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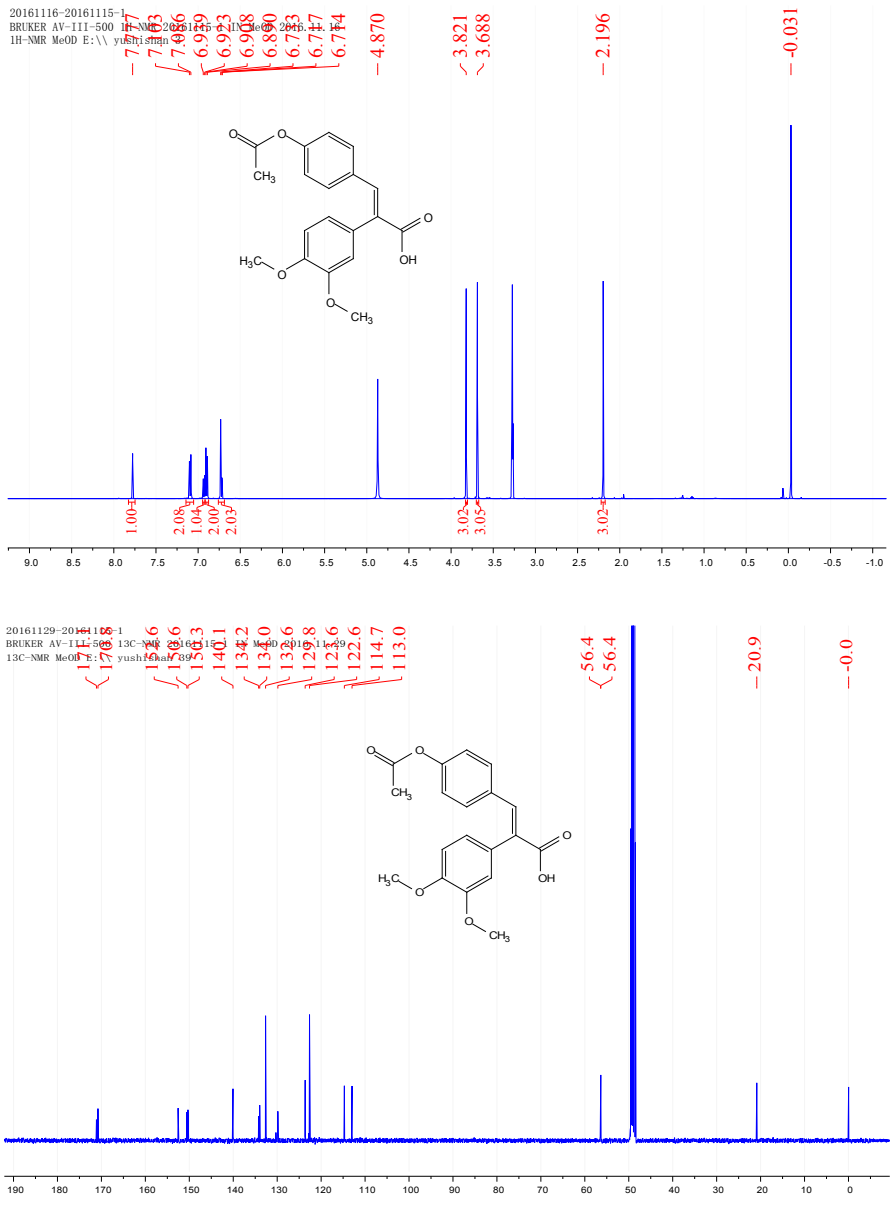
A novel and practical synthesis of CAT3: a phenanthroindolizidine alkaloid with potential in treating glioblastoma

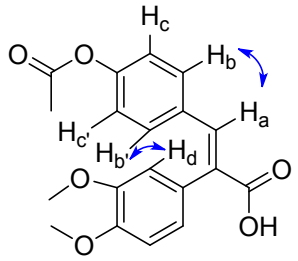
Ru-Bing Wang, Hai-Ning Lv, Shan-Shan Zhu,Xiao-Dong Ren, Song Xu,Shuang-Gang Ma, Yun-Bao Liu, and Shi-Shan Yu*

State Key Laboratory of Bioactive Substance and Function of Natural Medicines, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, China

Correspondence: E-mail: yushishan@imm.ac.cn



^{1}H NMR (500 MHz, CD_3OD) δ 7.78 (s, 1H), 7.08 (d, J = 8.7 Hz, 2H), 6.93 (d, J = 8.2 Hz, 1H), 6.90 (d, J = 8.7 Hz, 2H), 6.73 (s, 1H), 6.72 (dd, J = 8.2, 2.0 Hz, 1H), 3.82 (s, 3H), 3.69 (s, 3H), 2.20 (s, 3H)..^{13}C NMR (125 MHz, CD_3OD) δ 171.1, 170.8, 152.6, 150.6, 150.3, 140.1, 134.2, 133.9, 132.6, 129.9, 123.6, 122.6, 114.7, 112.97, 56.4, 49.5, 49.3, 49.2, 49.0, 48.8, 48.7, 48.5, 20.9.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Hc'
Hb'
Hd
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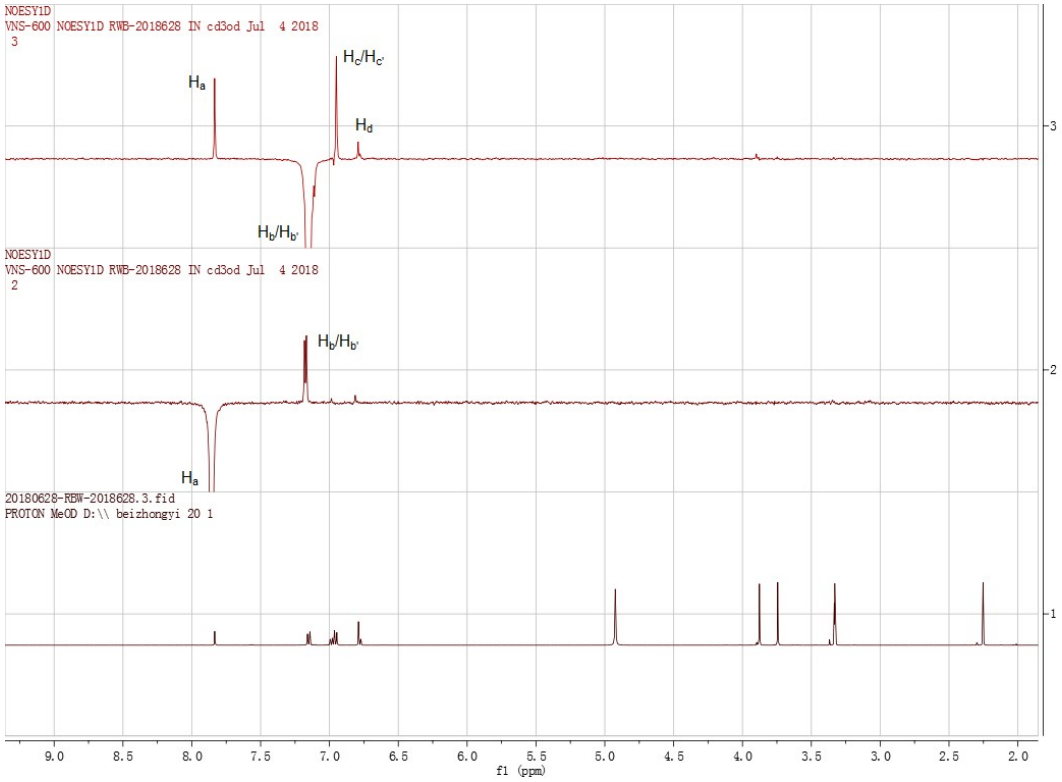
O
OH
O


NOESY1D
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3
Ha
Hc/Hc'
Hd
Hb/Hb'
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2
Hb/Hb'
Ha
20180628-RBW-2018628.3.fid
PROTON MeOD D:\\ beizhongyi 20 1
3
2
1
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8.5
8.0
7.5
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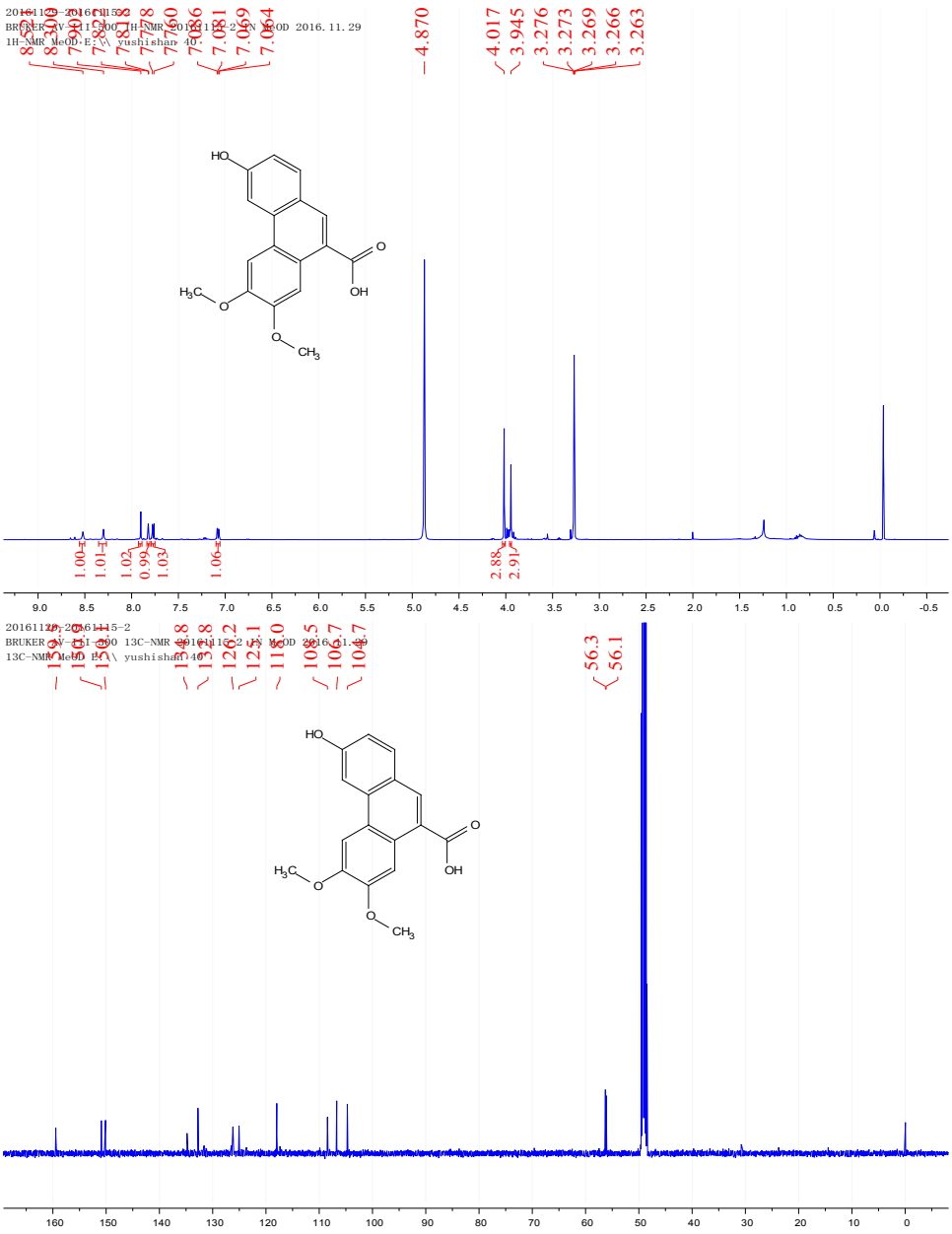
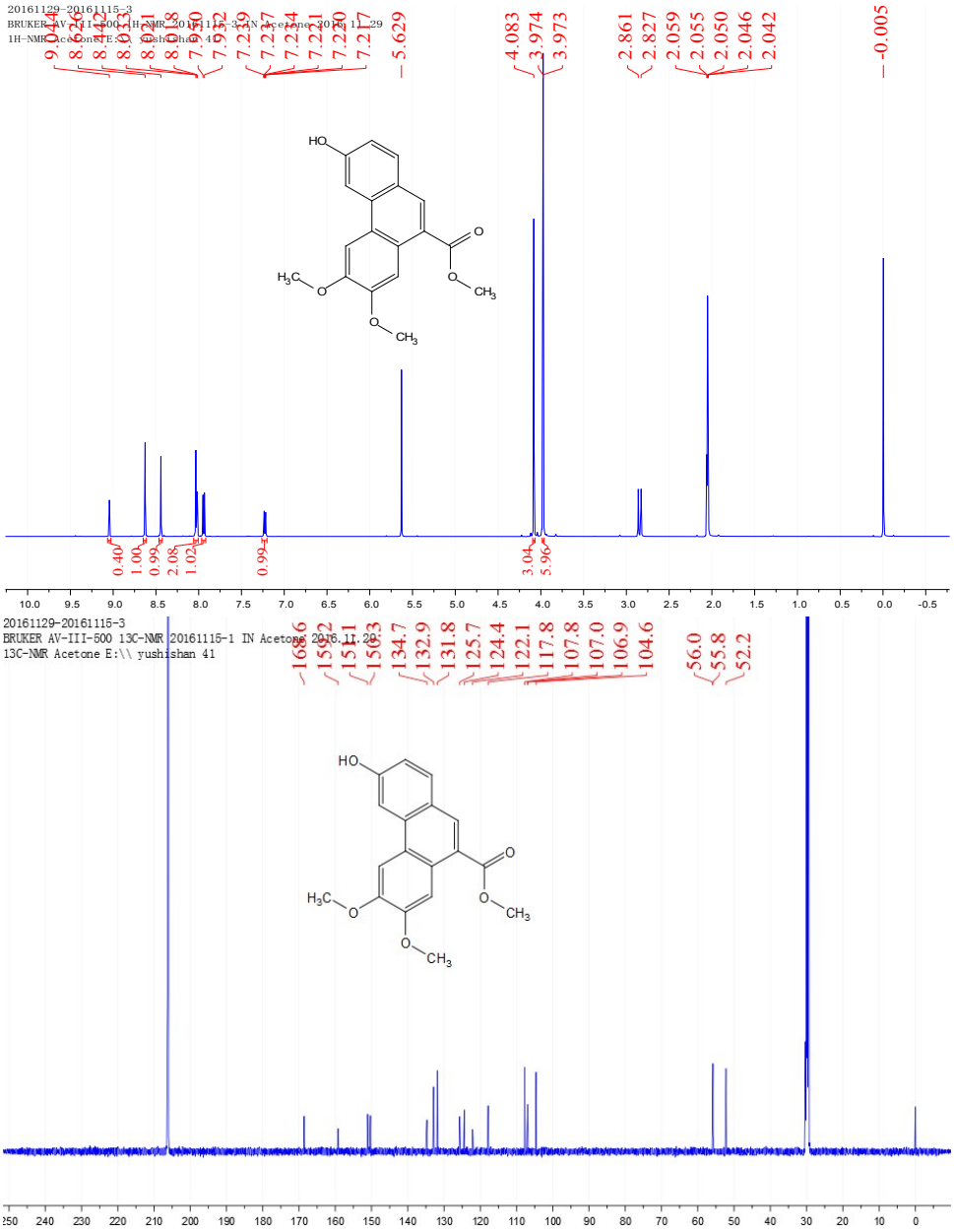
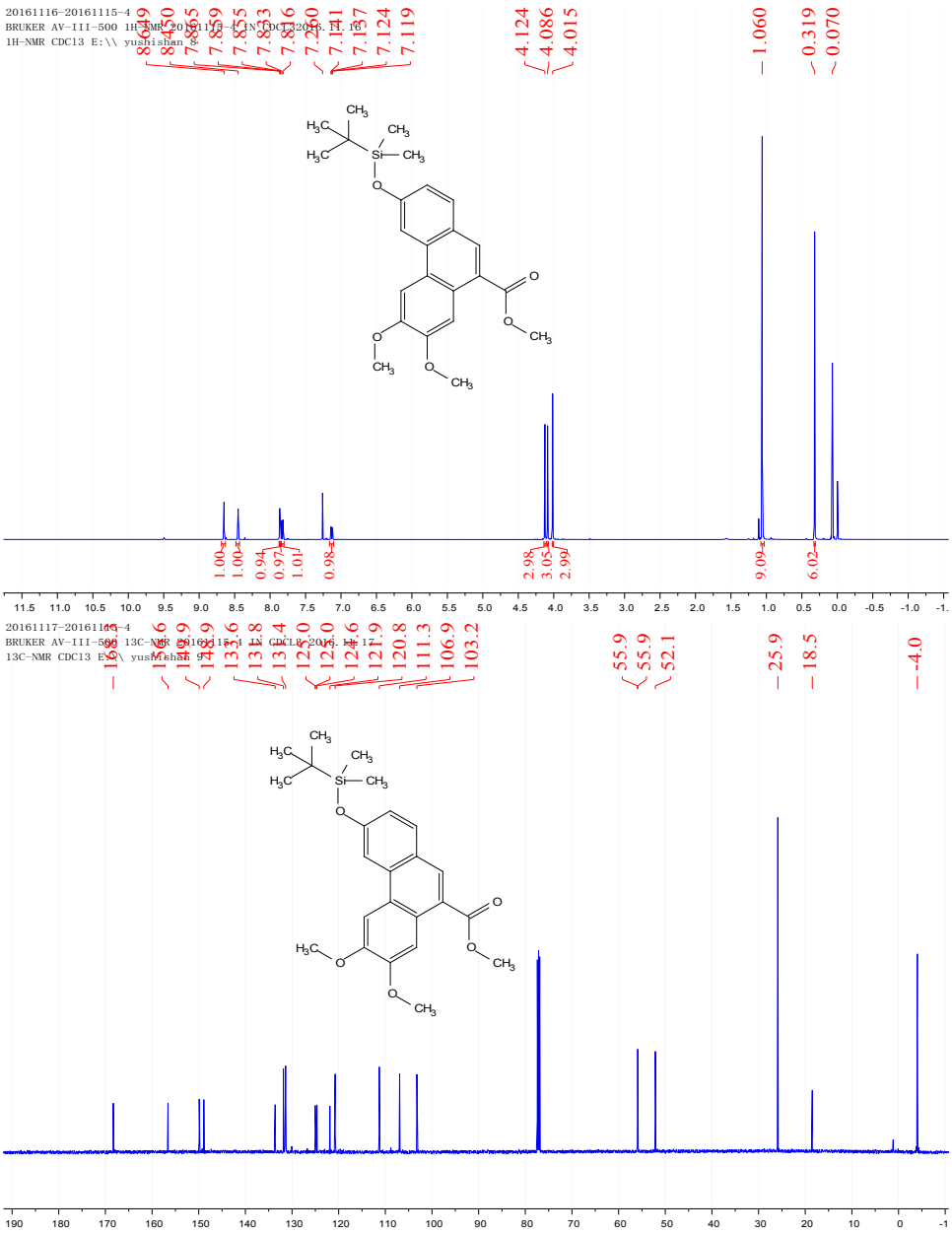


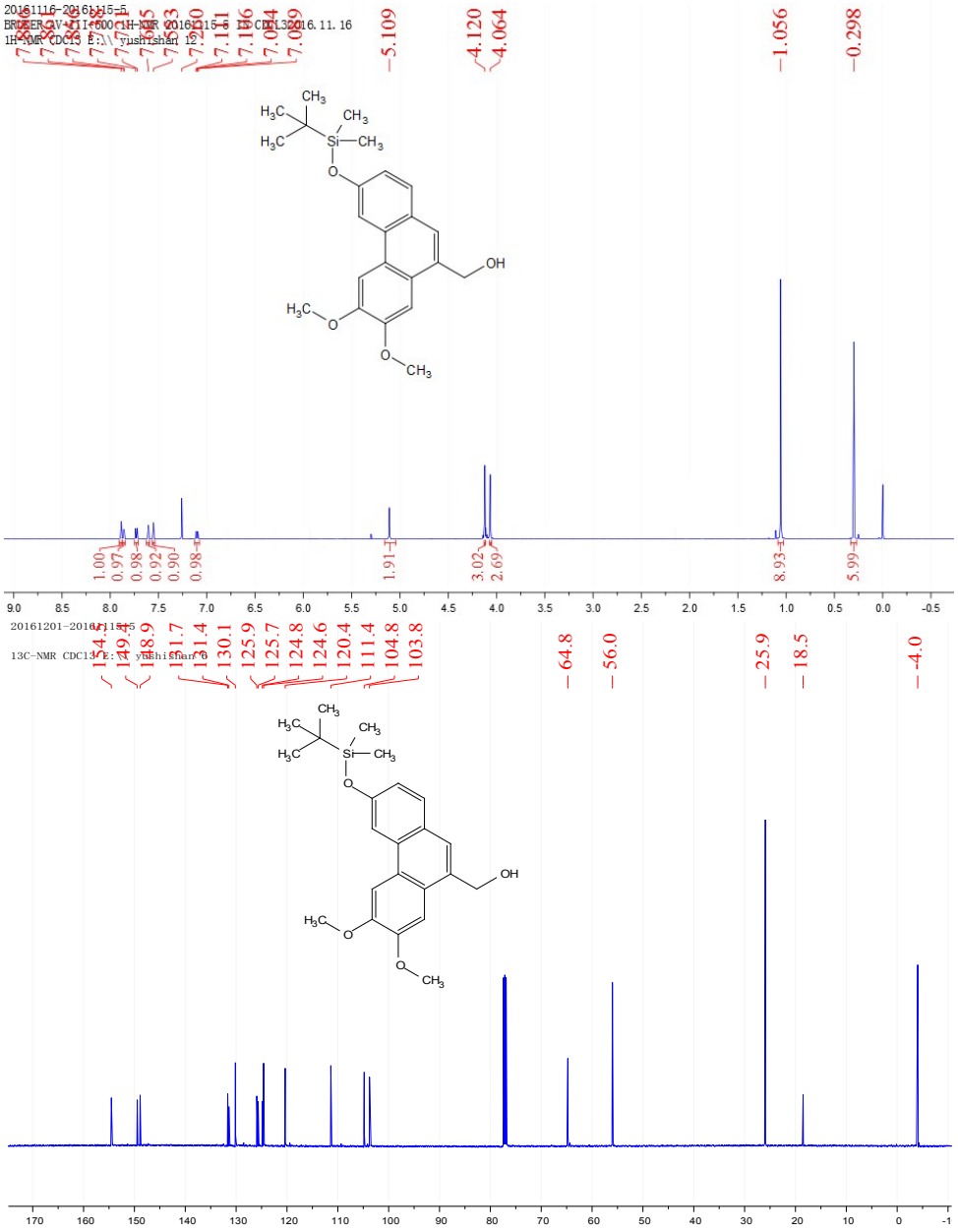
^{1}H NMR (500 MHz, CD_3OD) δ 8.52 (s, 1H), 8.30 (s, 1H), 7.90 (s, 1H), 7.82 (d, J = 2.2 Hz, 1H), 7.77 (d, J = 8.6 Hz, 1H), 7.07 (dd, J = 8.6, 2.2 Hz, 1H), 4.02 (s, 3H), 3.95 (s, 3H).^{13}C NMR (125 MHz, CD_3OD) δ 159.5, 150.9, 150.1, 134.8, 132.8, 126.2, 125.1, 118.0, 108.5, 106.7, 104.7, 56.3, 56.1.



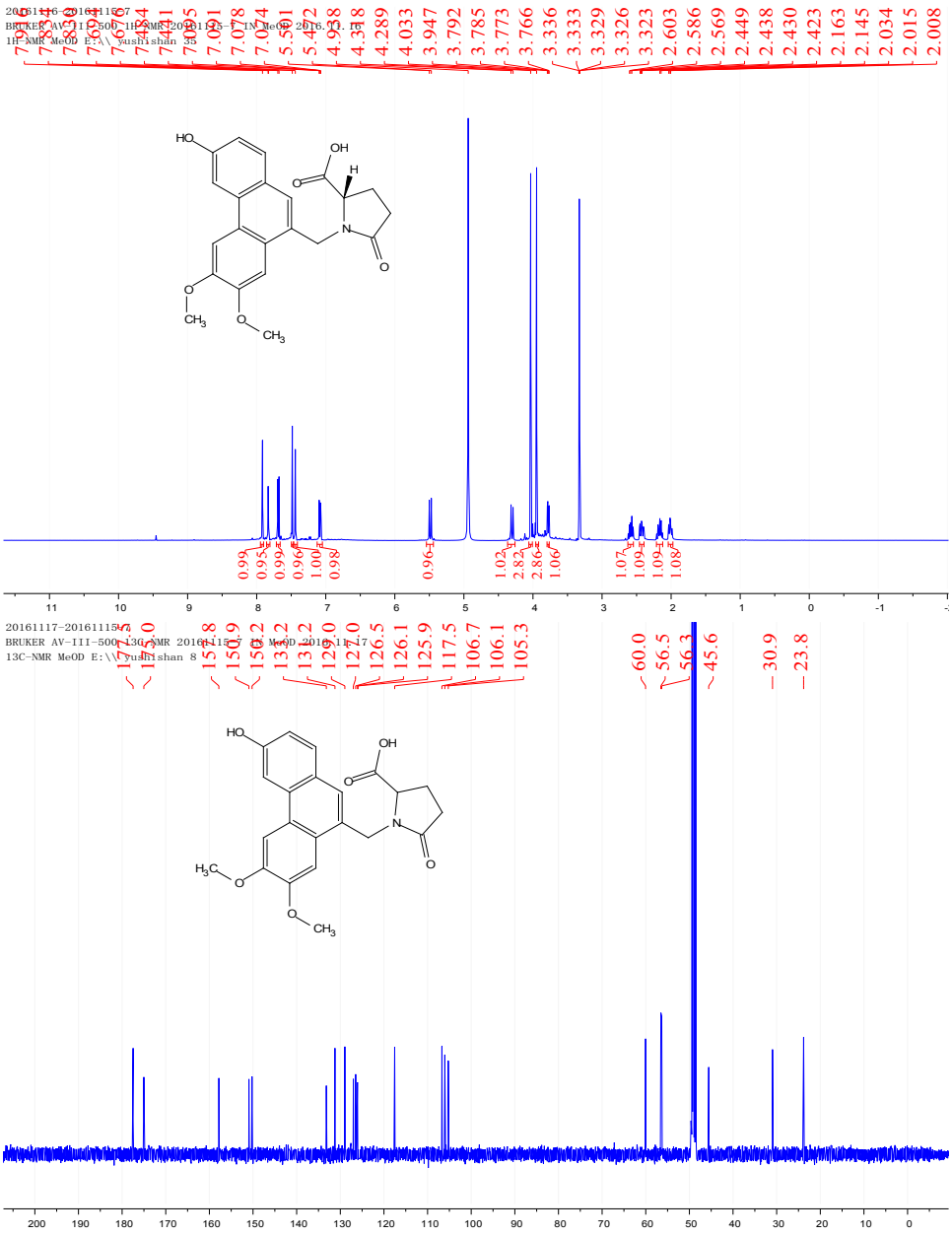
^{1}H NMR (500 MHz, CD_3COCD_3) δ 9.04 (s, 1H), 8.63 (s, 3H), 8.44 (s, 2H), 8.03 (s, 2H), 8.02 (d, J = 1.8 Hz, 2H), 7.94 (d, J = 8.6 Hz, 3H), 7.29 – 7.19 (m, 2H), 4.08 (s, 3H), 3.96 (s, 3H), 3.97 (s, 3H).^{13}C NMR (125 MHz, CD_3COCD_3) δ 168.6, 159.2, 151.1, 150.3, 134.7, 132.9, 131.8, 125.7, 124.4, 122.1, 117.8, 107.8, 107.0, 106.9, 104.6, 56.0, 55.8, 52.2.



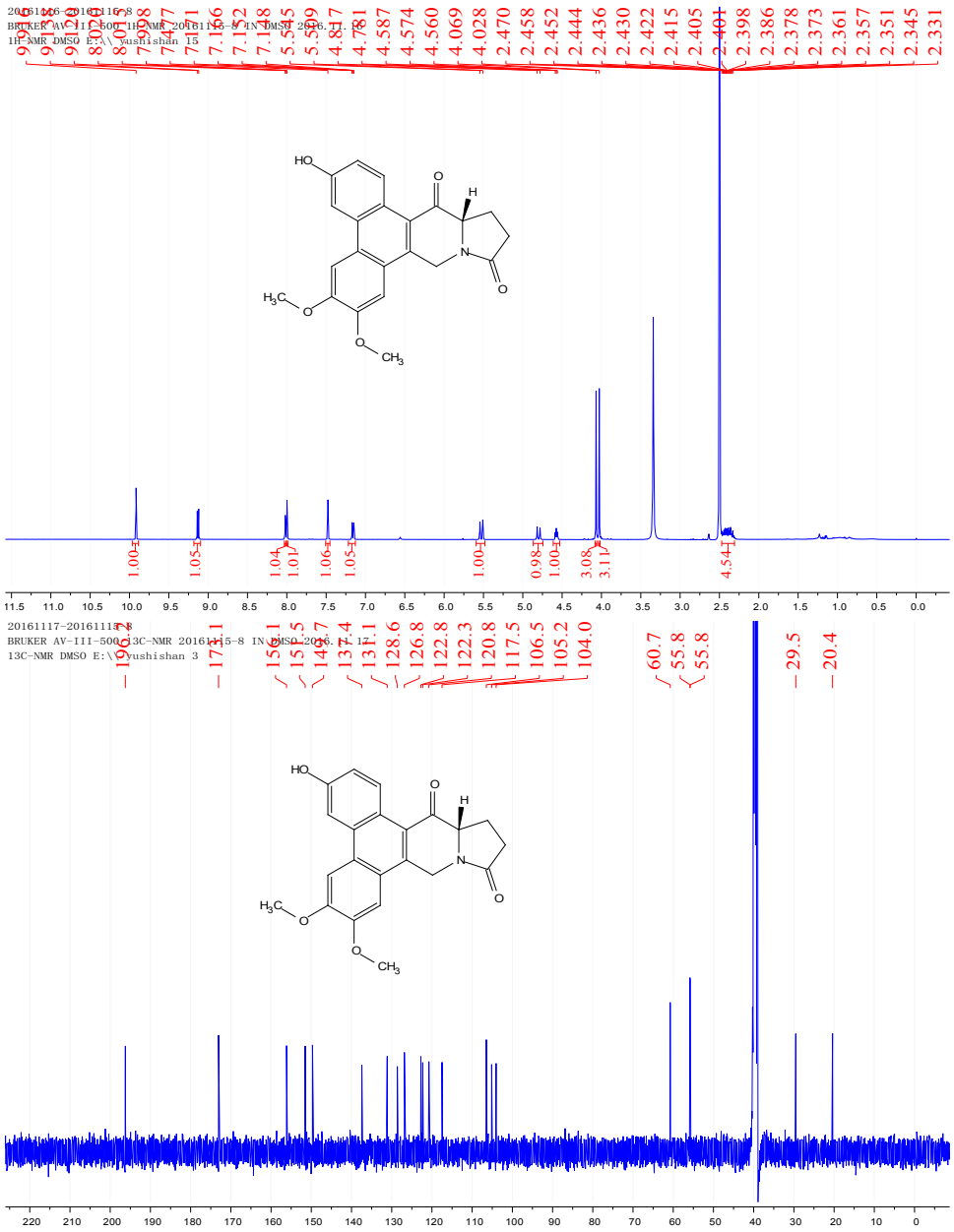
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.65 (s, 1H), 8.45 (s, 1H), 7.86 (s, 1H), 7.86 (d, J = 2.2 Hz, 1H), 7.82 (d, J = 8.6 Hz, 1H), 7.13 (dd, J = 8.6, 2.2 Hz, 1H), 4.12 (s, 3H), 4.09 (s, 3H), 4.02 (s, 3H), 1.06 (s, 9H), 0.32 (s, 6H).^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 156.6, 149.9, 148.9, 133.6, 131.9, 131.4, 125.0, 124.98, 124.7, 121.9, 120.8, 111.3, 106.9, 103.2, 55.95, 55.90, 52.1, 25.9, 18.5, -4.0.



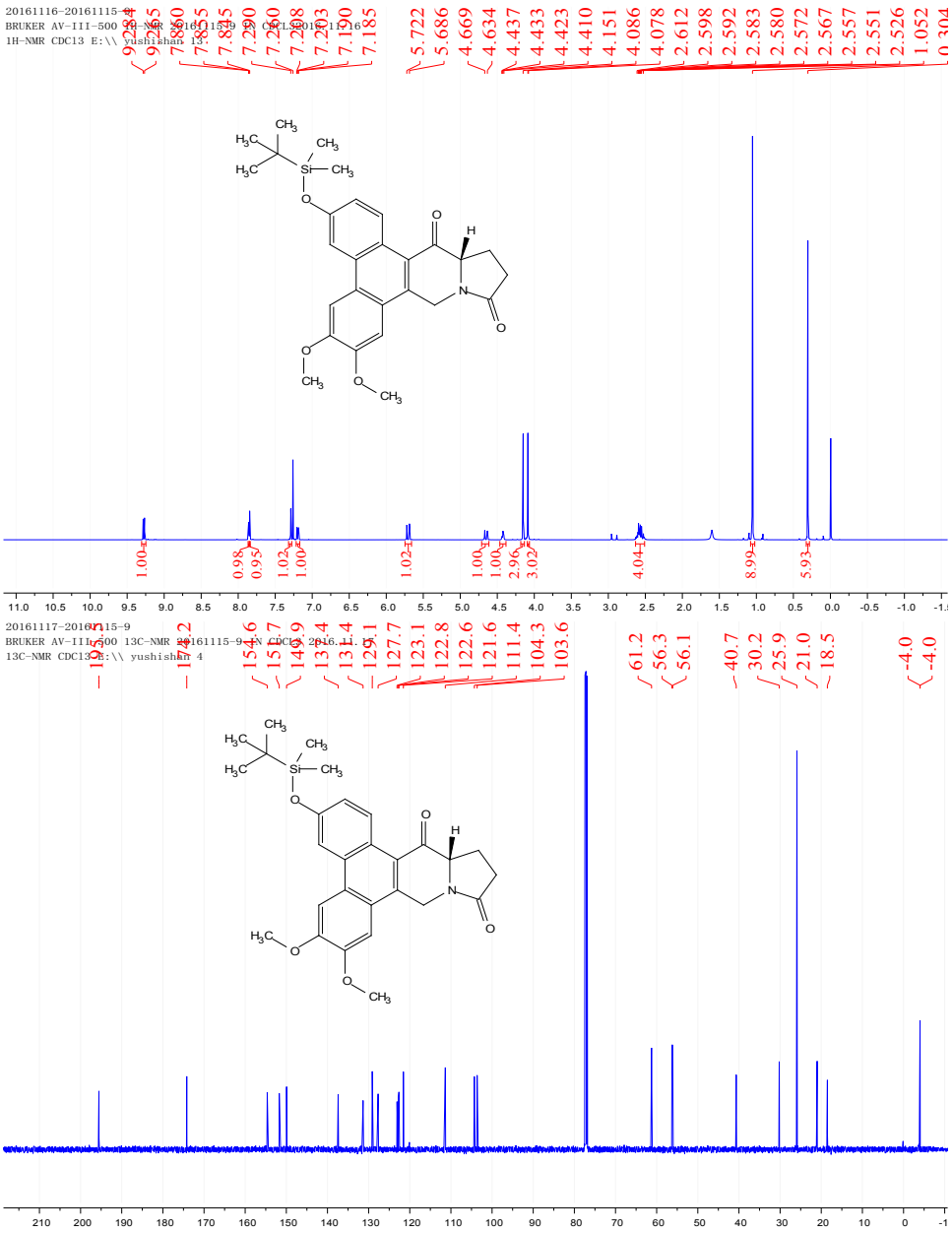
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.86 (d, J = 2.2 Hz, 1H), 7.73 (d, J = 8.6 Hz, 1H), 7.60 (s, 1H), 7.55 (s, 1H), 7.10 (dd, J = 8.6, 2.2 Hz, 1H), 5.11 (s, 2H), 4.12 (s, 3H), 4.06 (s, 3H), 1.06 (s, 9H), 0.30 (s, 6H).^{13}C NMR (125 MHz, $CDCl_3$) δ 154.5, 149.4, 148.9, 131.7, 131.4, 130.1, 125.9, 125.7, 124.9, 124.6, 120.4, 111.4, 104.8, 103.8, 64.7, 56.0, 25.9, 18.5, -4.1.



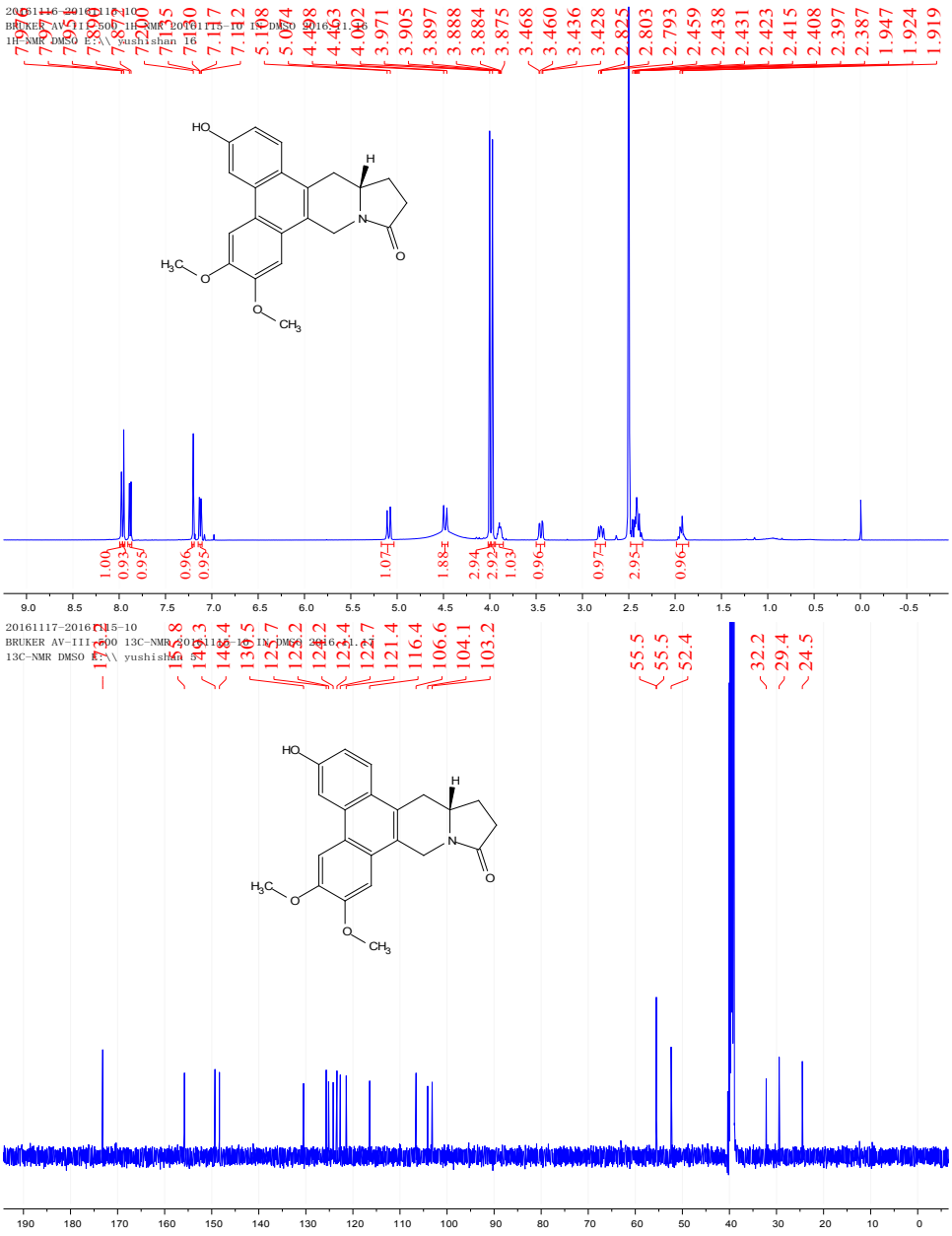
^{1}H NMR (500 MHz, CD_3OD) δ 7.92 (s, 1H), 7.83 (d, J = 2.1 Hz, 1H), 7.69 (d, J = 8.6 Hz, 1H), 7.48 (s, 1H), 7.44 (s, 1H), 7.08 (dd, J = 8.6, 2.1 Hz, 1H), 5.49 (d, J = 14.6 Hz, 1H), 4.30 (d, J = 14.6 Hz, 1H), 4.03 (s, 3H), 3.95 (s, 3H), 3.78 (dd, J = 9.4, 3.3 Hz, 1H), 2.62 – 2.55(m, 1H), 2.46 – 2.40 (m, 1H), 2.19 – 2.13(m, 1H), 2.04 – 1.98(m, 1H).^{13}C NMR (125 MHz, CD_3OD) δ 177.5, 175.0, 157.8, 150.9, 150.2, 133.2, 131.2, 129.0, 127.0, 126.5, 126.1, 125.9, 117.5, 106.7, 106.1, 105.3, 60.0, 56.5, 56.3, 45.6, 30.9, 23.8.



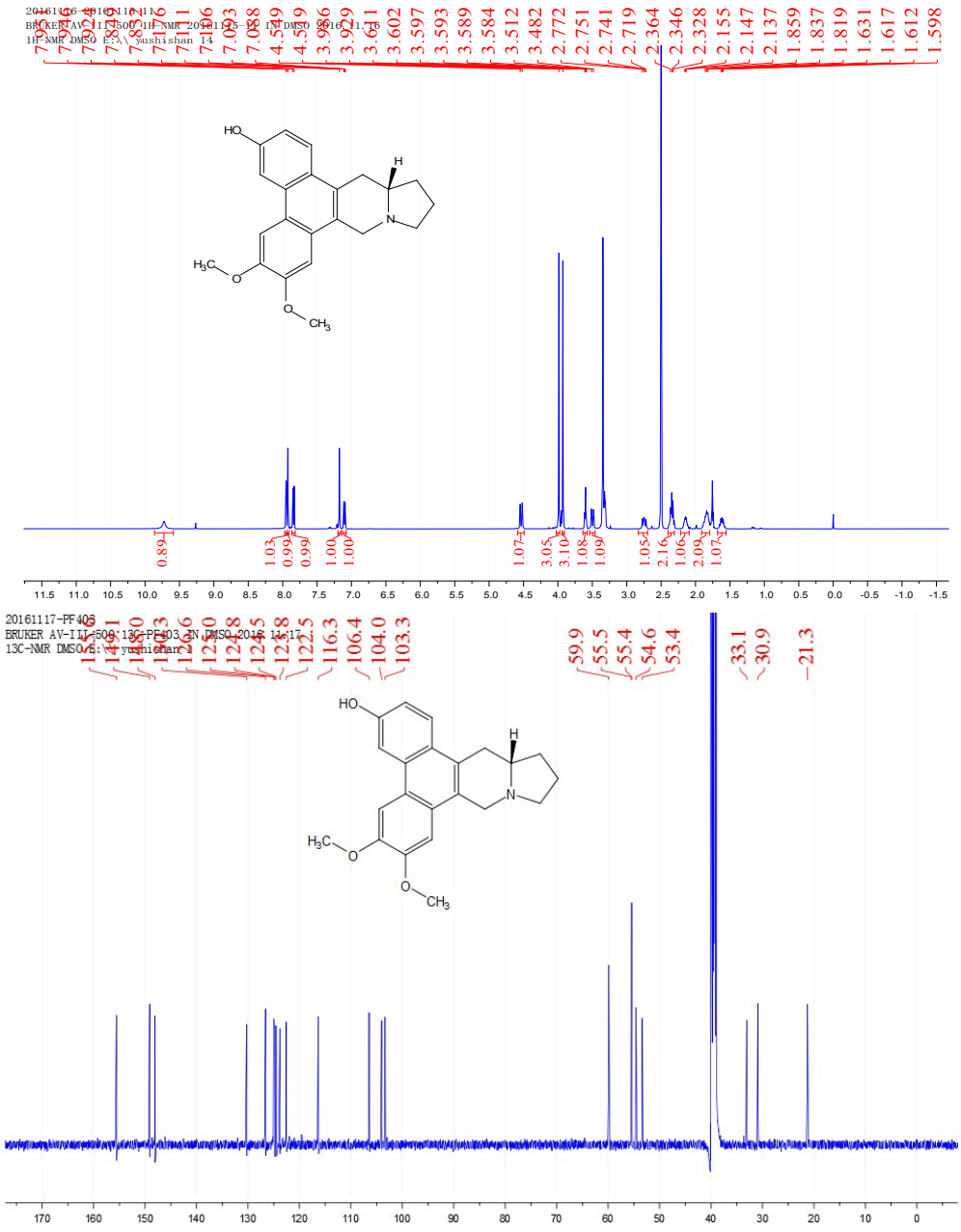
^{1}H NMR (500 MHz, DMSO-d_6) δ 9.92 (s, 1H), 9.13 (d, J = 9.2 Hz, 1H), 8.02 (d, J = 2.5 Hz, 1H), 8.00 (s, 1H), 7.48 (s, 1H), 7.16 (dd, J = 9.2, 2.5 Hz, 1H), 5.53 (d, J = 18.1 Hz, 1H), 4.80 (d, J = 18.1 Hz, 1H), 4.57 (t, J = 6.7 Hz, 1H), 4.07 (s, 3H), 4.03 (s, 3H), 2.48 – 2.29 (m, 4H).^{13}C NMR (125 MHz, DMSO-d_6) δ 196.2, 173.1, 156.2, 151.5, 149.7, 137.4, 131.1, 128.6, 126.9, 122.8, 122.3, 120.8, 117.5, 106.5, 105.2, 104.0, 60.8, 55.84, 55.79, 29.5, 20.4.



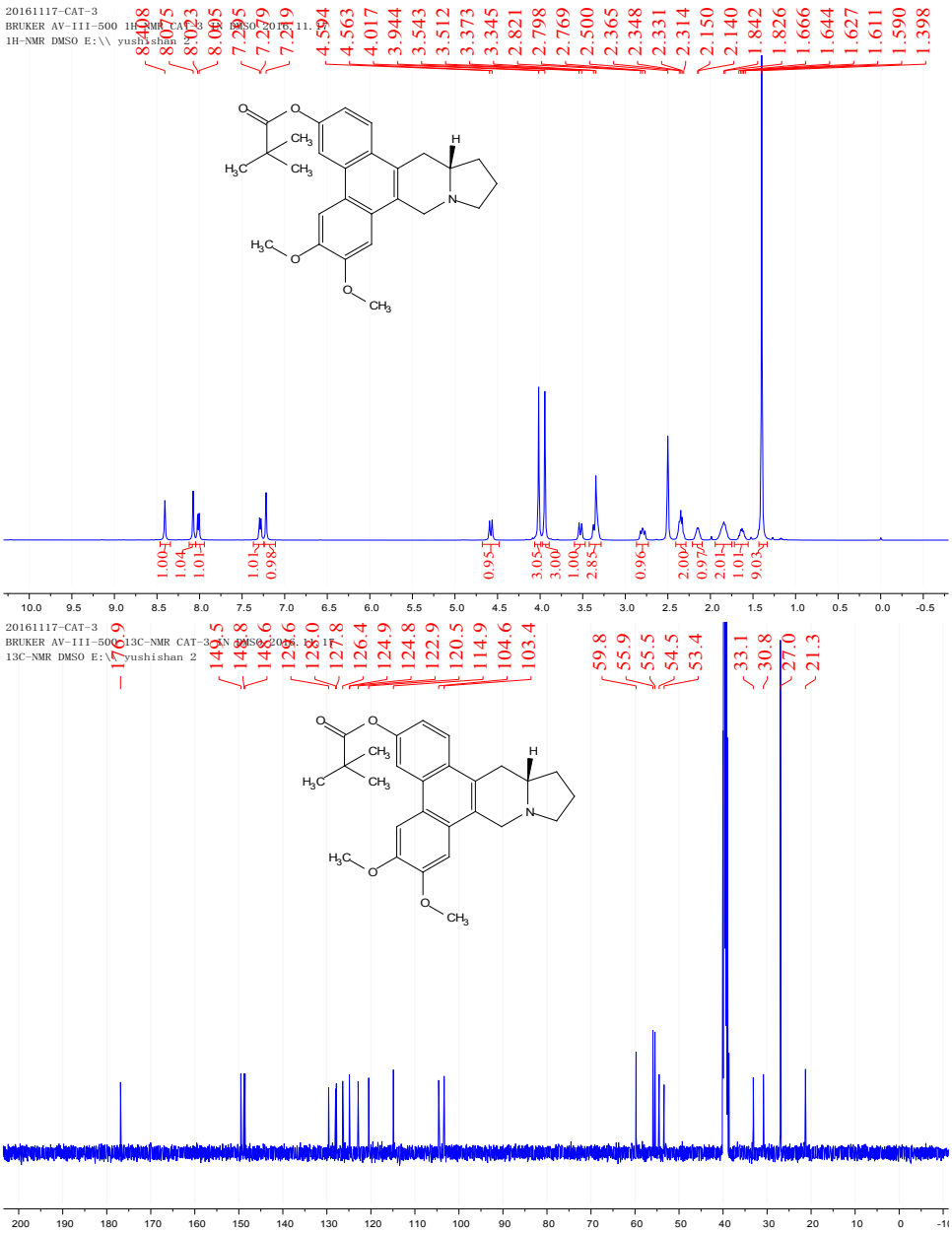
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.27 (d, J = 9.2 Hz, 1H), 7.86 (d, J = 2.5 Hz, 1H), 7.85 (s, 1H),7.29 (s, 1H), 7.20 (dd, J = 9.2, 2.5 Hz, 1H), 5.70 (d, J = 17.8 Hz, 1H), 4.65 (d, J = 17.8 Hz, 1H), 4.44 – 4.41 (m, 1H), 4.15 (s, 3H), 4.09 (s, 3H), 2.63 – 2.51 (m, 4H), 1.05 (s, 9H), 0.30 (s, 6H).^{13}C NMR (125 MHz, $CDCl_3$) δ 195.5, 174.2, 154.6, 151.7, 149.9, 137.4, 131.4, 129.1, 127.7, 123.1, 122.8, 122.6, 121.6, 111.4, 104.3, 103.6, 61.2, 56.3, 56.1, 40.7, 30.2, 25.9, 21.0, 18.5, -4.01, -4.02.



^{1}H NMR (500 MHz, DMSO-d_6) δ 7.97 (d, J = 2.4 Hz, 1H), 7.95 (s, 1H), 7.88 (d, J = 9.0 Hz, 1H), 7.20 (s, 1H), 7.12 (dd, J = 9.0, 2.4 Hz, 1H), 5.09 (d, J = 17.2 Hz, 1H), 4.48 (d, J = 17.2 Hz, 1H), 4.00 (s, 3H), 3.97 (s, 3H), 3.94 – 3.85 (m, 1H), 3.45 (dd, J = 16.2, 4.1 Hz, 1H), 2.80 (dd, J = 16.2, 10.9 Hz, 1H), 2.48 – 2.35 (m, 3H), 1.99 – 1.85 (m, 1H).^{13}C NMR (125 MHz, DMSO-d_6) δ 173.2, 155.8, 149.3, 148.4, 130.5, 125.7, 125.2, 124.2, 123.4, 122.7, 121.4, 116.4, 106.6, 104.1, 103.2, 55.53, 55.51, 52.4, 32.2, 29.4, 24.5.



^{1}H NMR (500 MHz, DMSO-d_6) δ 9.72 (s, 1H), 7.95 (d, J = 2.2 Hz, 1H), 7.92 (s, 1H), 7.84 (d, J = 8.9 Hz, 1H), 7.18 (s, 1H), 7.10 (dd, J = 8.9, 2.2 Hz, 1H), 4.53 (d, J = 15.0 Hz, 1H), 3.99 (s, 3H), 3.93 (s, 3H), 3.64 – 3.57 (m, 1H), 3.50 (d, J = 15.0 Hz, 1H), 2.75 (dd, J = 15.6, 10.6 Hz, 1H), 2.36 – 2.31(m, 2H), 2.22 – 2.09 (m, 1H), 1.91 – 1.79 (m, 2H), 1.78 – 1.73 (m, 1H), 1.68 – 1.56 (m, 1H).^{13}C NMR (125 MHz, DMSO-d_6) δ 155.6, 149.1, 148.0, 130.3, 126.6, 125.0, 124.8, 124.5, 123.8, 122.6, 116.3, 106.4, 104.0, 103.4, 59.9, 55.5, 55.4, 54.6, 53.4, 33.1, 30.9, 21.3.



^{1}H NMR (500 MHz, DMSO-d_6) δ 8.41 (s, 1H), 8.07 (s, 1H), 8.01 (d, J = 8.9 Hz, 1H), 7.29 (d, J = 8.0 Hz, 1H), 7.22 (s, 1H), 4.58 (d, J = 15.3 Hz, 1H), 4.02 (s, 3H), 3.94 (s, 3H), 3.53 (d, J = 15.3 Hz, 1H), 3.38 – 3.32 (m, 2H), 2.87 – 2.73 (m, 1H), 2.37 – 2.31 (m, 2H), 2.16 – 2.13 (m, 1H), 1.85 – 1.81 (m, 2H), 1.68 – 1.59 (m, 1H), 1.40 (s, 9H).^{13}C NMR (125 MHz, DMSO-d_6) δ 176.9, 149.5, 148.8, 148.6, 129.6, 128.0, 127.8, 126.4, 124.9, 124.8, 122.9, 120.5, 114.9, 104.6, 103.4, 59.8, 55.9, 55.5, 54.5, 53.4, 38.7, 33.1, 30.8, 27.0, 21.3.