

Semi-synthesis, Cytotoxic Evaluation, and Structure-Activity Relationships of Brefeldin A Derivatives with Antileukemia Activity

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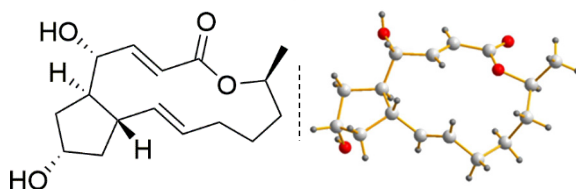
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Figure S46. ^1H NMR (500 MHz, CDCl_3) spectrum of compound **16**.

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Brefeldin A (1)



Known compound, white, amorphous powder; ^1H NMR (500 MHz, $\text{DMSO}-d_6$) δ 7.34 (1H, dd, J = 15.5, 3.0 Hz, H-3), 5.75–5.60 (2H, overlapped, H-2, H-11), 5.20 (1H, dd, J = 15.2, 9.6 Hz, H-10), 5.10 (1H, s, 4-OH), 4.71 (1H, m, H-15), 4.48 (1H, s, 7-OH), 4.04 (1H, m, H-7), 3.92 (1H, d, J = 9.2 Hz, H-4), 2.30 (1H, m, H-9), 2.02–1.87 (2H, overlapped, H-8, H-12), 1.87–1.60 (6H, overlapped, H-5, H-6a, H-6b, H-12, H-13, H-14), 1.47 (1H, m, H-14), 1.30 (1H, m, H-8), 1.18 (3H, d, J = 6.3 Hz, 16- CH_3), 0.75 (1H, m, H-13); ^{13}C NMR (125 MHz, $\text{DMSO}-d_6$) δ 165.7 (C-1), 154.4 (C-3), 137.1 (C-10), 129.2 (C-11), 116.3 (C-2), 74.3 (C-4), 70.9 (C-15), 70.5 (C-7), 51.7 (C-5), 43.3 (C-9), 43.1 (C-8), 40.9 (C-6), 33.4 (C-14), 31.5 (C-12), 26.5 (C-13), 20.7 (C-16); ESIMS m/z 281.17 $[\text{M} + \text{H}]^+$, 263.19 $[\text{M} + \text{H} - \text{H}_2\text{O}]^+$, 245.19 $[\text{M} + \text{H} - 2\text{H}_2\text{O}]^+$.

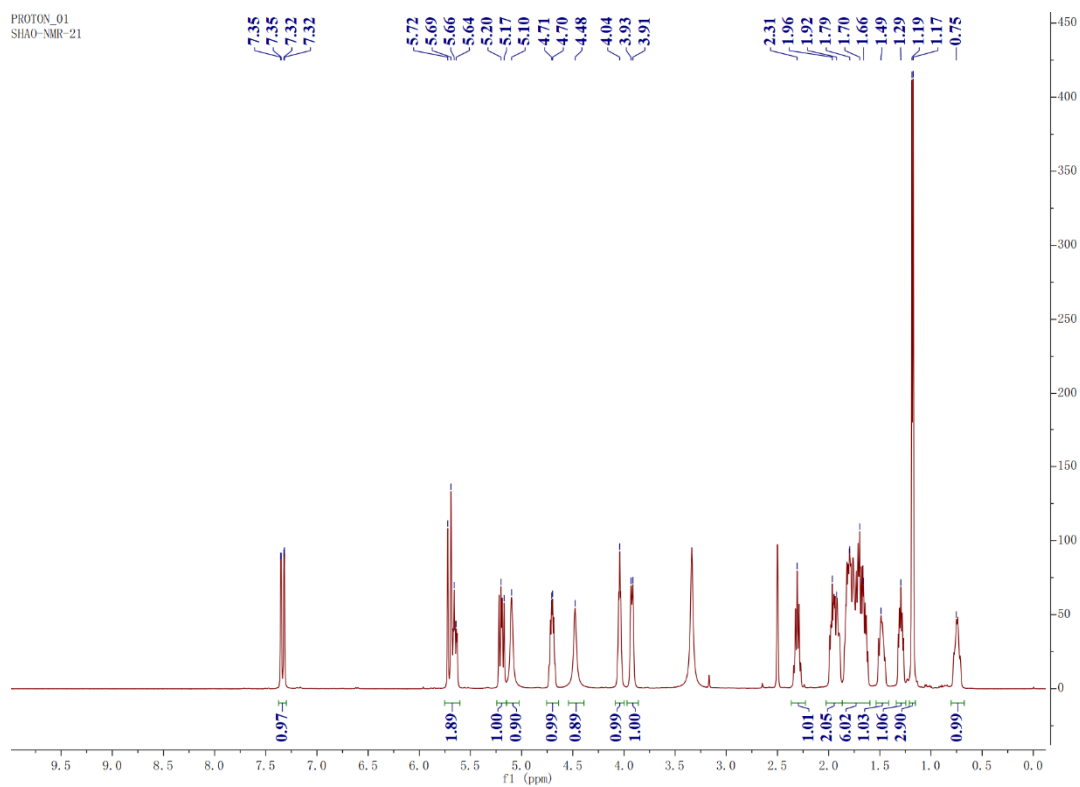


Figure S1. ^1H NMR (500 MHz, $\text{DMSO}-d_6$) spectrum of compound **1**.

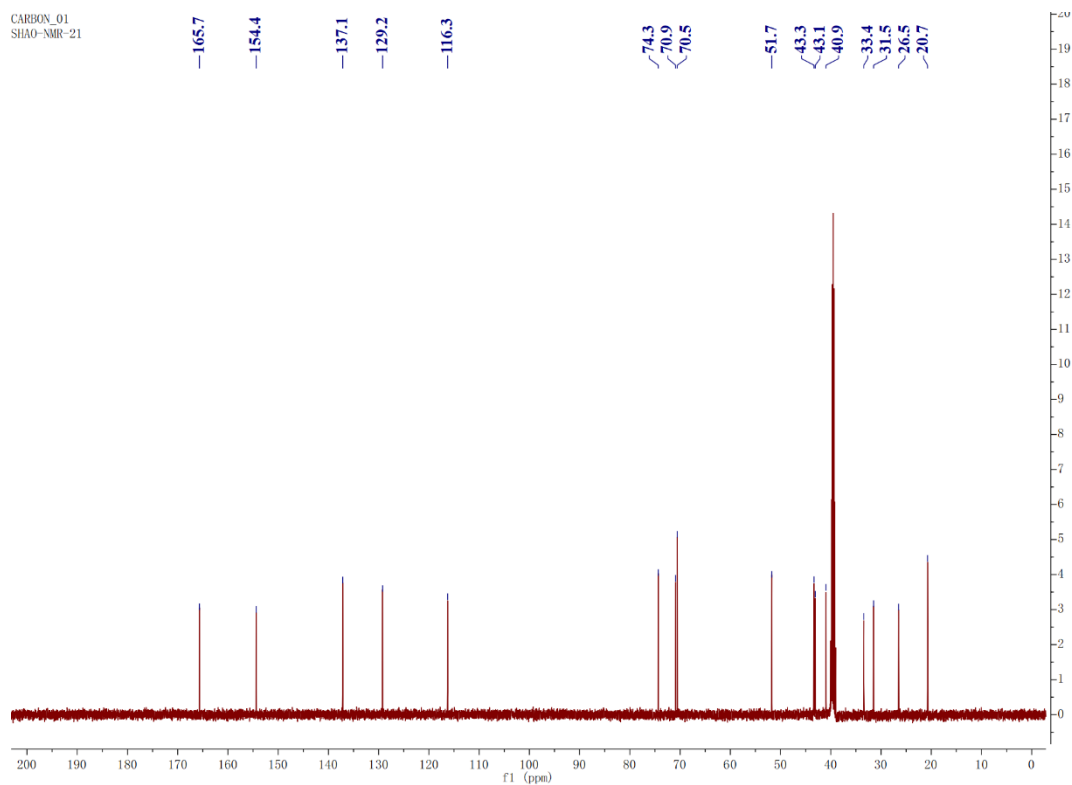


Figure S2. ^{13}C NMR (125 MHz, $\text{DMSO}-d_6$) spectrum of compound **1**.

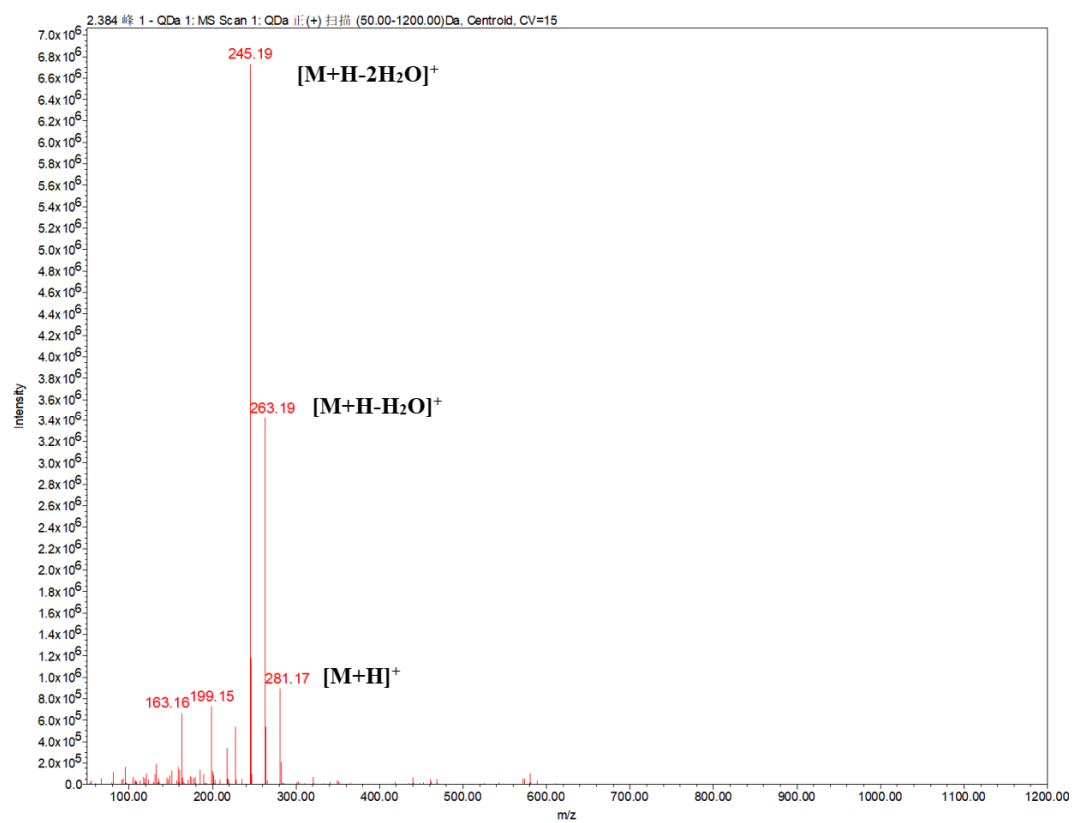
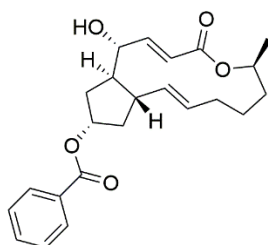


Figure S3. ESIMS spectrum of compound **1**.

Brefeldin A 7-O-benzoate (2)



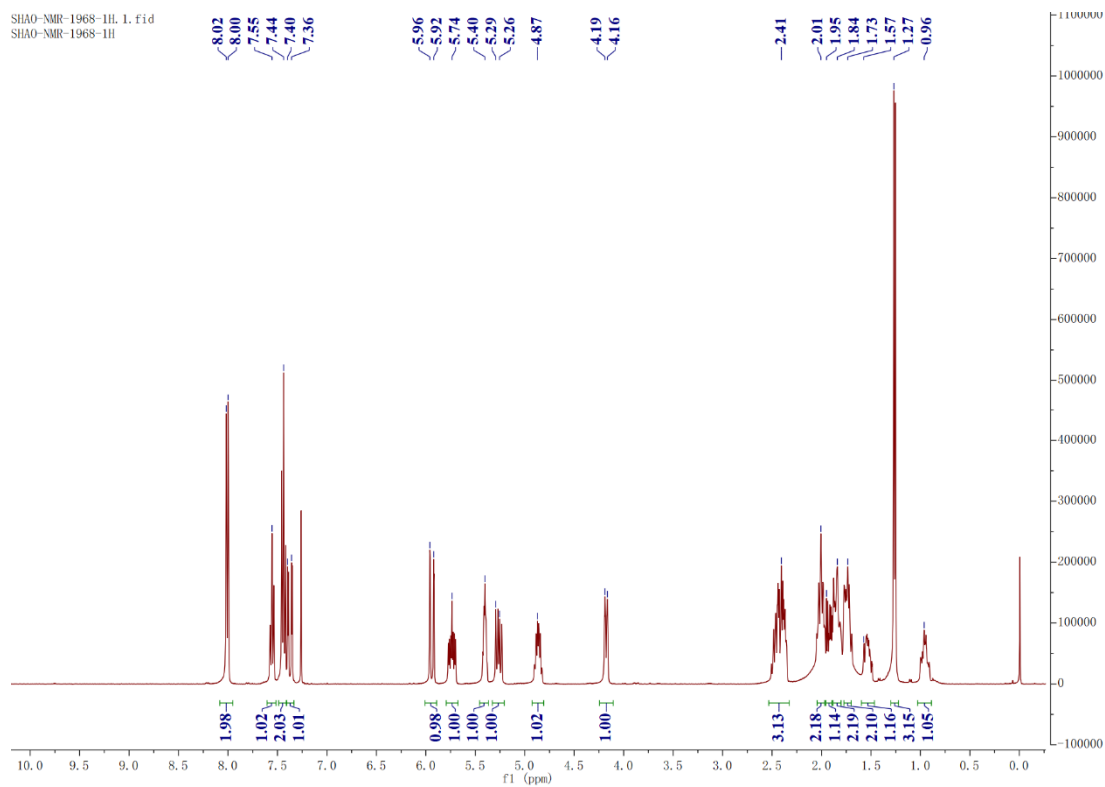


Figure S4. ^1H NMR (400 MHz, CDCl_3) spectrum of compound **2**.

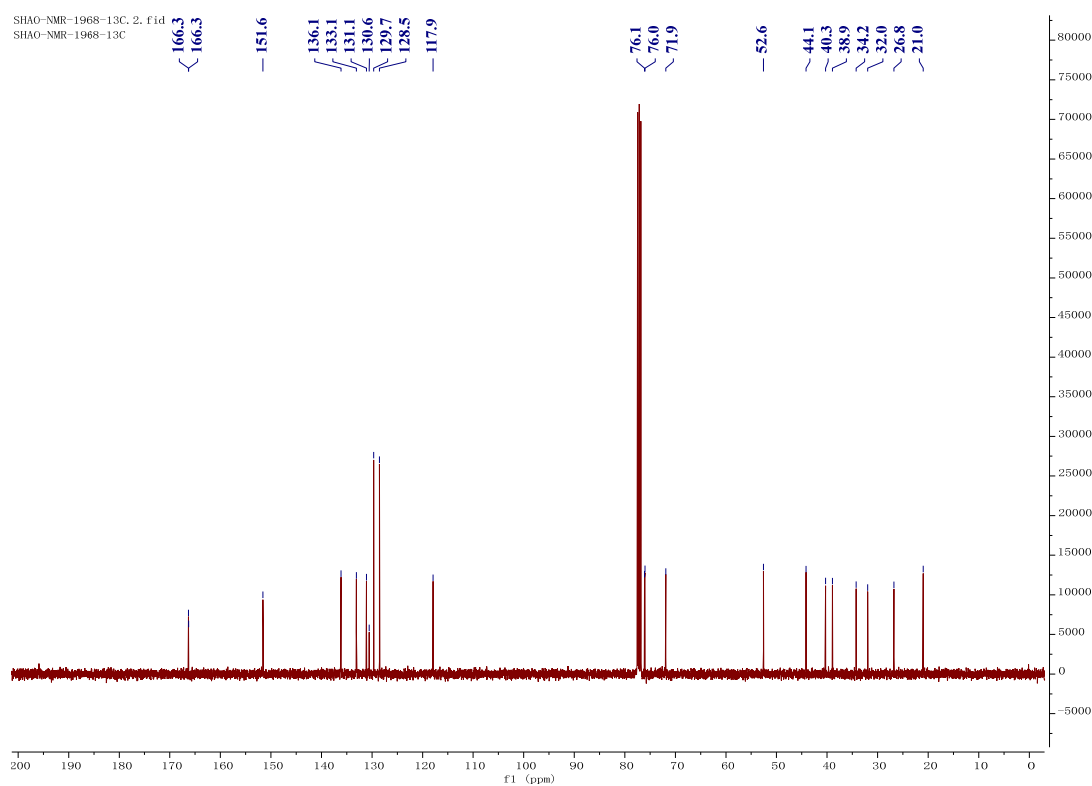


Figure S5. ^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **2**.

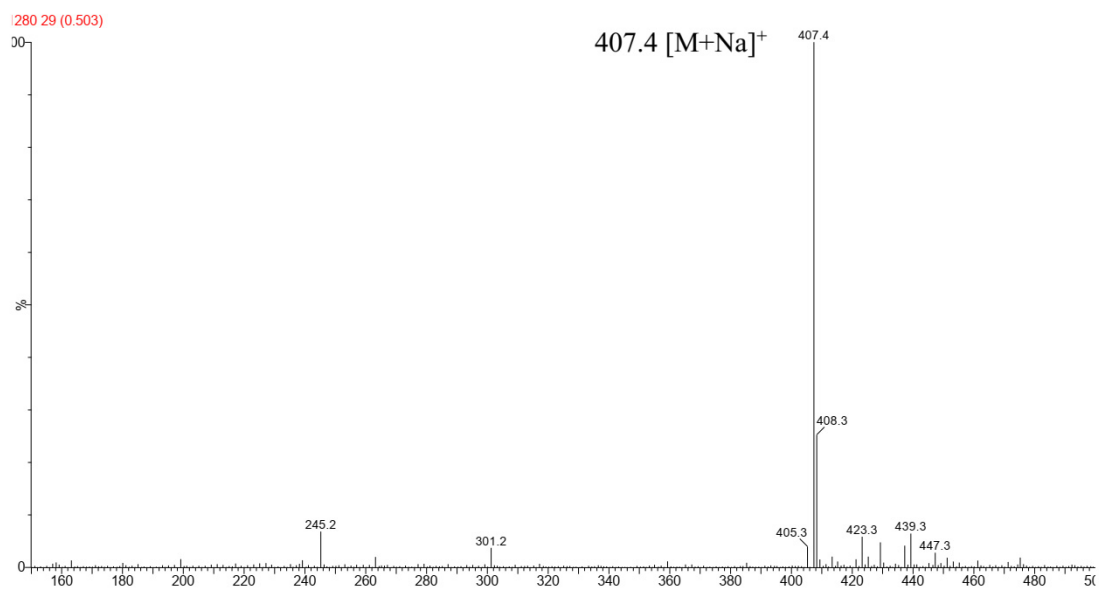


Figure S6. ESIMS spectrum of compound **2**.

Brefeldin A 4,7-O-dibenzoate (3)

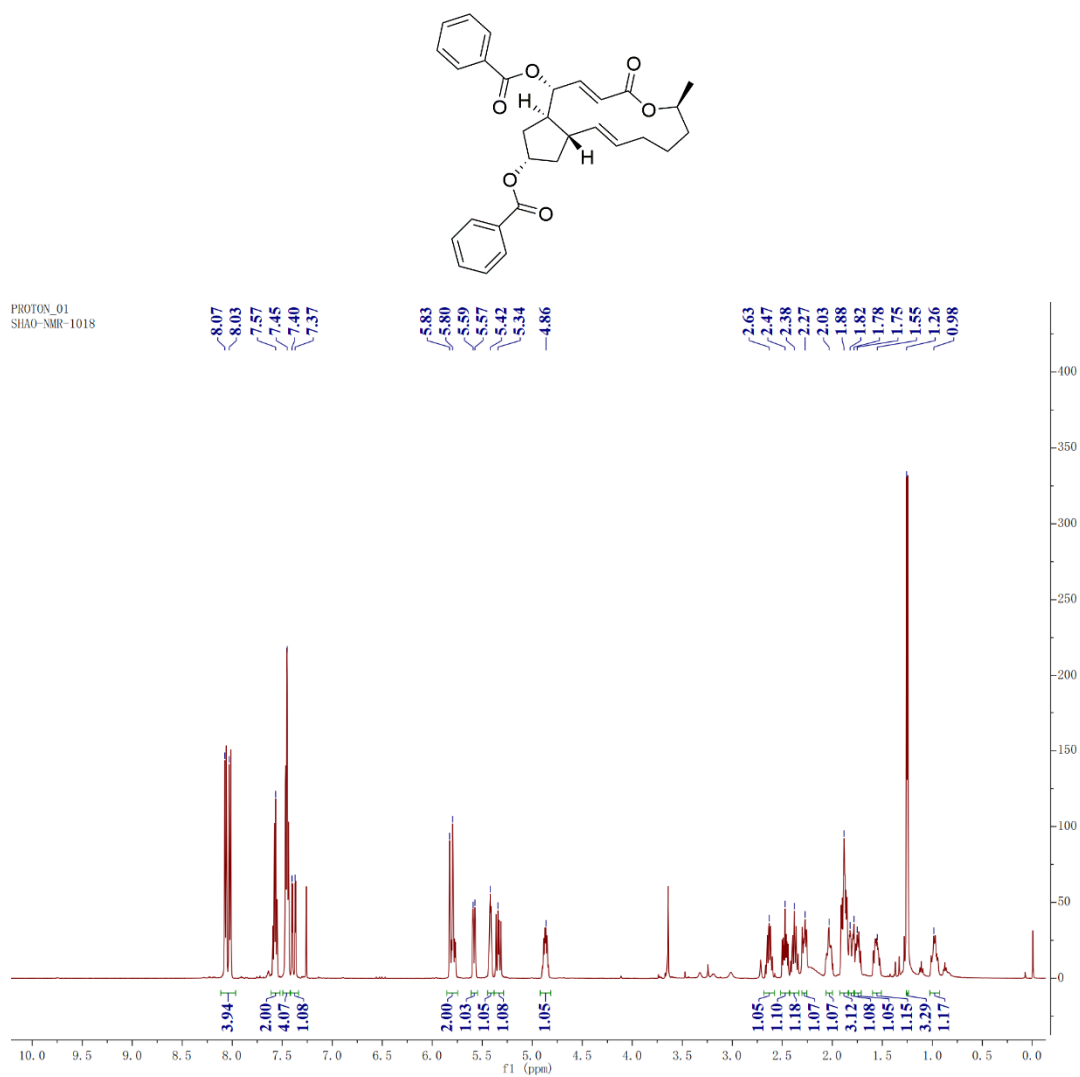


Figure S7. ^1H NMR (500 MHz, CDCl_3) spectrum of compound **3**.

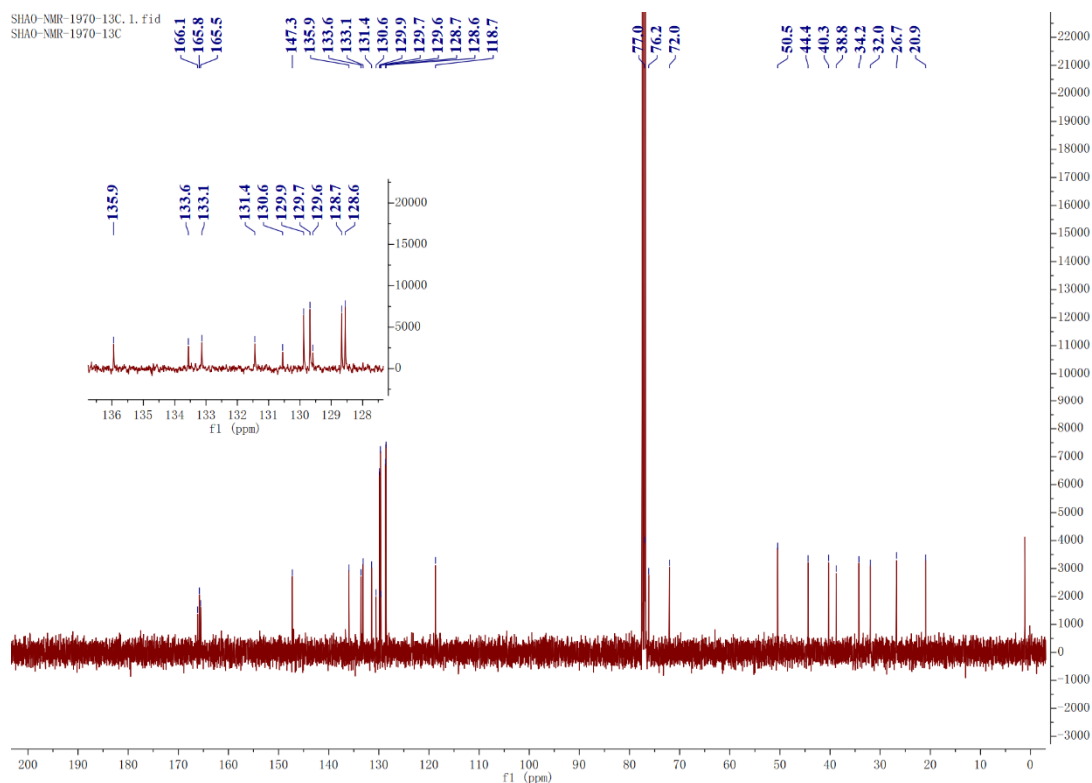


Figure S8. ^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **3**.

CHNQD-01222 #485 RT: 4.73 AV: 1 NL: 4.61E5
T: FTMS + p ESI Full ms [100.0000-1500.0000]

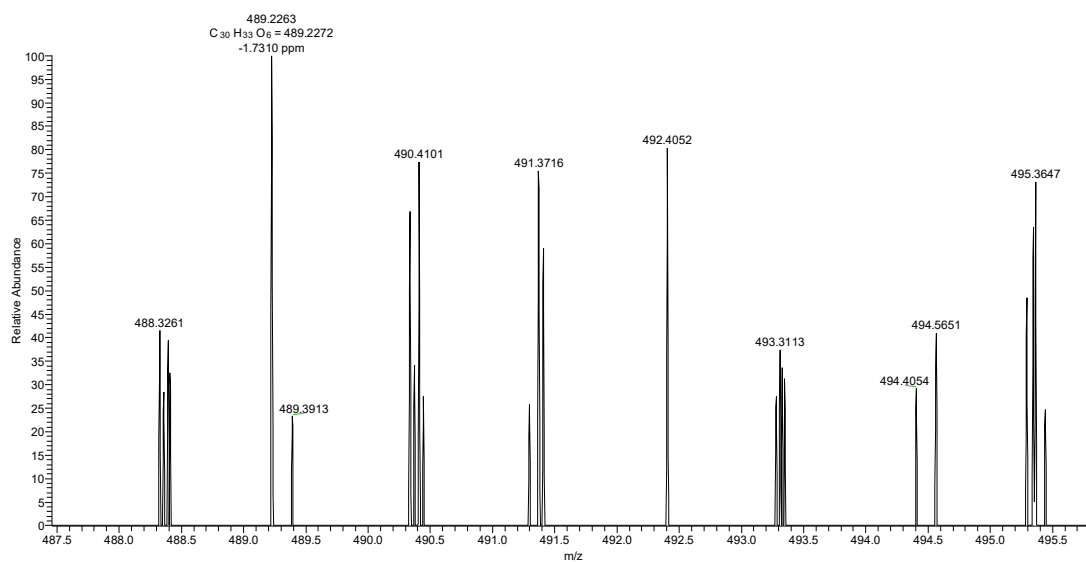


Figure S9. ESIMS spectrum of compound **3**.

Brefeldin A 4-O-benzoate (4)

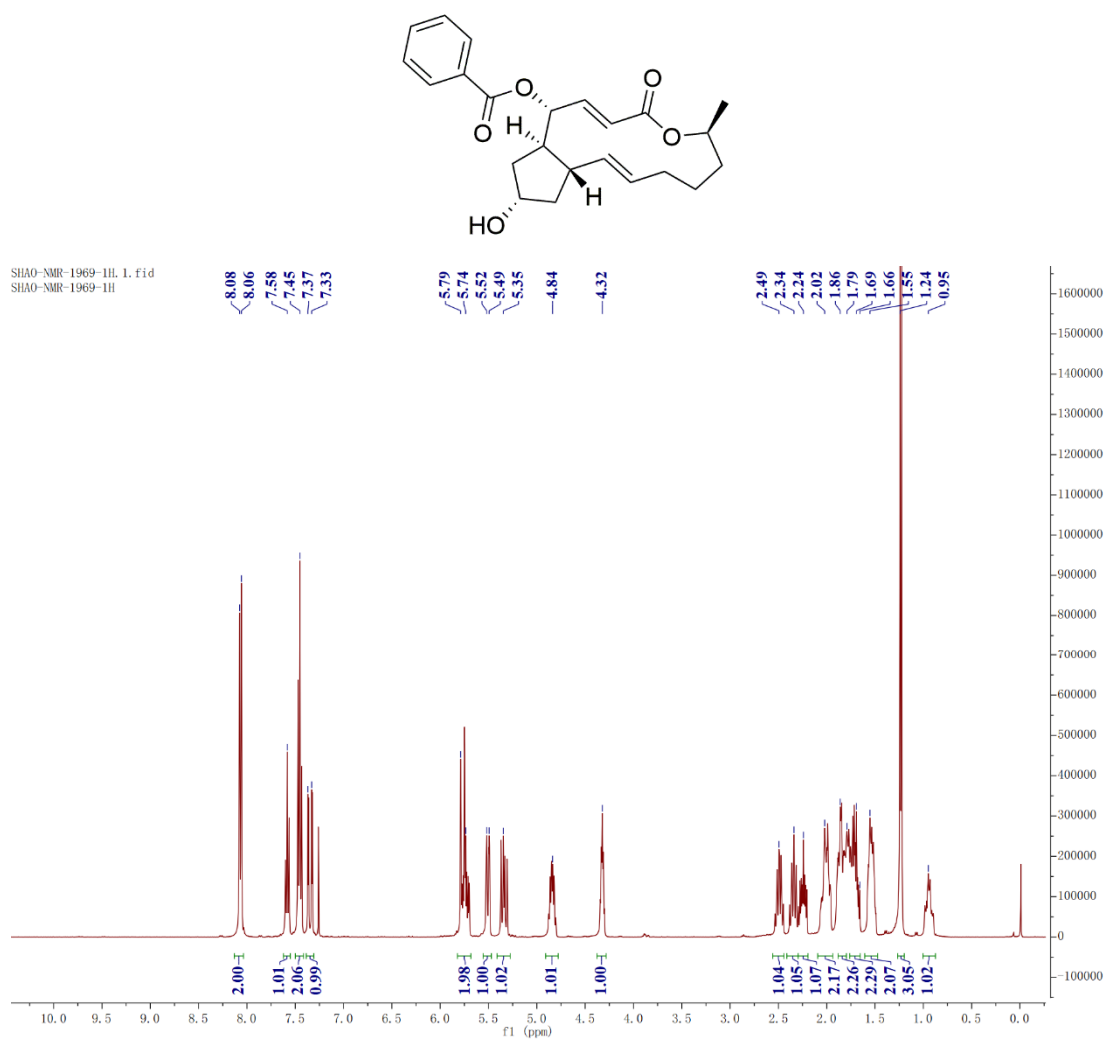


Figure S10. ¹H NMR (400 MHz, CDCl₃) spectrum of compound **4**.

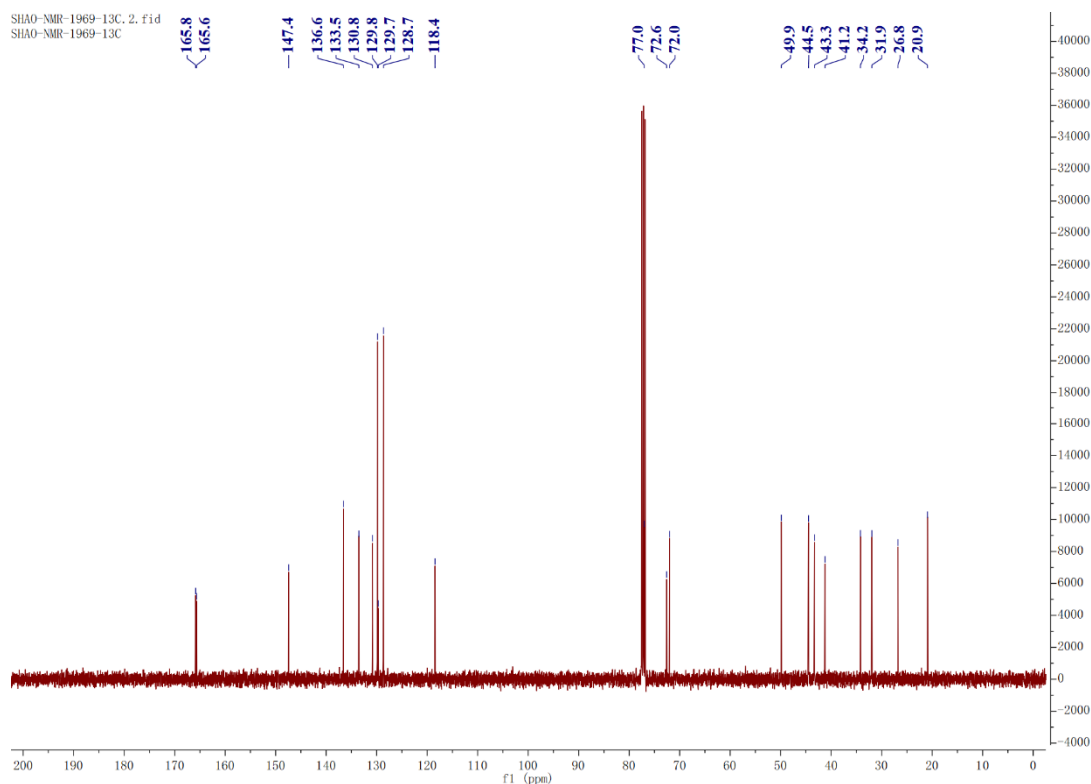


Figure S11. ^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **4**.

CHNQD-01279 #13 RT: 0.16 AV: 1 NL: 4.58E6
T: FTMS + p ESI Full ms [100.0000-1500.0000]

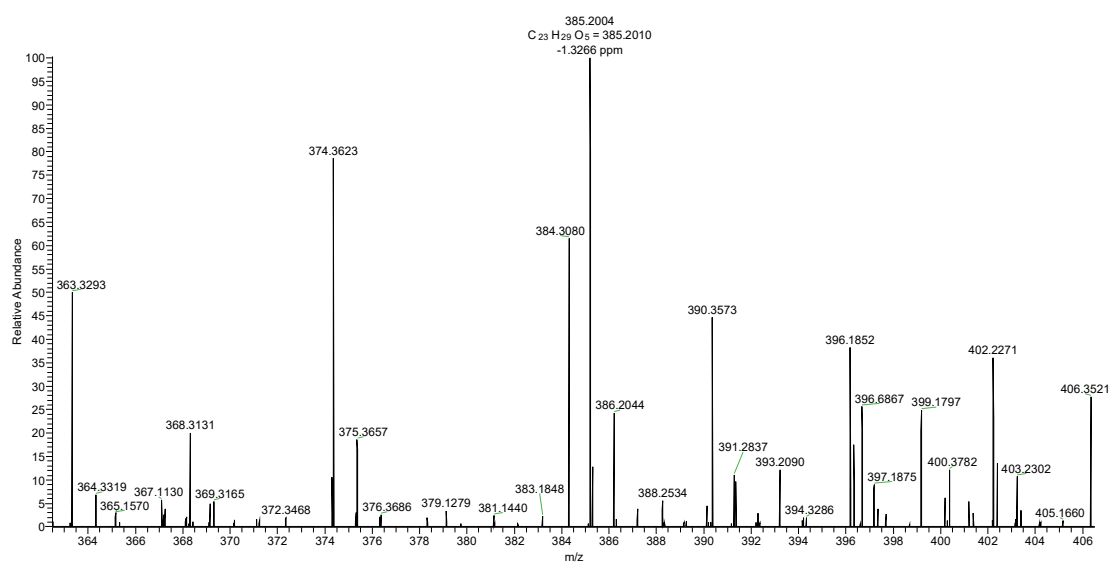


Figure S12. HRESIMS spectrum of compound **4**.

Brefeldin A 7-O-(2,3,4)-trifluorobenzoate (5)

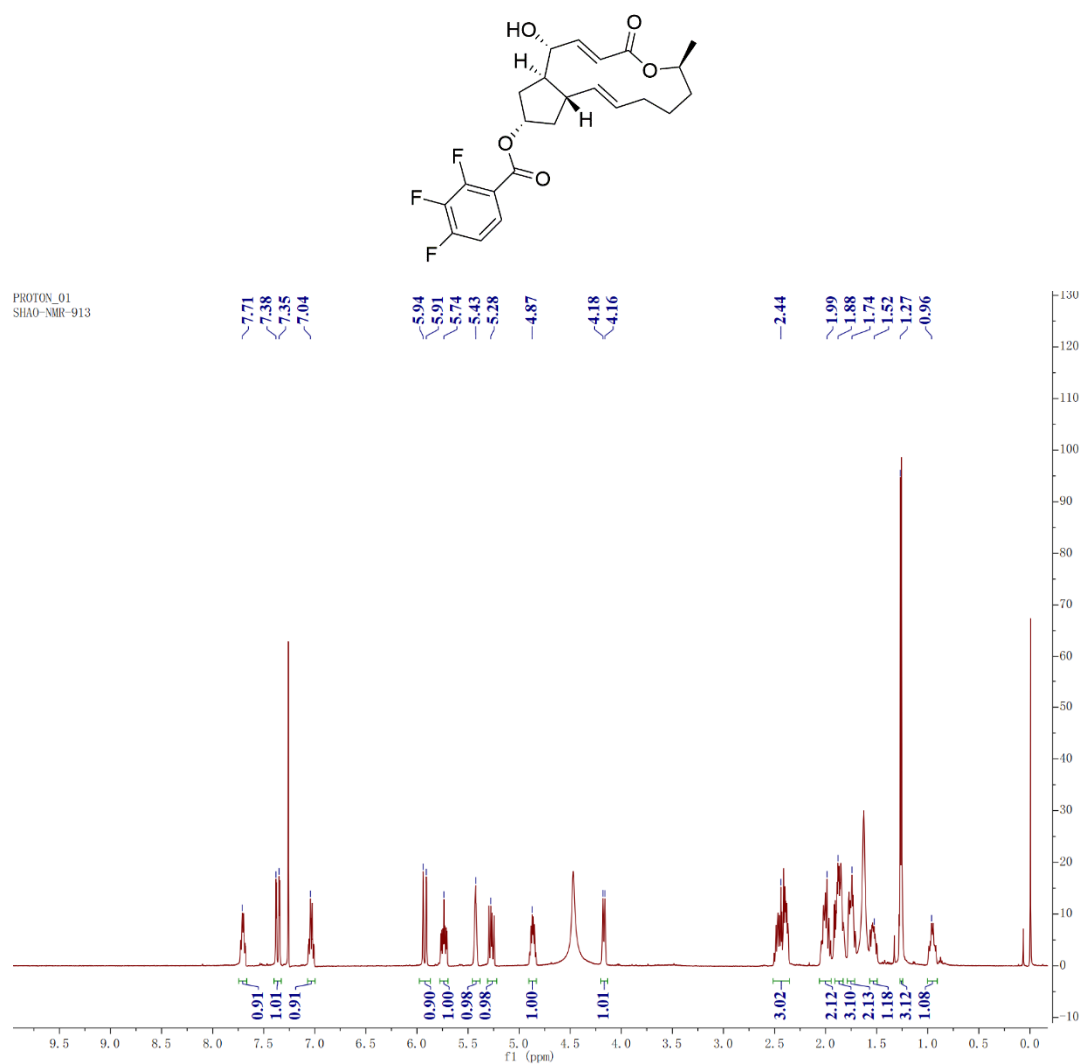


Figure S13. ¹H NMR (500 MHz, CDCl₃) spectrum of compound 5.

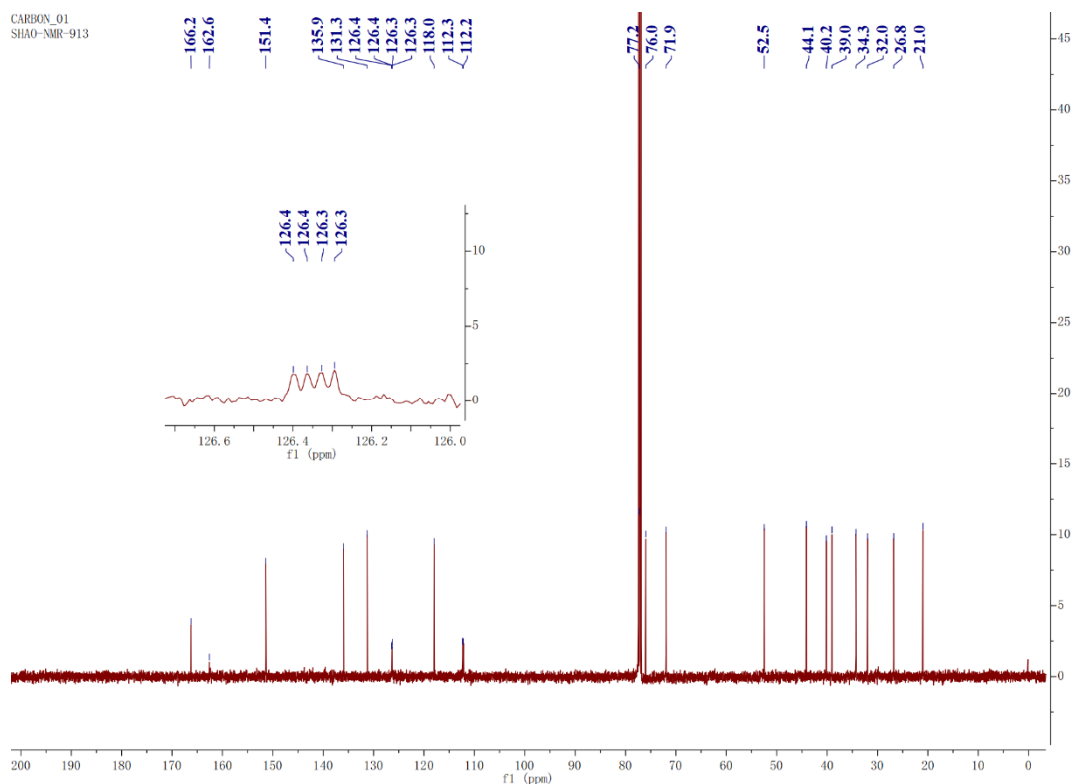


Figure S14. ^{13}C NMR (125 MHz, CDCl_3) spectrum of compound **5**.

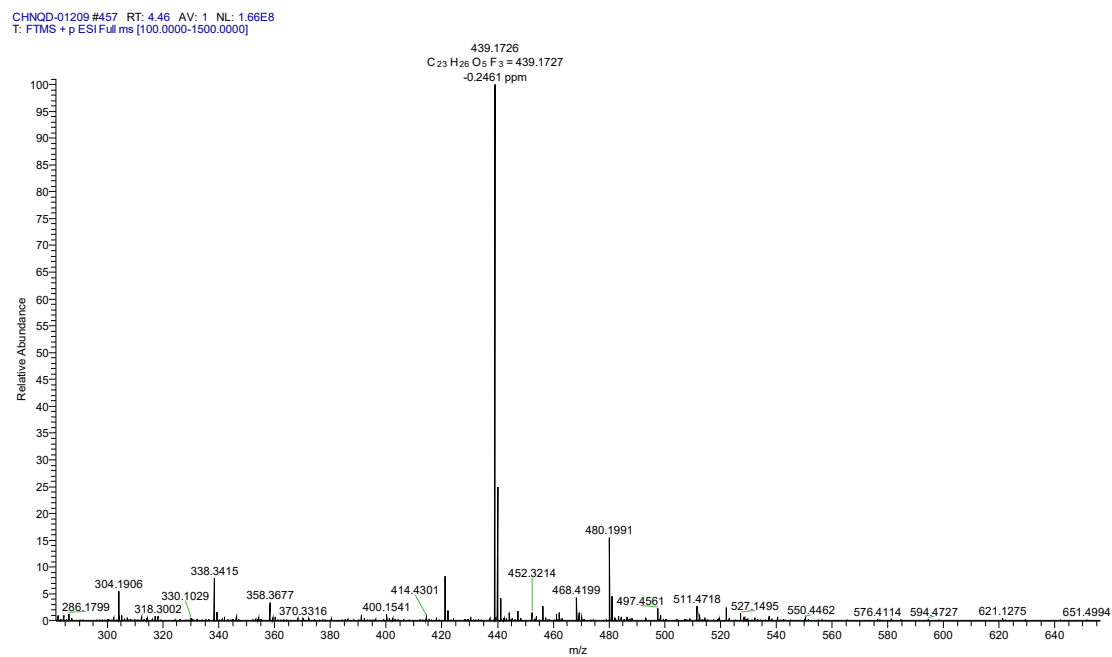


Figure S15. HRESIMS spectrum of compound **5**.

Brefeldin A 4-O-(2,3,4)-trifluorobenzoate (6)

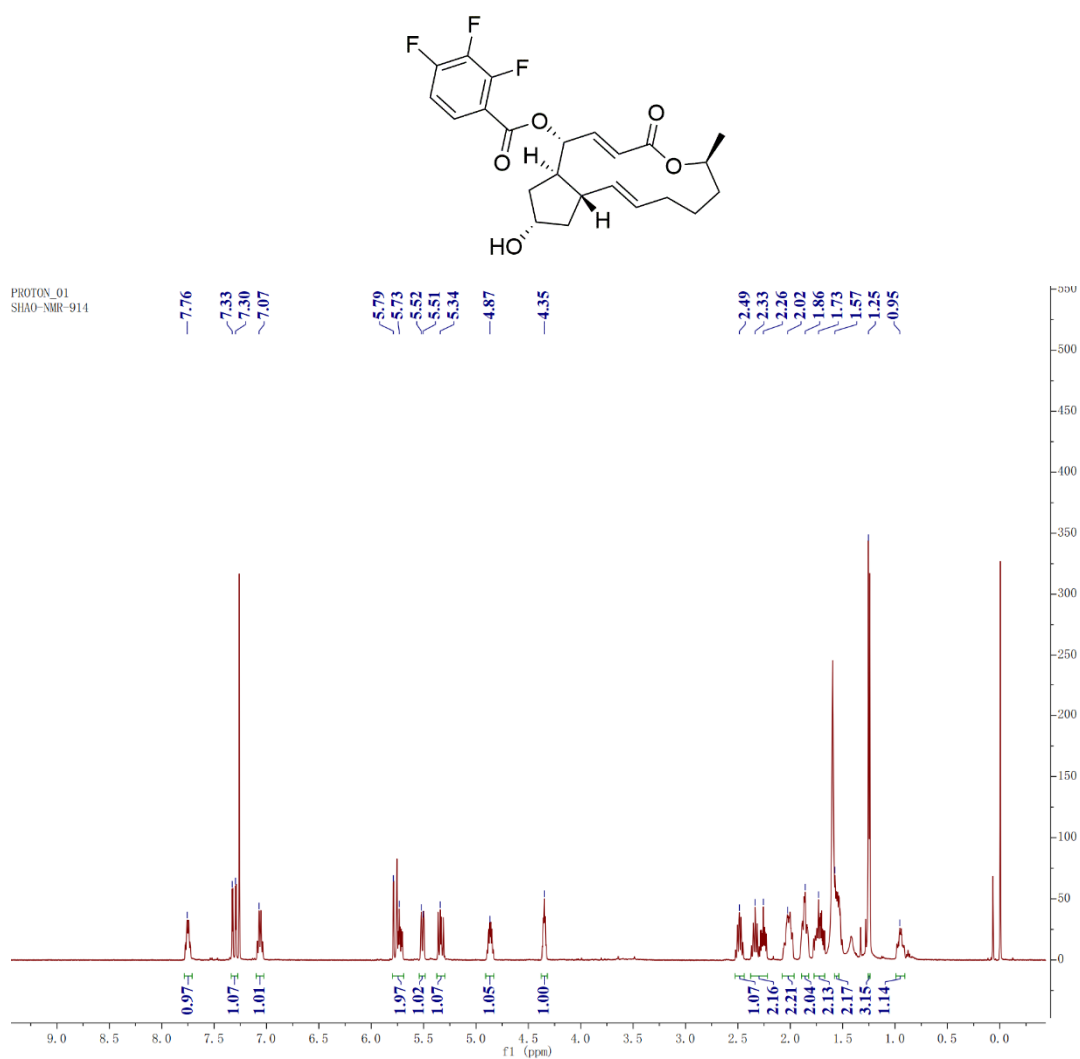


Figure S16. ^1H NMR (500 MHz, CDCl_3) spectrum of compound 6.

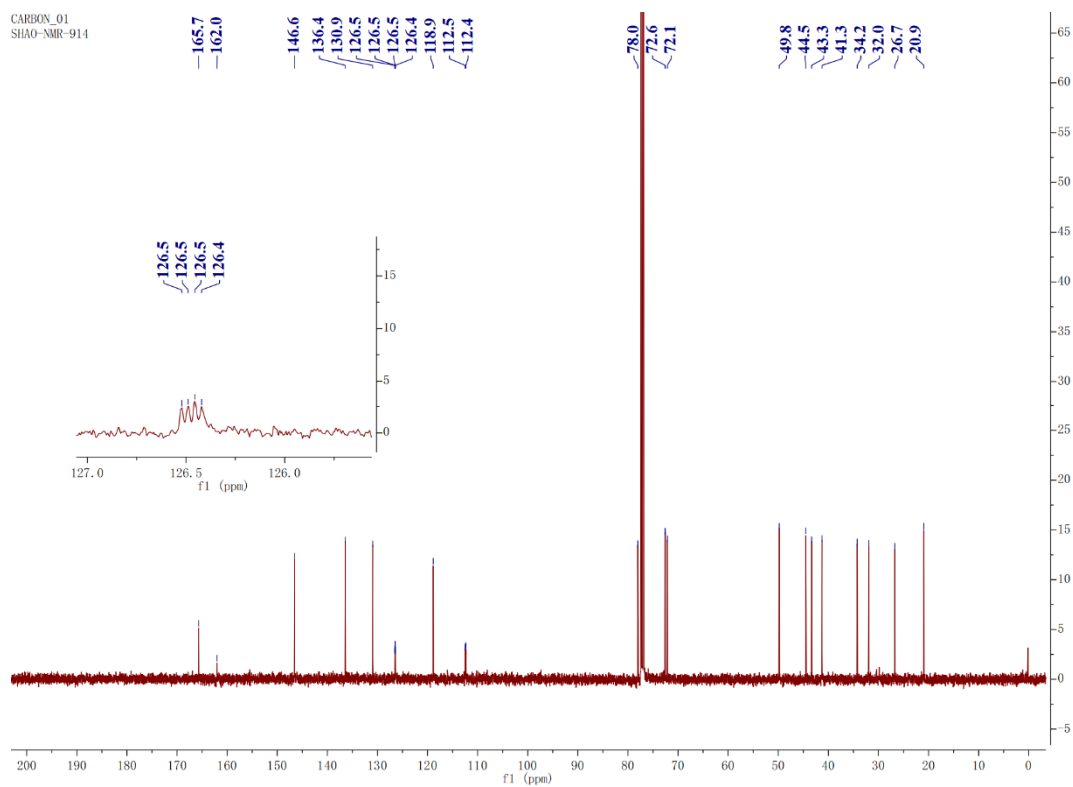


Figure S17. ^{13}C NMR (125 MHz, CDCl_3) spectrum of compound **6**.

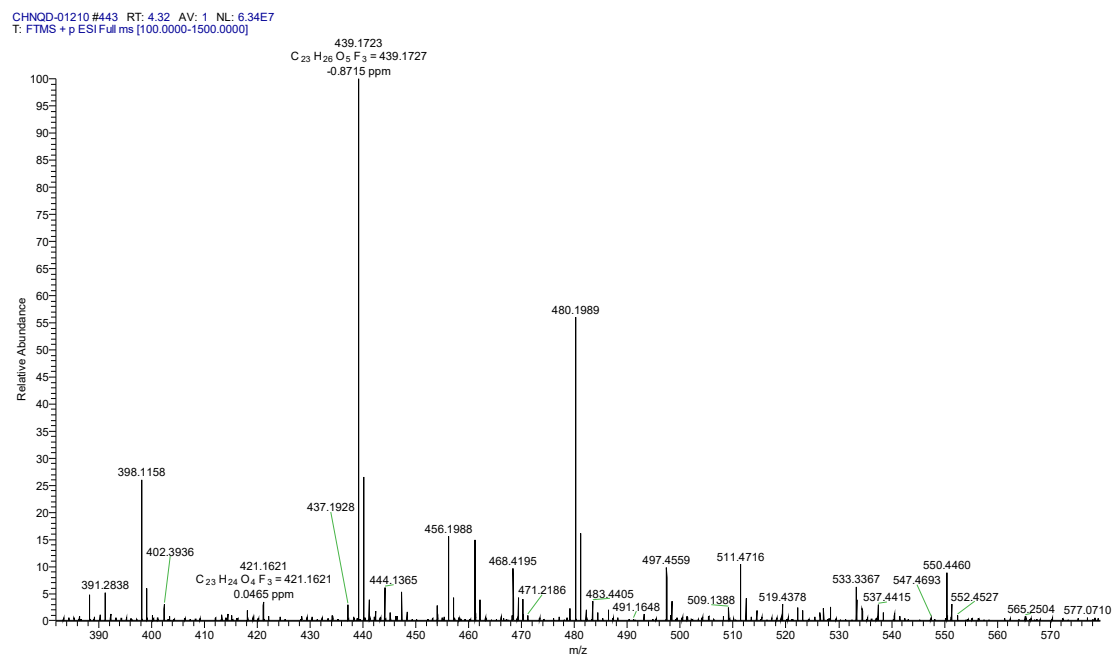


Figure S18. HRESIMS spectrum of compound **6**.

Brefeldin A 7-O-2-chloro-4,5-difluorobenzoate (7)

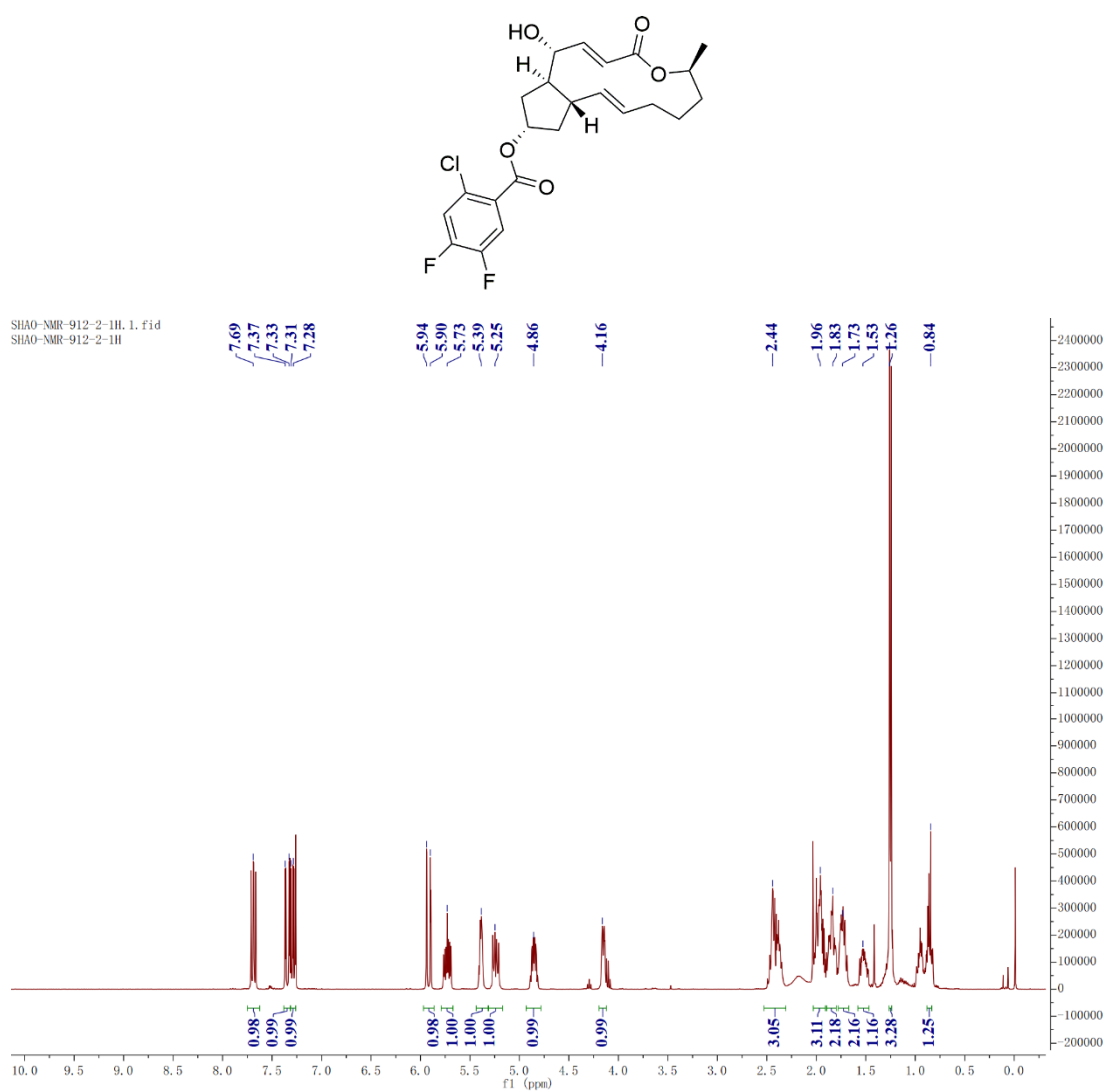


Figure S19. ^1H NMR (400 MHz, CDCl_3) spectrum of compound **7**.

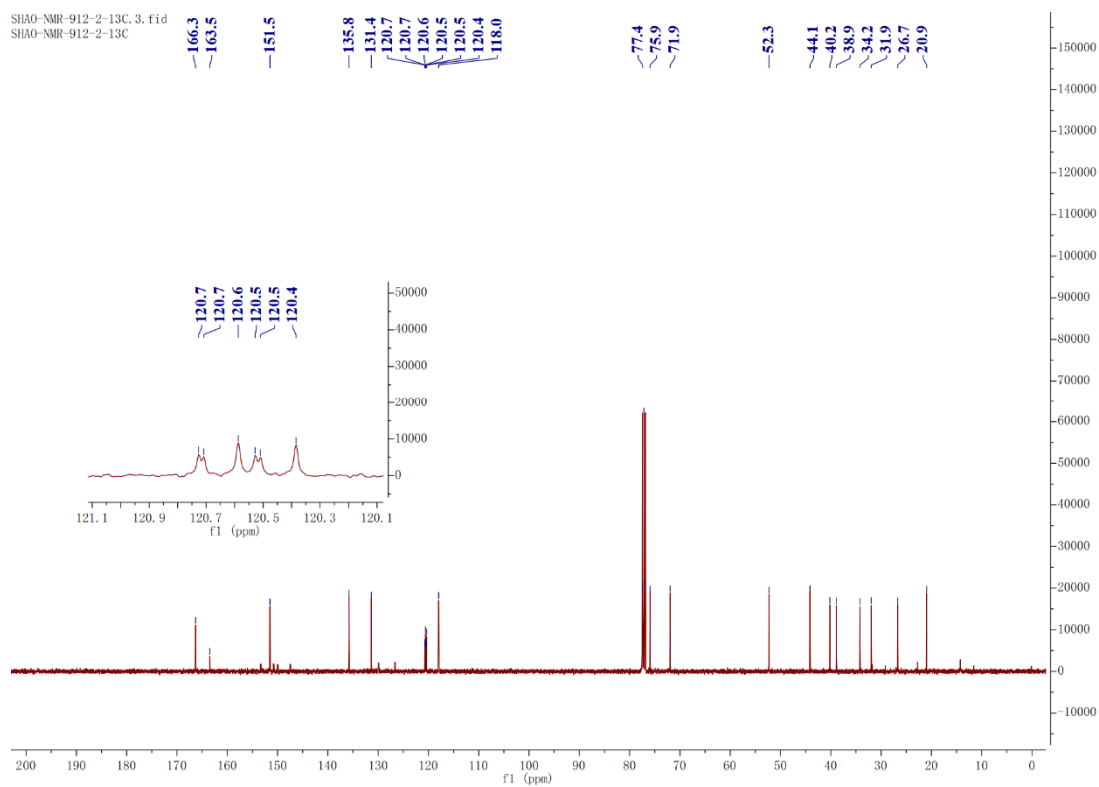


Figure S20. ^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **7**.

CHNQD-01212-#471 RT: 4.60 AV: 1 NL: 1.83E8
T: FTMS + p ESI Full ms [100.0000-1500.0000]

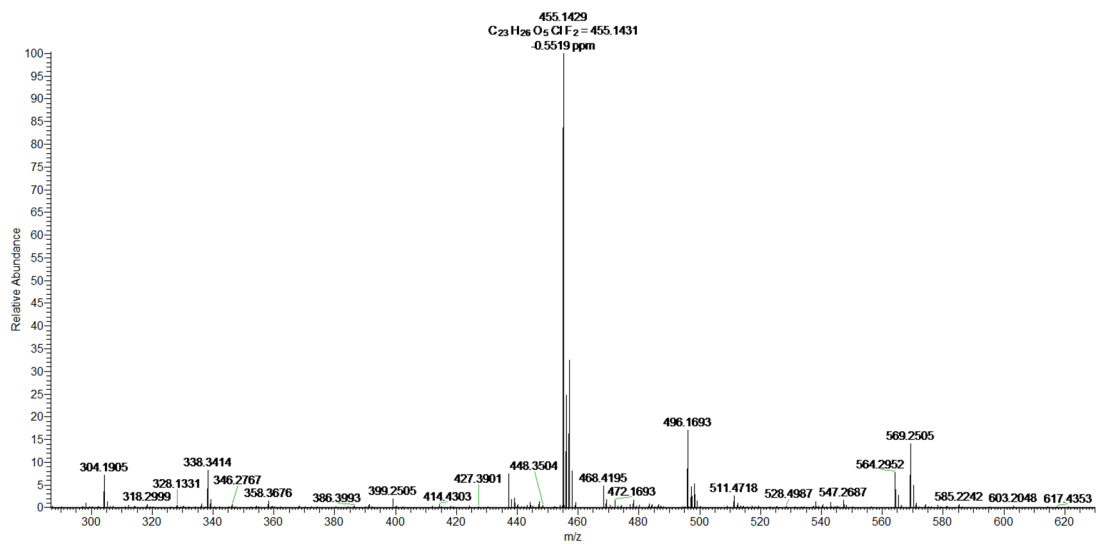


Figure S21. HRESIMS spectrum of compound **7**.

Brefeldin A 4-O-2-chloro-4,5-difluorobenzoate (8)

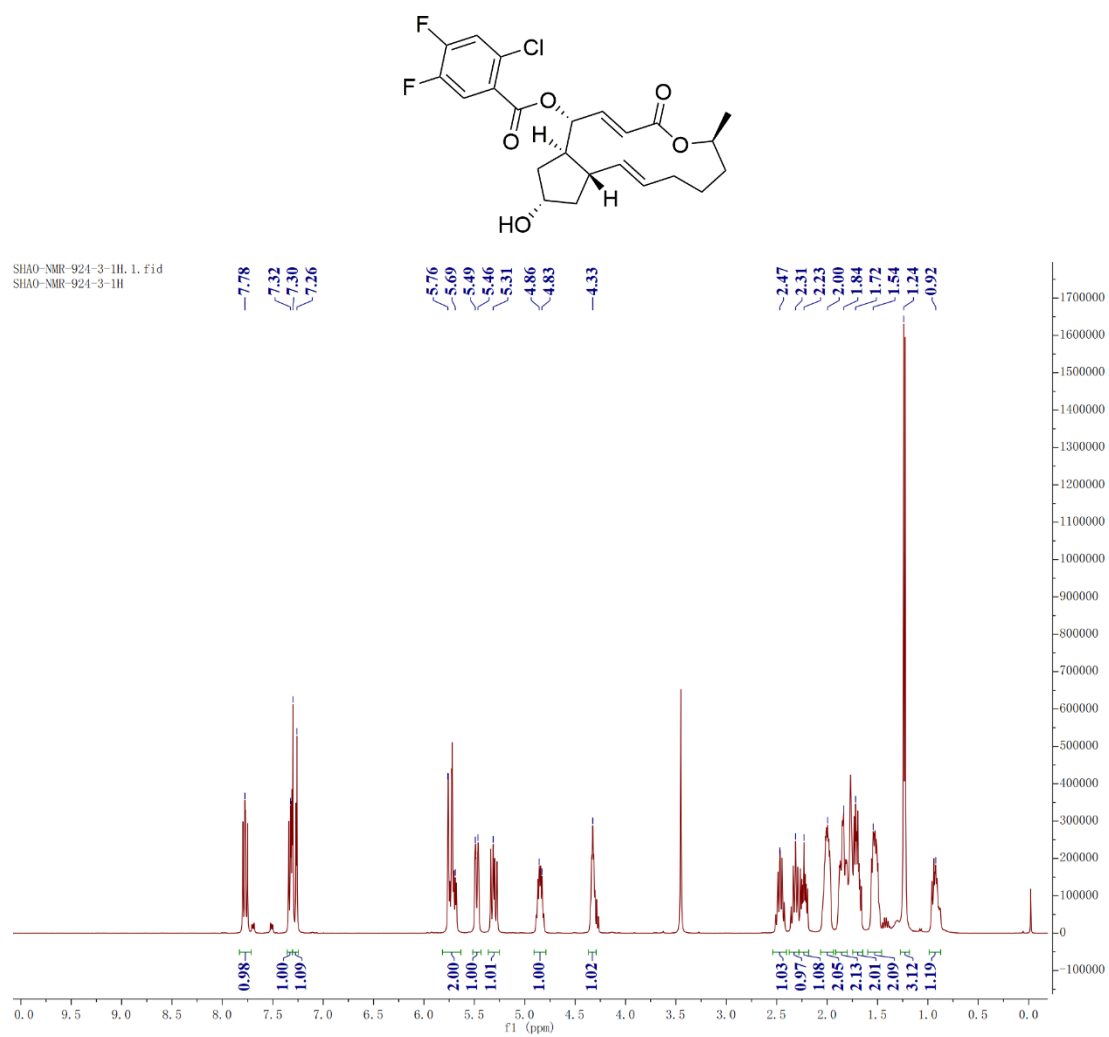


Figure S22. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 8.

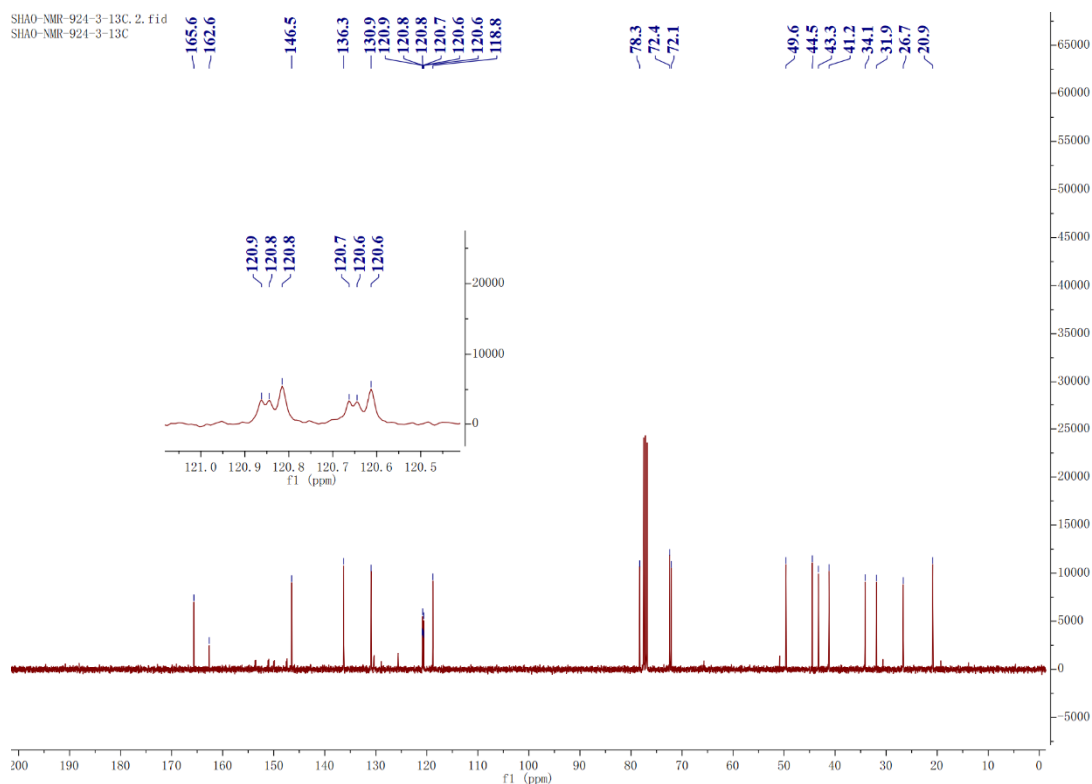


Figure S23. ^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **8**.

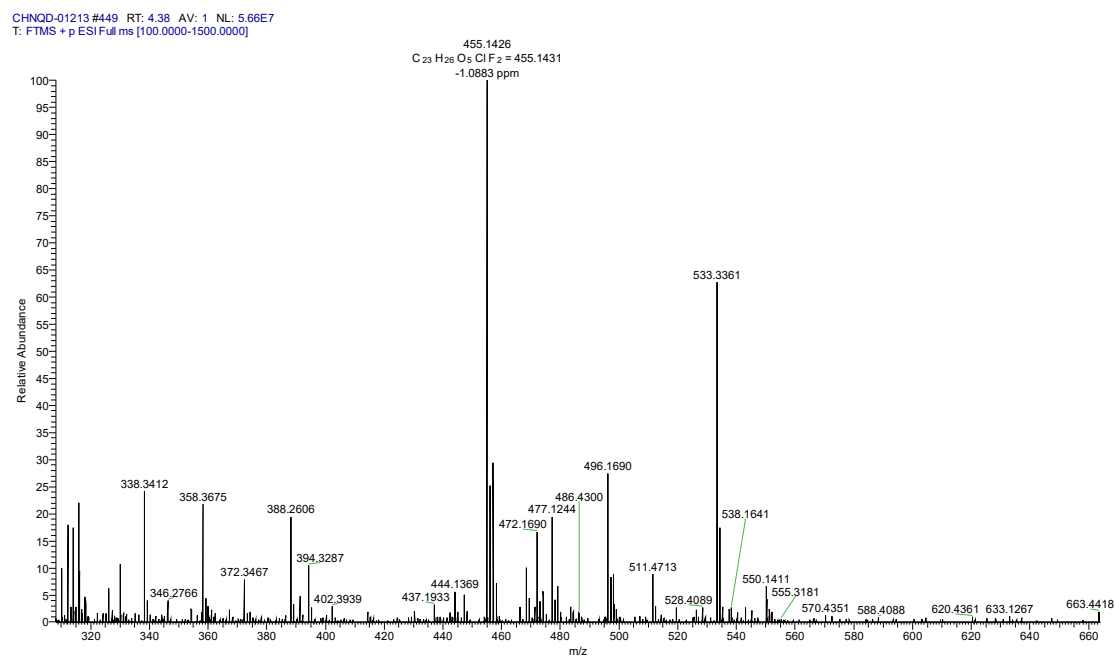
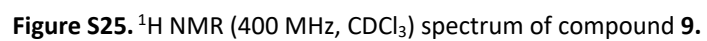
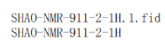


Figure S24. HRESIMS spectrum of compound **8**.

Brefeldin A 4,7-O-di-2-chloro-4,5-difluorobenzoate (9)



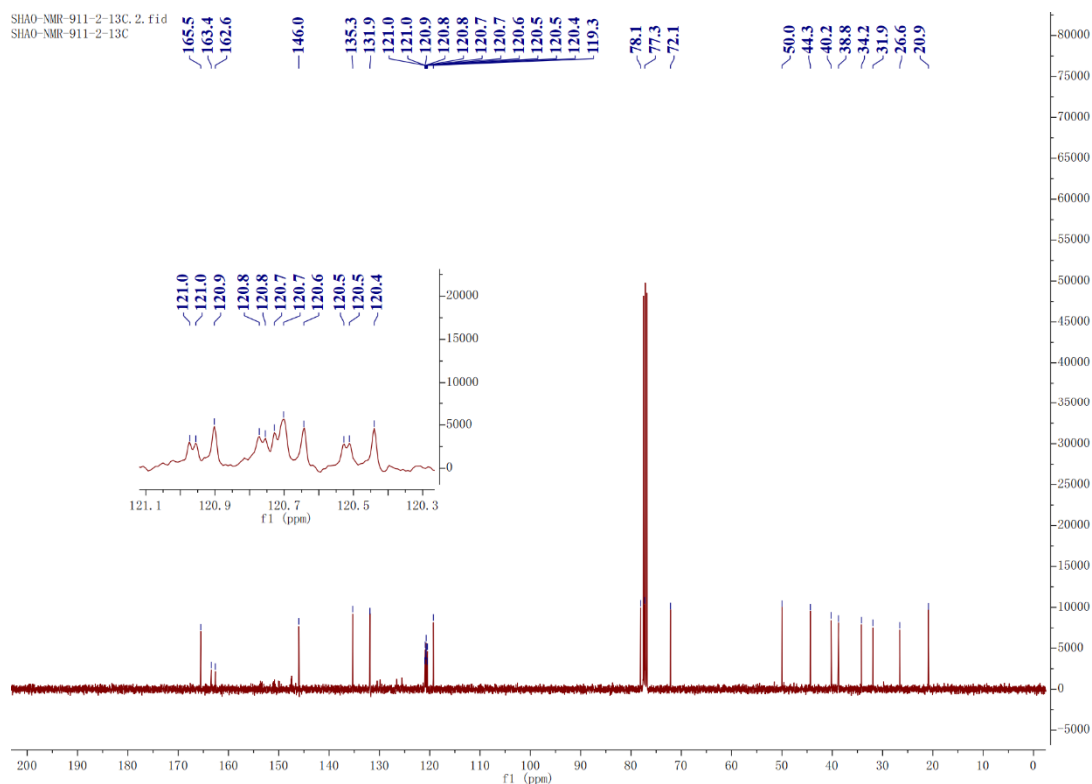


Figure S26. ^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **9**.

CHNQD-012111 #17 RT: 0.20 AV: 1 NL: 1.03E5
T: FTMS + p ESI Full ms [100.0000-1500.0000]

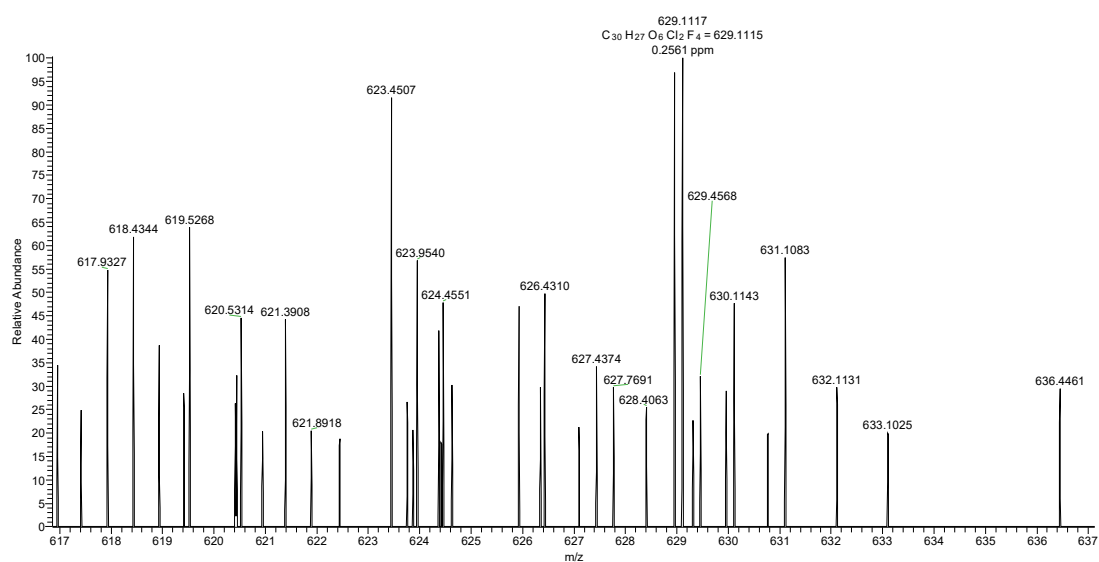


Figure S27. HRESIMS spectrum of compound **9**.

Brefeldin A 7-O-(4)-chlorobenzoate (10)

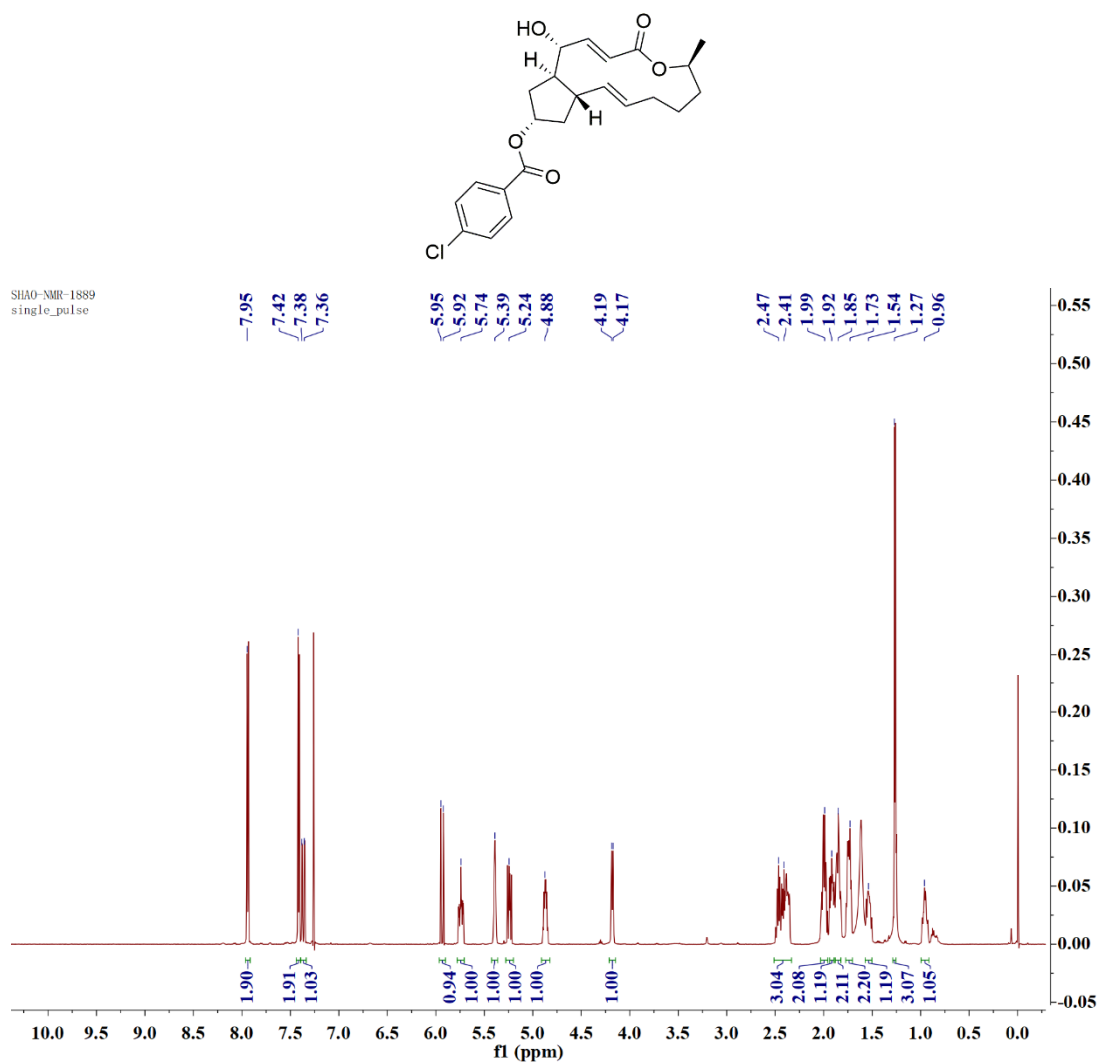


Figure S28. ^1H NMR (600 MHz, CDCl_3) spectrum of compound 10.

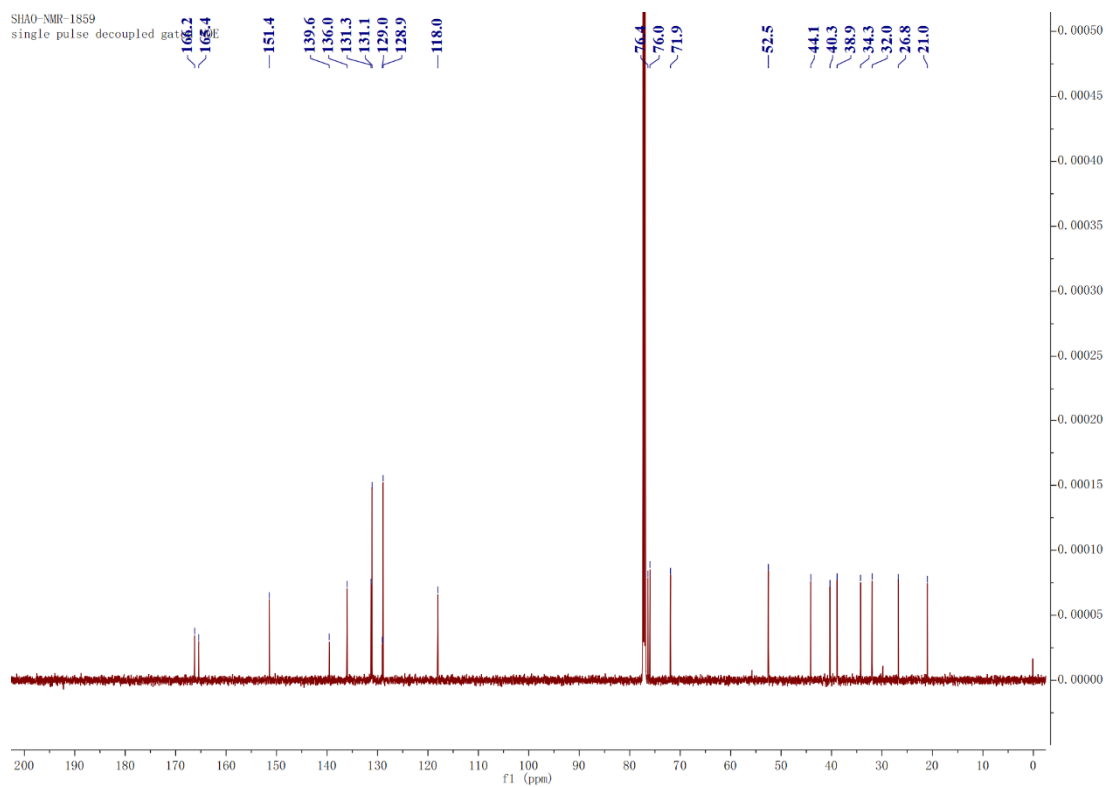


Figure S29. ^{13}C NMR (150 MHz, CDCl_3) spectrum of compound **10**.

CHNQD-01218 #479 RT: 4.67 AV: 1 NL: 5.90E7
T: FTMS + p ESI Full ms [100.0000-1500.0000]

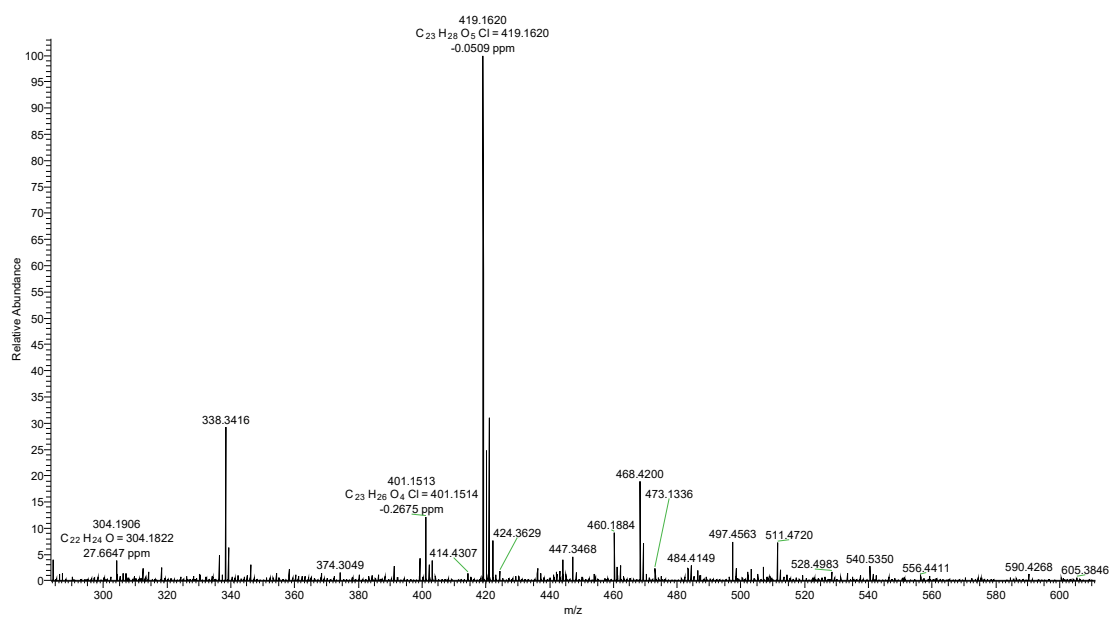


Figure S30. HRESIMS spectrum of compound **10**.

Brefeldin A 4-O-(4-chlorobenzoate (11)

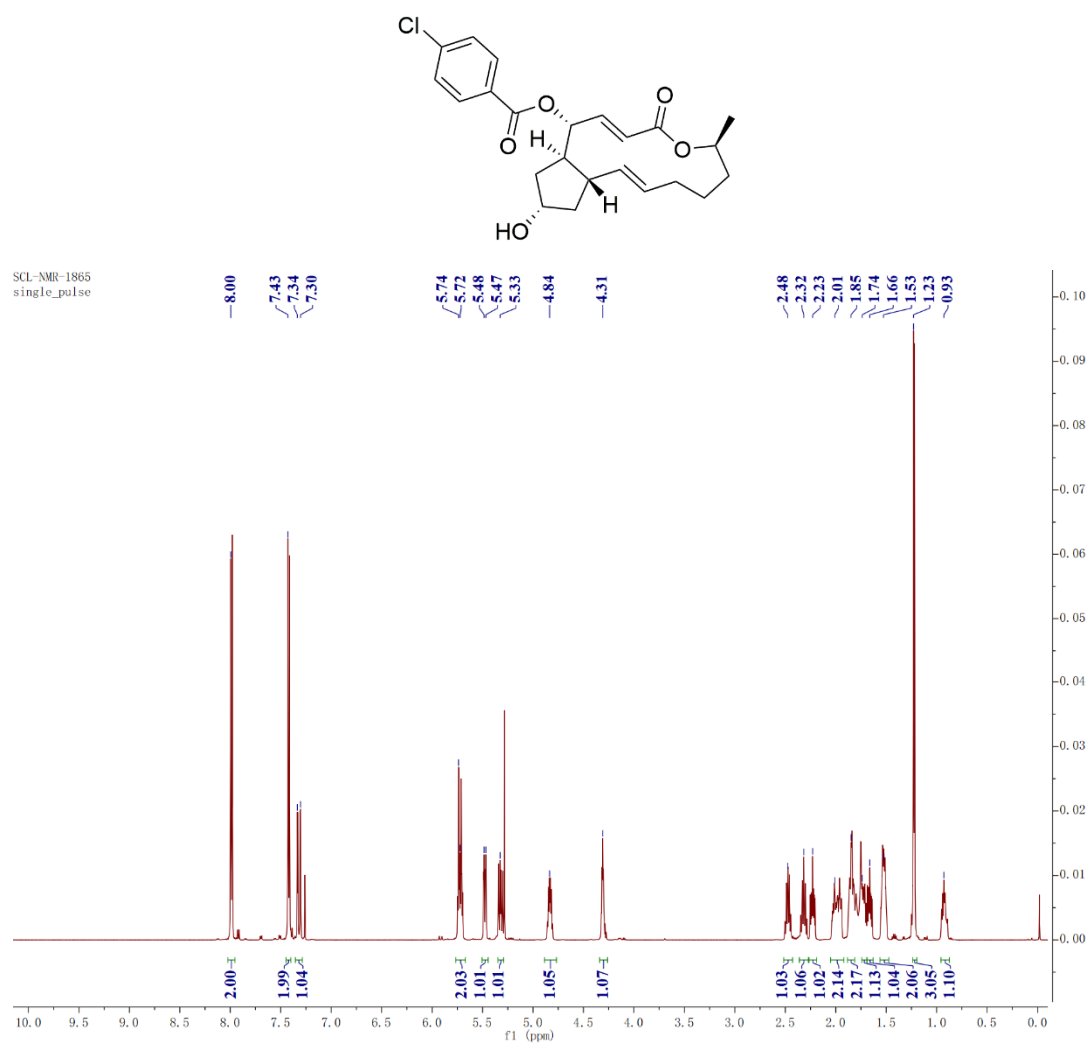


Figure S31. ^1H NMR (600 MHz, CDCl_3) spectrum of compound 11.

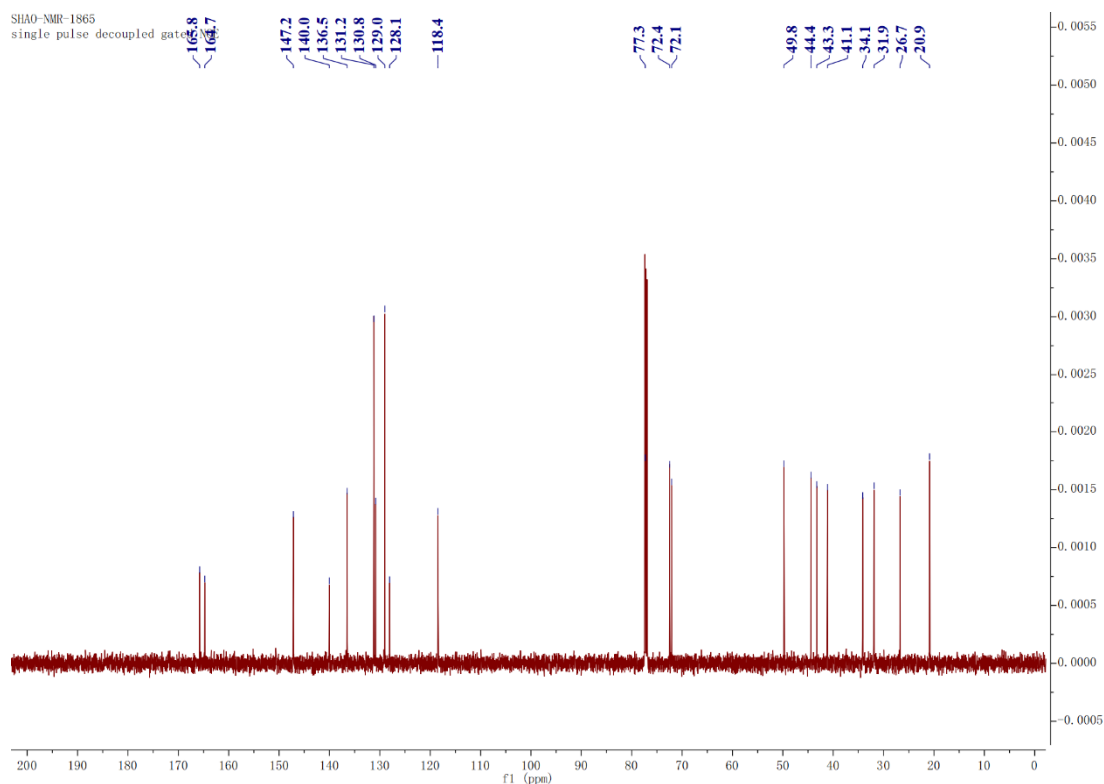


Figure S32. ^{13}C NMR (150 MHz, CDCl_3) spectrum of compound **11**.

26_200119204721 #453 RT: 4.44 AV: 1 NL: 4.57E7
T: FTMS + p ESI Full ms [100.0000-1500.0000]

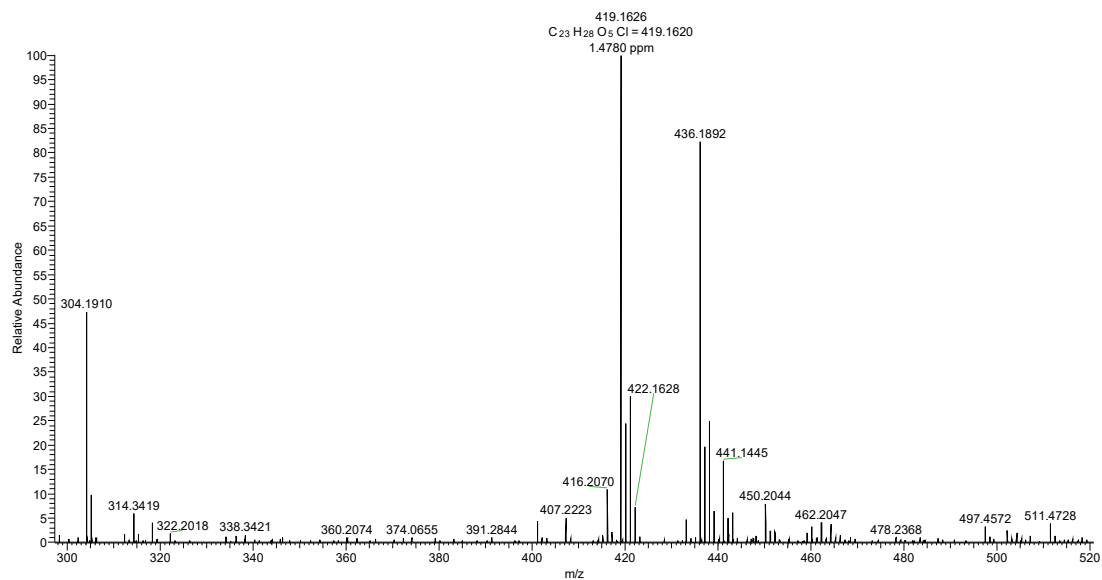


Figure S33. HRESIMS spectrum of compound **11**.

Brefeldin A 4,7-O-di-(4)-chlorobenzoate (12)

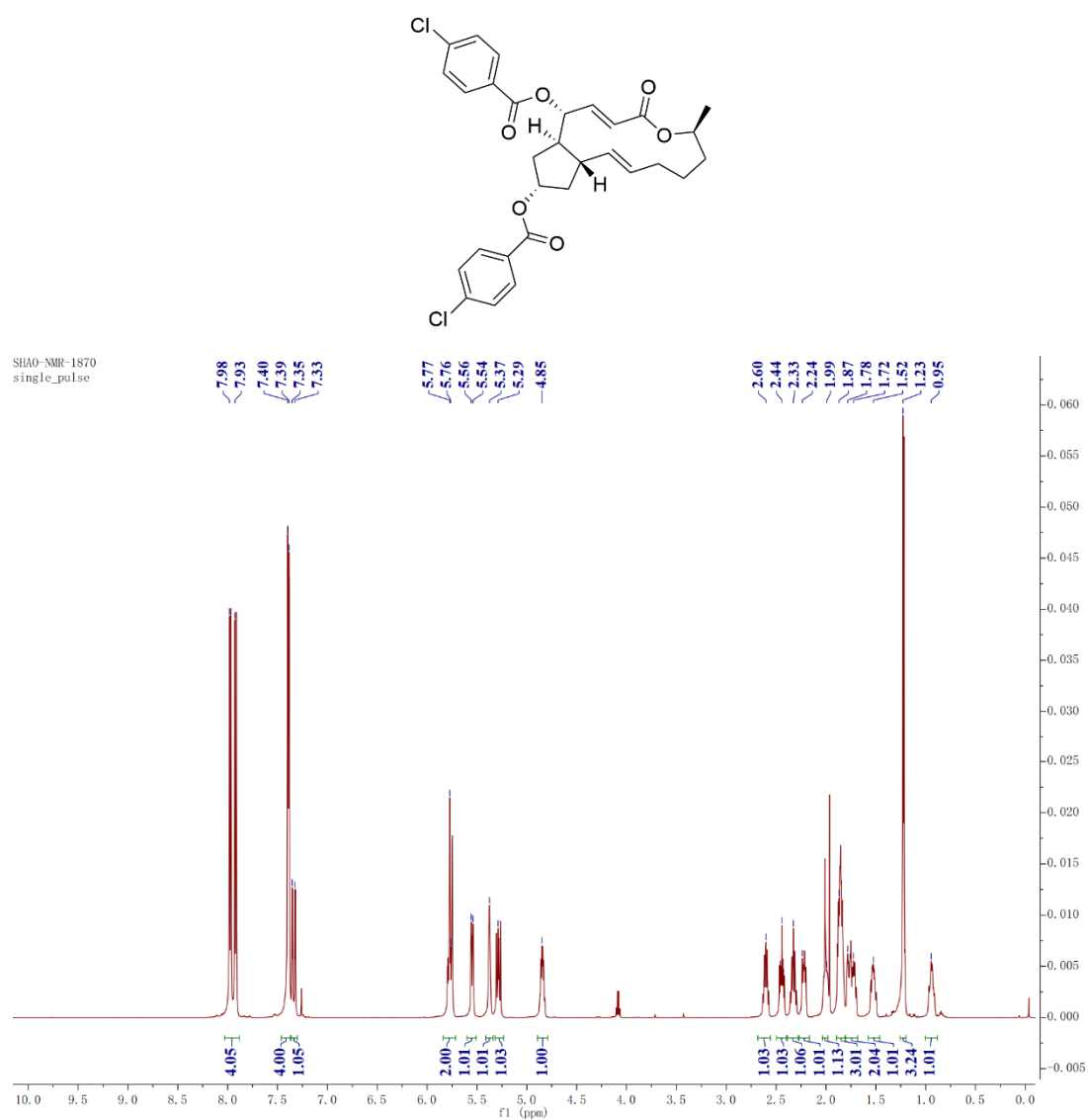


Figure S34. ¹H NMR (600 MHz, CDCl₃) spectrum of compound 12.

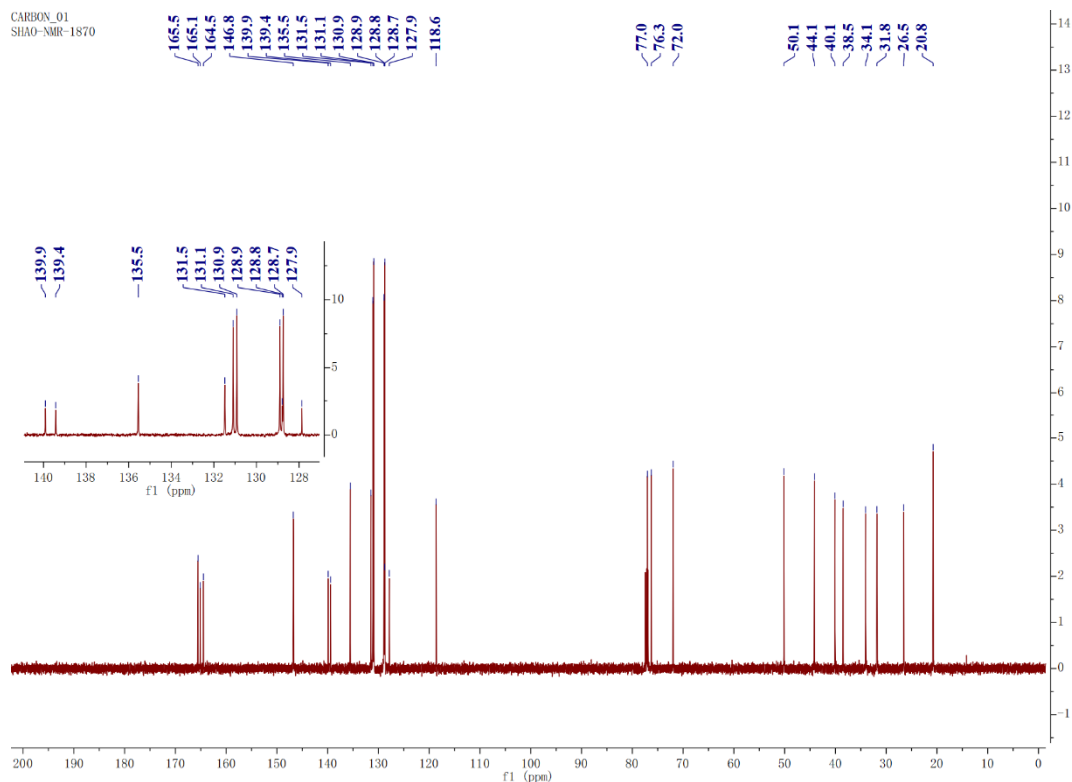


Figure S35. ^{13}C NMR (125 MHz, CDCl_3) spectrum of compound **12**.

CHNQD-01217 #17 RT: 0.20 AV: 1 NL: 2.37E5
T: FTMS + p ESI Full ms [100.0000-1500.0000]

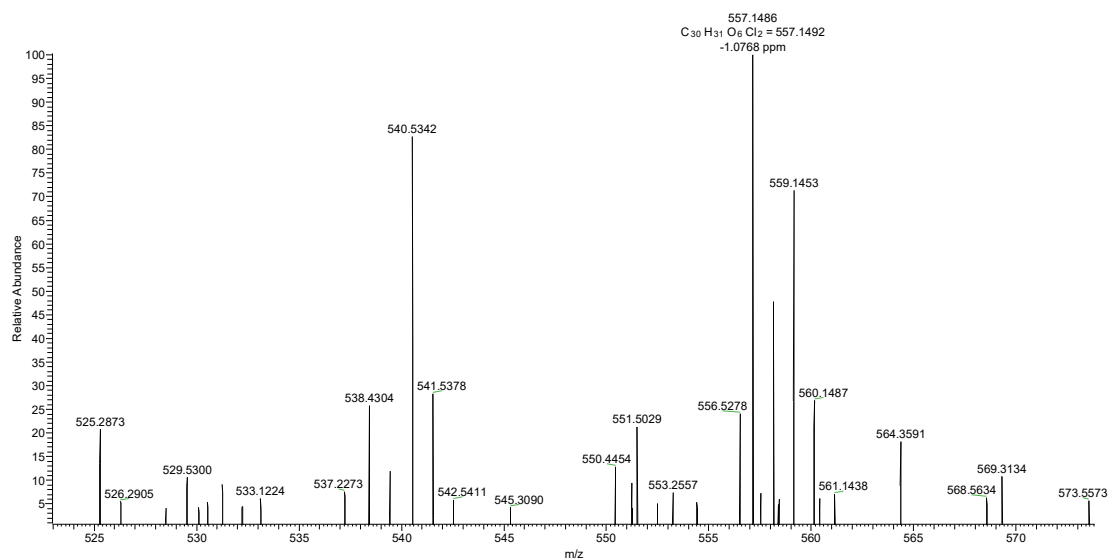


Figure S36. HRESIMS spectrum of compound **12**.

Brefeldin A 7-O-2-chloro-4-fluorobenzoate (13)

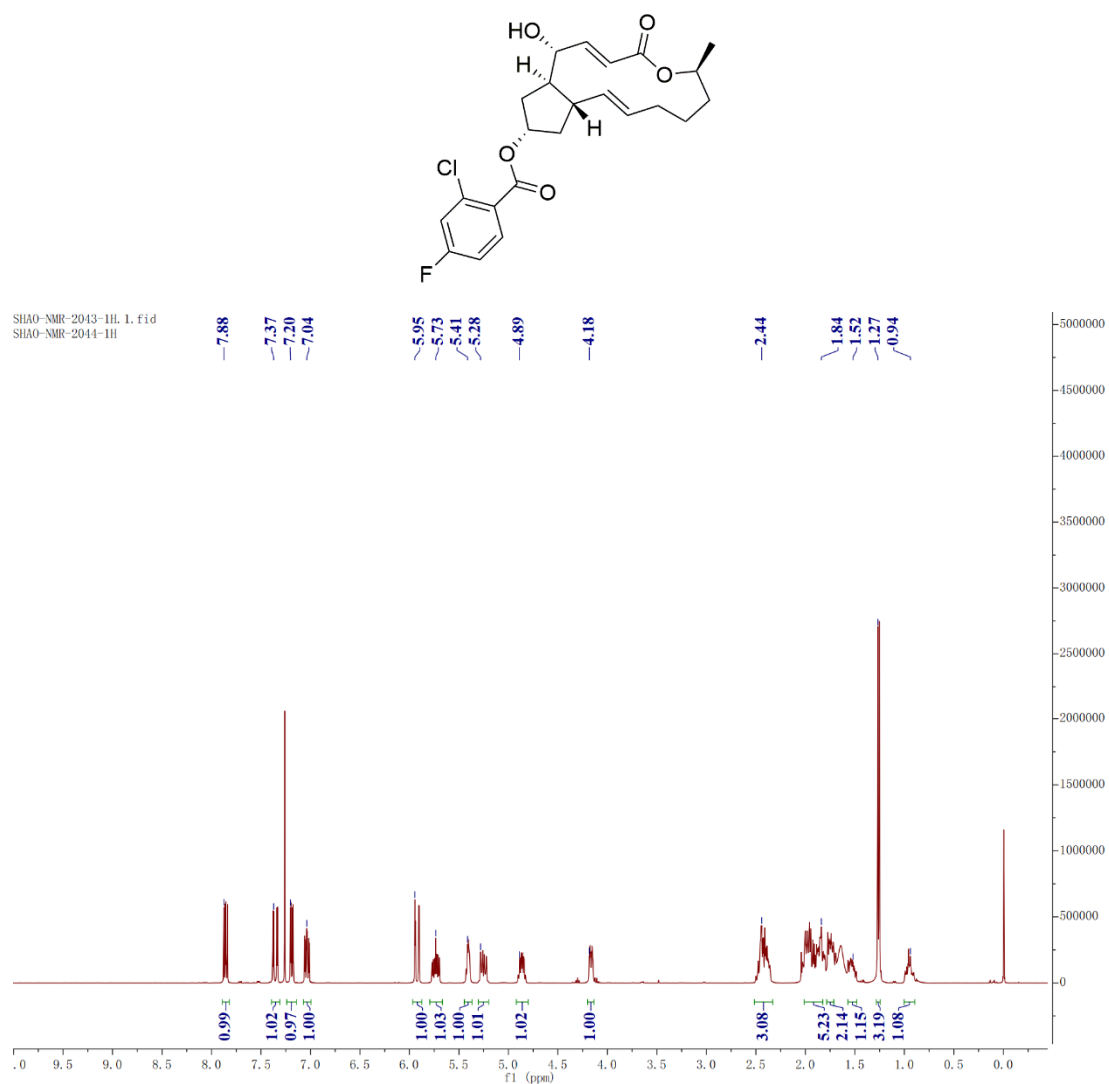


Figure S37. ^1H NMR (400 MHz, CDCl_3) spectrum of compound **13**.

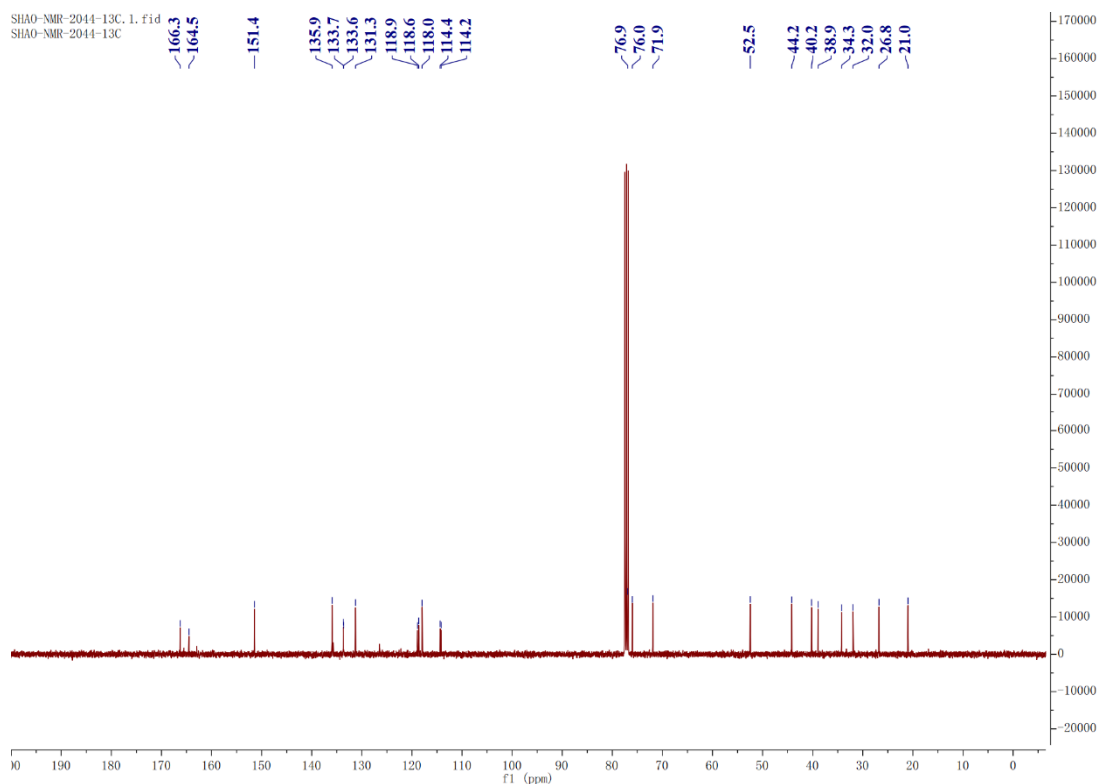


Figure S38. ^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **13**.

CHNQD-01297 #13 RT: 0.16 AV: 1 NL: 8.76E6
T: FTMS + p ESI Full ms [100.0000-1500.0000]

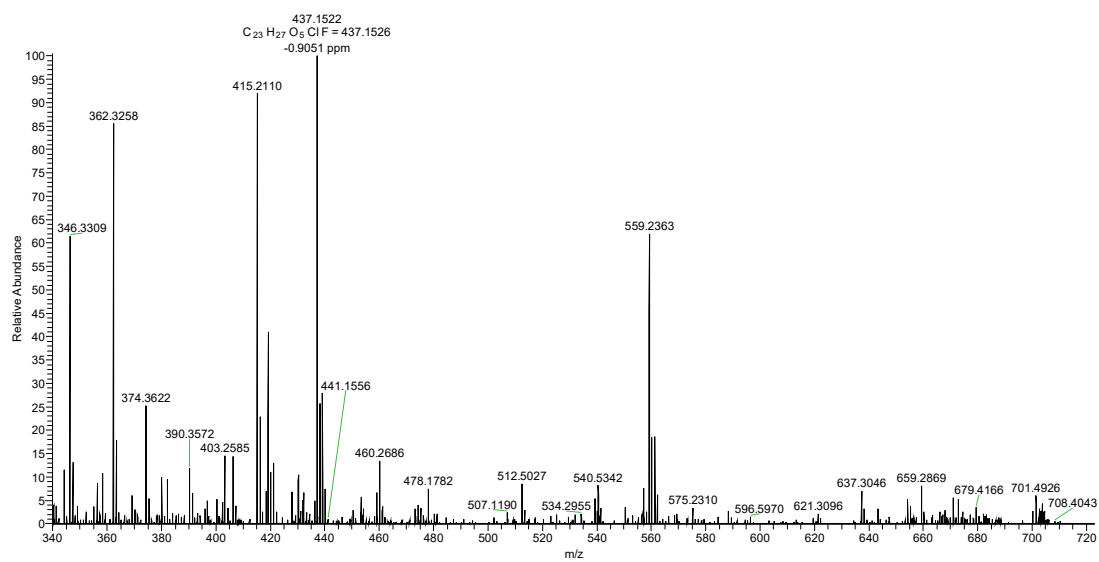


Figure S39. HRESIMS spectrum of compound **13**.

Brefeldin A 4-O-2-chloro-4-fluorobenzoate (14)

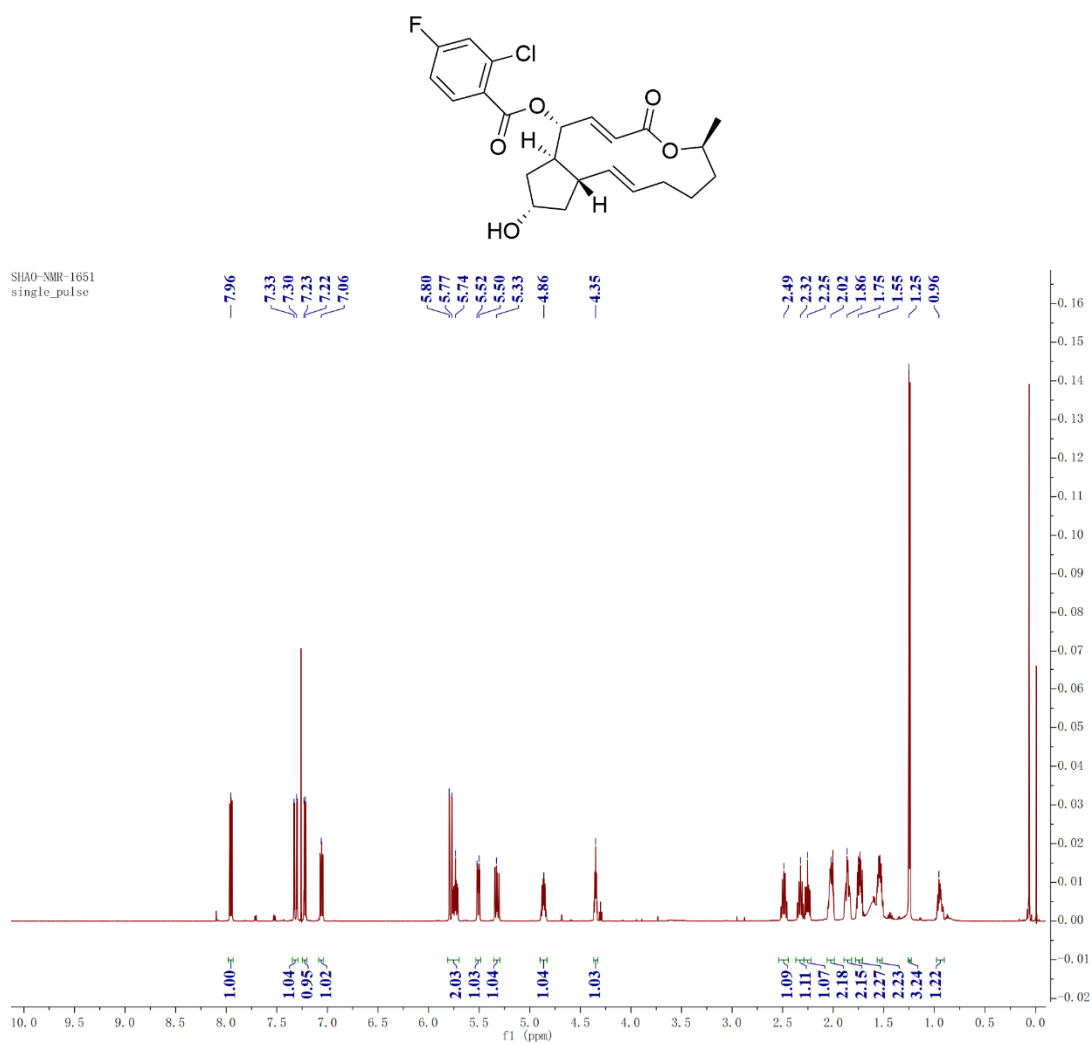


Figure S40. ¹H NMR (600 MHz, CDCl₃) spectrum of compound **14**.

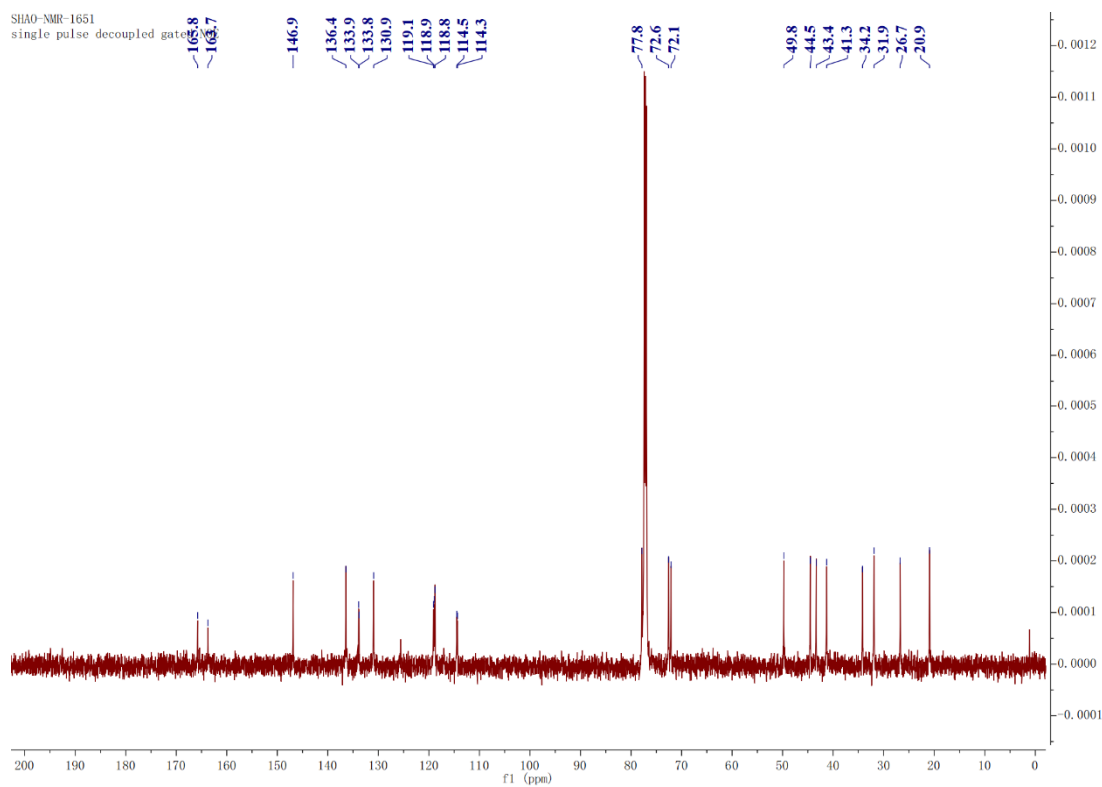


Figure S41. ^{13}C NMR (150 MHz, CDCl_3) spectrum of compound **14**.

14_200119191355 #443 RT: 4.33 AV: 1 NL: 5.23E7
T: FTMS + p ESI Full ms [100.0000-1500.0000]

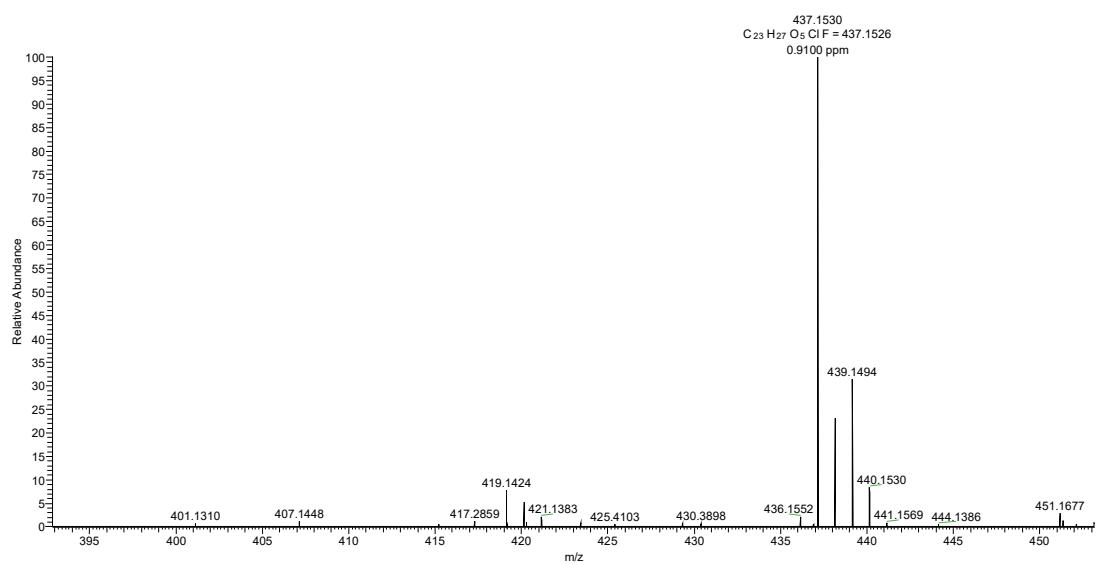


Figure S42. HRESIMS spectrum of compound **14**.

Brefeldin A 4,7-O-di-2-chloro-4-fluorobenzoate (15)

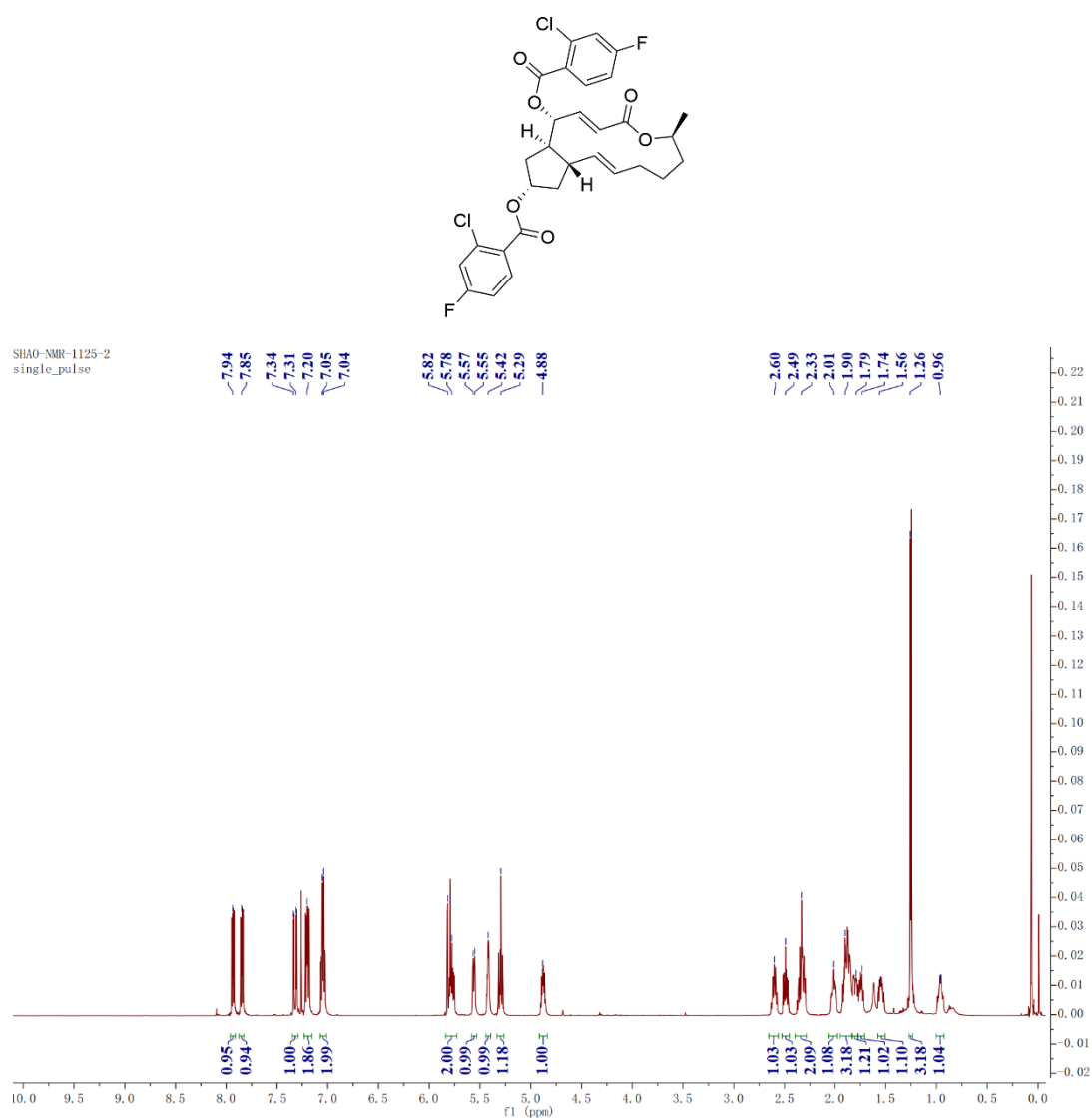


Figure S43. ^1H NMR (600 MHz, CDCl_3) spectrum of compound **15**.

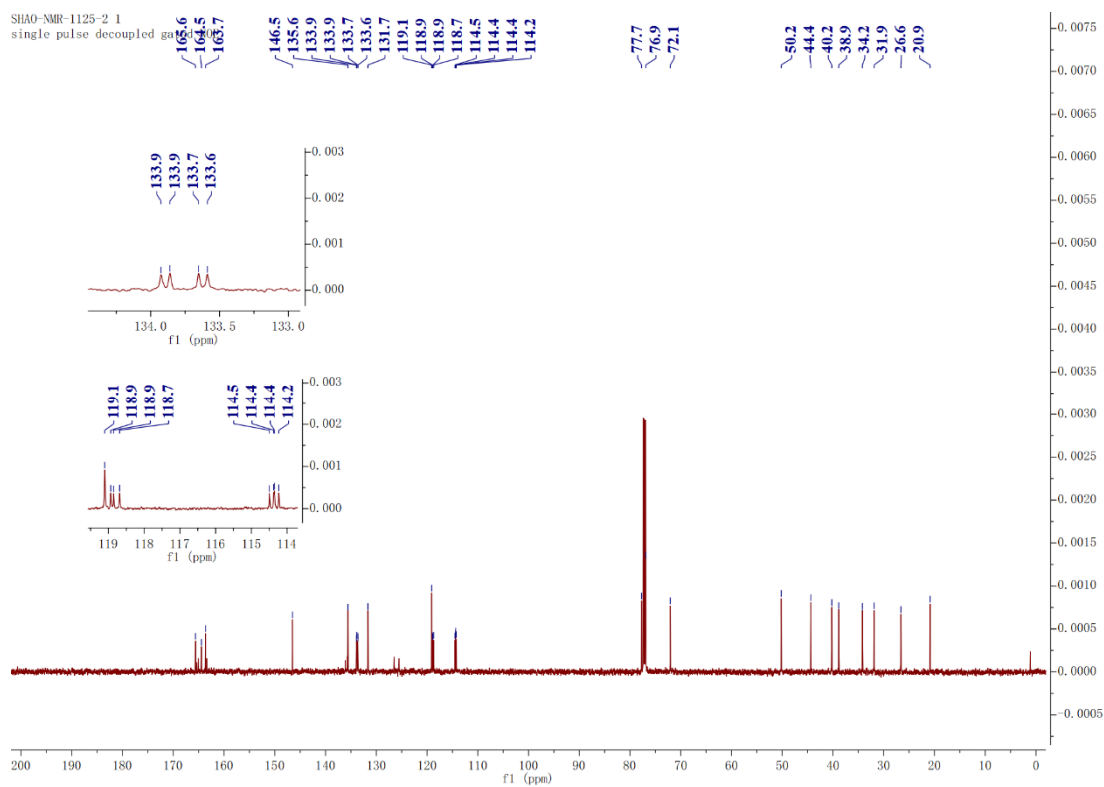


Figure S44. ^{13}C NMR (150 MHz, CDCl_3) spectrum of compound **15**.

CHNQD-01246 #13 RT: 0.16 AV: 1 NL: 2.01E5
T: FTMS + p ESI Full ms [100.0000-1500.0000]

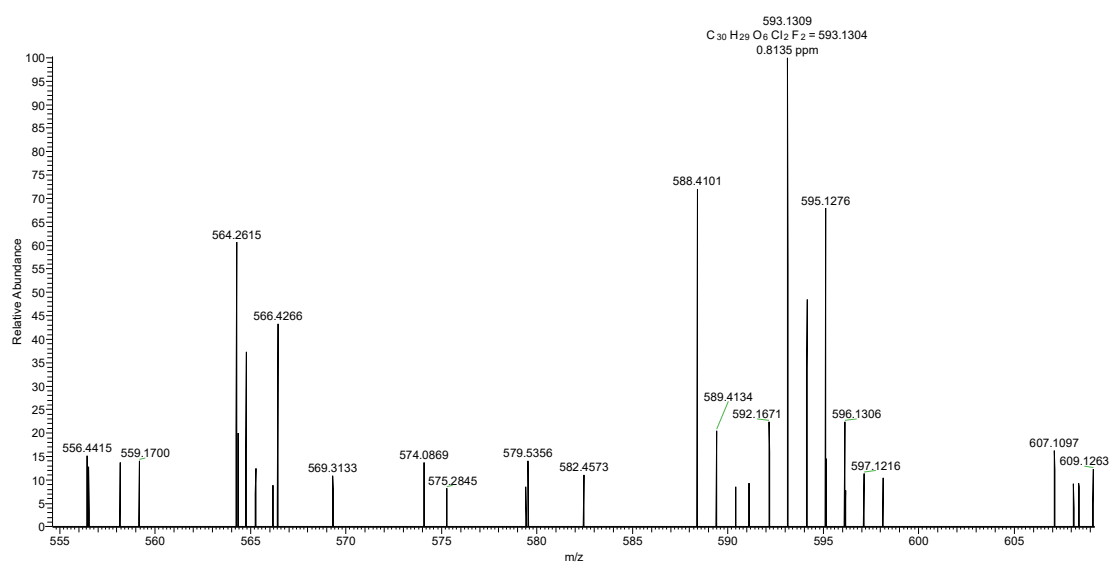


Figure S45. HRESIMS spectrum of compound **15**.

Brefeldin A 7-O-(2,4,6)-trichlorobenzoate (16)

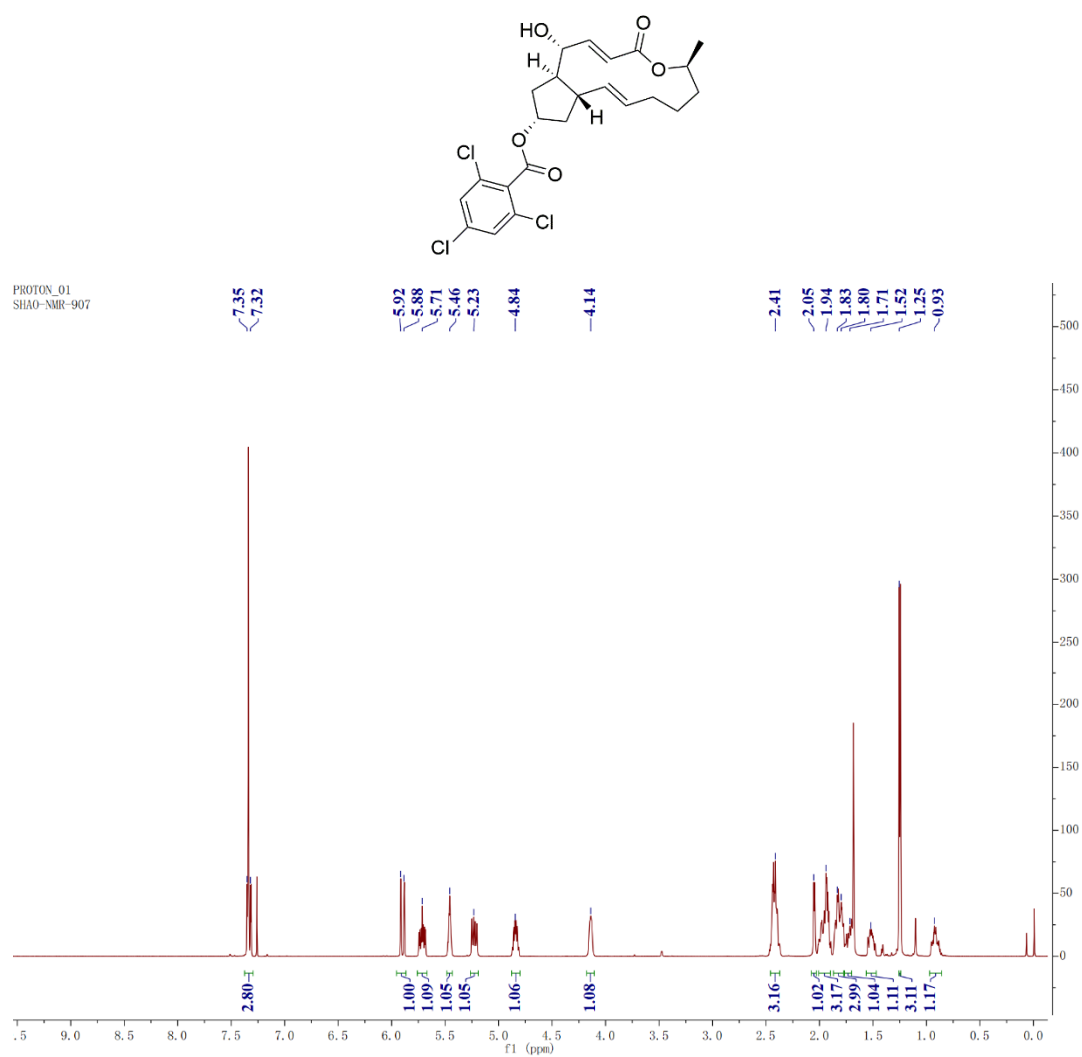


Figure S46. ¹H NMR (500 MHz, CDCl₃) spectrum of compound 16.

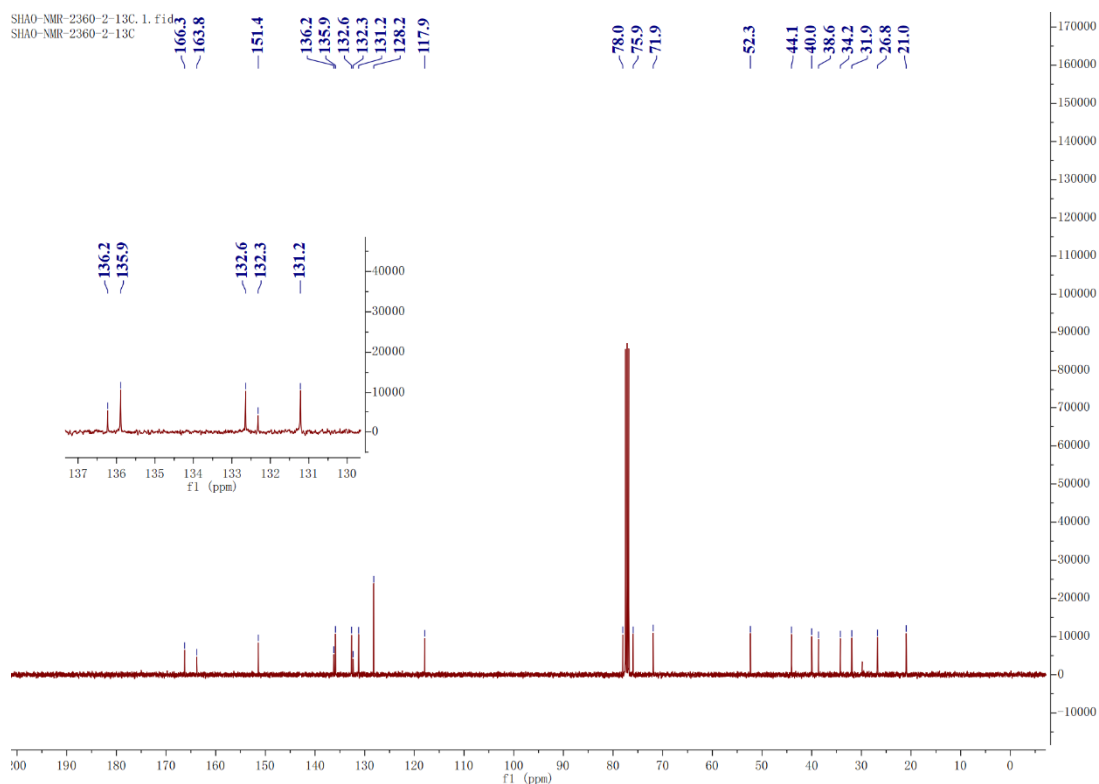


Figure S47. ^{13}C NMR (100 MHz, CDCl_3) spectrum of compound **16**.

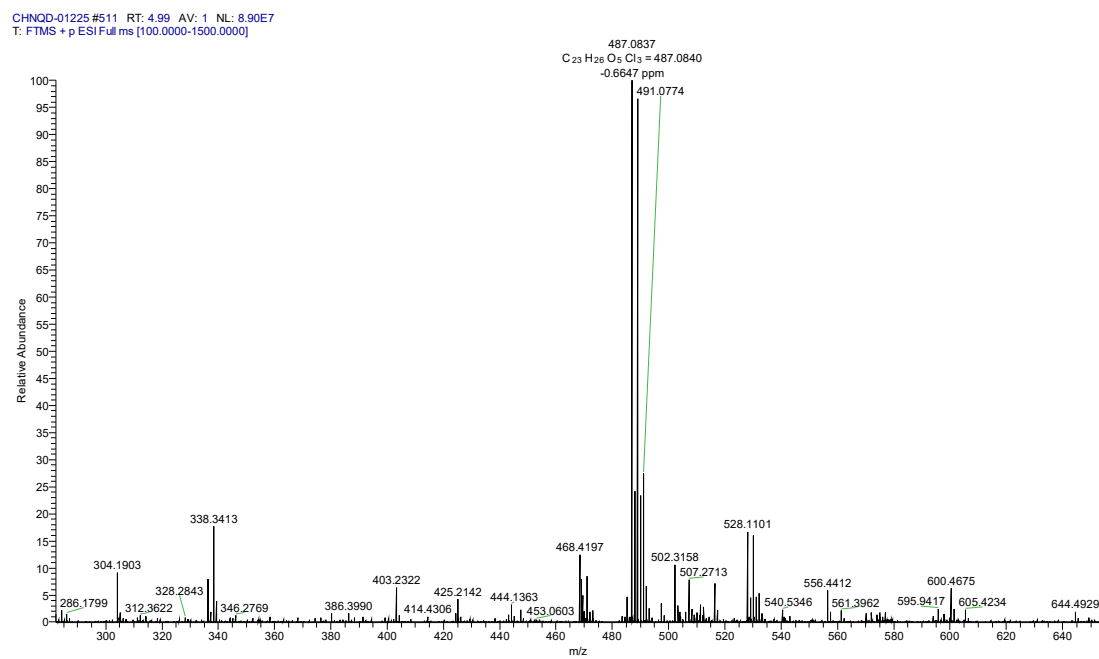


Figure S48. HRESIMS spectrum of compound **16**.