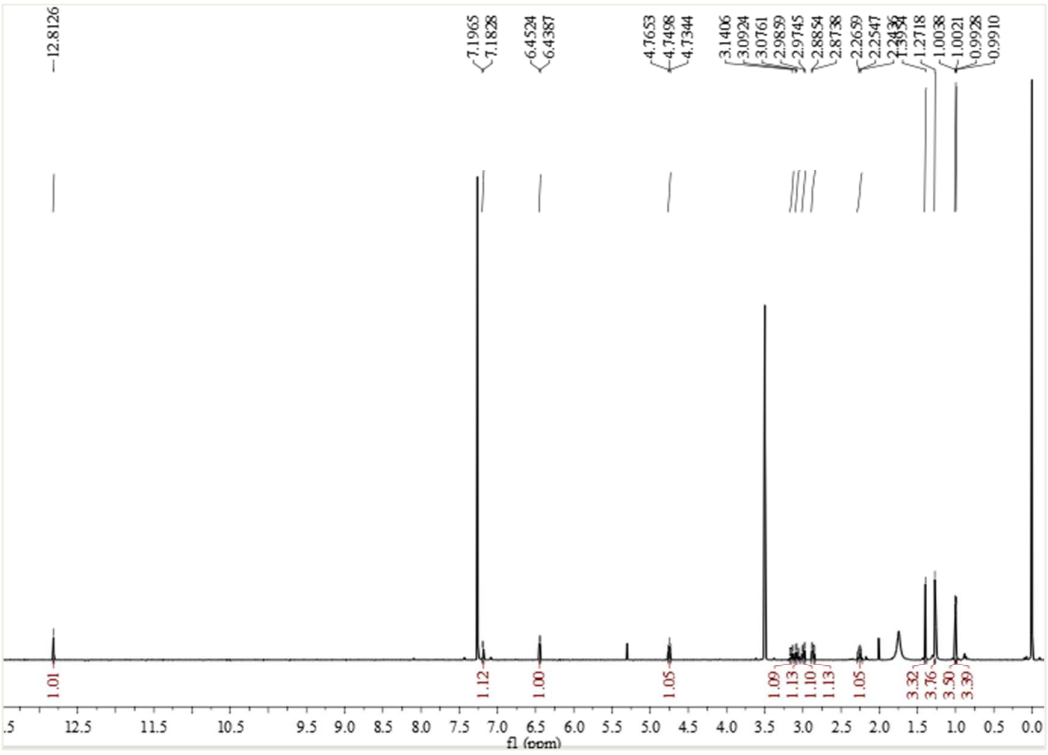
S57. The molecular energy profiles of conformational flexibility of compound **8**



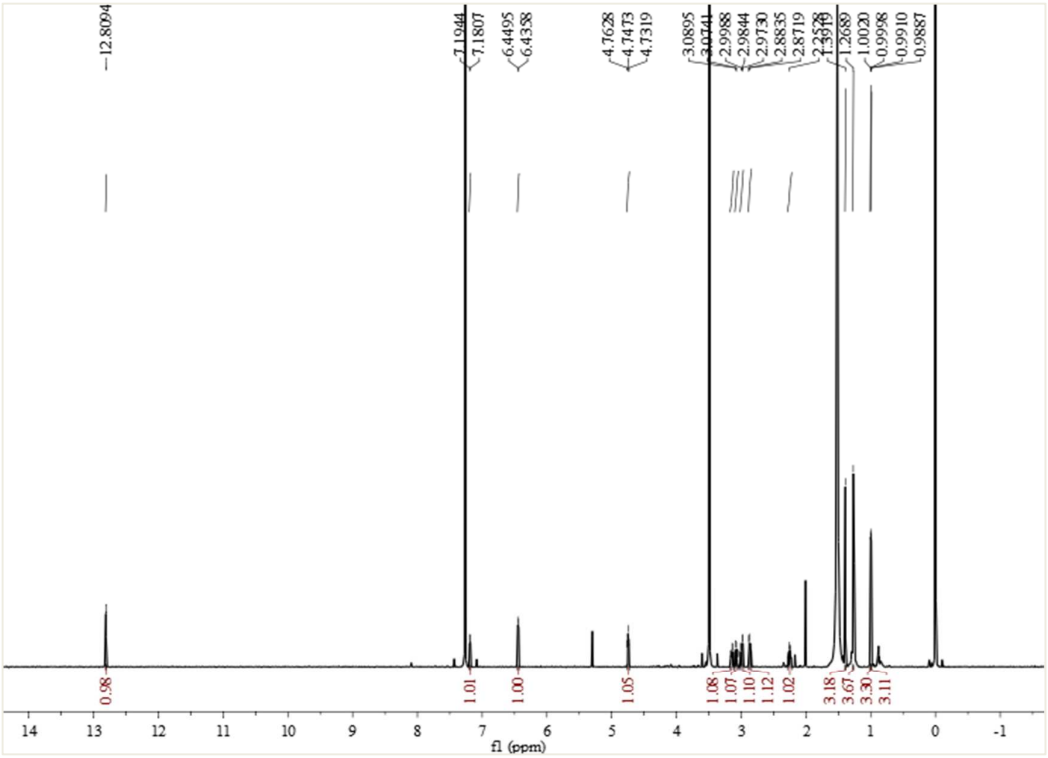
S58. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of lupulone H (**9**).



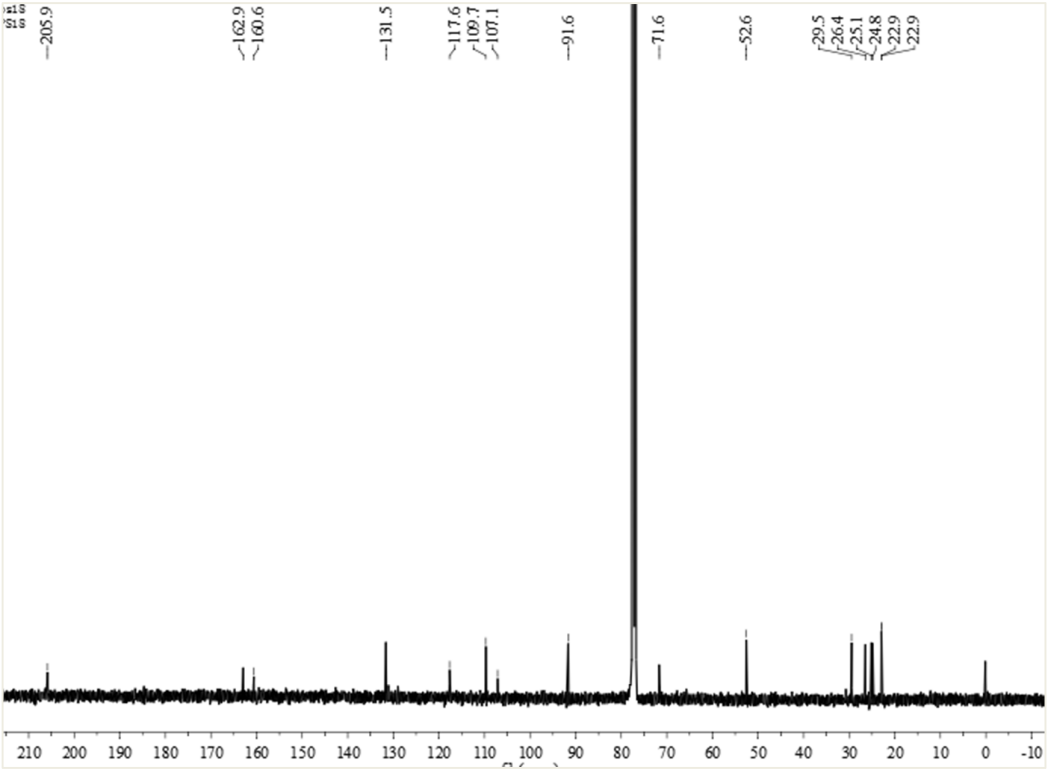
S59. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of (*R*)-lupulone H (**9a**).



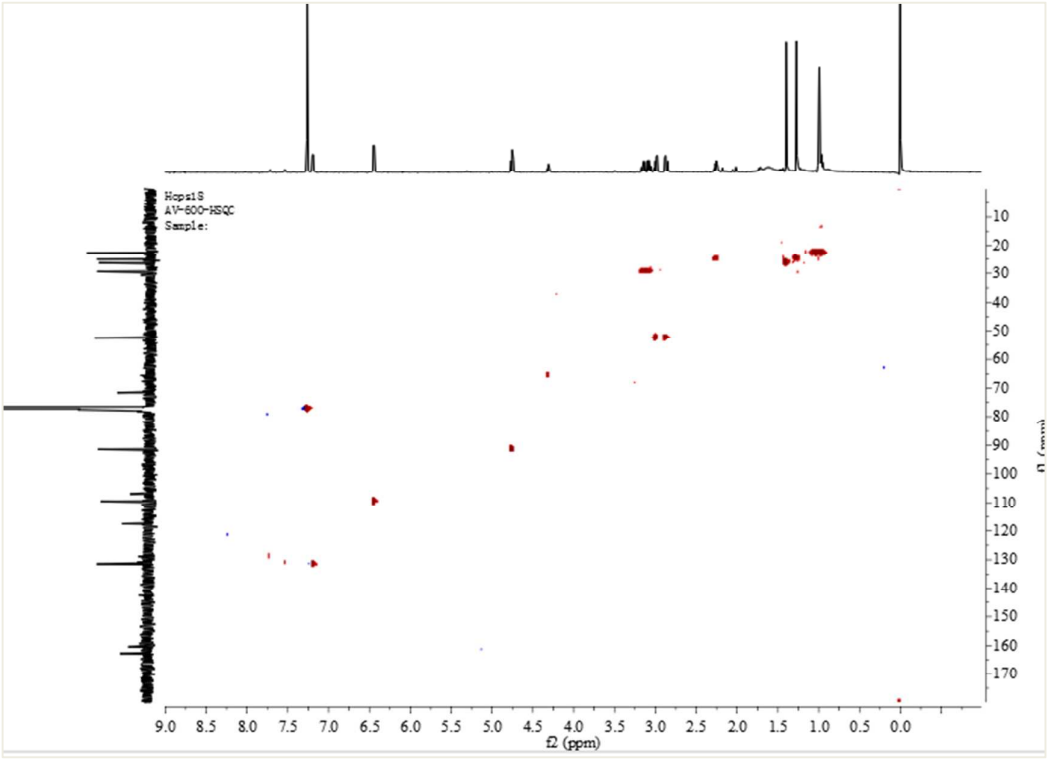
S60. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of (*S*)-lupulone H (**9b**).



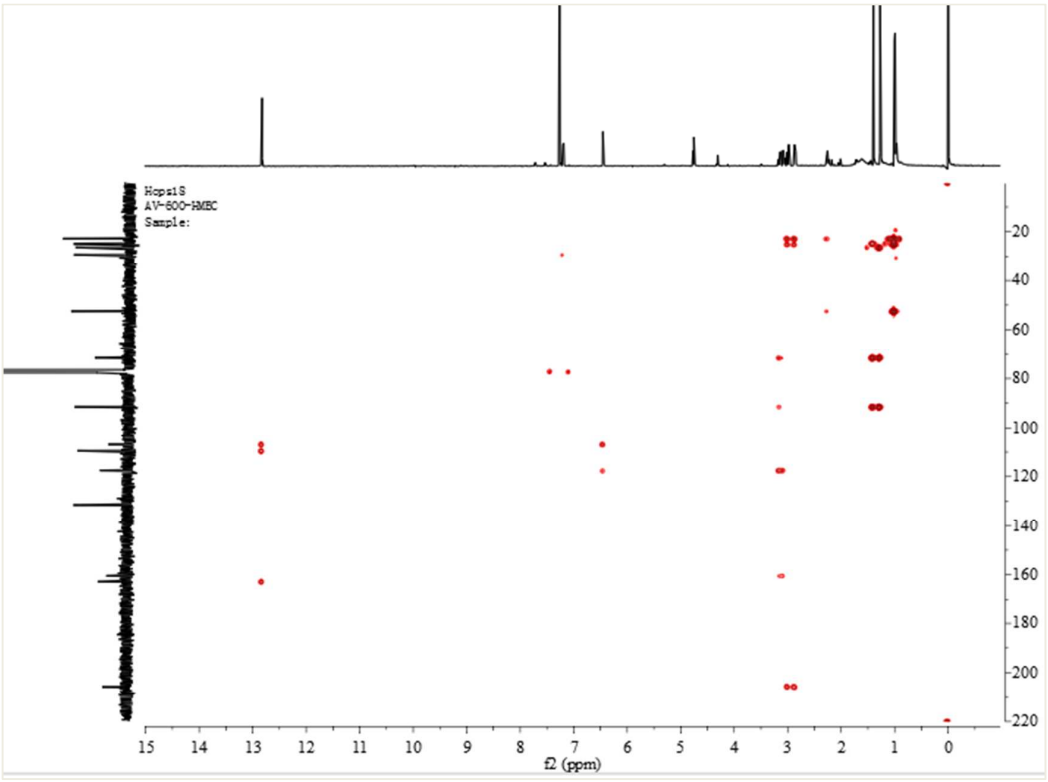
S61. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of lupulone H (**9**).



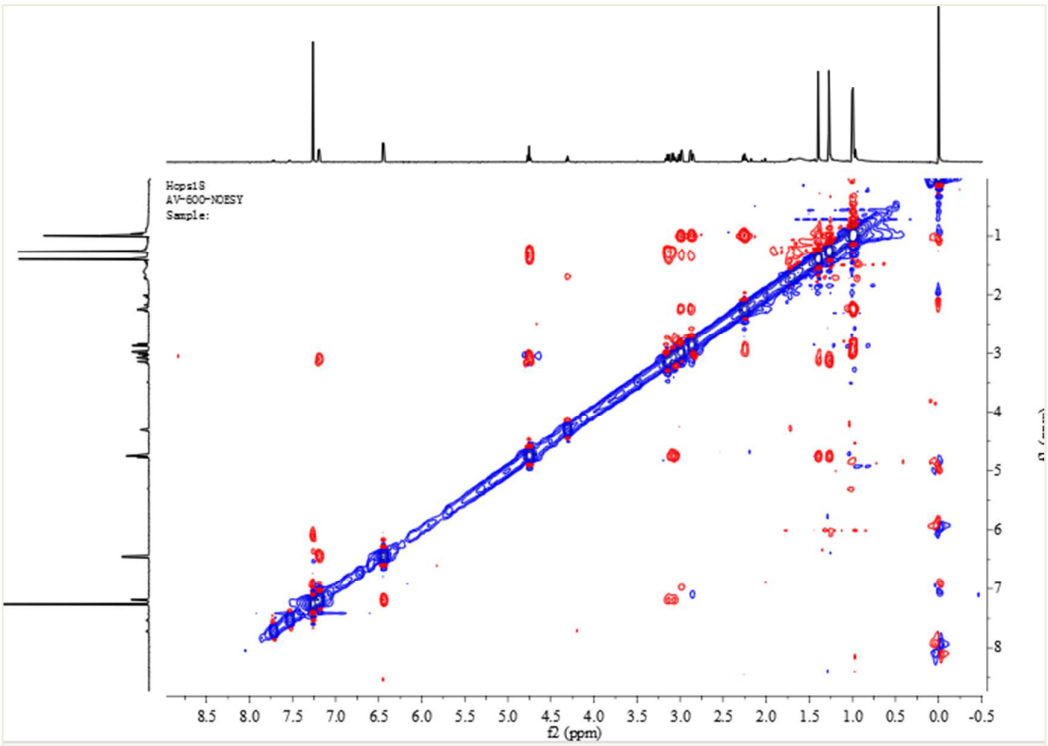
S62. HSQC (600 MHz, $CDCl_3$) spectrum of lupulone H (**9**).



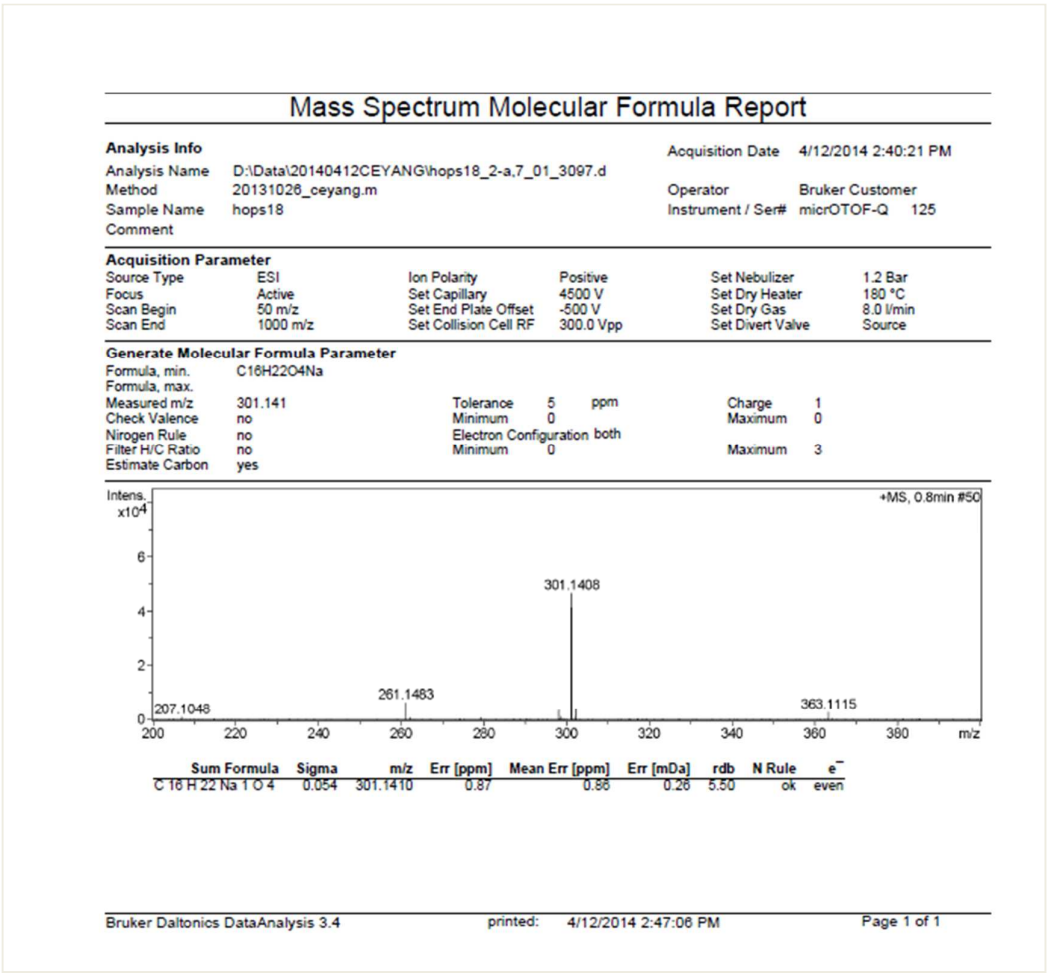
S63. HMBC (600 MHz, $CDCl_3$) spectrum of lupulone H (**9**).



S64. NOESY (600 MHz, $CDCl_3$) spectrum of lupulone H (**9**).



S65. HRESIMS spectrum of lupulone H (**9**).



Mass Spectrum Molecular Formula Report

Analysis Info

Analysis Name	D:\Data\20140412CEYANG\hops18_2-a,7_01_3097.d	Acquisition Date	4/12/2014 2:40:21 PM
Method	20131026_ceyang.m	Operator	Bruker Customer
Sample Name	hops18	Instrument / Ser#	micrOTOF-Q 125
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.2 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	1000 m/z	Set Collision Cell RF	300.0 Vpp	Set Divert Valve	Source

Generate Molecular Formula Parameter

Formula, min.	C16H22O4Na				
Formula, max.					
Measured m/z	301.141	Tolerance	5 ppm	Charge	1
Check Valence	no	Minimum	0	Maximum	0
Nirogen Rule	no	Electron Configuration	both		
Filter H/C Ratio	no	Minimum	0	Maximum	3
Estimate Carbon	yes				

Sum Formula	Sigma	m/z	Err [ppm]	Mean Err [ppm]	Err [mDa]	rdb	N Rule	e⁻
C 16 H 22 Na 1 O 4	0.054	301.1410	0.87	0.86	0.26	5.50	ok	even

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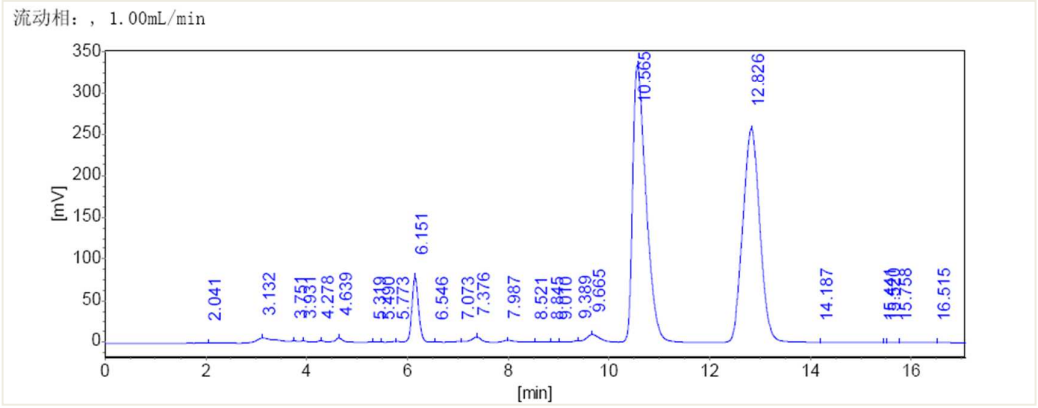
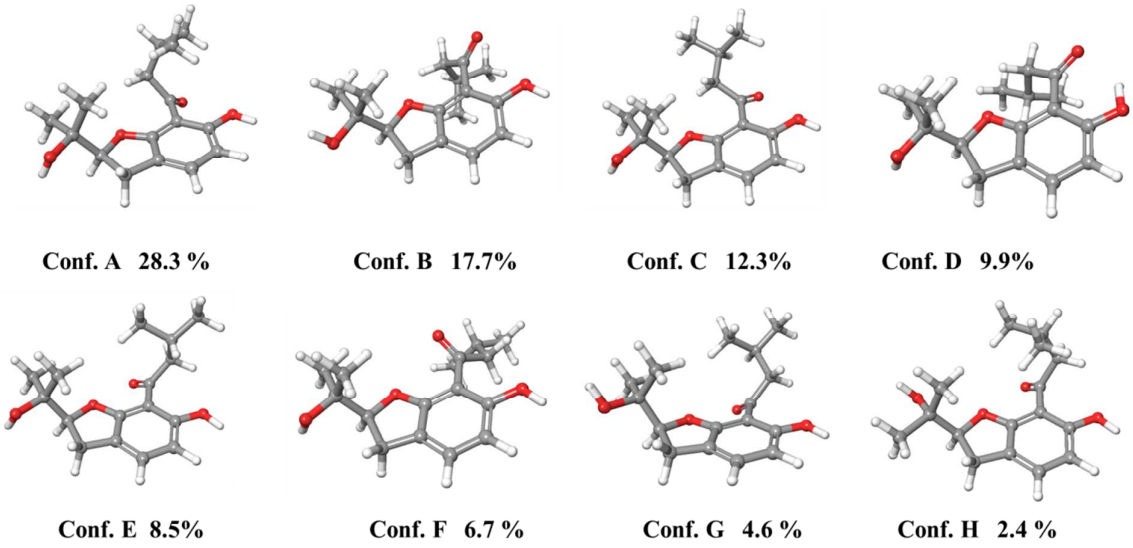
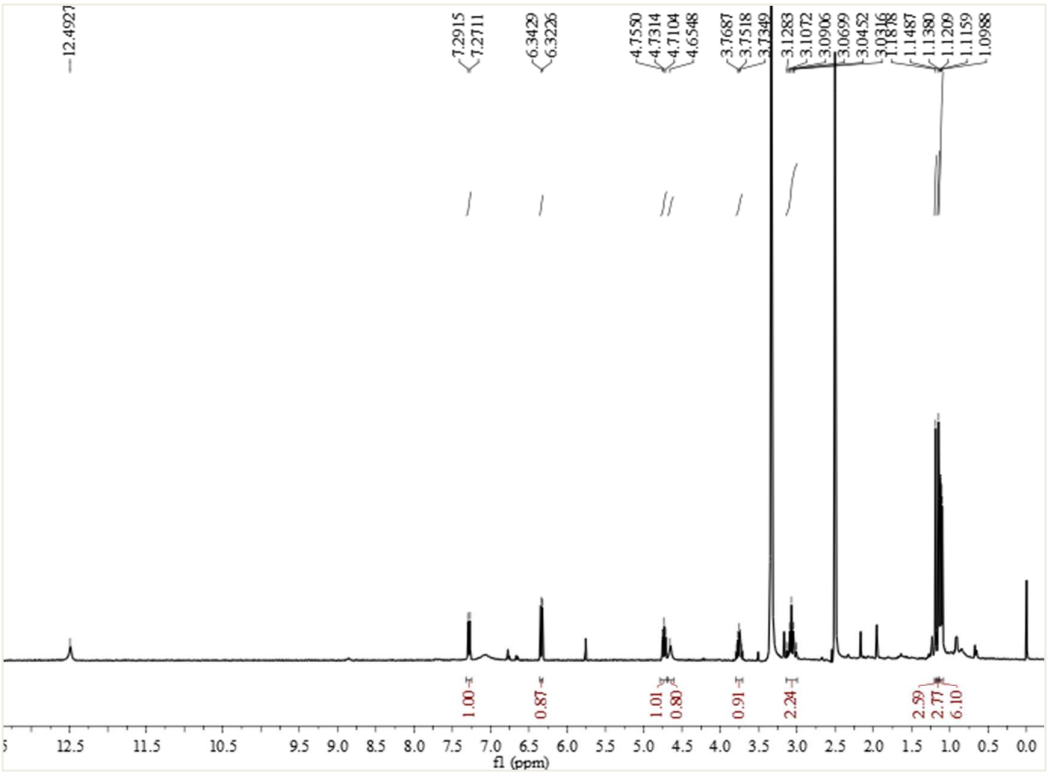
S66. The HPLC of chiral column analysis of lupulone H (**9**).



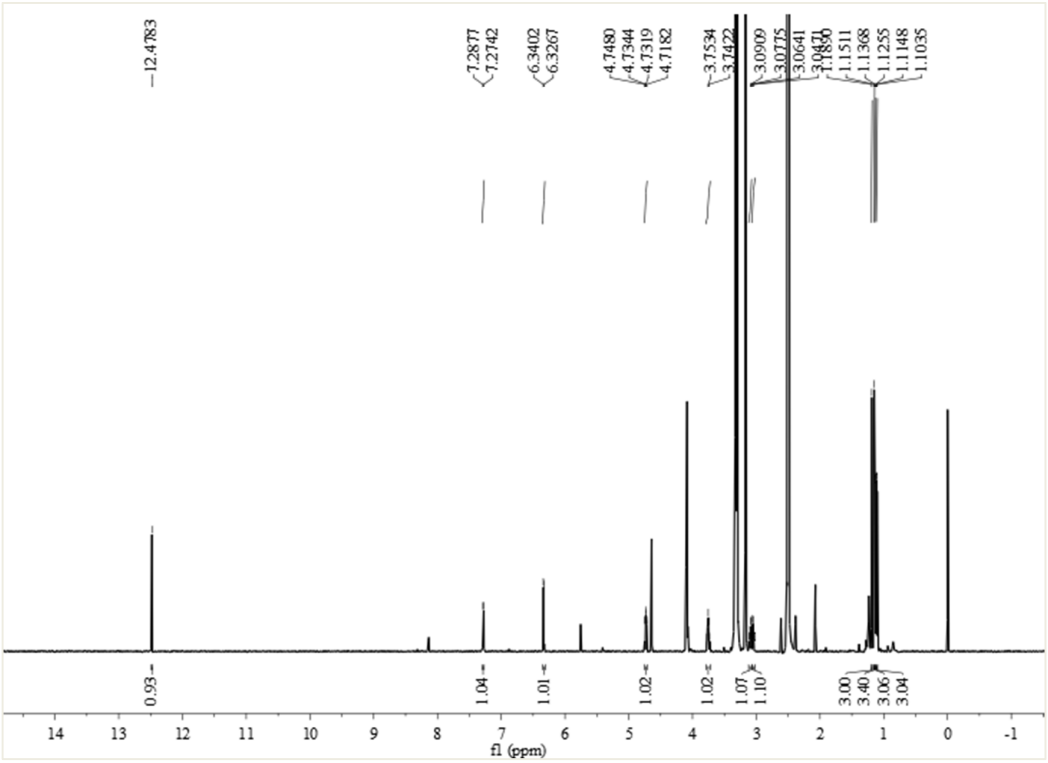
S67. Structures and populations of the low-energy B3LYP/6-31G (d) in *vacuo* conformers (>2%) of (2*S*)-**9**.



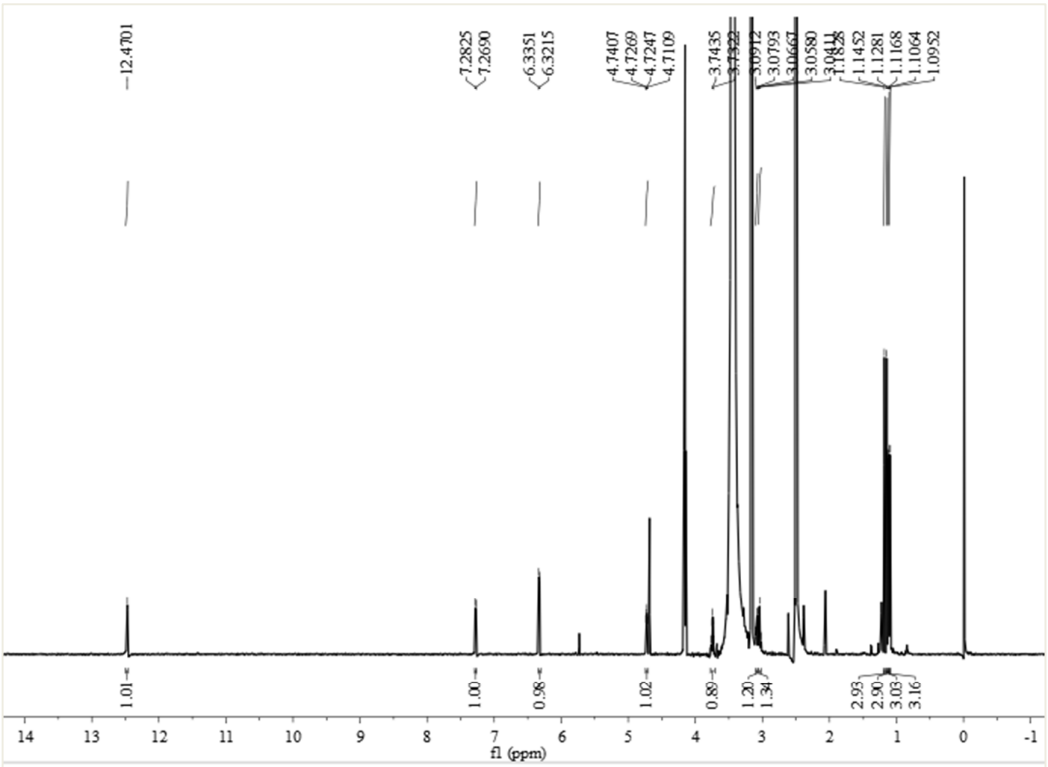
S68. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of lupulone G (**10**)



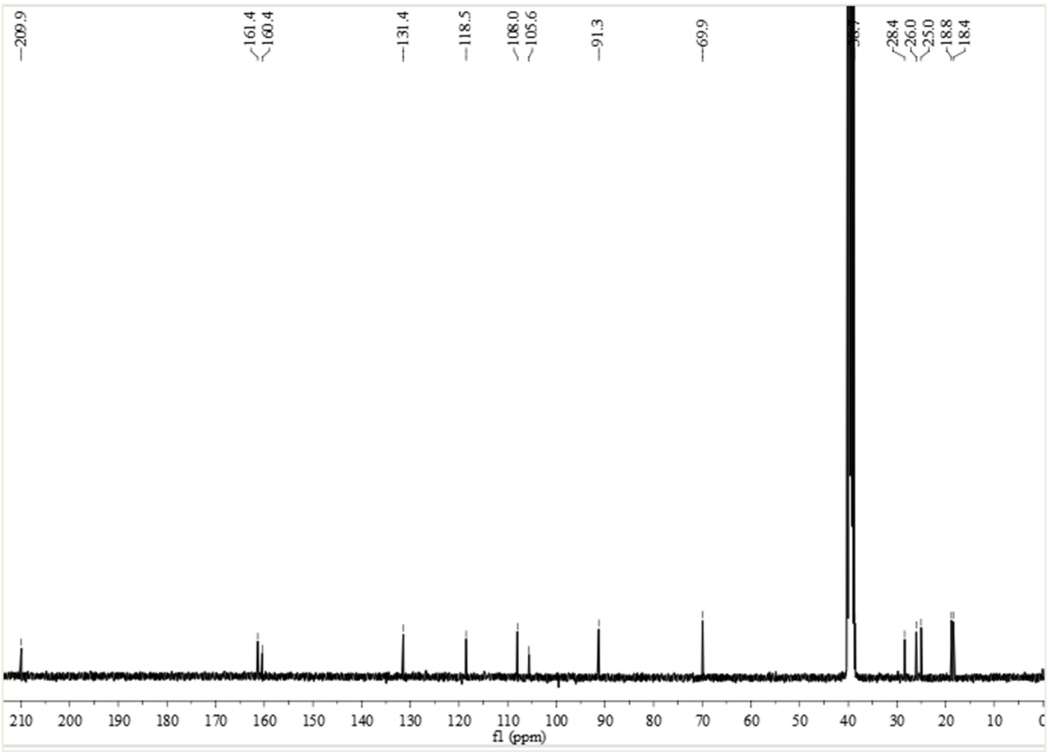
S69. ^{1}H NMR (600 MHz, DMSO-d_6) spectrum of (*R*)-lupulone G (**10a**)



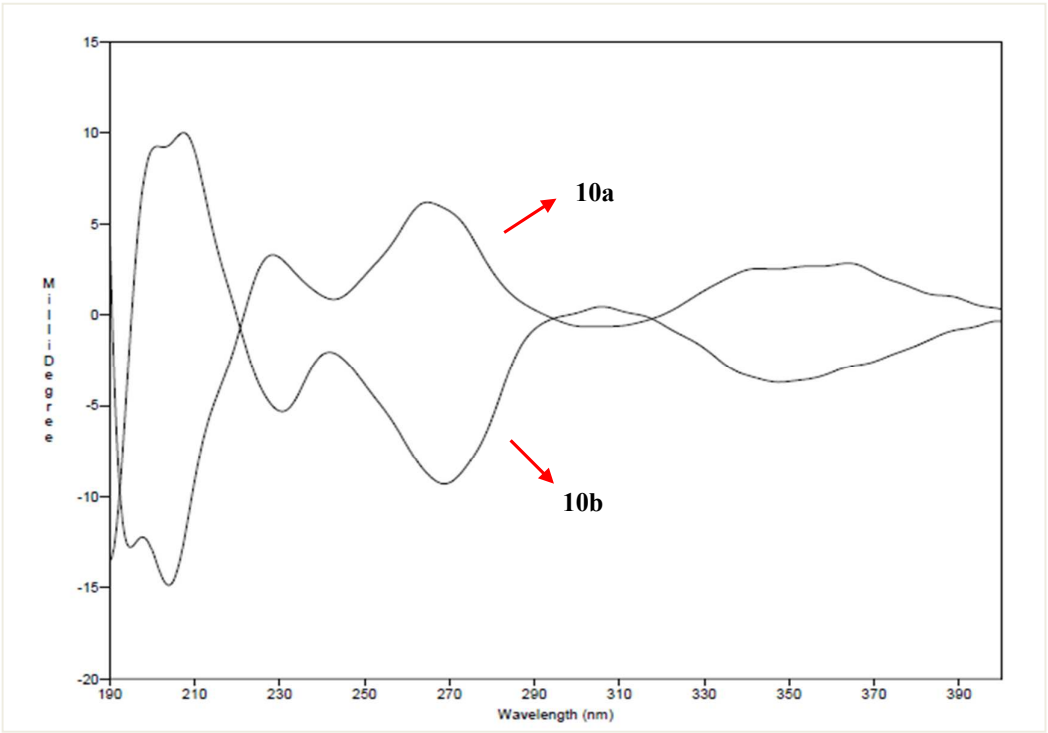
S70. ^{1}H NMR (600 MHz, DMSO-d_6) spectrum of (*S*)-lupulone G (**10b**)



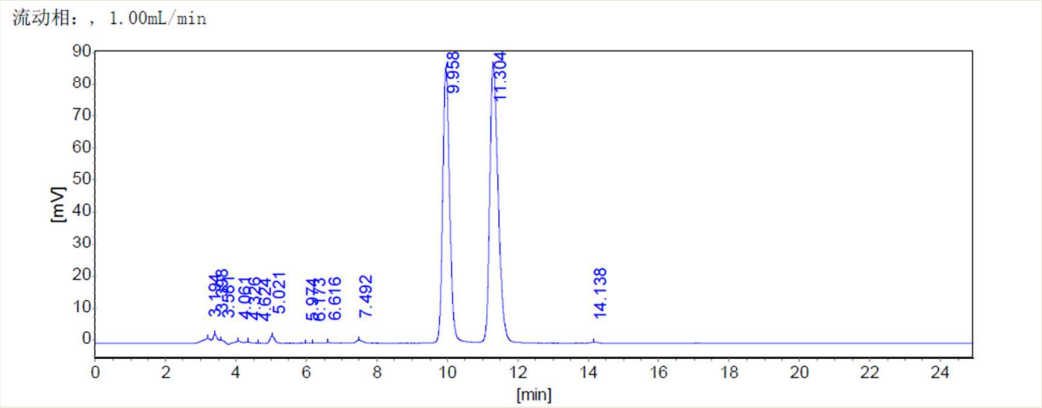
S71. ^{13}C NMR (100 MHz, DMSO-d_6) spectrum of lupulone G (**10**).



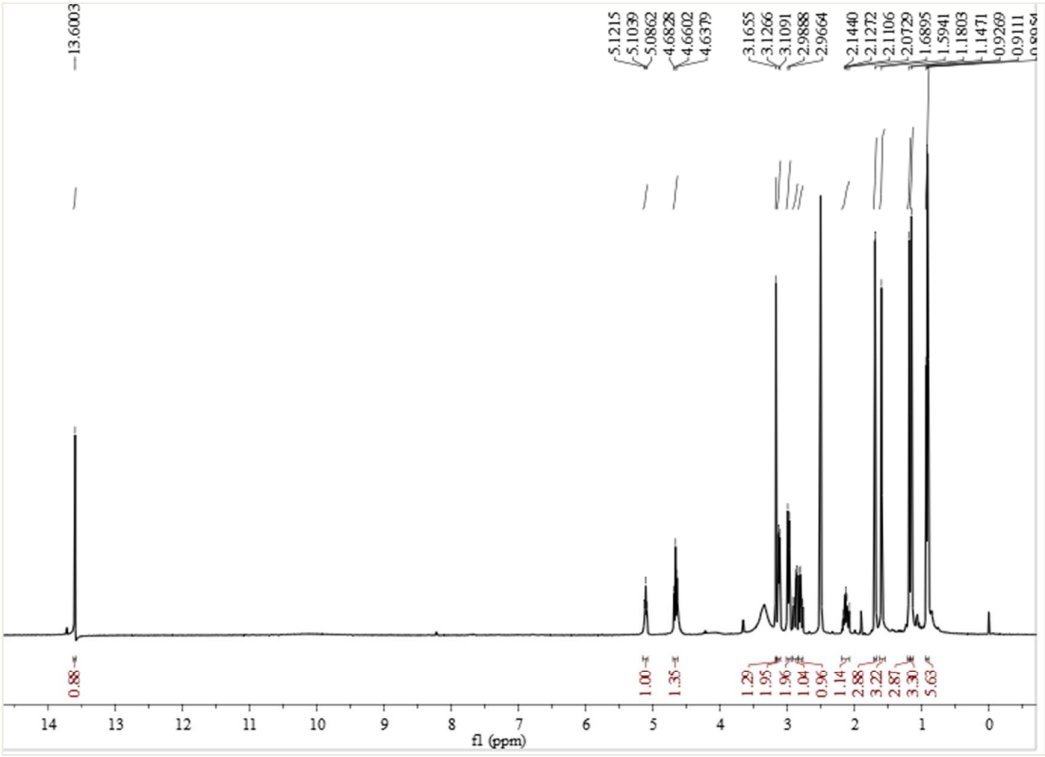
S72. Experimental CD spectrum of (*R*)-lupulone G (**10a**) and (*S*)-lupulone G (**10b**).



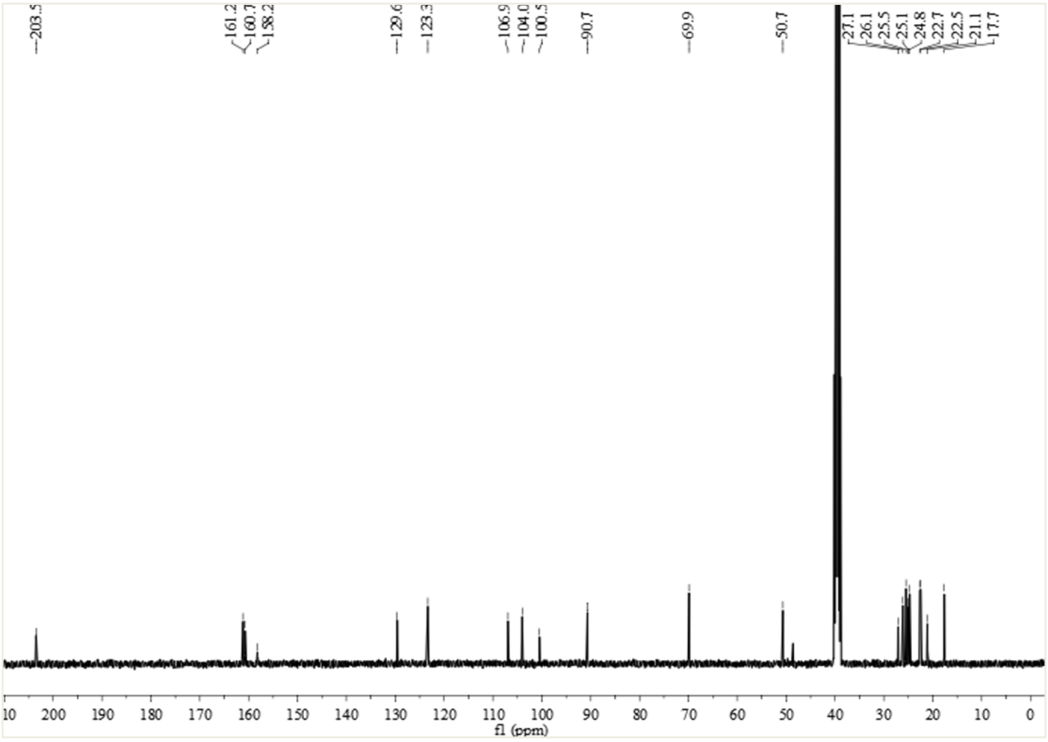
S73. The HPLC of chiral column analysis of lupulone G (**10**).



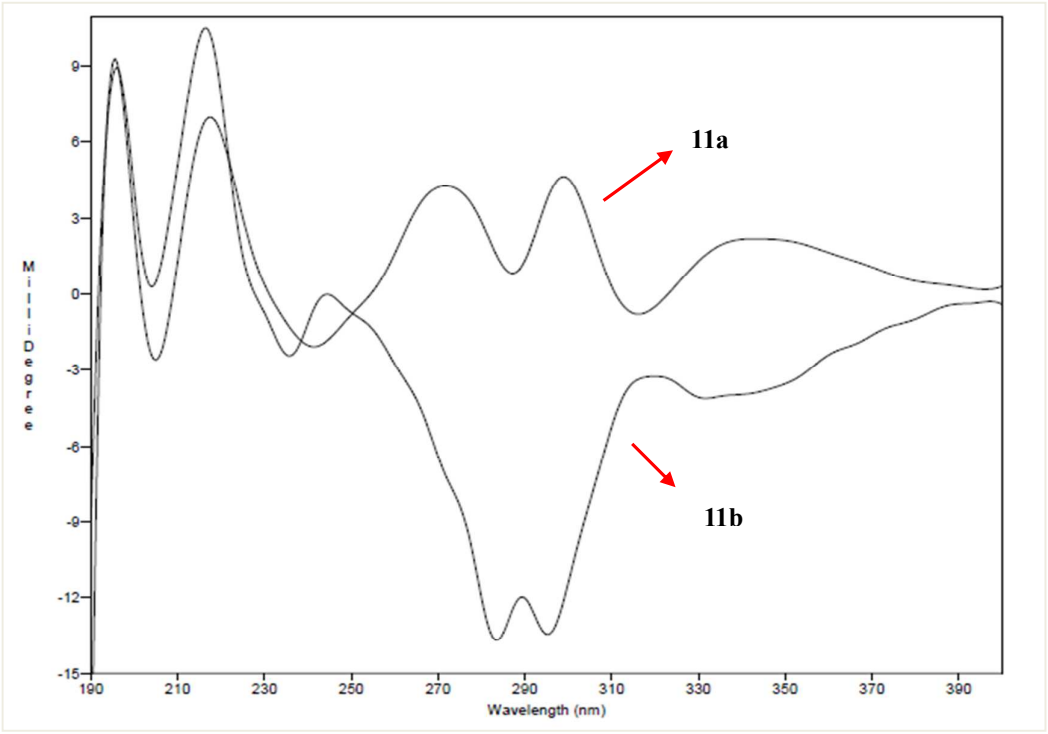
S74. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of 5-deprenyllupulonol C (**11**).



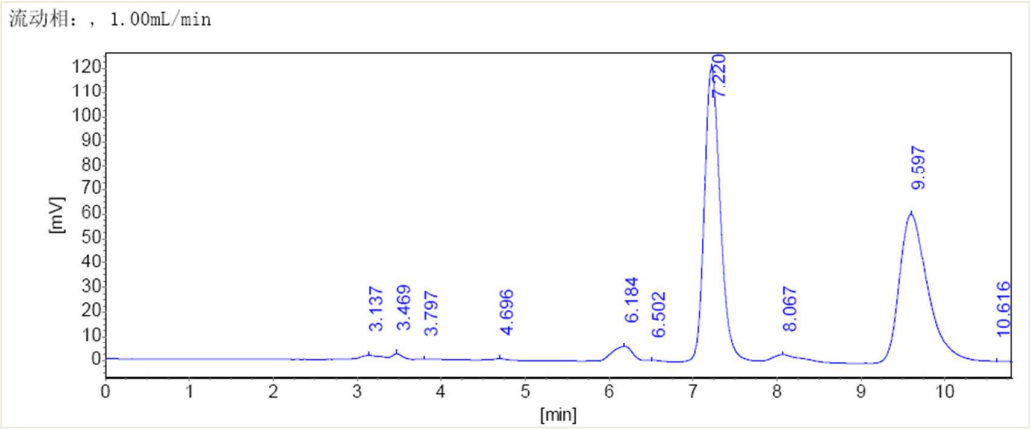
S75. ^{13}C NMR (100 MHz, DMSO-d_6) spectrum of 5-deprenyllupulonol C (**11**).



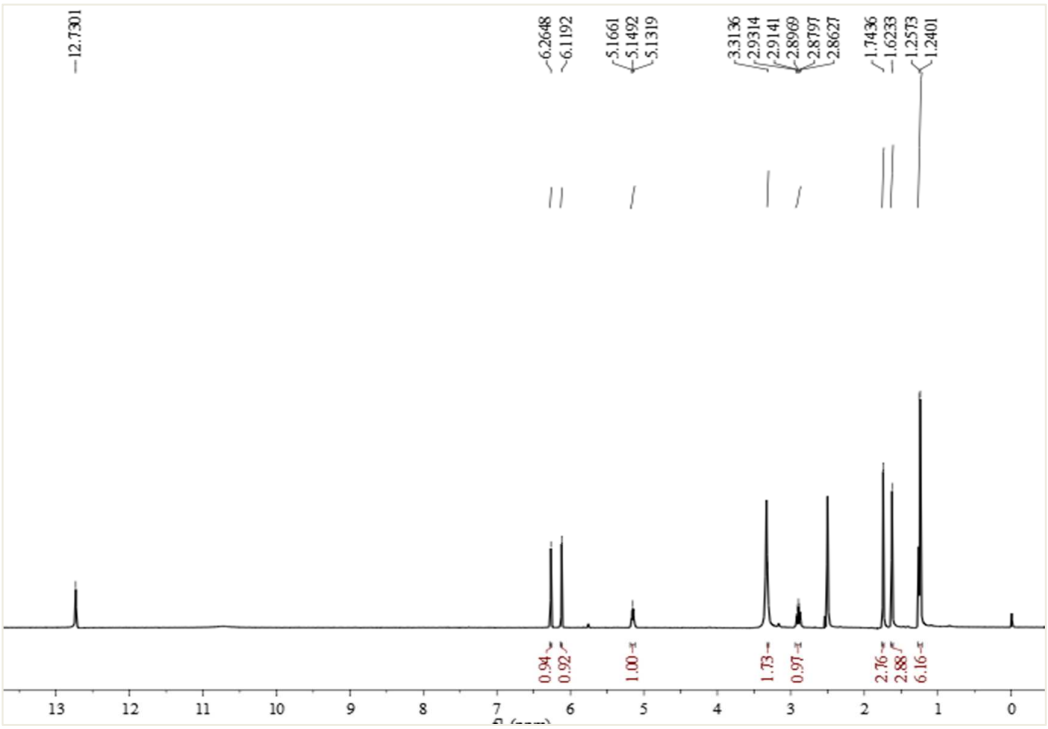
S76. Experimental CD spectrum of (*R*)-5-deprenyllupulonol C (**11a**) and (*S*)-5-deprenyllupulonol C (**11b**).



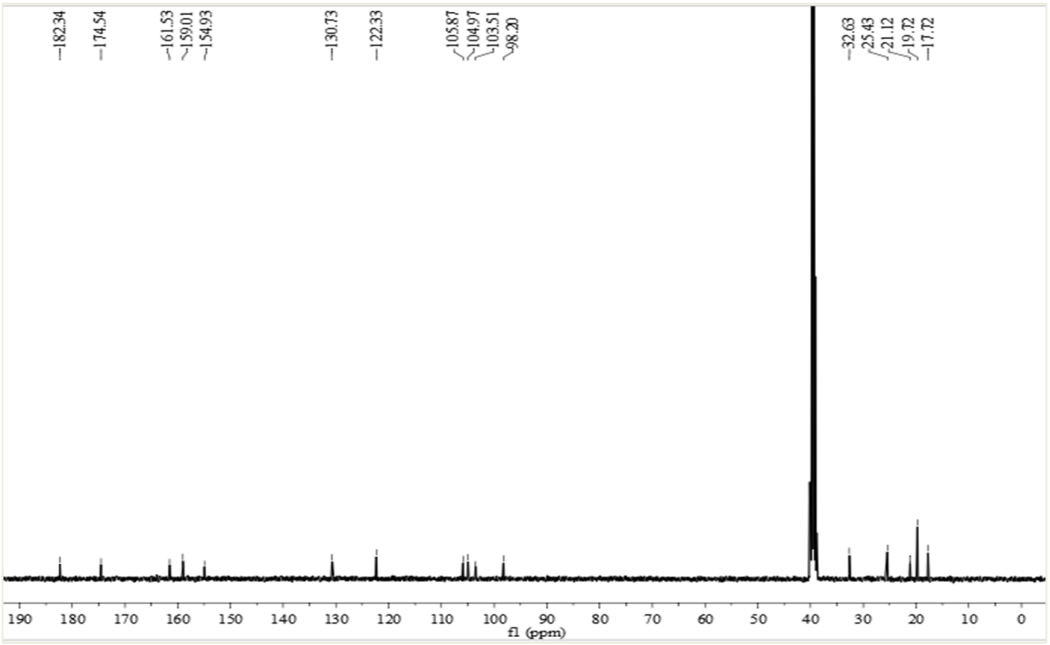
S77. The HPLC of chiral column analysis of 5-deprenyllupulonol C (**11**).



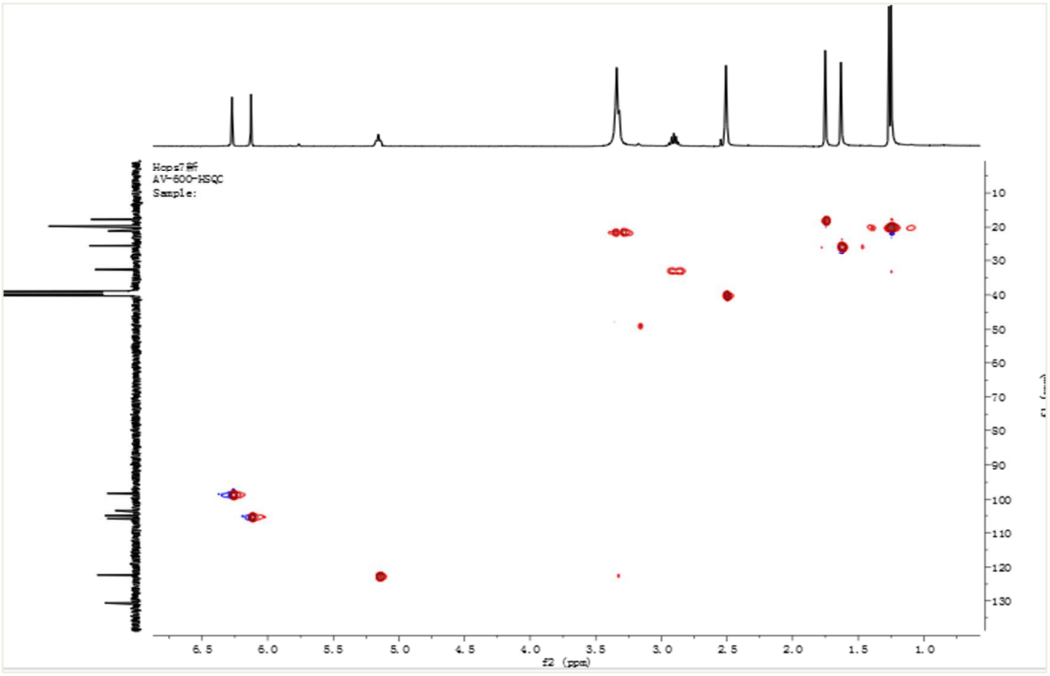
S78. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of 5,7-dihydroxy-2-isopropyl-8-prenylchromone (**12**).



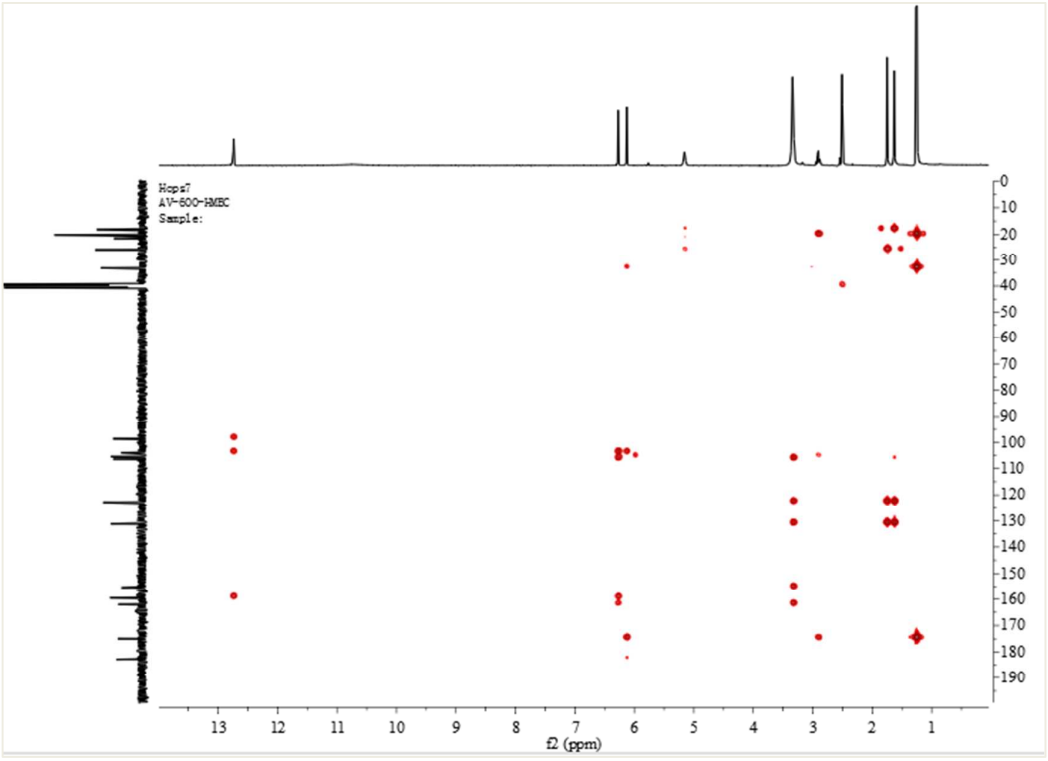
S79. ^{13}C NMR (100 MHz, DMSO-d_6) spectrum of 5,7-dihydroxy-2-isopropyl-8-prenylchromone (**12**).



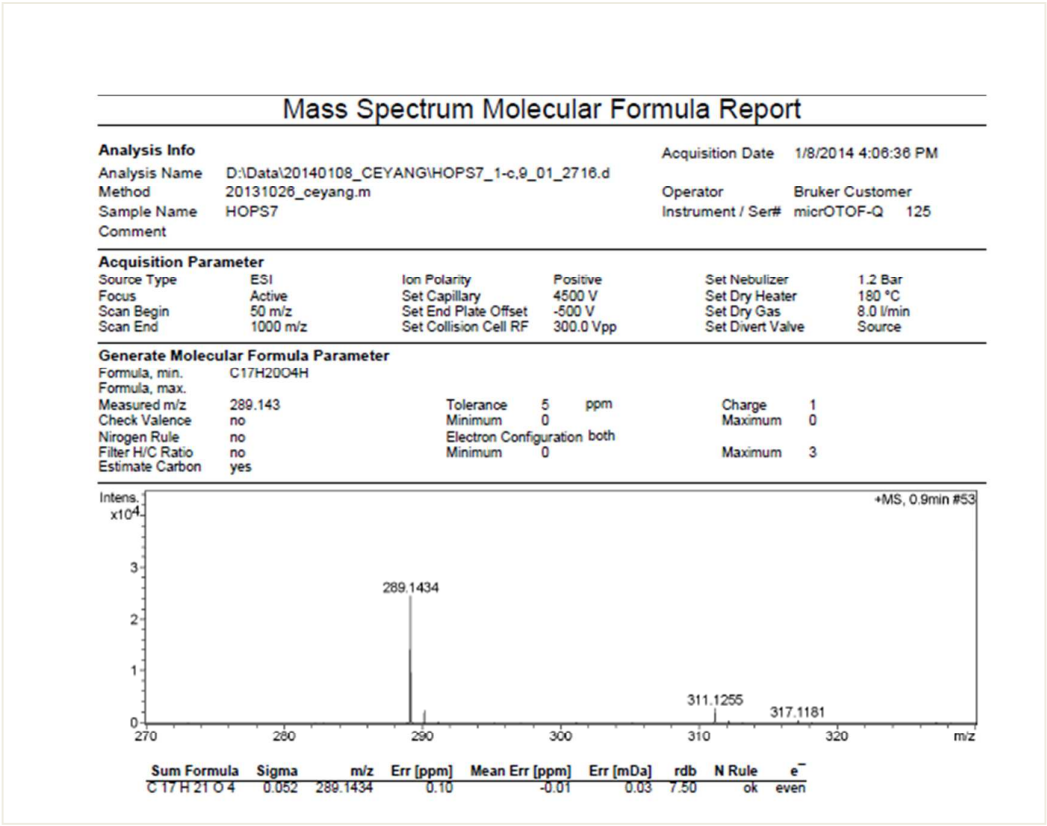
S80. HSQC (600 MHz, DMSO-d_6) spectrum of 5,7-dihydroxy-2-isopropyl-8-prenylchromone (**12**).



S81. HMBC (600 MHz, DMSO-d_6) spectrum of 5,7-dihydroxy-2-isopropyl-8-prenylchromone (**12**).



S82. HRESIMS spectrum of 5,7-dihydroxy-2-isopropyl-8-prenylchromone (**12**).



Mass Spectrum Molecular Formula Report

Analysis Info

Analysis Name	D:\Data\20140108_CEYANG\HOPS7_1-c,9_01_2716.d	Acquisition Date	1/8/2014 4:06:36 PM
Method	20131026_ceyang.m	Operator	Bruker Customer
Sample Name	HOPS7	Instrument / Ser#	micrOTOF-Q 125
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.2 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	1000 m/z	Set Collision Cell RF	300.0 Vpp	Set Divert Valve	Source

Generate Molecular Formula Parameter

Formula, min.	C17H20O4H				
Formula, max.					
Measured m/z	289.143	Tolerance	5 ppm	Charge	1
Check Valence	no	Minimum	0	Maximum	0
Nirogen Rule	no	Electron Configuration	both		
Filter H/C Ratio	no	Minimum	0	Maximum	3
Estimate Carbon	yes				

Sum Formula	Sigma	m/z	Err [ppm]	Mean Err [ppm]	Err [mDa]	rdb	N Rule	e⁻
C 17 H 21 O 4	0.052	289.1434	0.10	-0.01	0.03	7.50	ok	even

S83. The experimental method used for ECD calculations of compounds **1**, **4**, **5**, **7**, **8** and **9**

All structures were established by Schrodinger 2013 package. Conformational searches were performed using the bioactive search function of conformational search protocol of the Schrodinger 2013 package with 50 target conformers. The conformers generated from conformational search were optimized at the B3LYP/6-31G (d) level using Gaussian09 package. The optimized conformers were aligned using the flexible ligand alignment protocol to examine if there were identical conformers for some structurally similar conformers would lead to the totally identical conformer after structure optimization. After merging the identical conformers, the remaining conformers were subjected to frequent analysis at the B3LYP/6-31G (d) level and the population of each conformer was determined based on Boltzmann distribution. For compound **7** and **9**, eight conformers that contributes over 2 % of the population were used for ECD calculation. For compounds with high flexibility, the geometries from

the conformational searches studies would not represent the real geometries in the solution. Whereas NOE correlations were tested in liquid environments, giving more detailed information of a stereo-structure. Thus, for compounds **1**, **4** and **5**, the optimized geometries were subjected to intensive NOE analysis for the relative location of the isopentenyl at C-8 versus C-2'/C-1' of **1** and isopentenyl at C-7 versus the -$C(CH_3)_2OH$ group at C-2 of **4** and **5** could predominate the ECD curves as the isopentenyl at C-8 was a large group besides the chromophore composed of C-8a, 4a, 5, 6, 7 in compound **1** (C-3a, 7a, 4, 5, 6 in compound **4** and **5**). The geometries that did not match the experimental NOE correlations were excluded for ECD calculations and finally 6 conformers for **1** and **4** (4 conformers for compound **5**) were used for further ECD calculation. For compound **8**, the conformational flexibility of the molecule was depicted in the molecular energy profiles (Figure S57 Supporting Information) with respect to the dihedral angle C2'-C3'-C3-C2, ranging from -180° to 180° at the B3LYP/6-31G(d) level of theory. As can be seen from Figure S57, the most stable conformer is obtained for 170° having energy of -1072.13358515 Hartree. Keeping C2'-C3'-C3-C2 at 170°, the conformer of lowest energy (170°) was used to perform conformational search, structure optimization and identical conformer merging studies by the same way as compounds **1**, **4**, **5**, **7** and **9** did and finally 3 conformers were generated for ECD calculation. ECD computations for all conformers were carried out at the B3LYP/6-31G (d) level in the gas phase. The calculated ECD spectrums were visualized and Boltzmann averaged using specdis software[1-3].

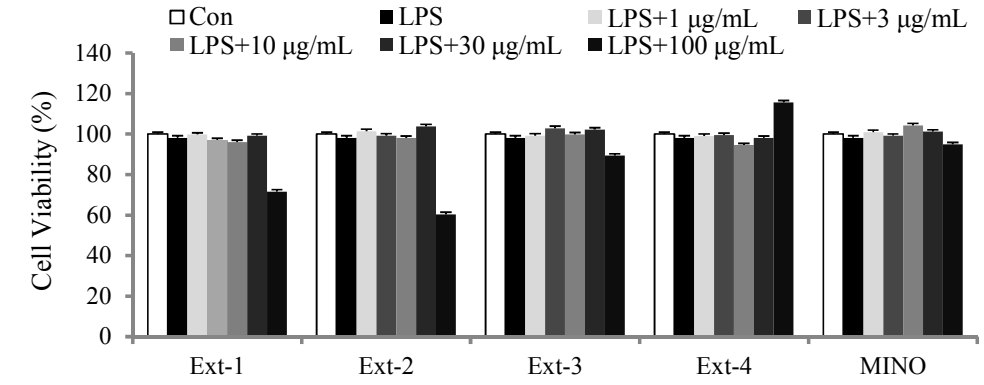
REFERENCES

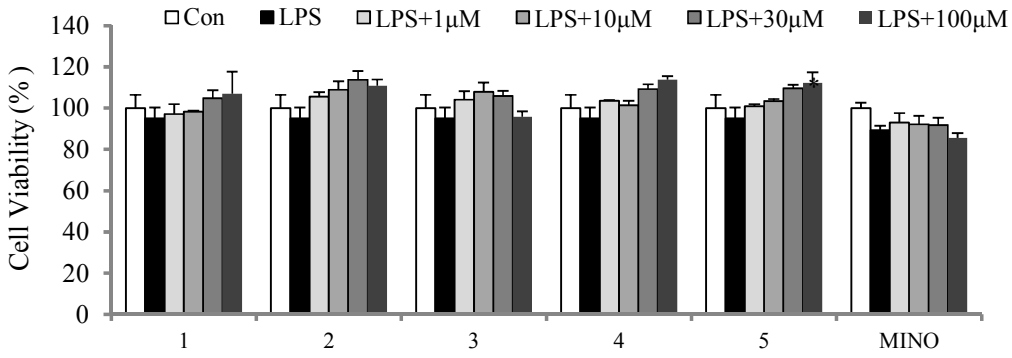
(1) Bruhn, T.; Schaumlöffel, A.; Hemberger, Y.; Pecitelli, G. Berlin. Germany, 2017.

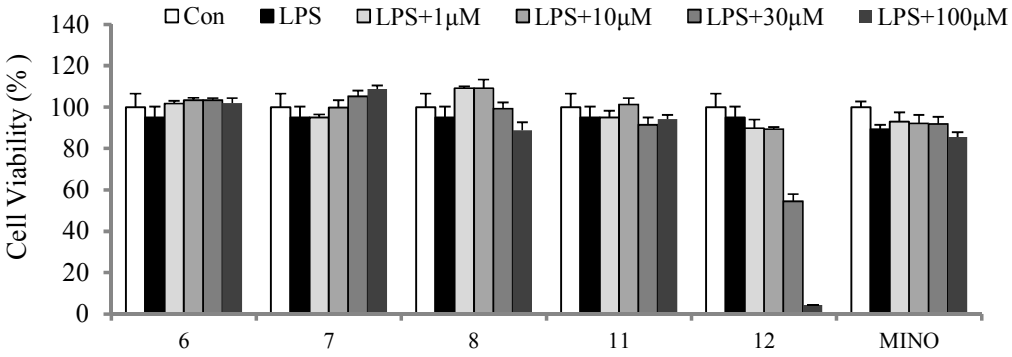
(2) Bruhn, T.; Schaumlöffel, A.; Hemberger, Y.; Bringmann, G. *Chirality*. **2013**, *25*, 243-249.

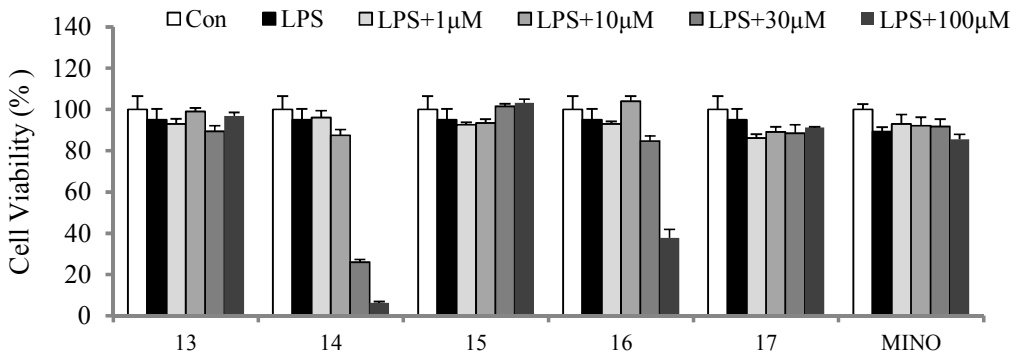
(3) Pescitelli, G.; Bruhn, T. *Chirality*. **2016**, *28*, 466-47.

S84. BV-2 cell viability assay and effect of the extracts and isolated compounds **1-8, 13-17** on LPS-induced NO production in BV-2 microglial cells.








Con
LPS
LPS+1μM
LPS+10μM
LPS+30μM
LPS+100μM
Cell Viability (%)
140
120
100
80
60
40
20
0
13
14
15
16
17
MINO