

Synthesis and evaluation of neuroprotective 4-*O*-substituted chrysotoxine derivatives as potential multi-functional agents for the treatment of Alzheimer's disease

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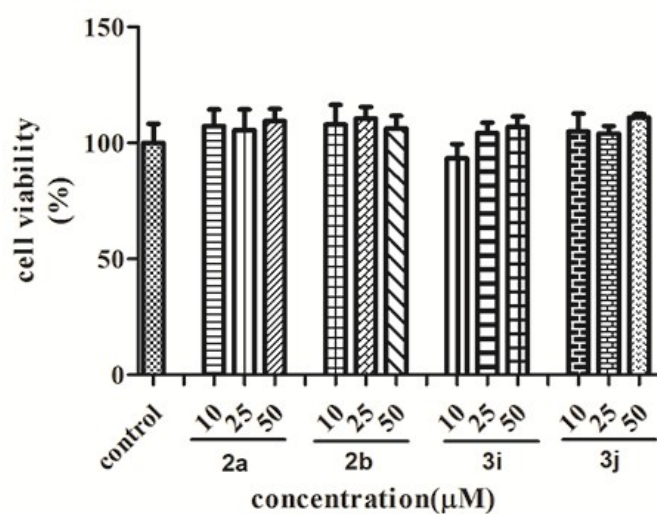


Fig S1 Effects of **2a**, **2b**, **3i** and **3j** on A β_{25-35} -untreated normal PC12 cells for 24 h. Data were the means $\pm$ SD expressed as percentages of control group. Results are the mean of 3 independent experiments in triplicate. Their cell viability does not have significant difference compared to control group (ANOVA followed by Newman-Keuls Test).

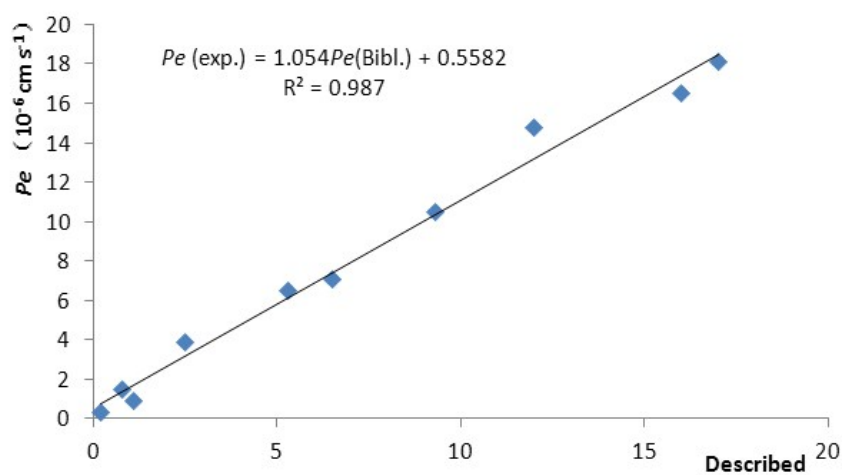


Fig S2 Linear correlation between the experimental and the reported permeabilities ¹of commercial drugs using the PAMPA-BBB assay. $Pe \text{ (exp.)} = 1.054Pe(\text{Bibl.}) + 0.5582$ ($R^2 = 0.987$)

¹ L. Di, E. H. Kerns, K. Fan, O. J. McConnell and G. T. Carter, *Euro. J. Med. Chem.*, 2003, **38**, 223-232

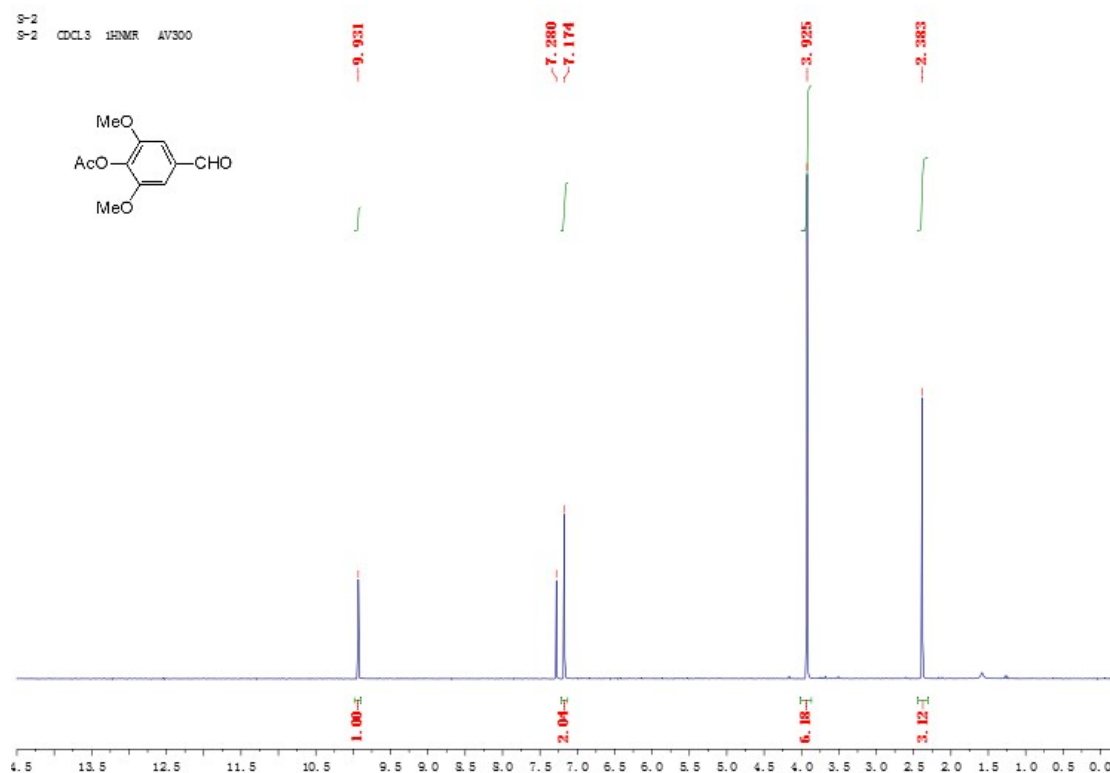


Fig S3.1.1 ¹H-NMR spectrum of compound **3** (300 MHz, CDCl₃)

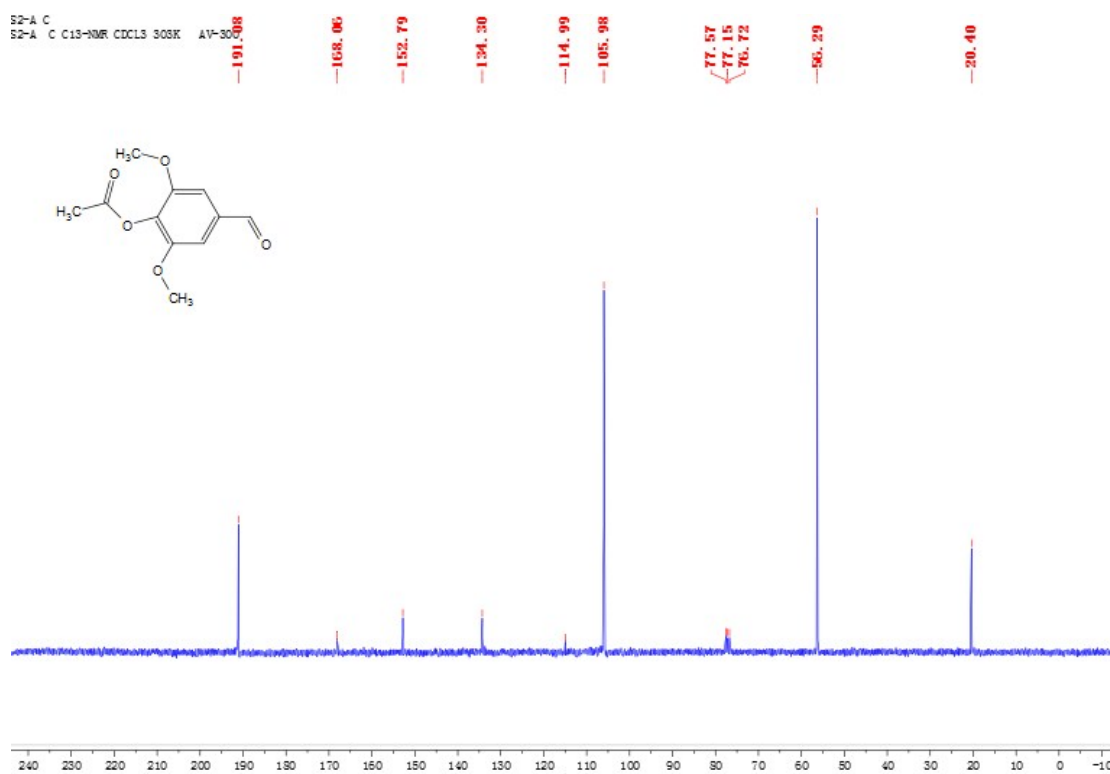


Fig S3.1.2 ¹³C-NMR spectrum of compound 3 (75 MHz, CDCl₃)

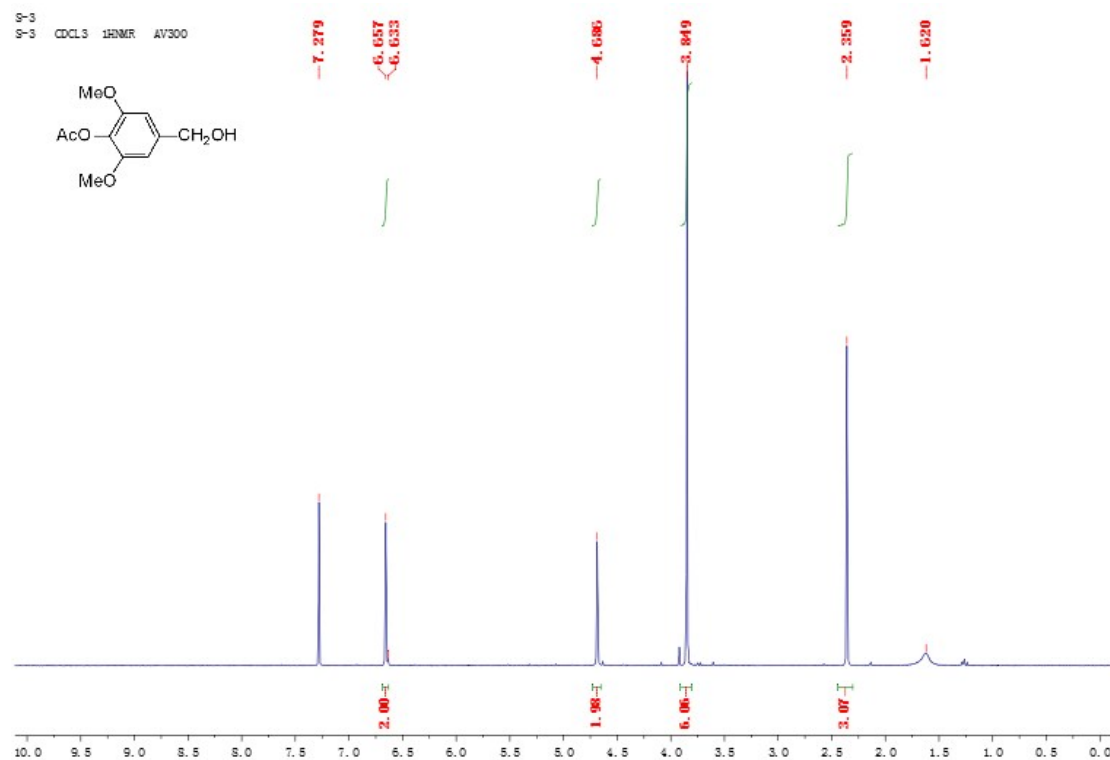


Fig S3.2.1 ¹H-NMR spectrum of compound 4 (300 MHz, CDCl₃)

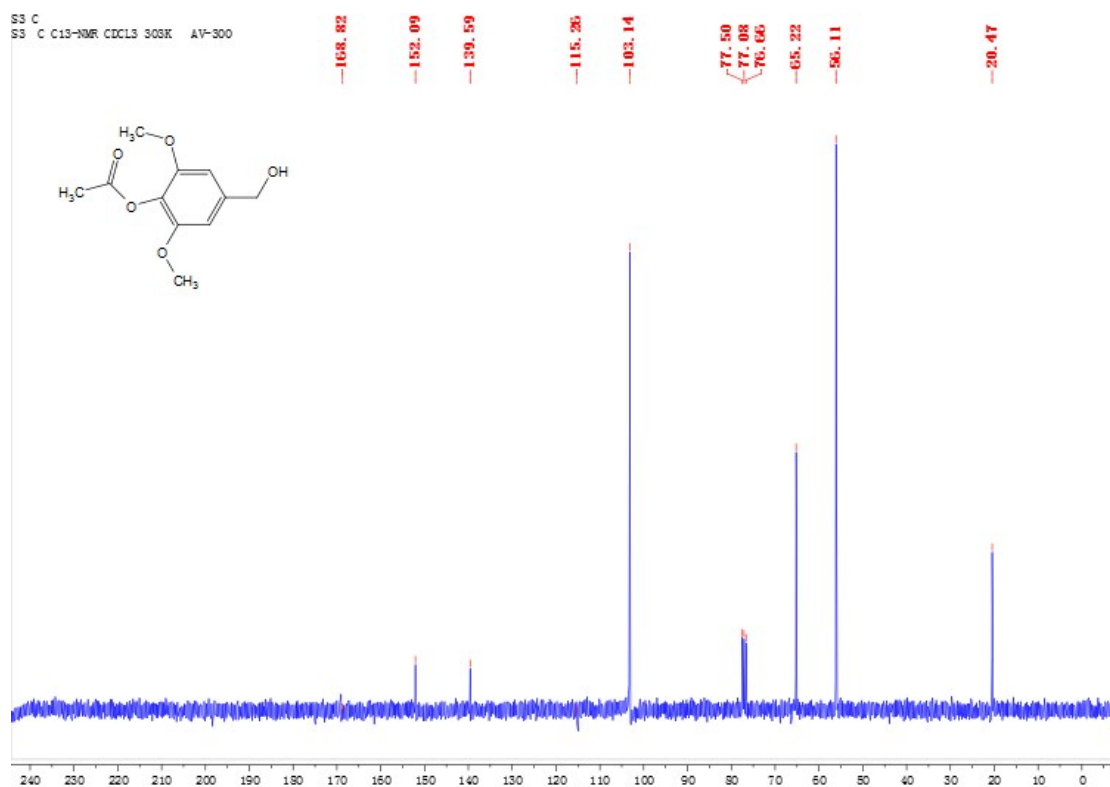


Fig S3.2.2 ^{13}C -NMR spectrum of compound 4 (75 MHz, CDCl_3)

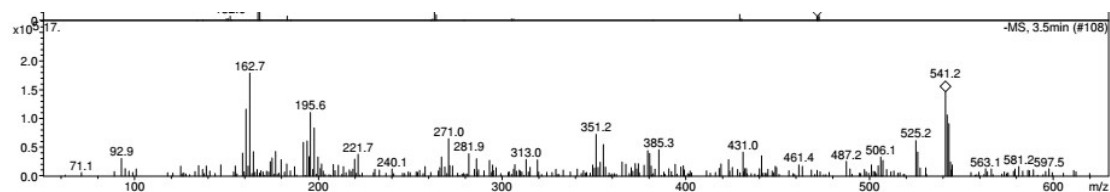


Fig S3.3.1 ESI-MS spectrum of compound 6

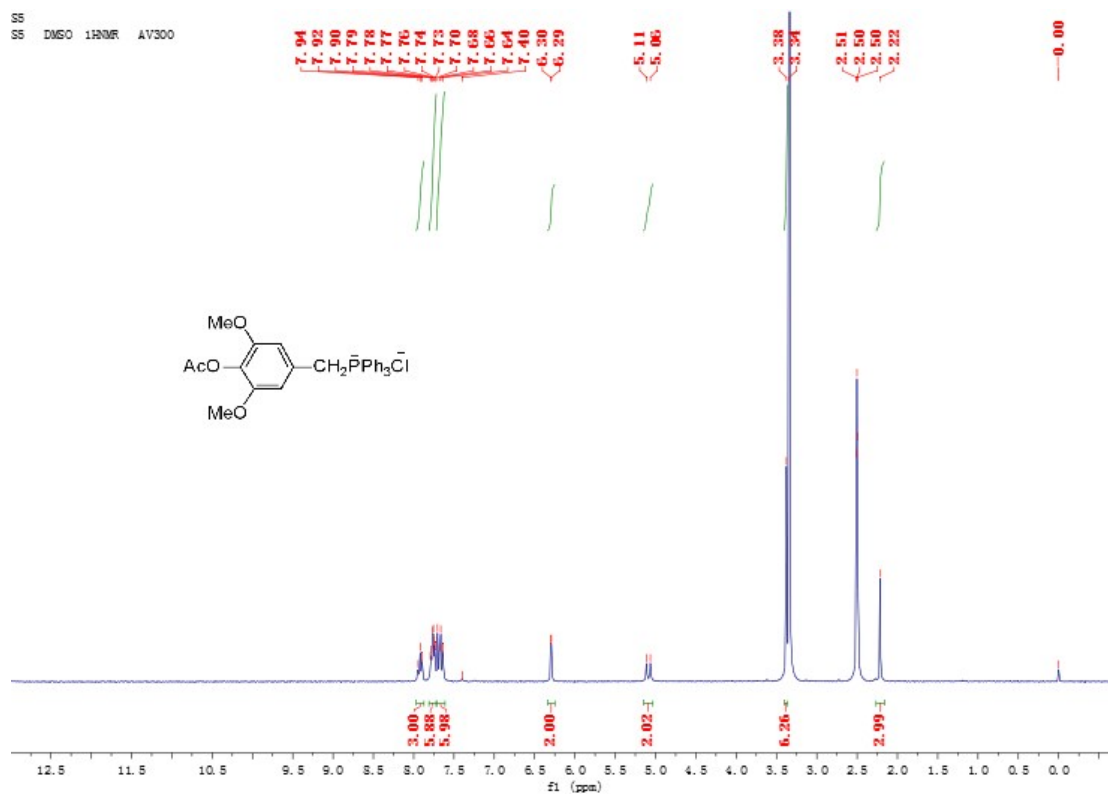


Fig S3.3.2 ^1H -NMR spectrum of compound **6** (300MHz, DMSO)

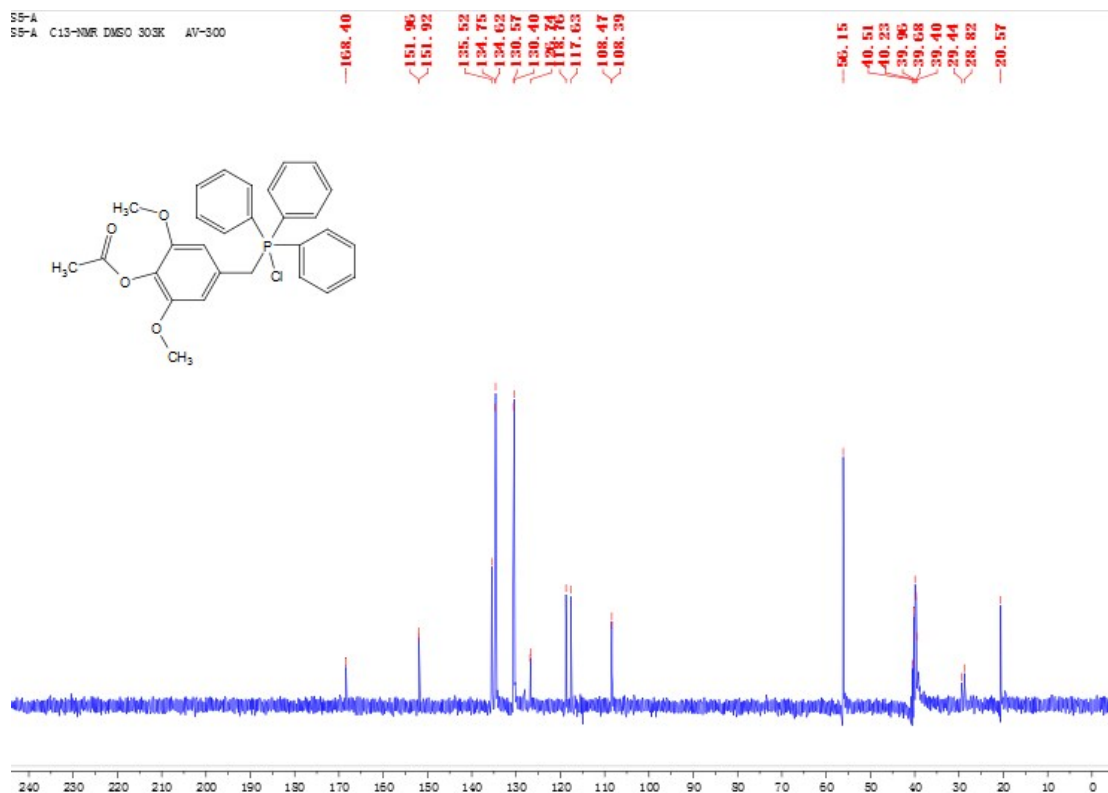


Fig S3.3.3 ^{13}C -NMR spectrum of compound **6** (75 MHz, CDCl_3)

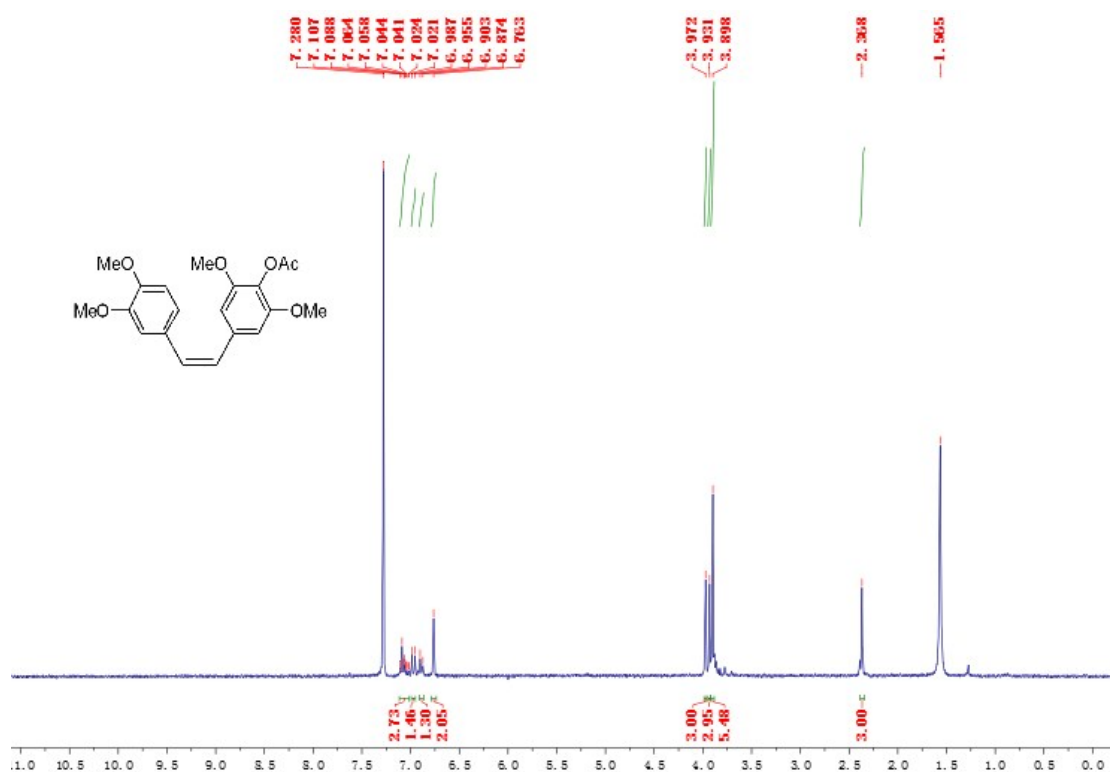


Fig S3.4.1 ¹H-NMR spectrum of compound 7(Z) (300MHz, CDCl₃)

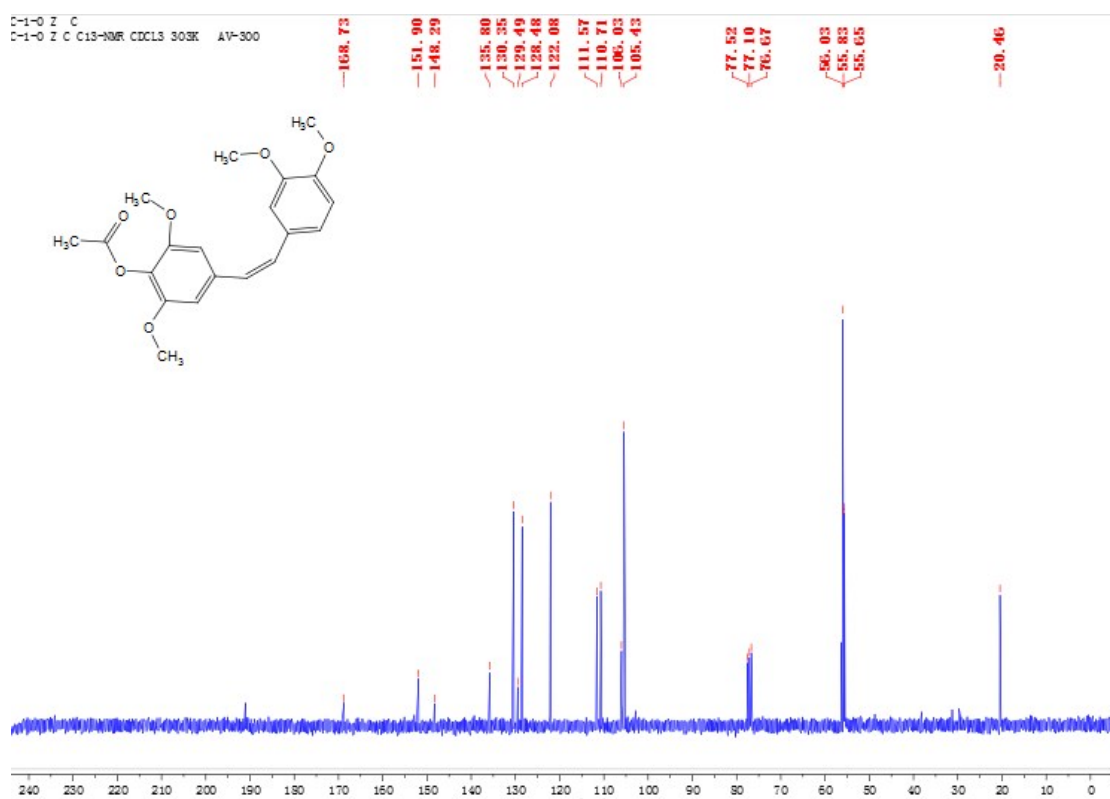


Fig S3.4.2 ¹³C-NMR spectrum of compound 7(Z) (75 MHz, CDCl₃)

ZZ-3
ZZ-3 CDC13 1H-NMR AV300

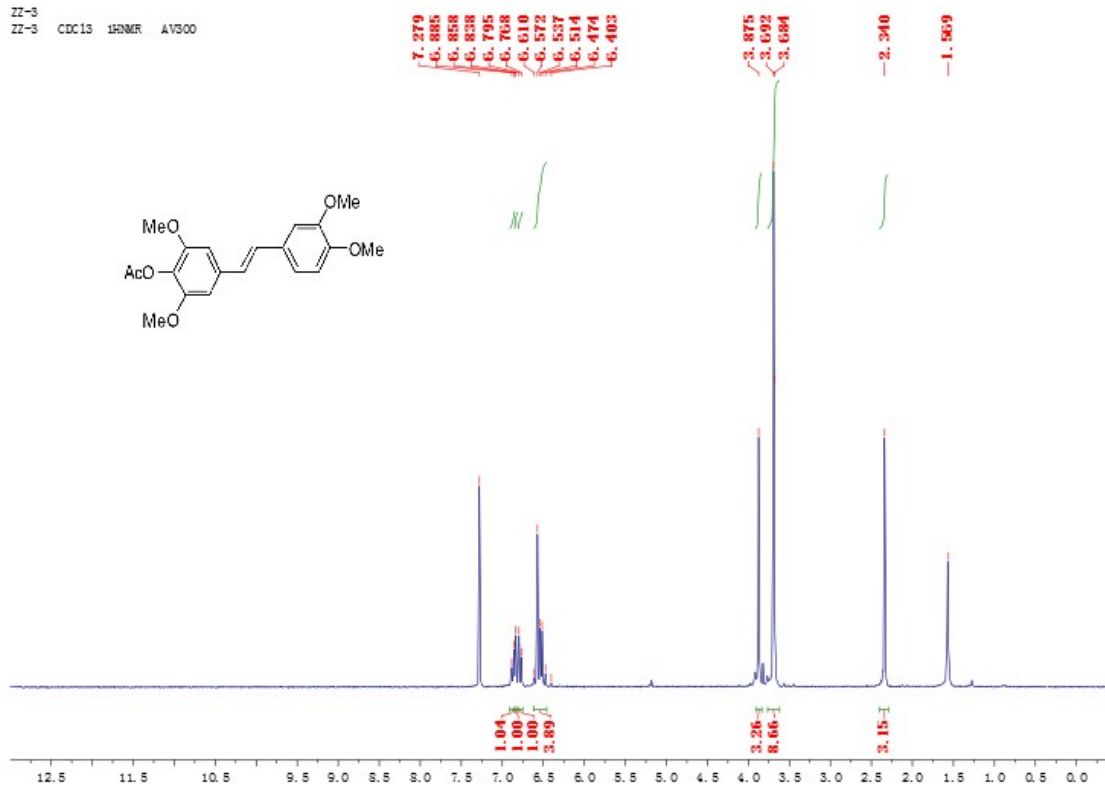


Fig S3.5.1 ¹H-NMR spectrum of compound 7(E) (300MHz, CDCl₃)

C-1-O H C
C-1-O H C C13-NMR CDCL3 303K AV-300

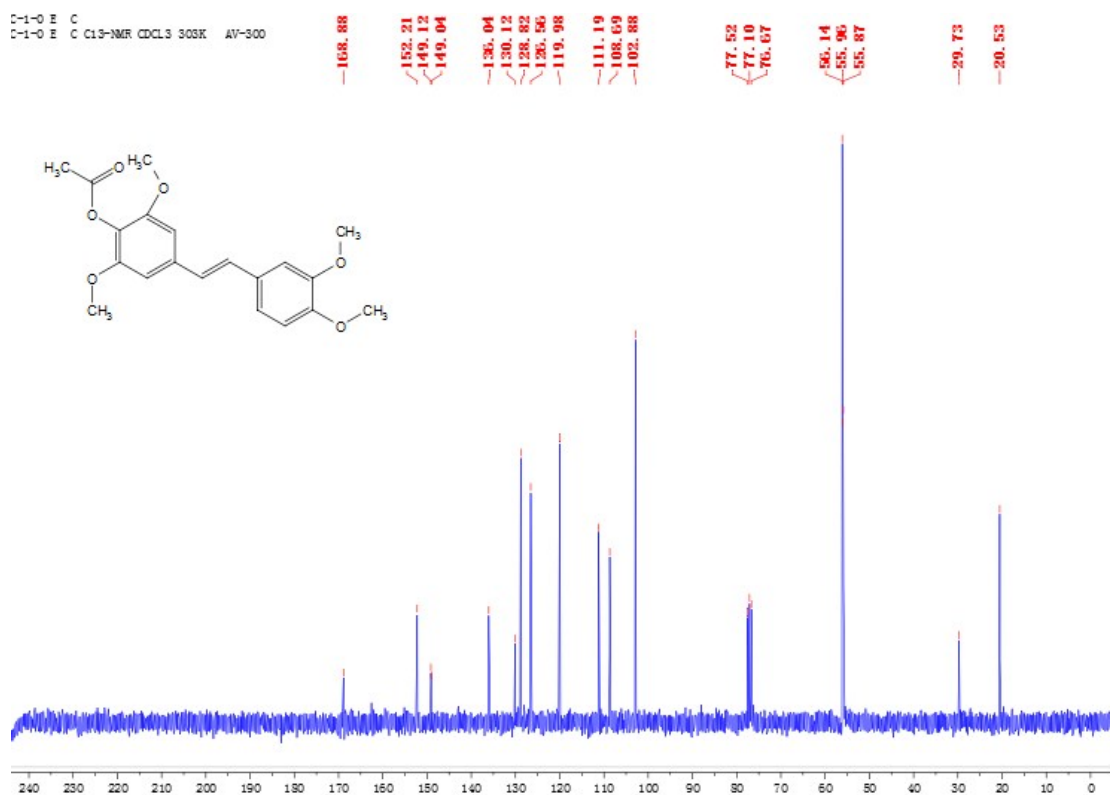


Fig S3.5.2 ¹³C-NMR spectrum of compound 7(E) (75 MHz, CDCl₃)

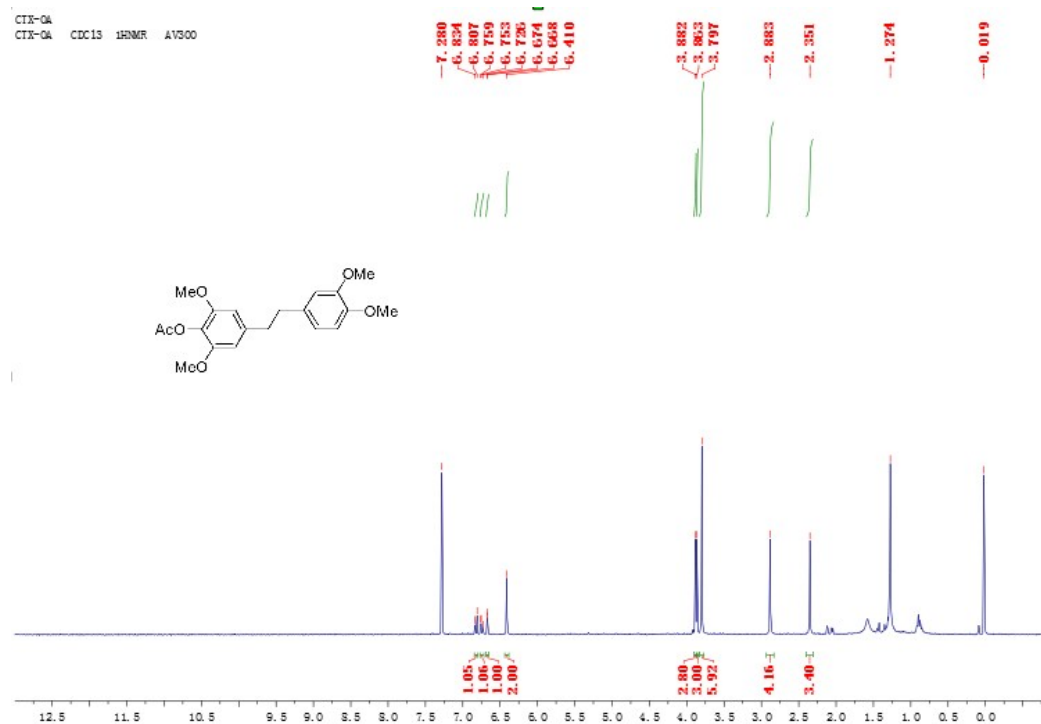


Fig S3.6.1 ¹H-NMR spectrum of compound CTX-0 (300MHz, CDCl₃)

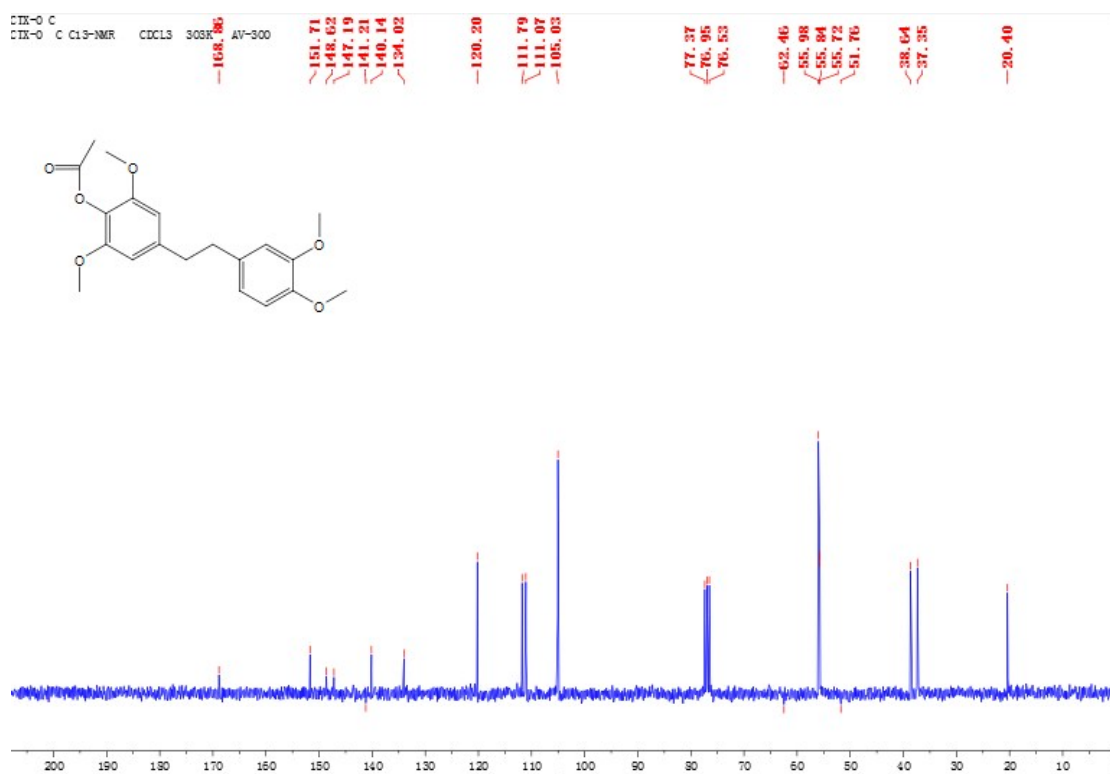


Fig S3.6.2 ¹³C-NMR spectrum of compound CTX-0 (75 MHz, CDCl₃)

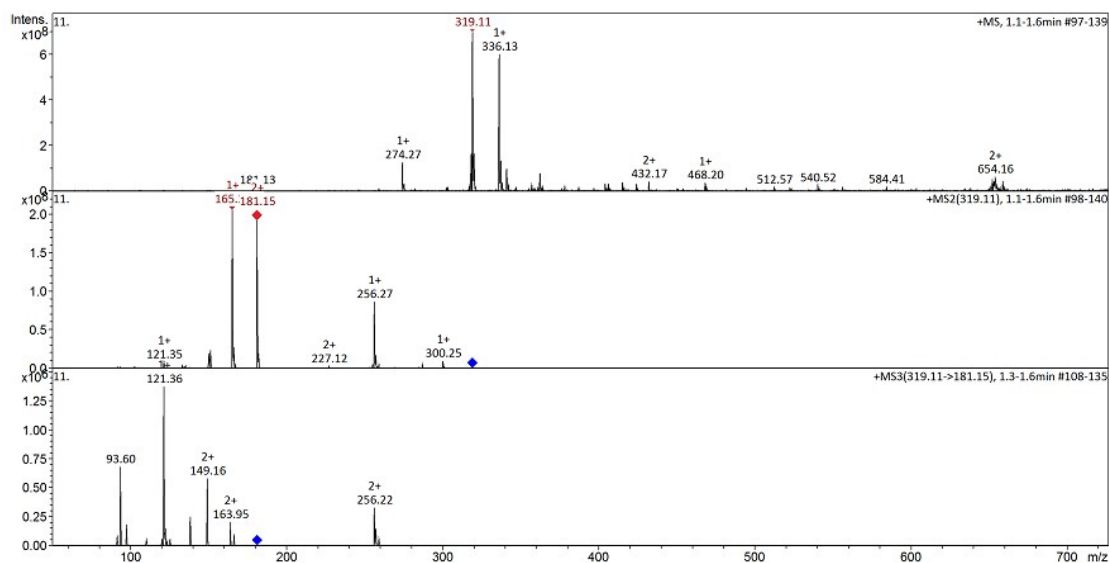


Fig S3.7.1 ESI-MS spectrum of compound CTX

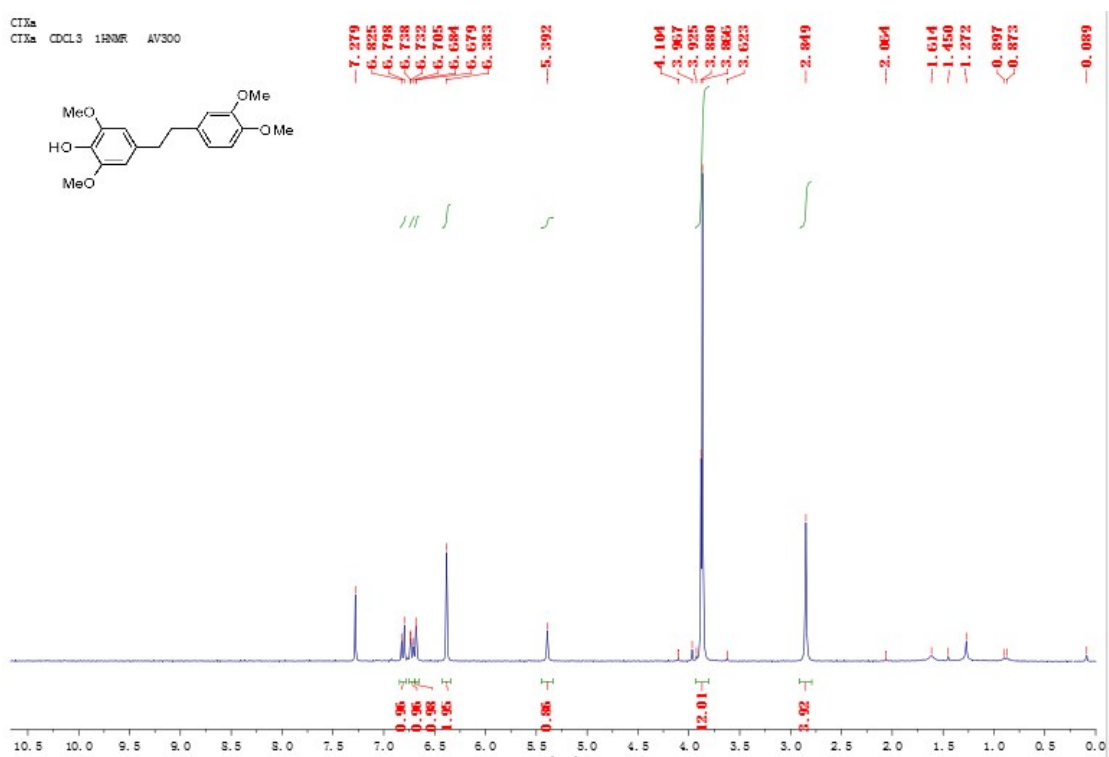


Fig S3.7.2 ^1H -NMR spectrum of compound CTX (300 MHz, CDCl_3)

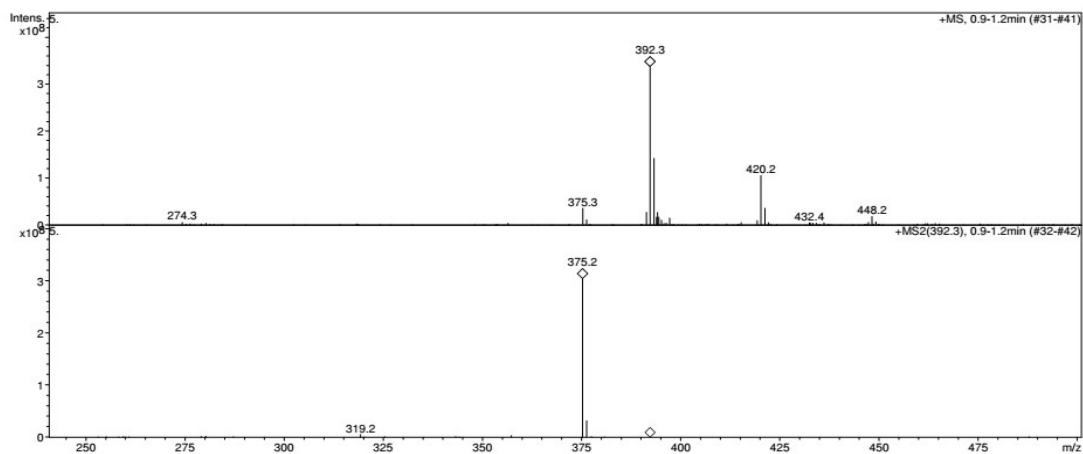


Fig S3.8.1 ESI-MS spectrum of compound **1a**

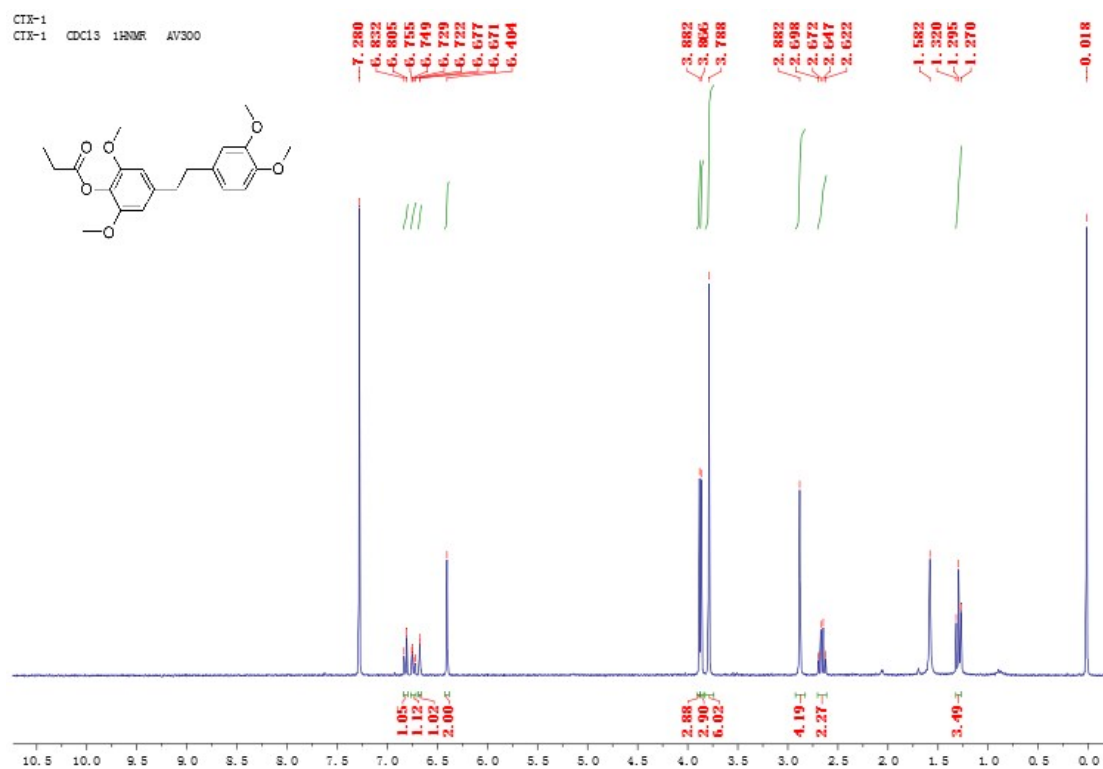


Fig S3.8.2 ¹H-NMR spectrum of compound **1a** (300 MHz, CDCl₃)

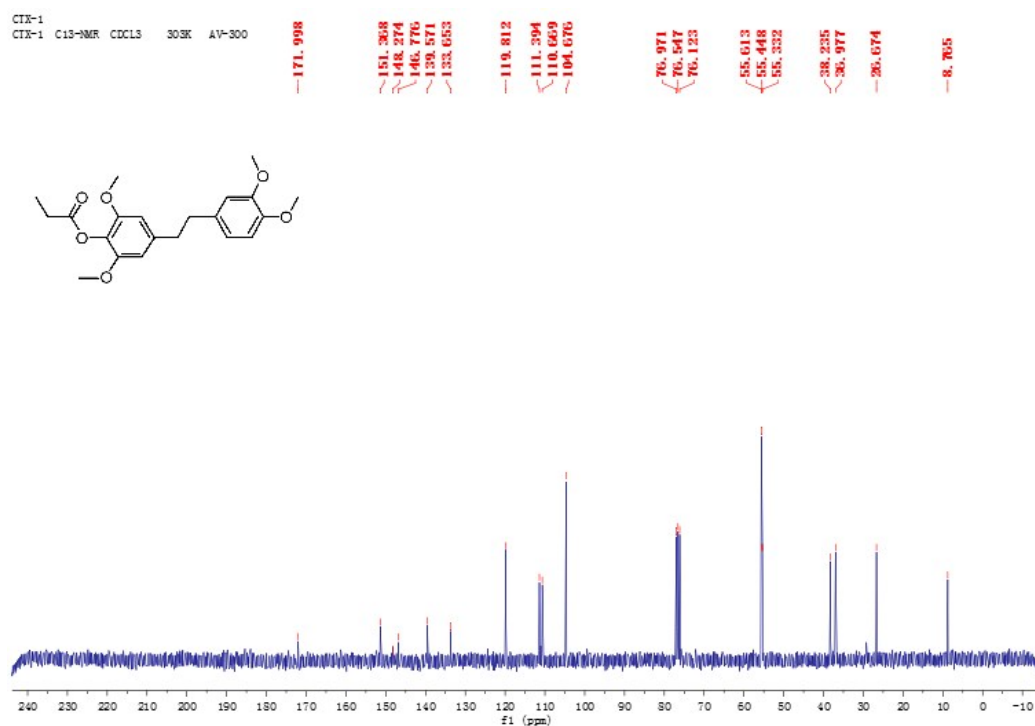


Fig S3.8.3 ¹³C-NMR spectrum of compound 1a (75 MHz, CDCl₃)

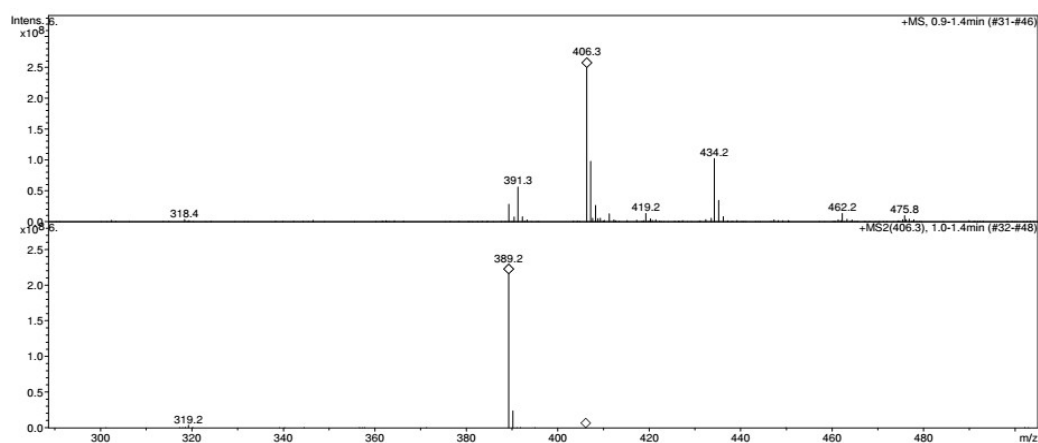


Fig S3.9.1 ESI-MS spectrum of compound 1b

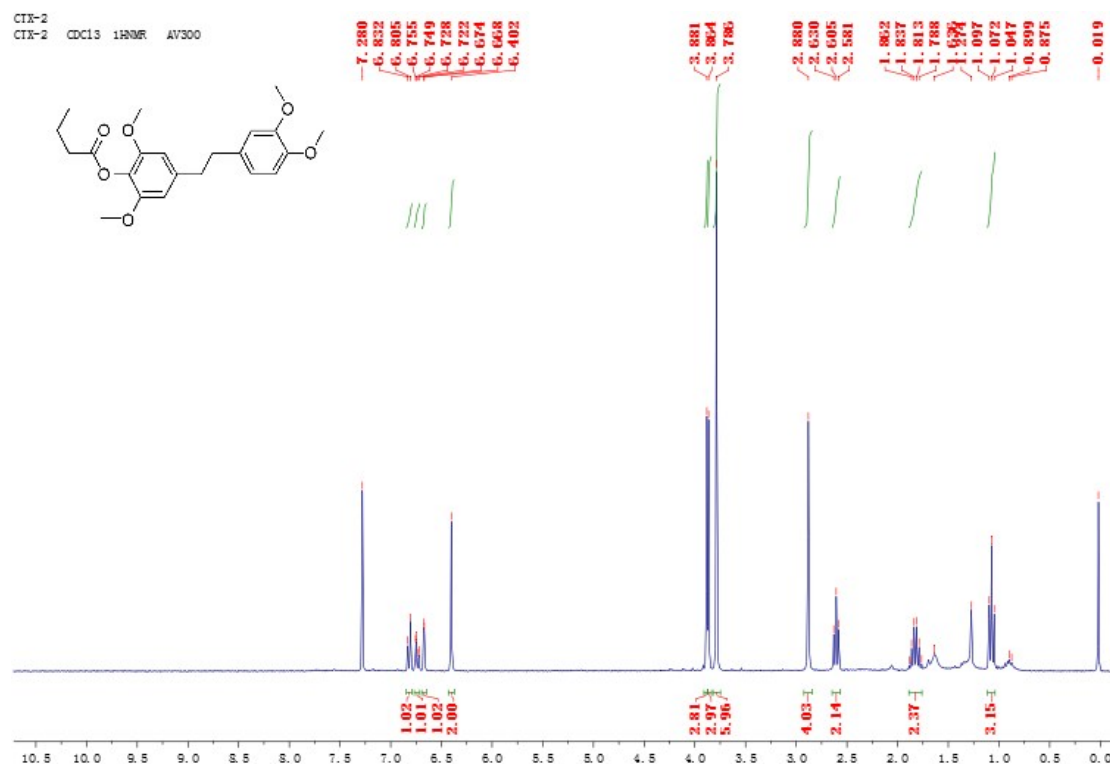


Fig S3.9.2 ¹H-NMR spectrum of compound **1b** (300MHz, CDCl₃)

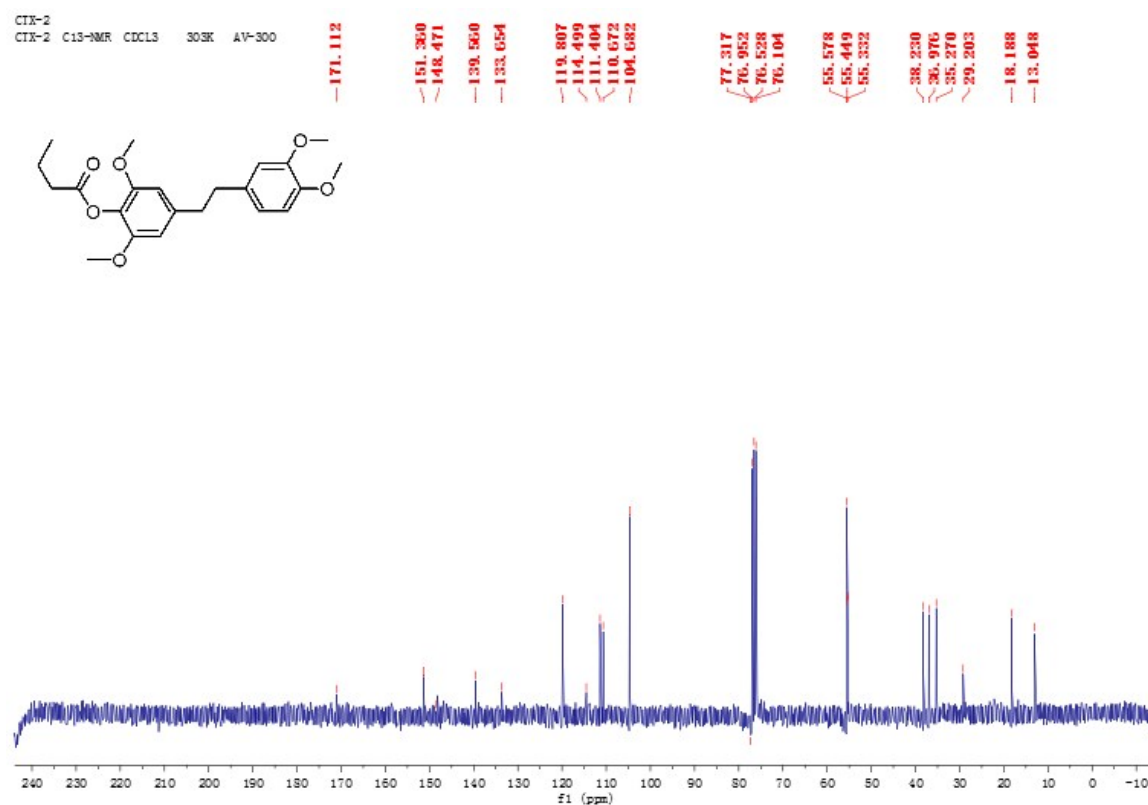


Fig S3.9.3 ¹³C-NMR spectrum of compound **1b** (75 MHz, CDCl₃)

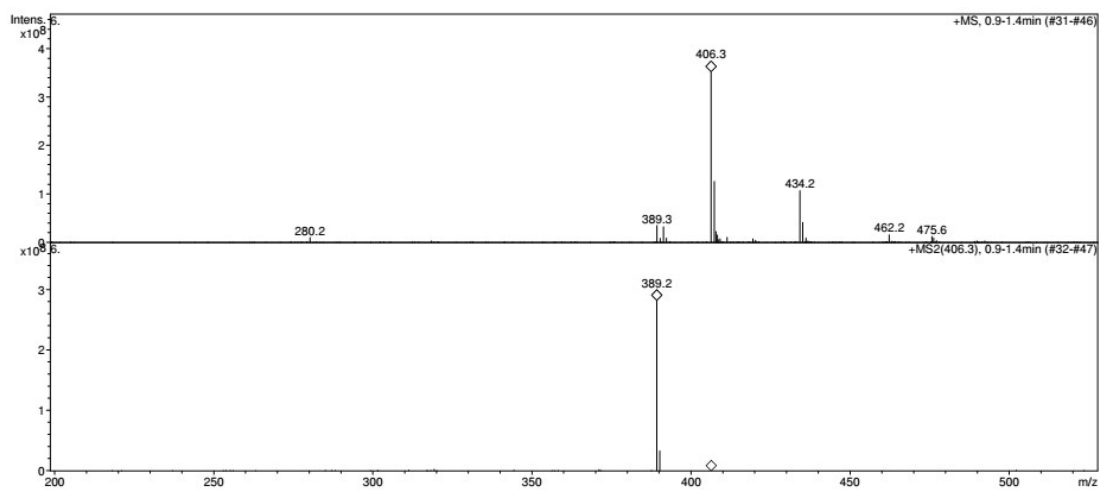


Fig S3.10.1 ESI-MS spectrum of compound **1c**

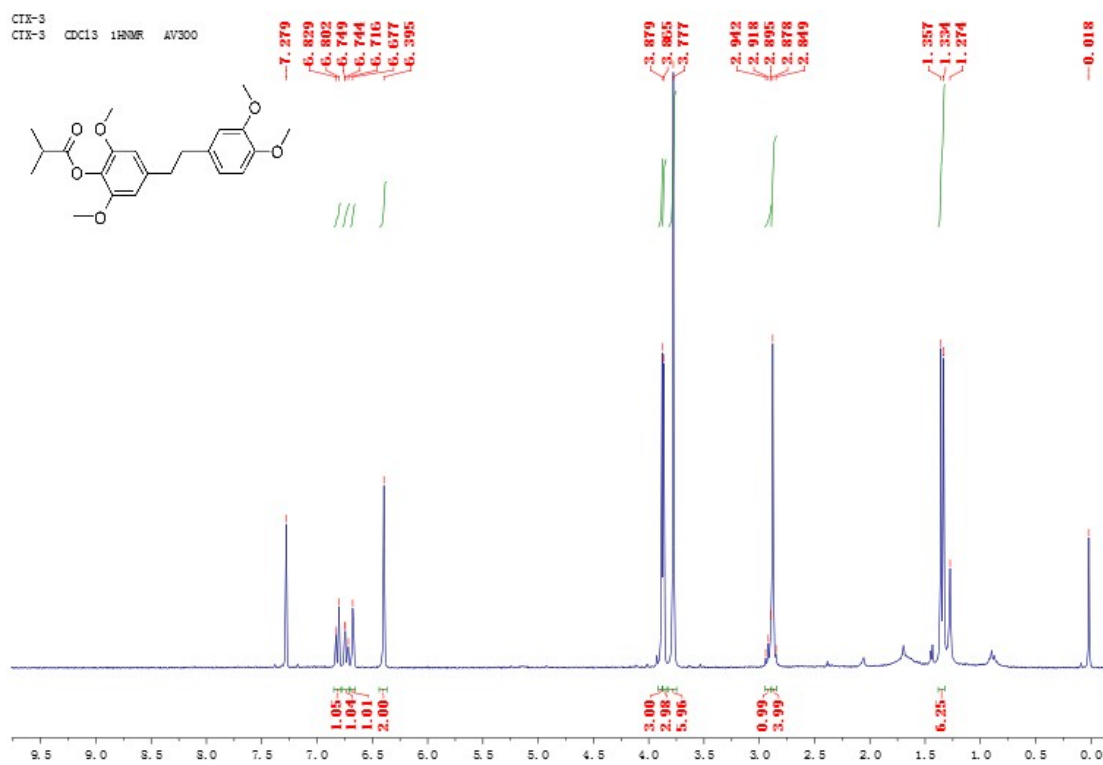
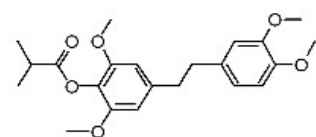


Fig S3.10.2 ^1H -NMR spectrum of compound **1c** (300MHz, CDCl_3)

CTX-3
CTX-3 C13-NMR CDCl3 303K AV-300



174.662

151.424
148.481
146.774
139.440
133.674

119.820
114.528
111.401
110.673
104.751

76.961
76.537
76.114

55.635
55.449
55.325

38.216
36.985
33.360

18.622

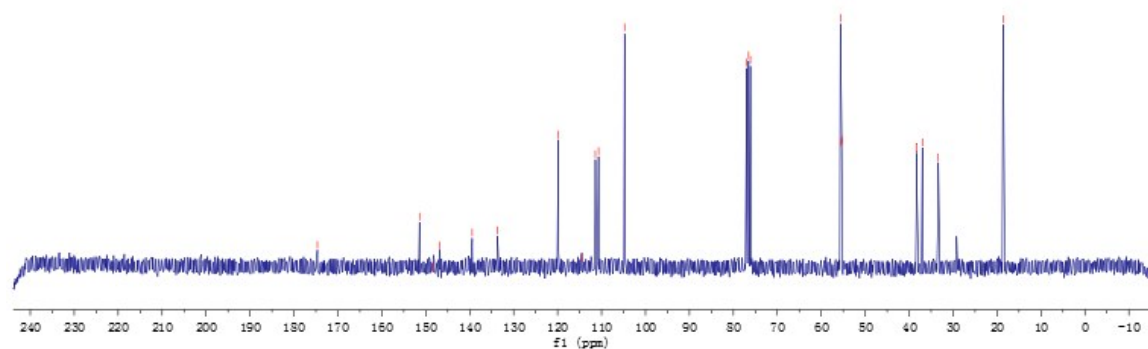


Fig S3.10.3 ¹³C-NMR spectrum of compound 1c (75 MHz, CDCl₃)

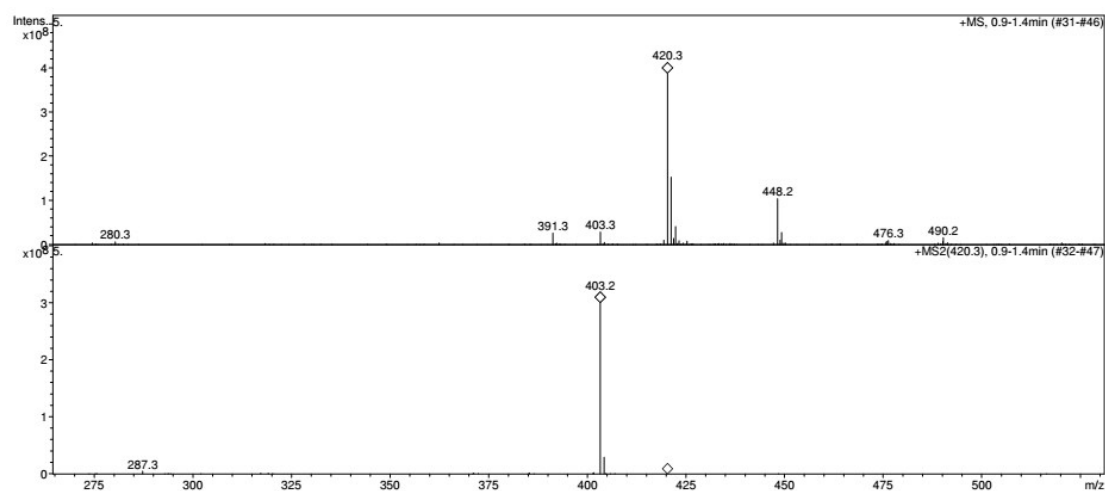


Fig S3.11.1 ESI-MS spectrum of compound 1d

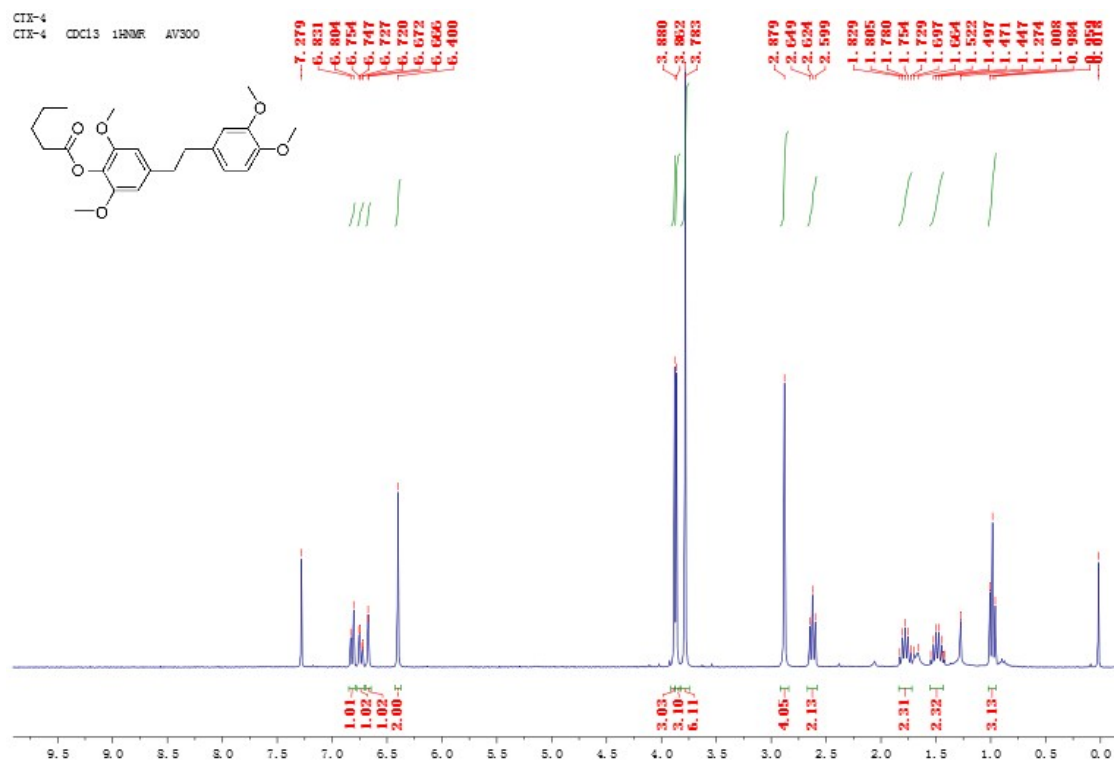


Fig S3.11.2 ¹H-NMR spectrum of compound **1d** (300MHz, CDCl₃)

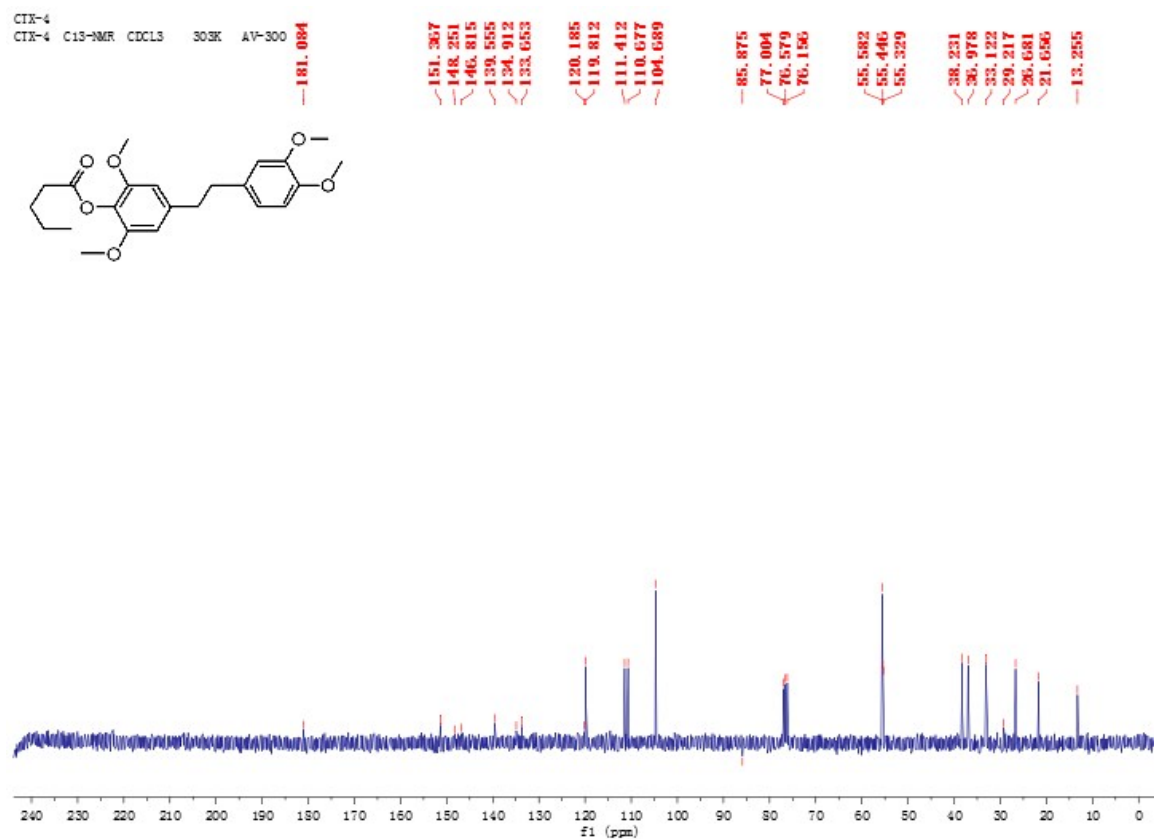


Fig S3.11.3 ¹³C-NMR spectrum of compound **1d** (75 MHz, CDCl₃)

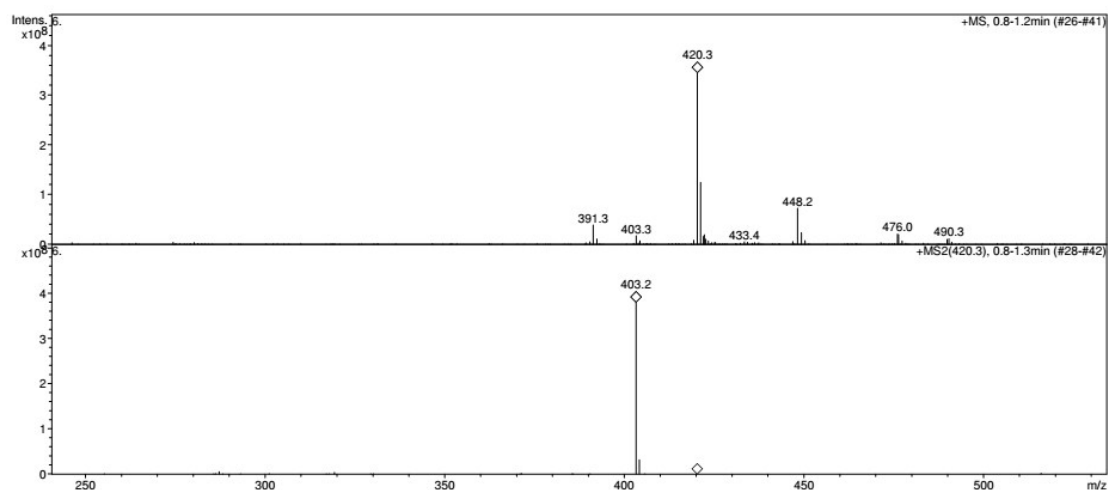


Fig S3.12.1 ESI-MS spectrum of compound **1e**

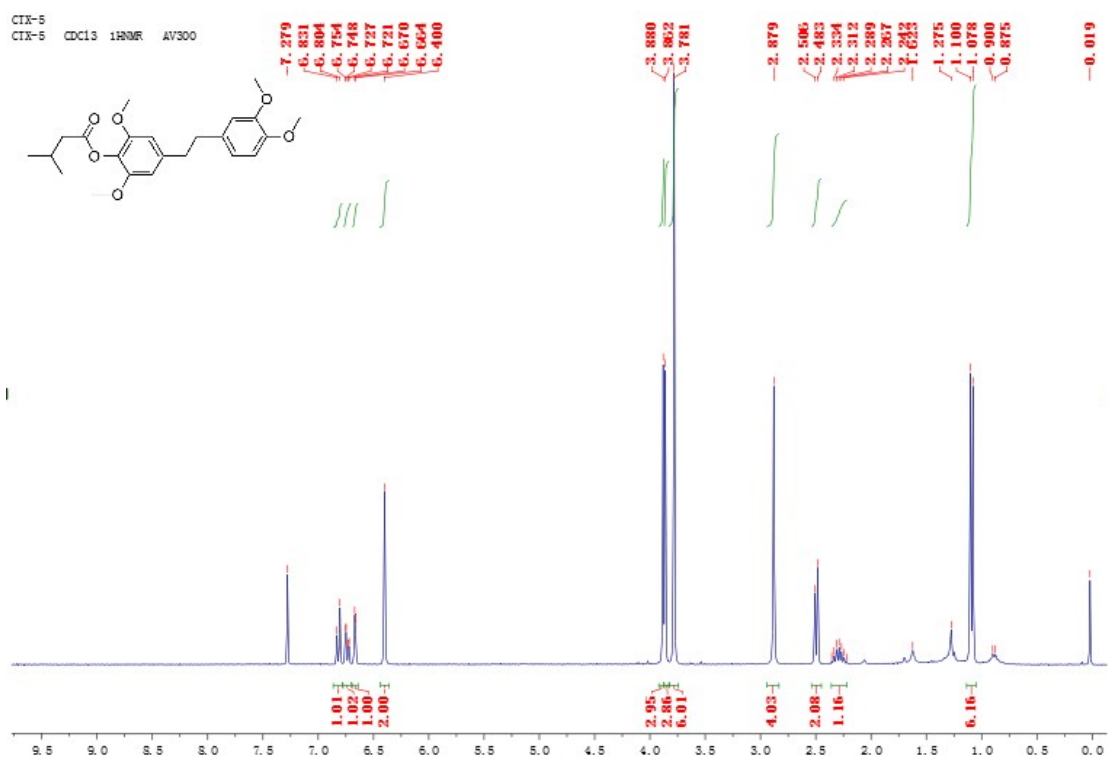


Fig S3.12.2 ^1H -NMR spectrum of compound **1e** (300MHz, CDCl_3)

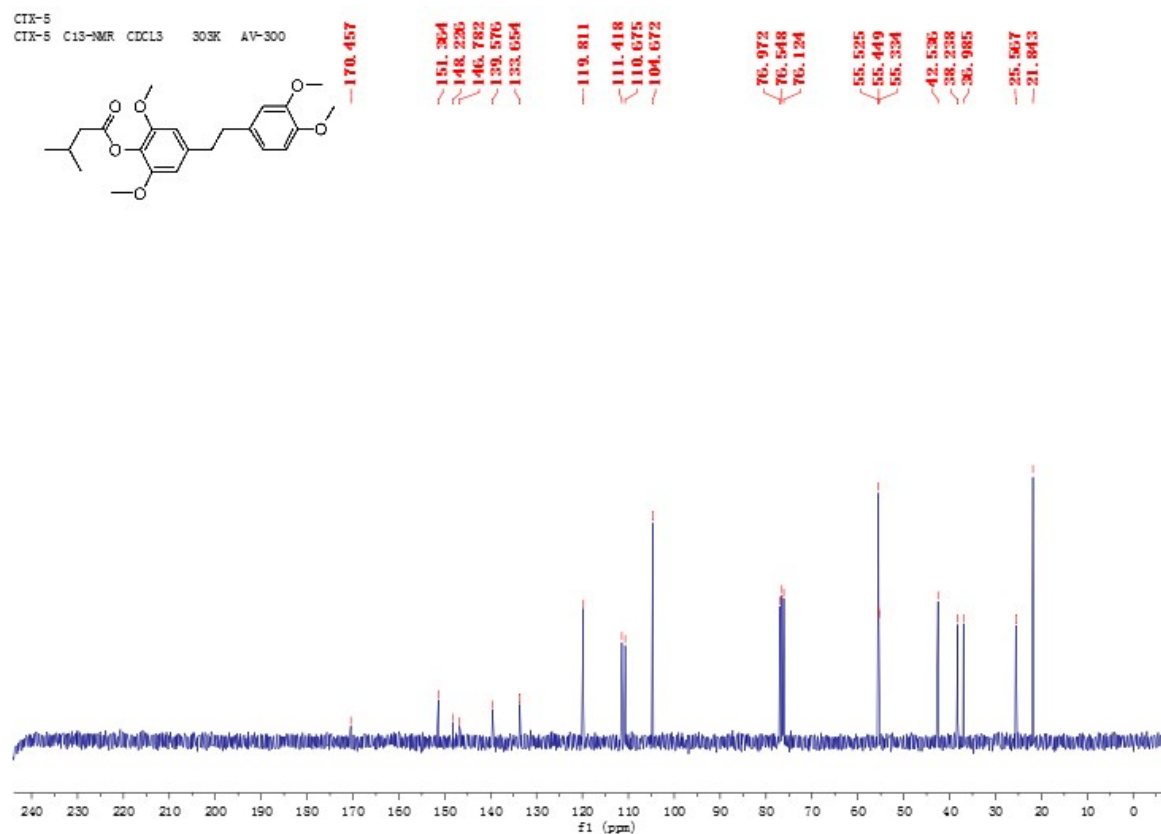


Fig S3.12.3 ¹³C-NMR spectrum of compound **1e** (75 MHz, CDCl₃)

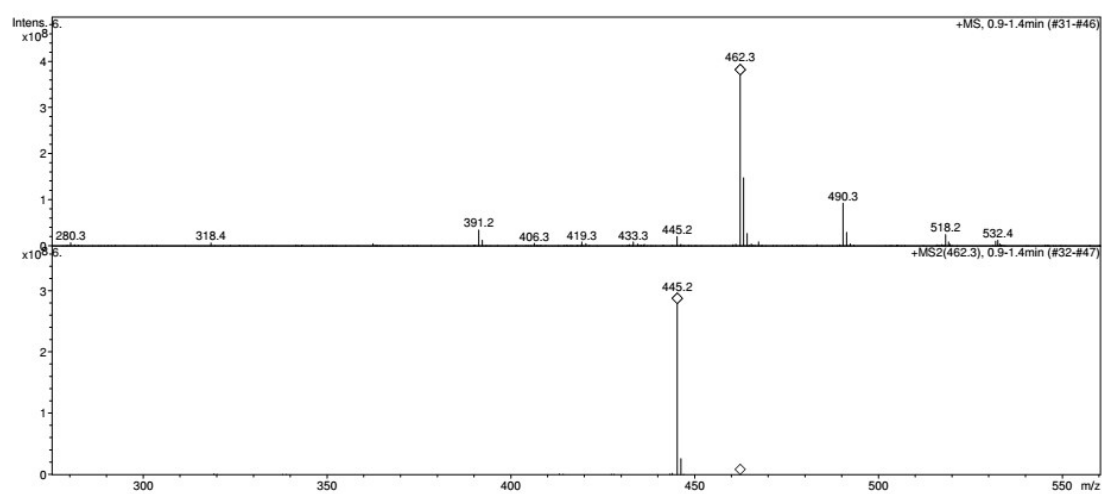


Fig S3.13.1 ESI-MS spectrum of compound **1f**

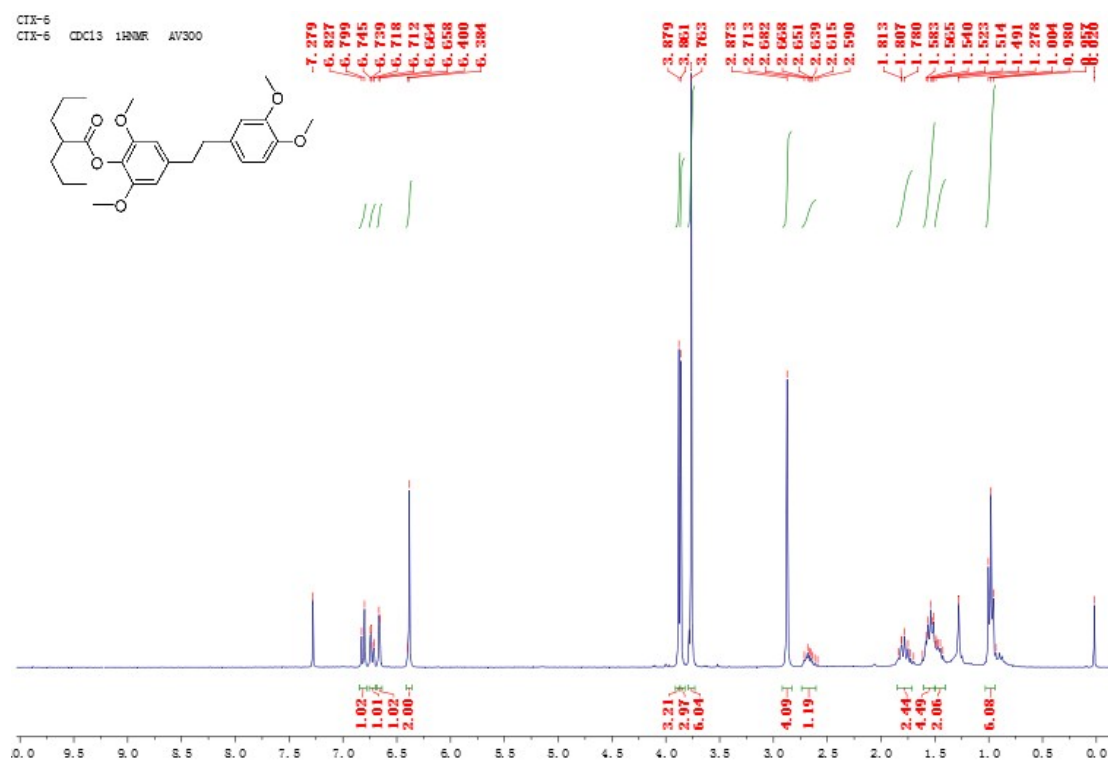


Fig S3.13.2 ¹H-NMR spectrum of compound **1f** (300MHz, CDCl₃)

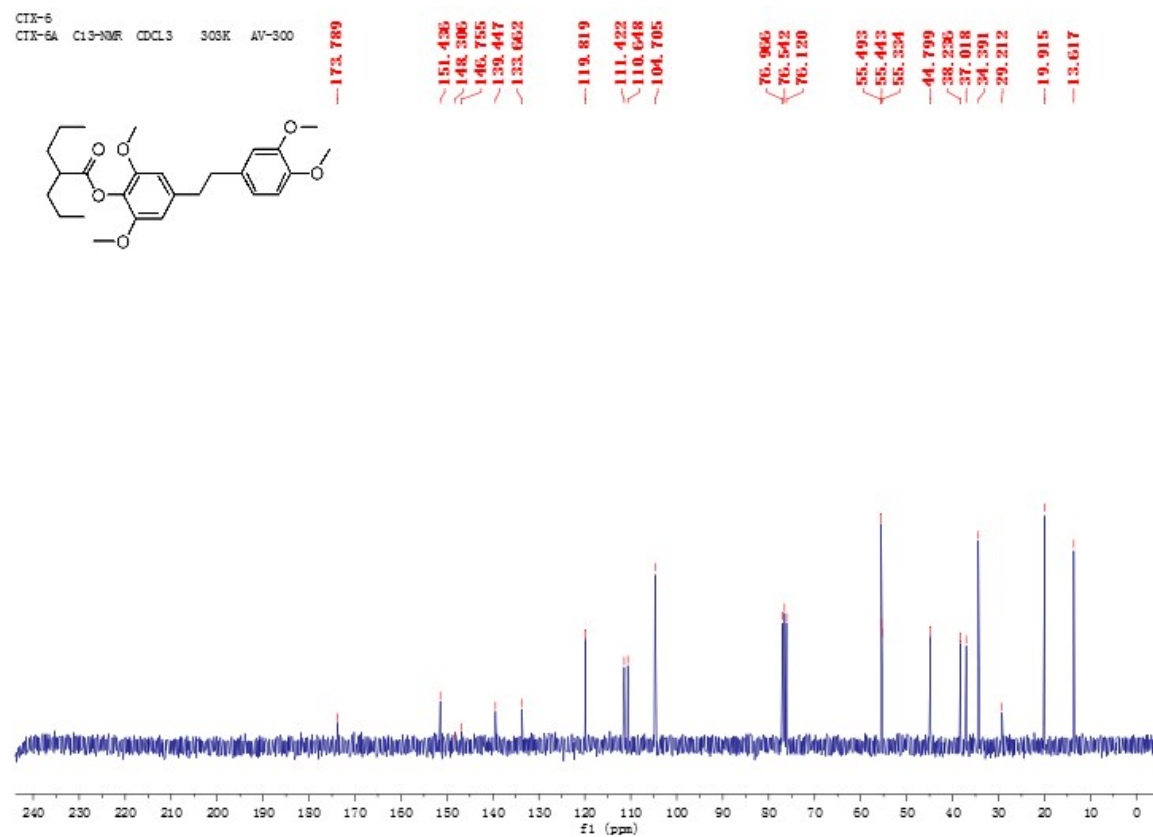


Fig S3.13.3 ¹³C-NMR spectrum of compound **1f** (75 MHz, CDCl₃)

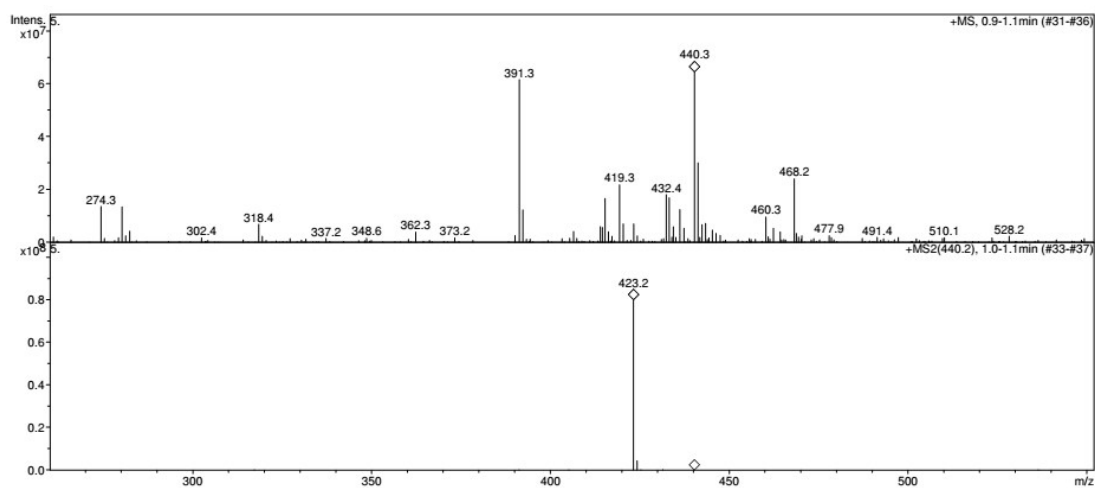


Fig S3.14.1 ESI-MS spectrum of compound **2a**

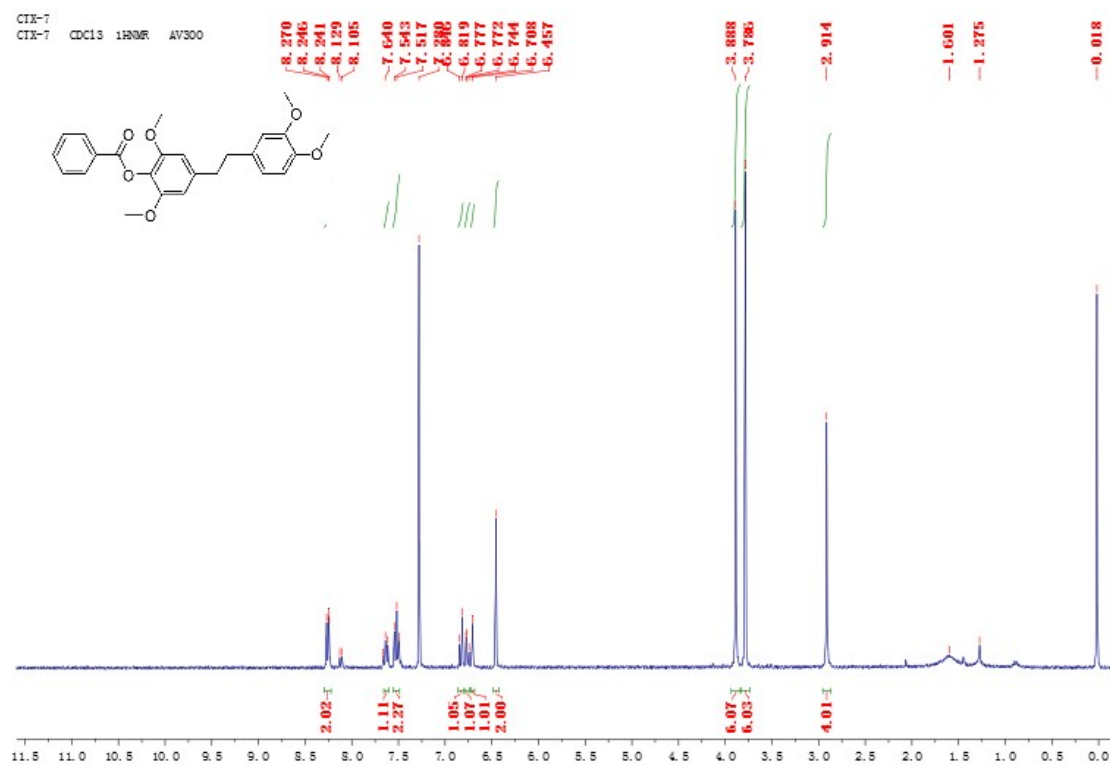


Fig S3.14.2 ^1H -NMR spectrum of compound **2a** (300MHz, CDCl_3)

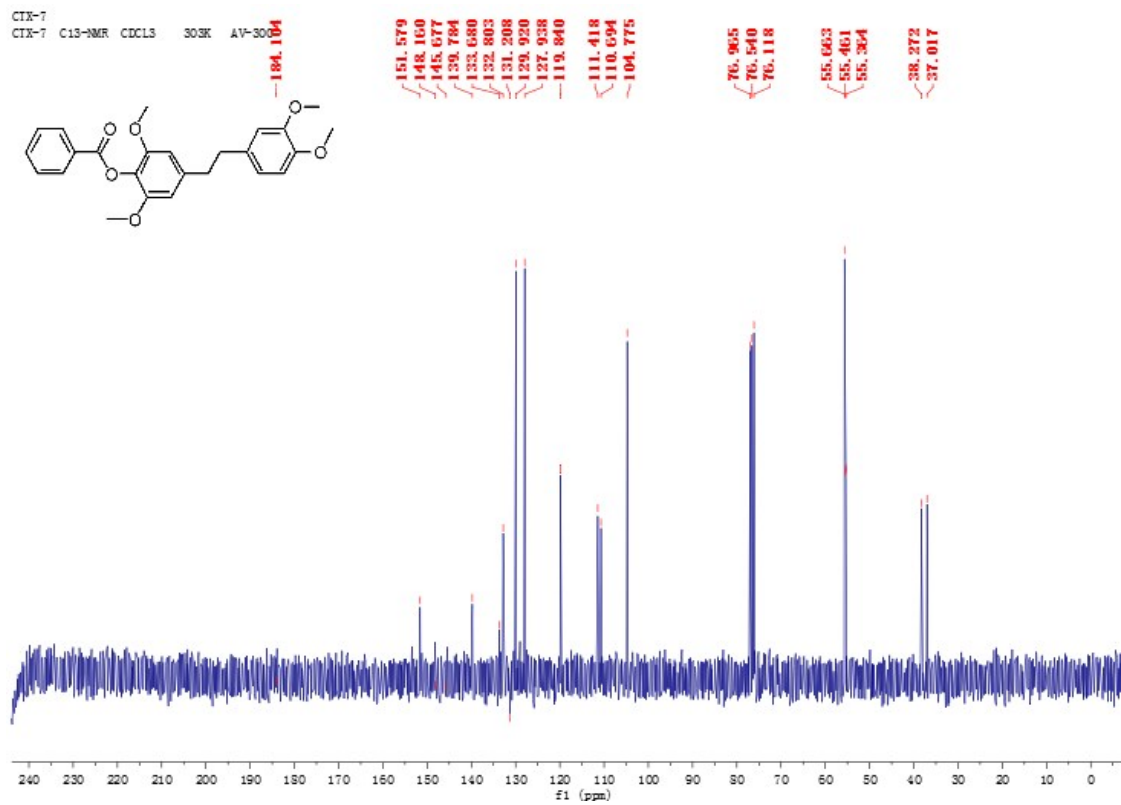


Fig S3.14.3 ^{13}C -NMR spectrum of compound **2a** (75 MHz, CDCl_3)

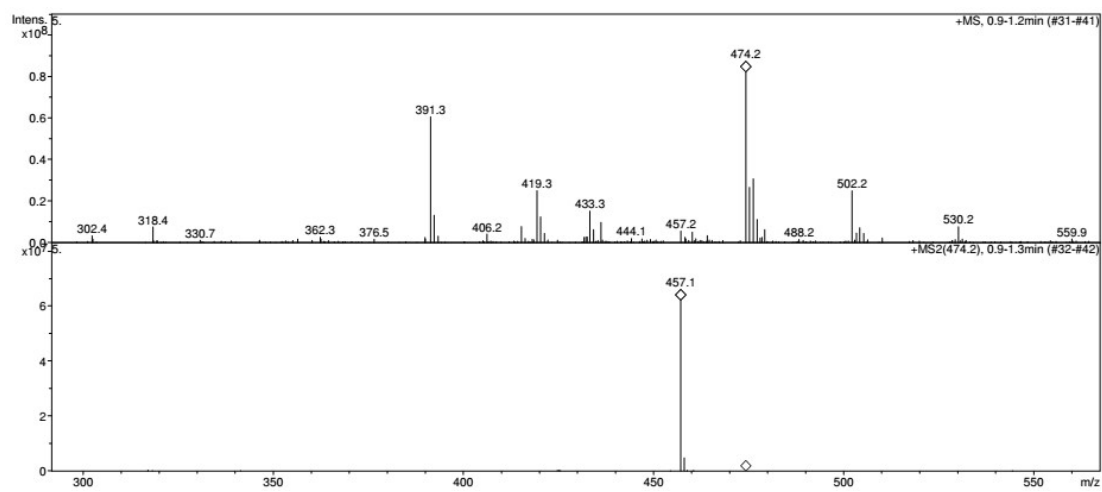


Fig S3.15.1 ESI-MS spectrum of compound **2b**

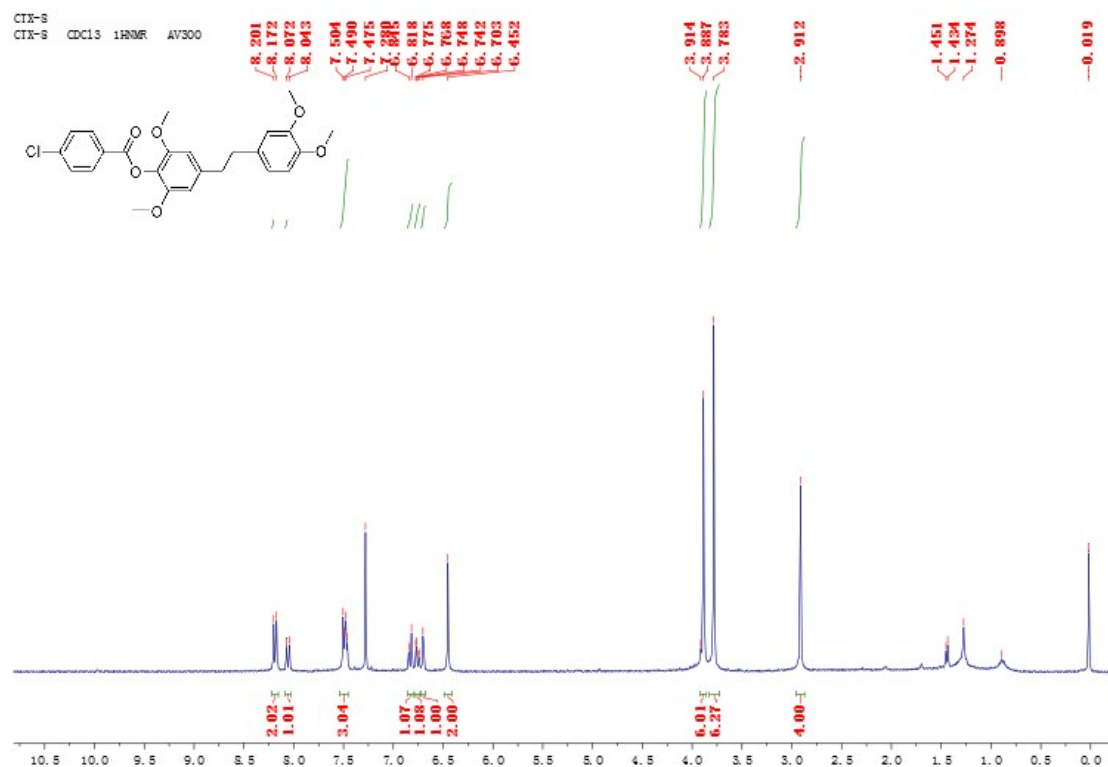


Fig S3.15.2 ¹H-NMR spectrum of compound **2b** (300MHz, CDCl₃)

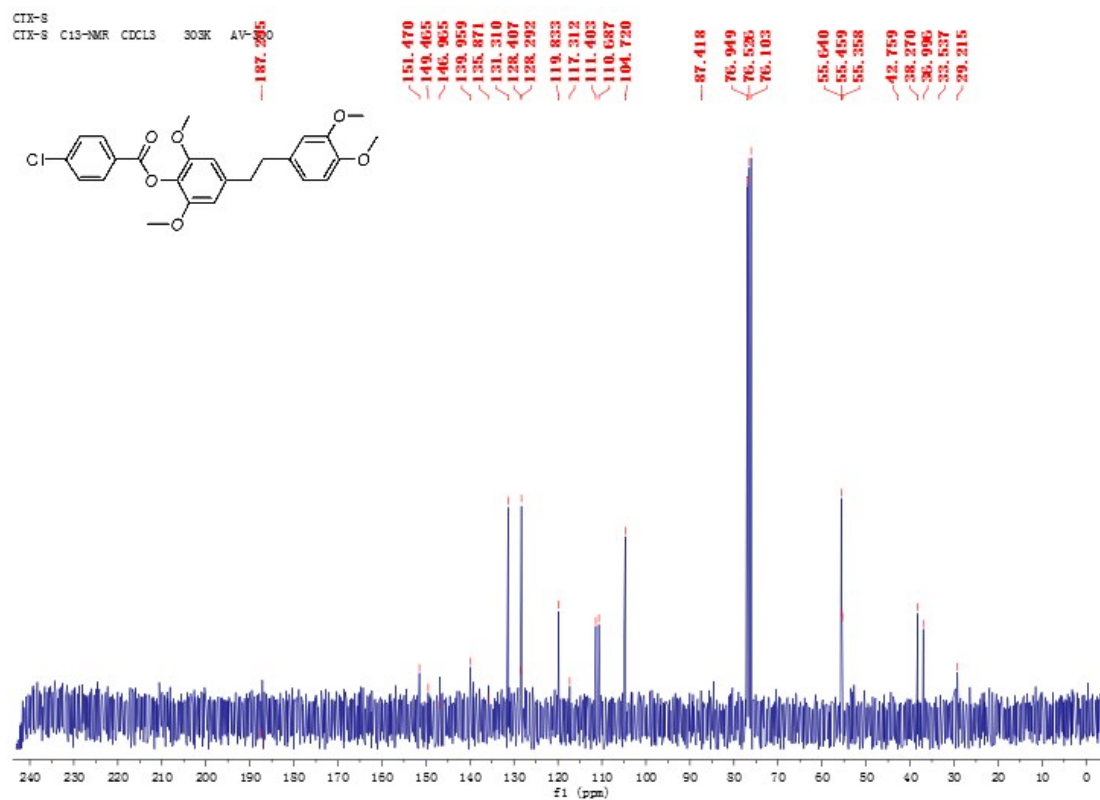


Fig S3.15.3 ¹³C-NMR spectrum of compound **2b** (75 MHz, CDCl₃)

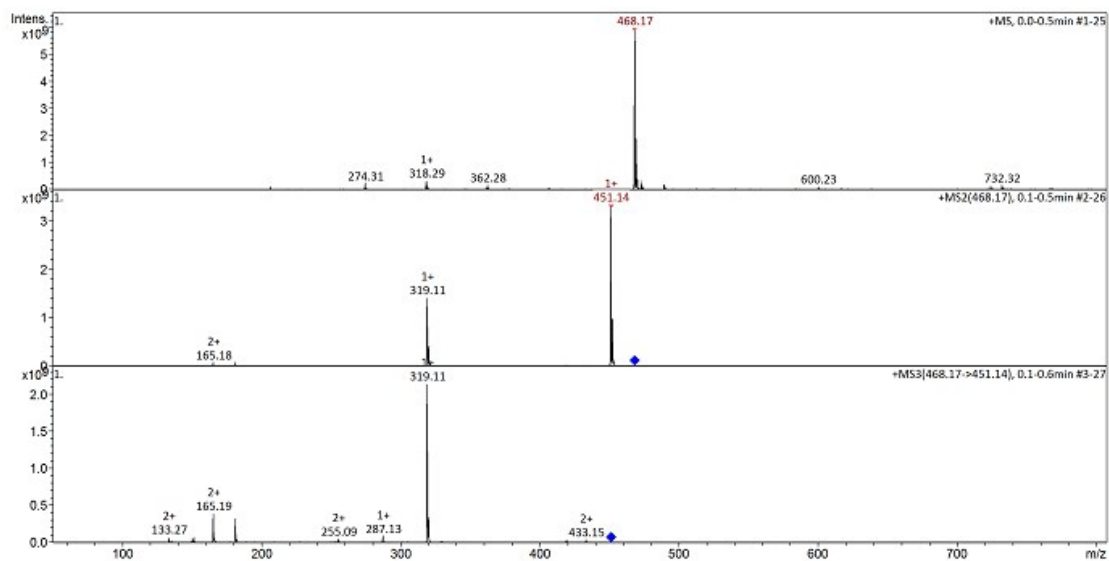


Fig S3.16.1 ESI-MS spectrum of compound **2c**

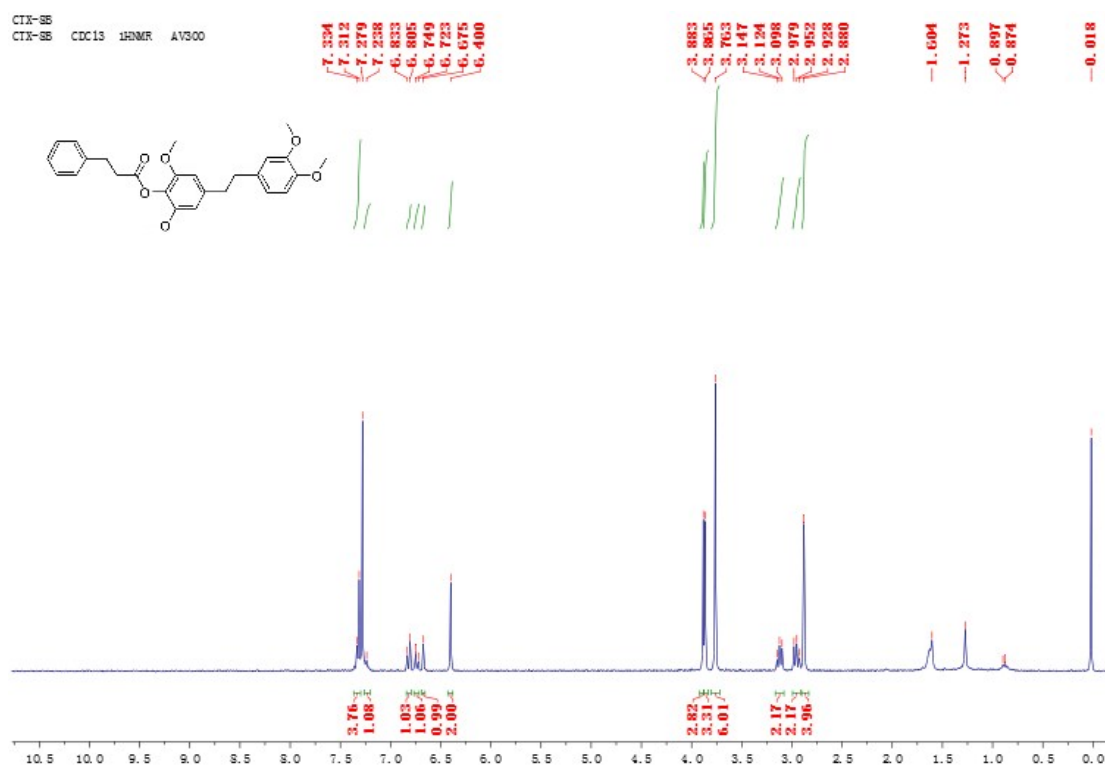


Fig S3.16.2 ¹H-NMR spectrum of compound **2c** (300MHz, CDCl₃)

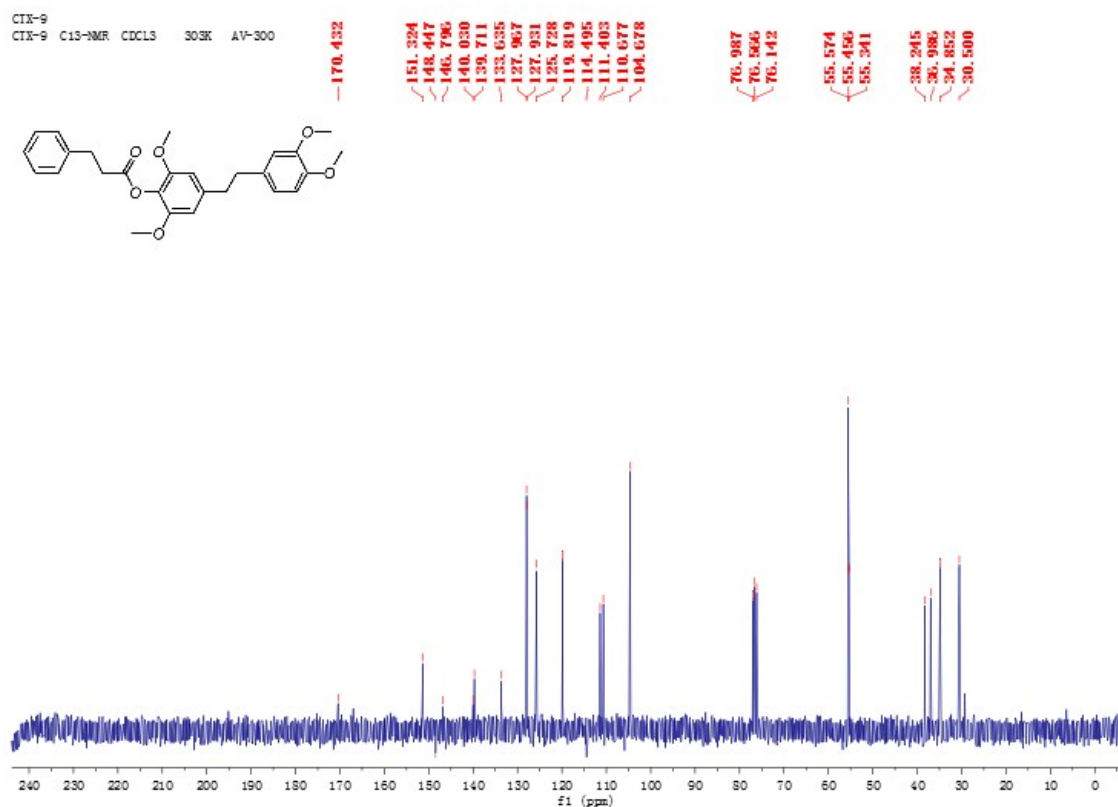


Fig S3.16.3 ¹³C-NMR spectrum of compound 2c (75 MHz, CDCl₃)

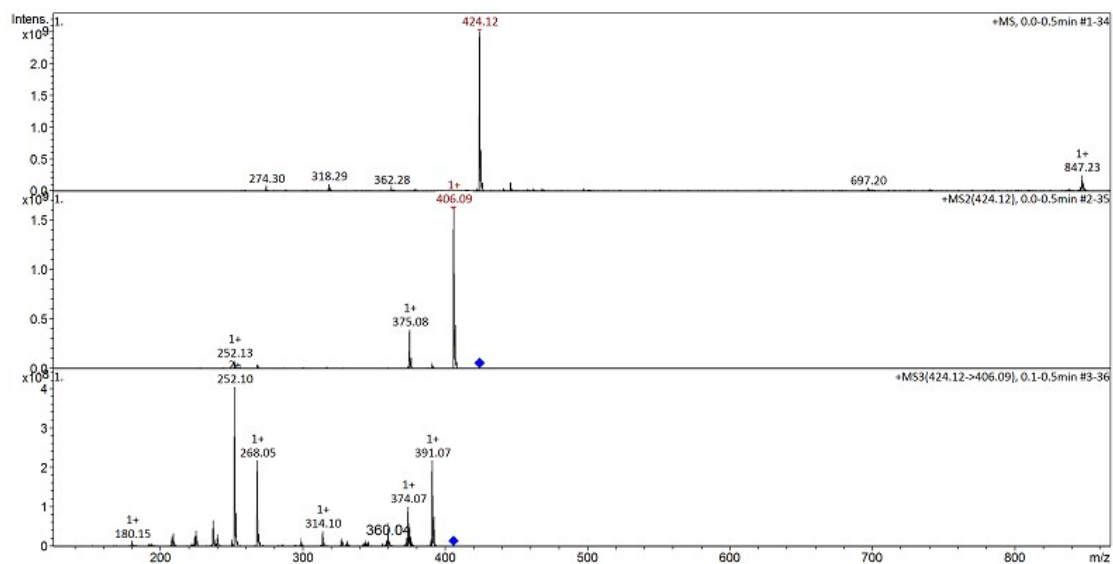


Fig S3.17.1 ESI-MS spectrum of compound 2d

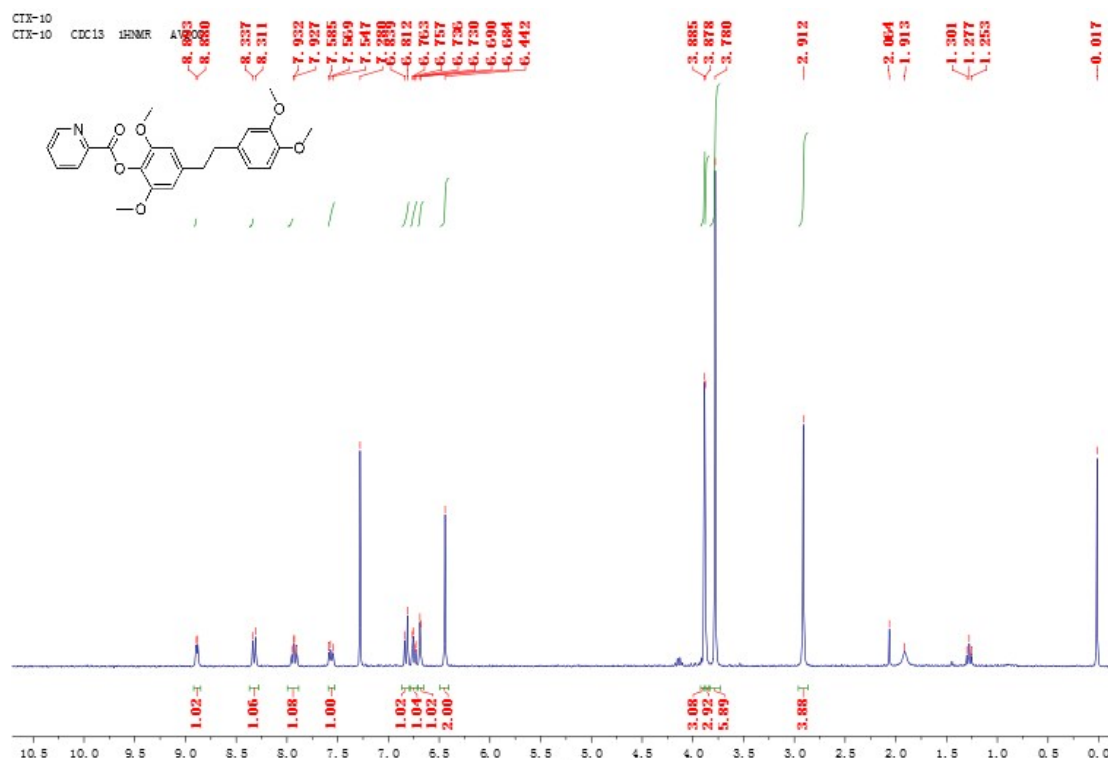


Fig S3.17.2 ¹H-NMR spectrum of compound **2d** (300MHz, CDCl₃)

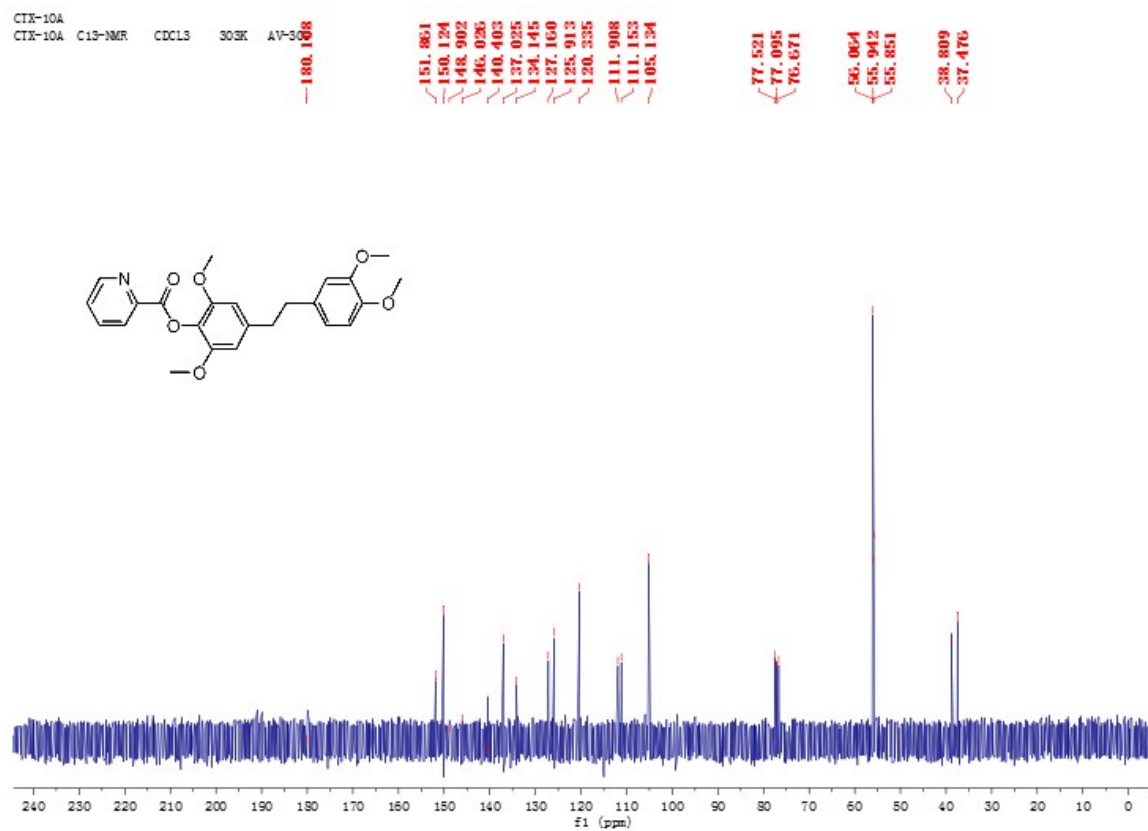


Fig S3.17.3 ¹³C-NMR spectrum of compound **2d** (75 MHz, CDCl₃)

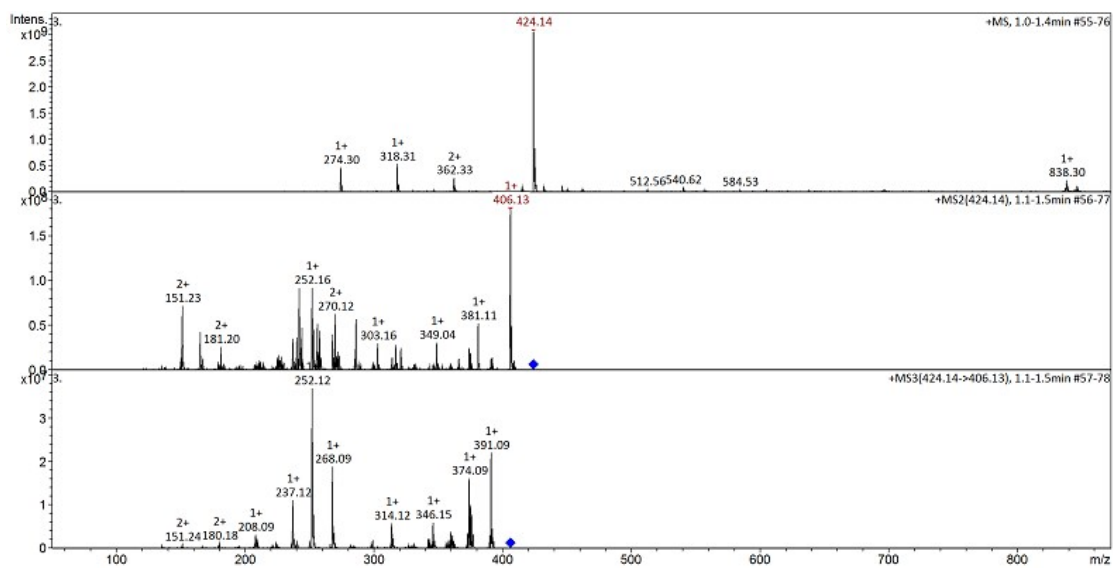


Fig S3.18.1 ESI-MS spectrum of compound **2e**

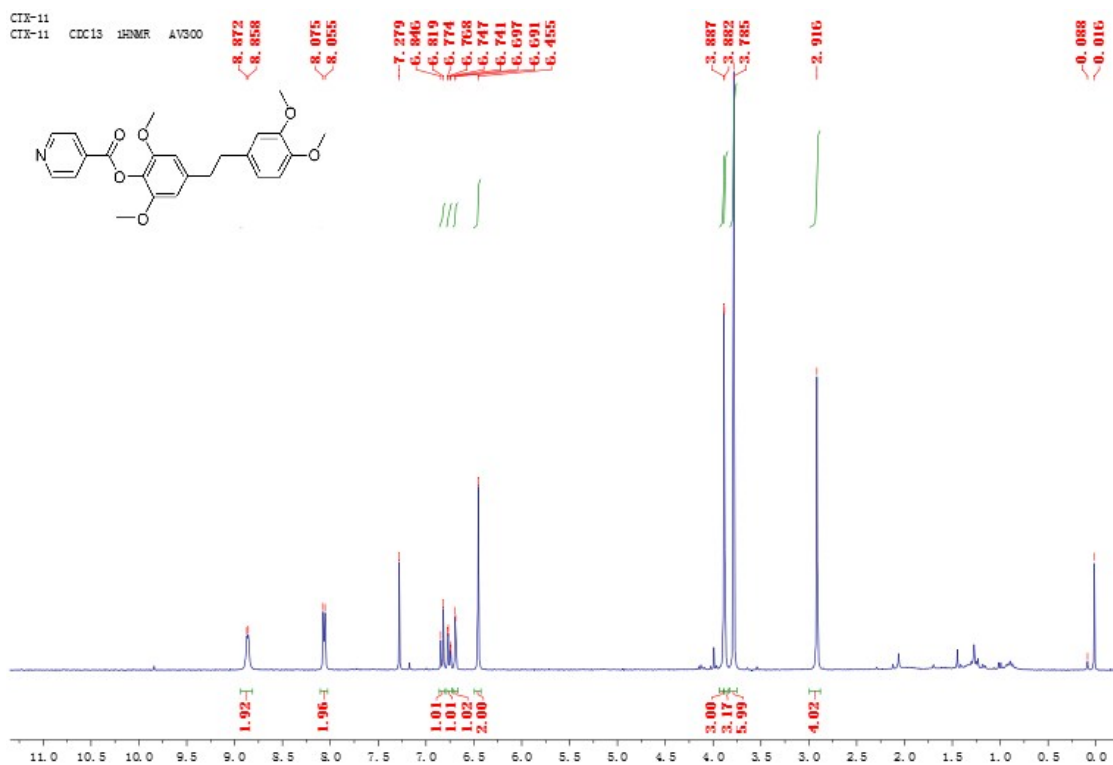


Fig S3.18.2 ¹H-NMR spectrum of compound **2e** (300MHz, CDCl₃)

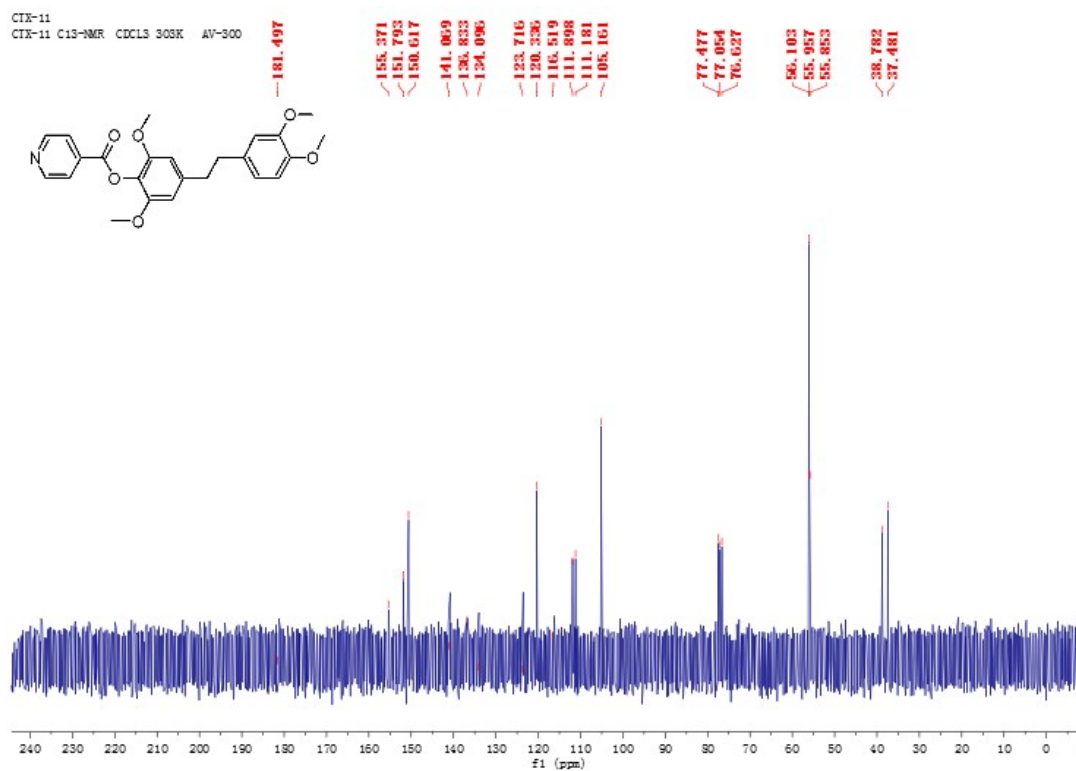


Fig S3.18.3 ^{13}C -NMR spectrum of compound 2e (75 MHz, CDCl_3)

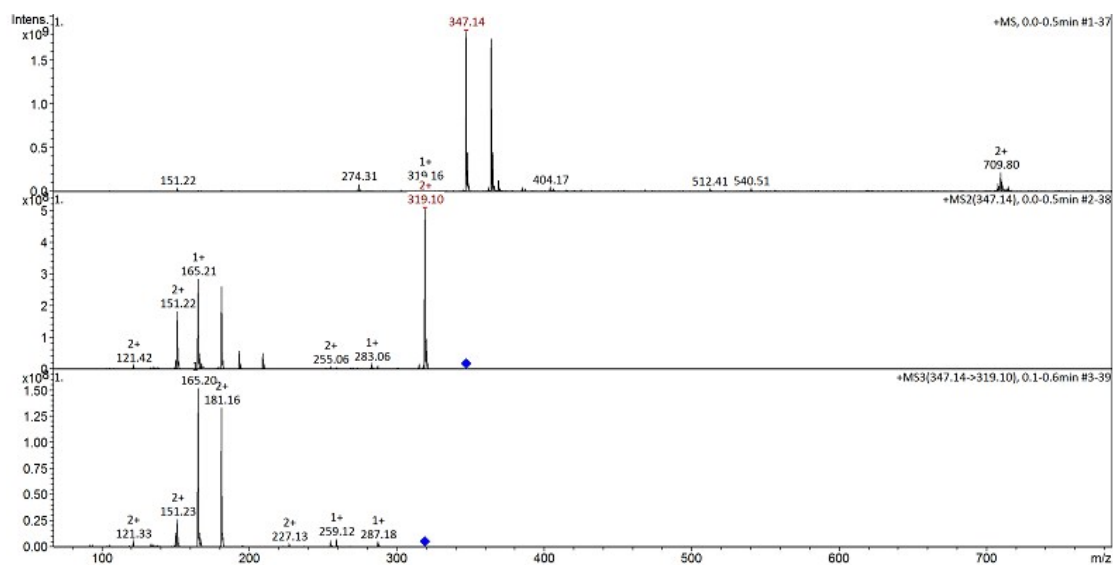


Fig S3.19.1 ESI-MS spectrum of compound 3a

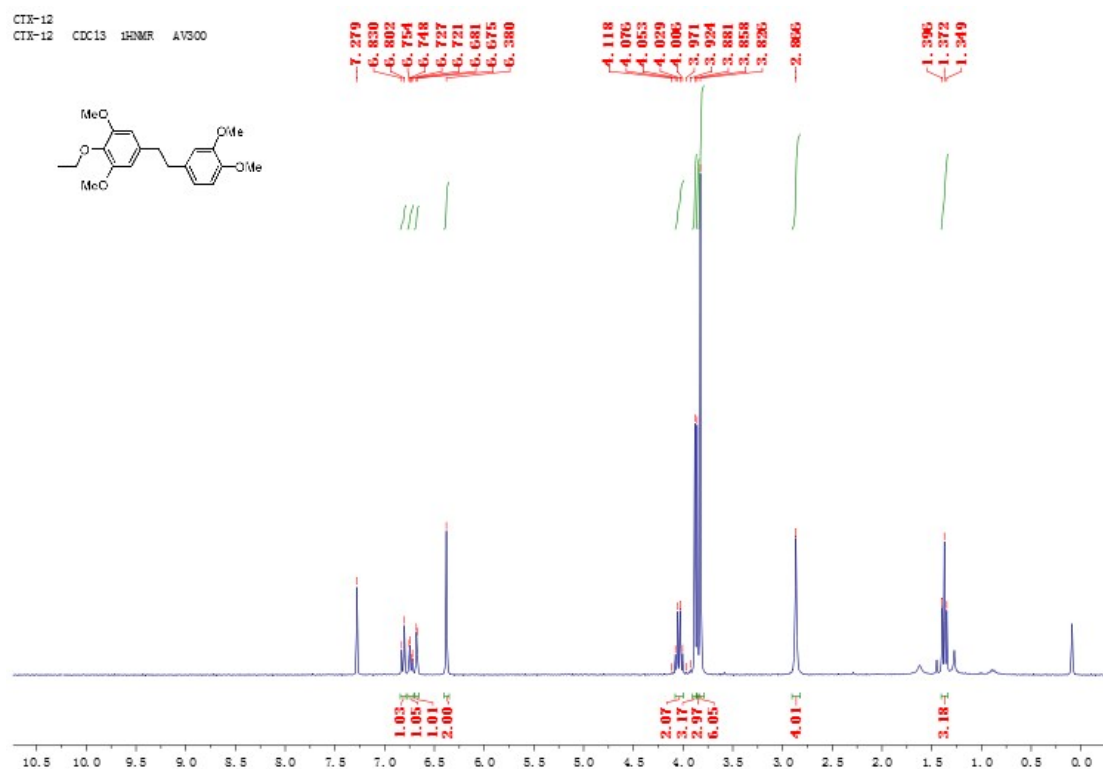


Fig S3.19.2 ¹H-NMR spectrum of compound 3a (300MHz, CDCl₃)

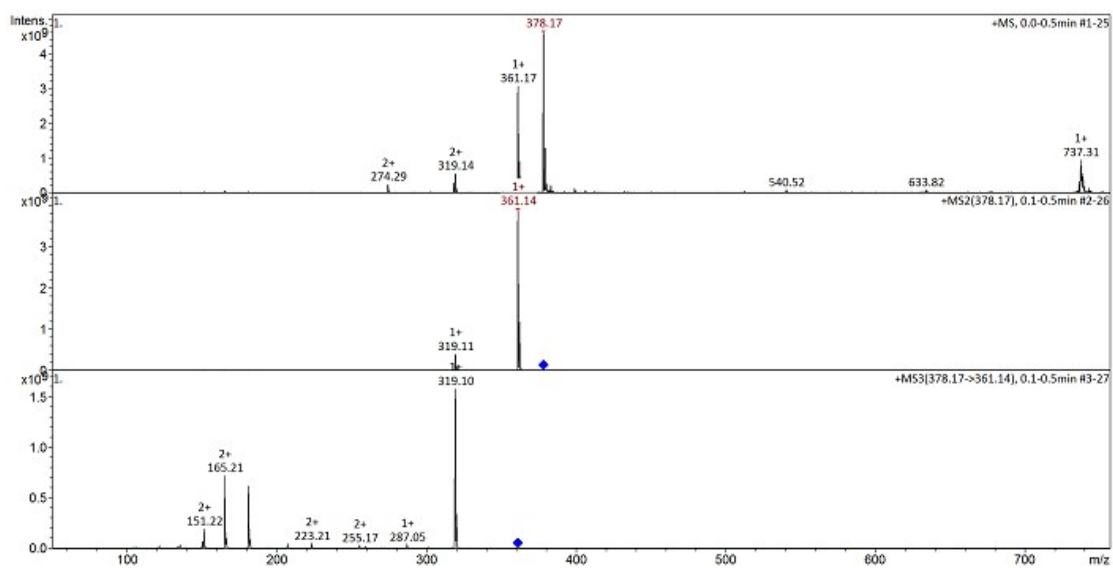


Fig S3.20.1 ESI-MS spectrum of compound 3b

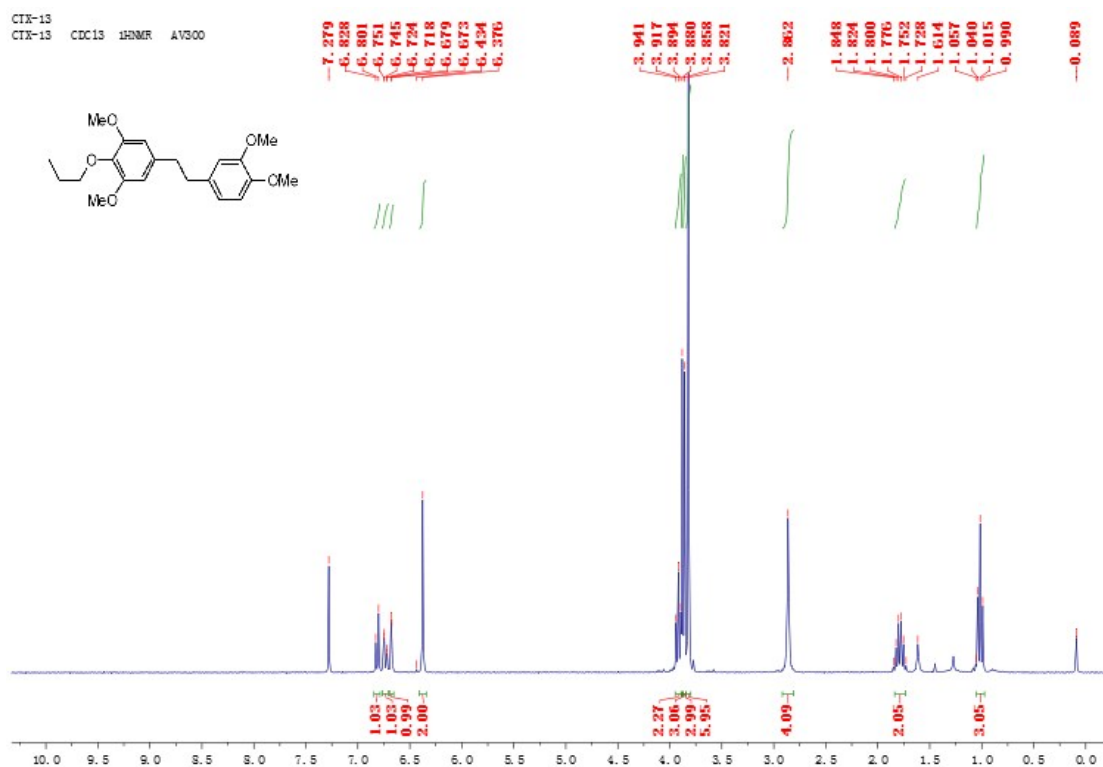


Fig S3.20.2 ¹H-NMR spectrum of compound **3b** (300MHz, CDCl₃)

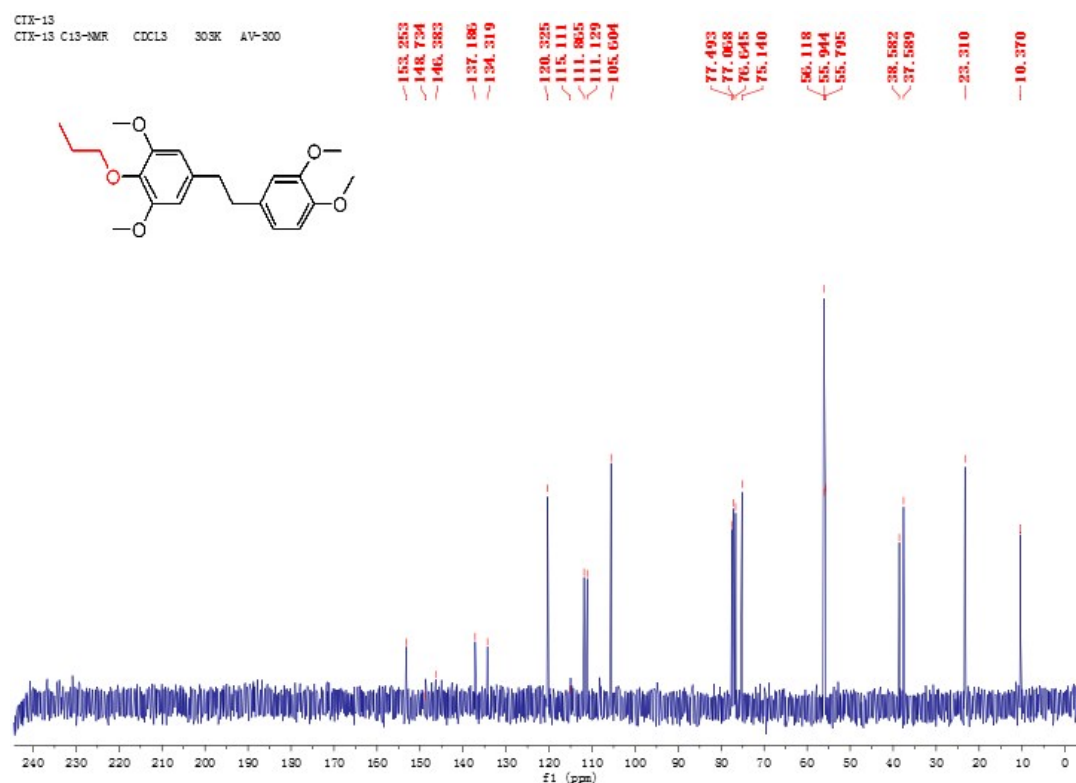


Fig S3.20.3 ¹³C-NMR spectrum of compound **3b** (75 MHz, CDCl₃)

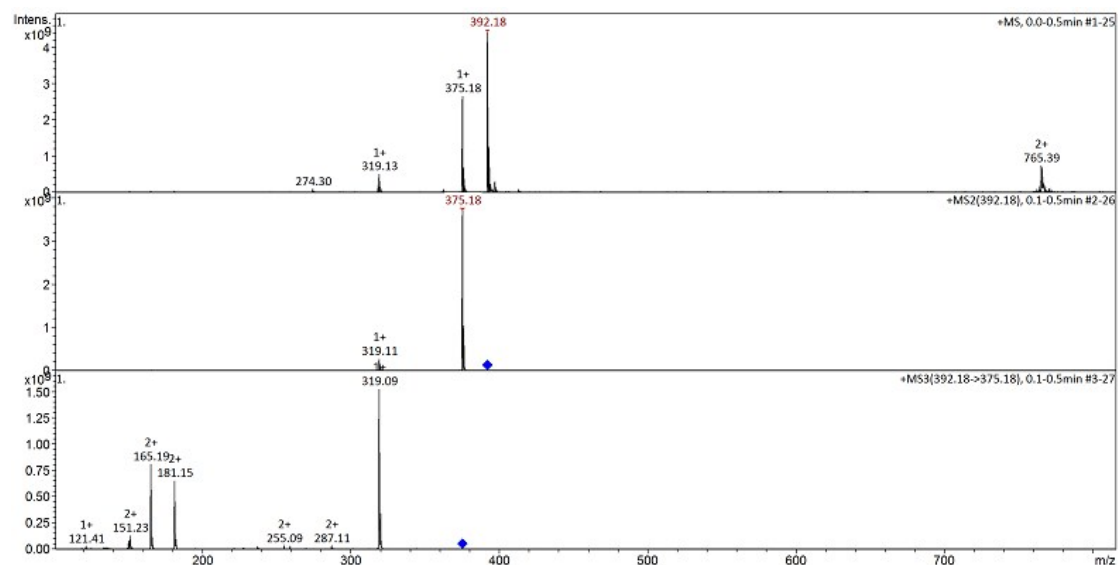


Fig S3.21.1 ESI-MS spectrum of compound 3c

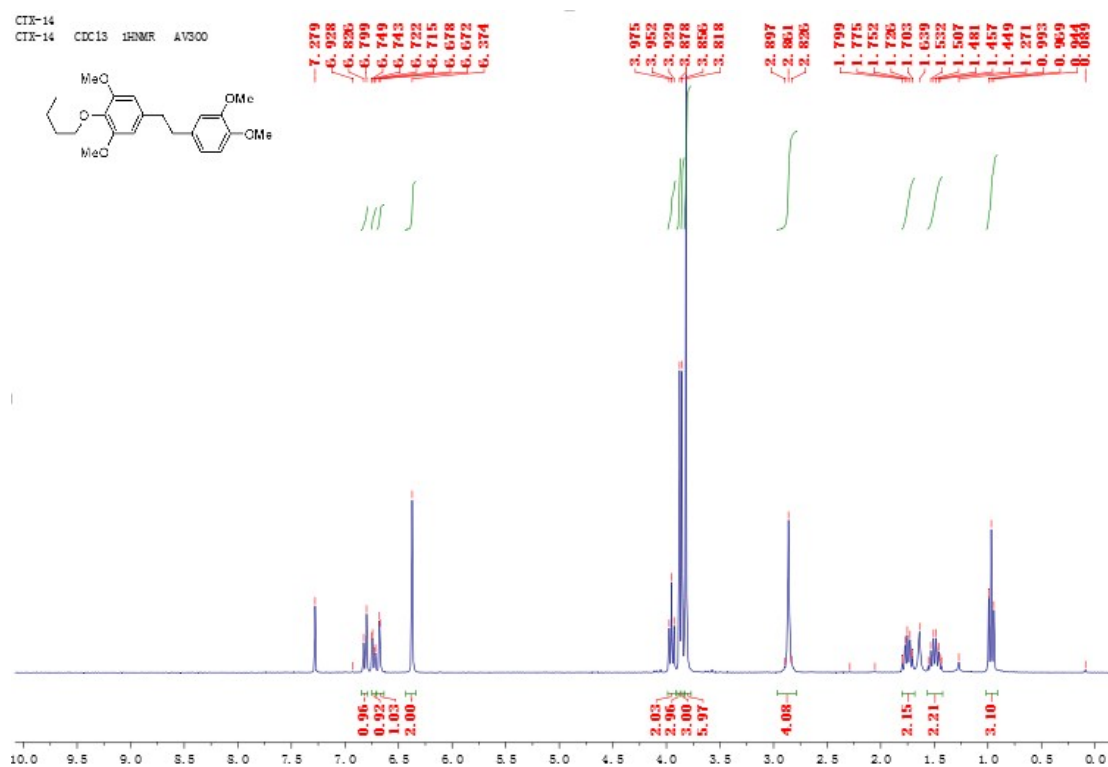


Fig S3.21.2 ¹H-NMR spectrum of compound 3c (300MHz, CDCl₃)

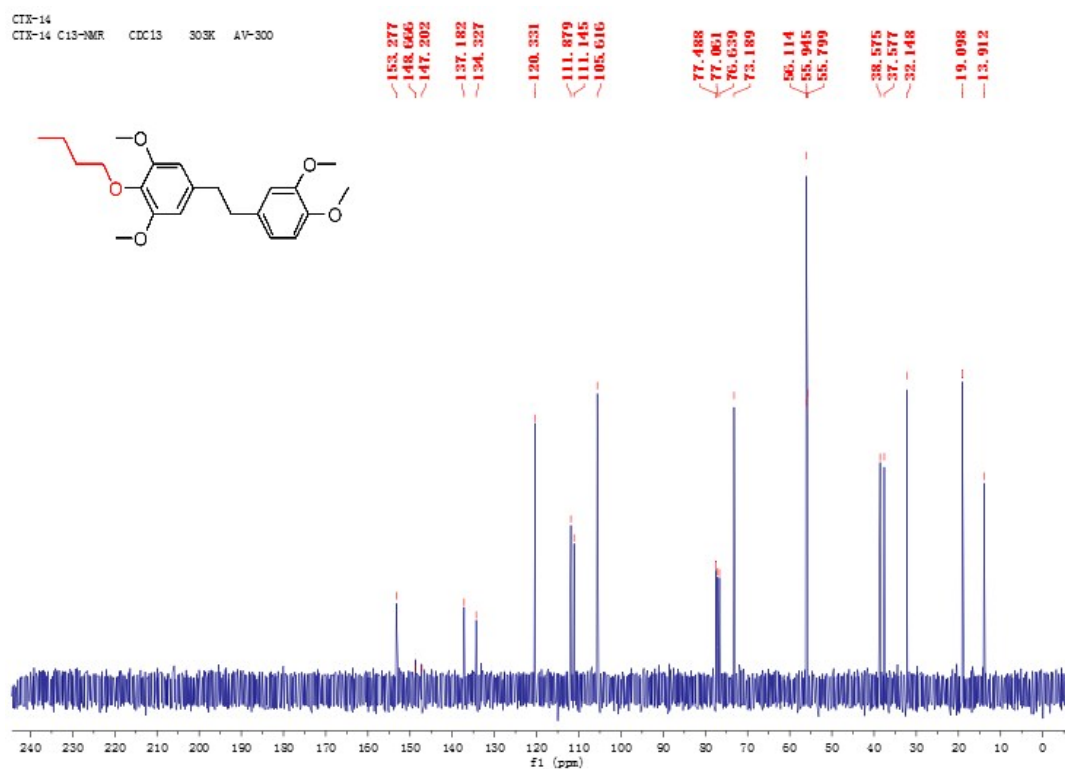


Fig S3.21.3 ^{13}C -NMR spectrum of compound 3c (75 MHz, CDCl_3)

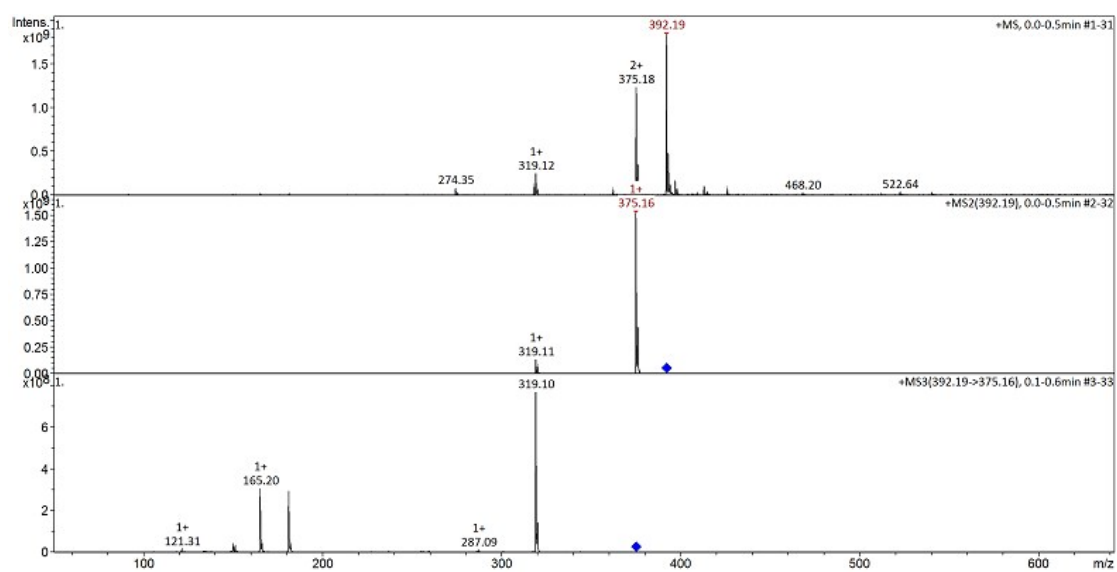


Fig S3.22.1 ESI-MS spectrum of compound 3d

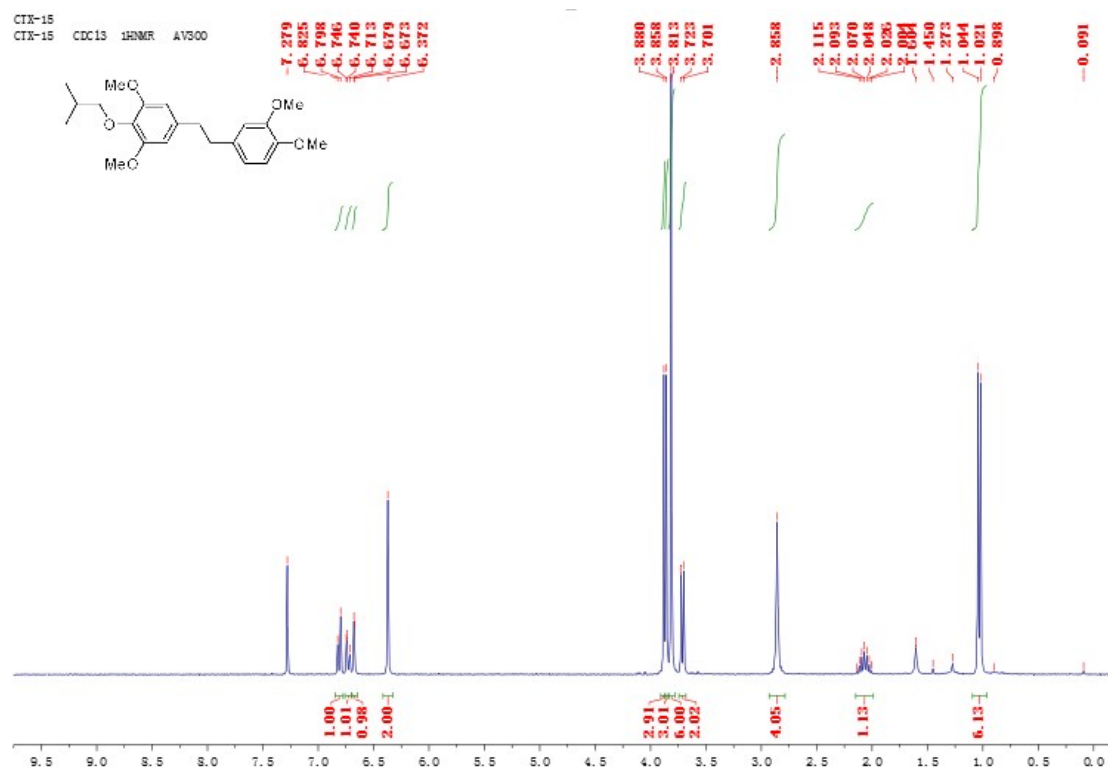


Fig S3.22.2 ^1H -NMR spectrum of compound **3d** (300MHz, CDCl_3)

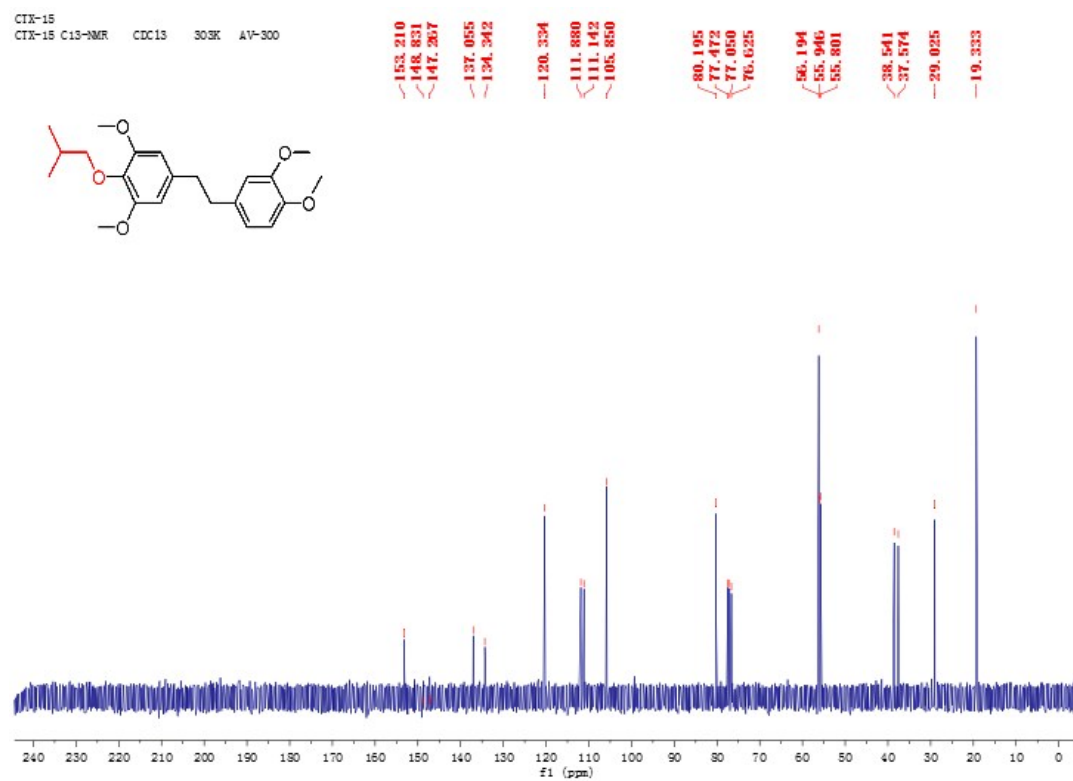


Fig S3.22.3 ^{13}C -NMR spectrum of compound **3d** (75 MHz, CDCl_3)

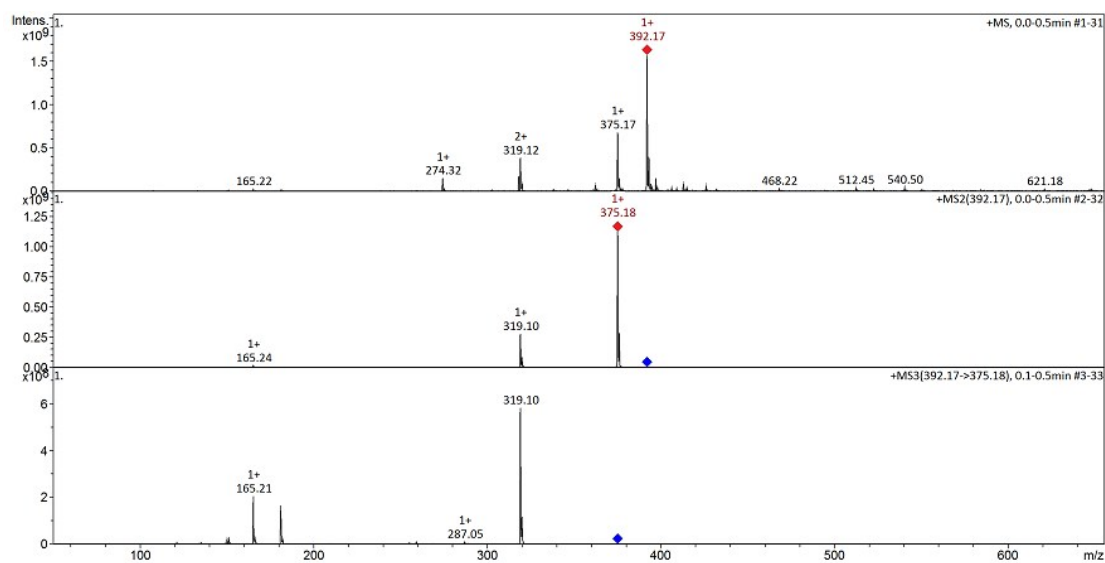


Fig S3.23.1 ESI-MS spectrum of compound **3e**

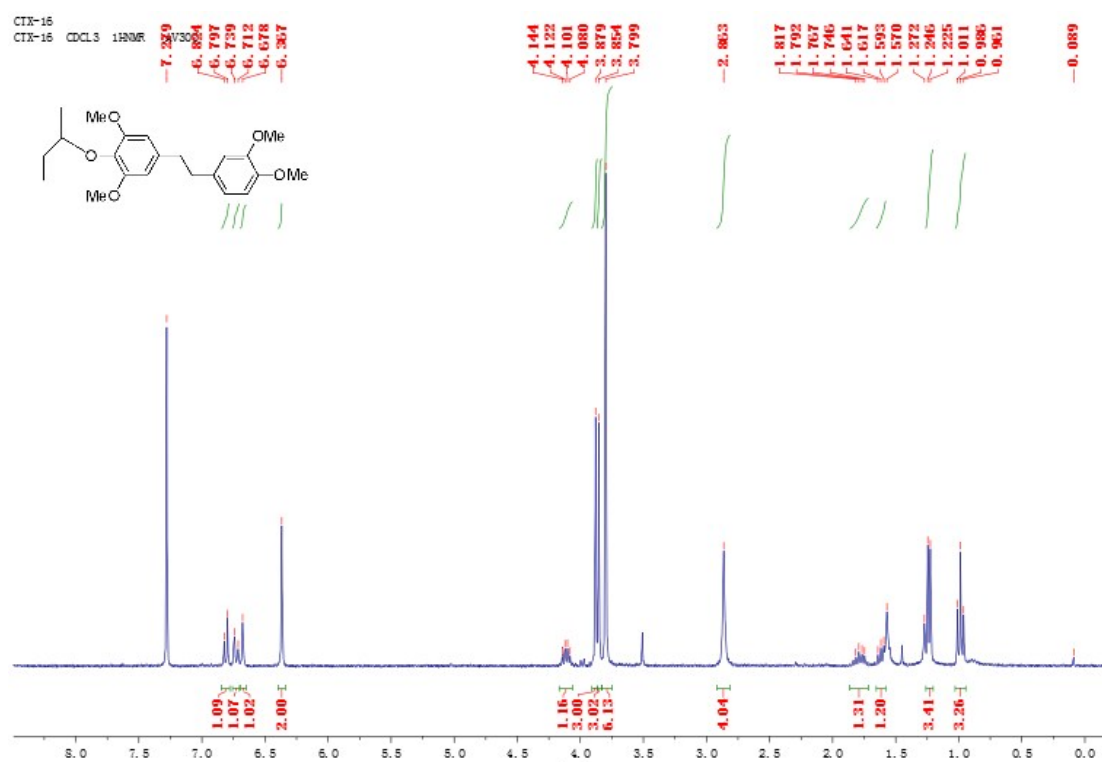


Fig S3.23.2 ¹H-NMR spectrum of compound **3e** (300MHz, CDCl₃)

CTX-16
CTX-16 C13-NMR CDCl3 303K AV-300

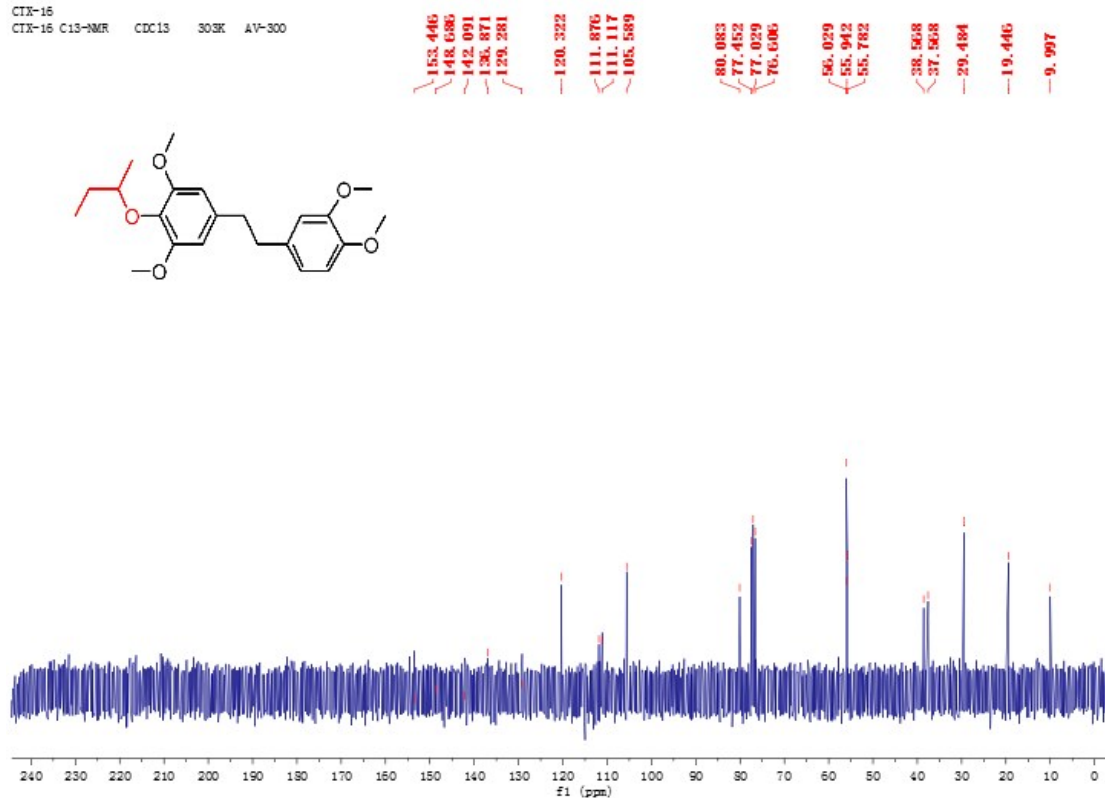


Fig S3.23.3 ^{13}C -NMR spectrum of compound 3e (75 MHz, CDCl_3)

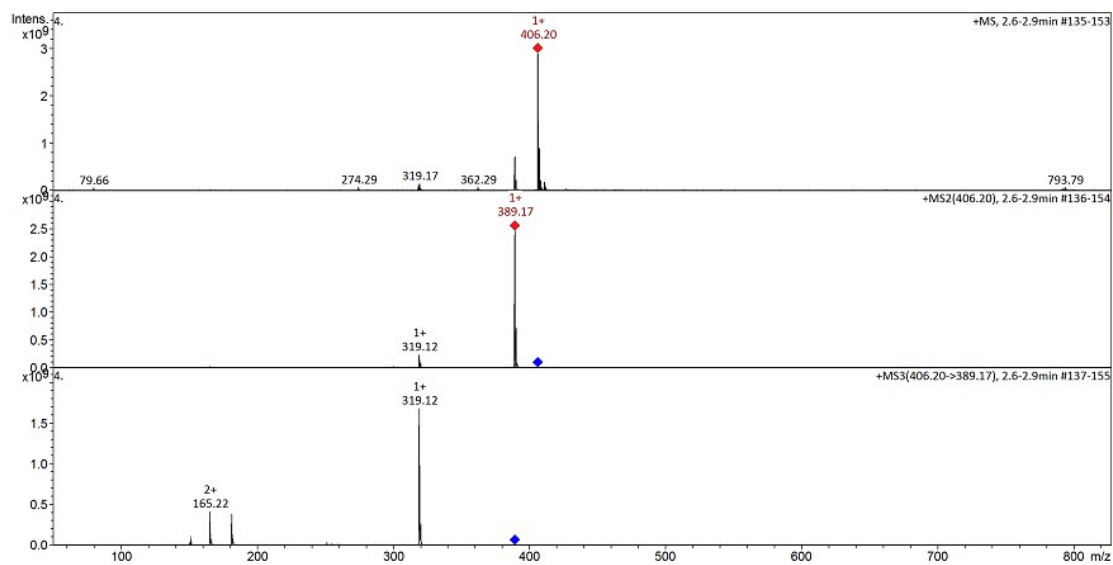


Fig S3.24.1 ESI-MS spectrum of compound 3f

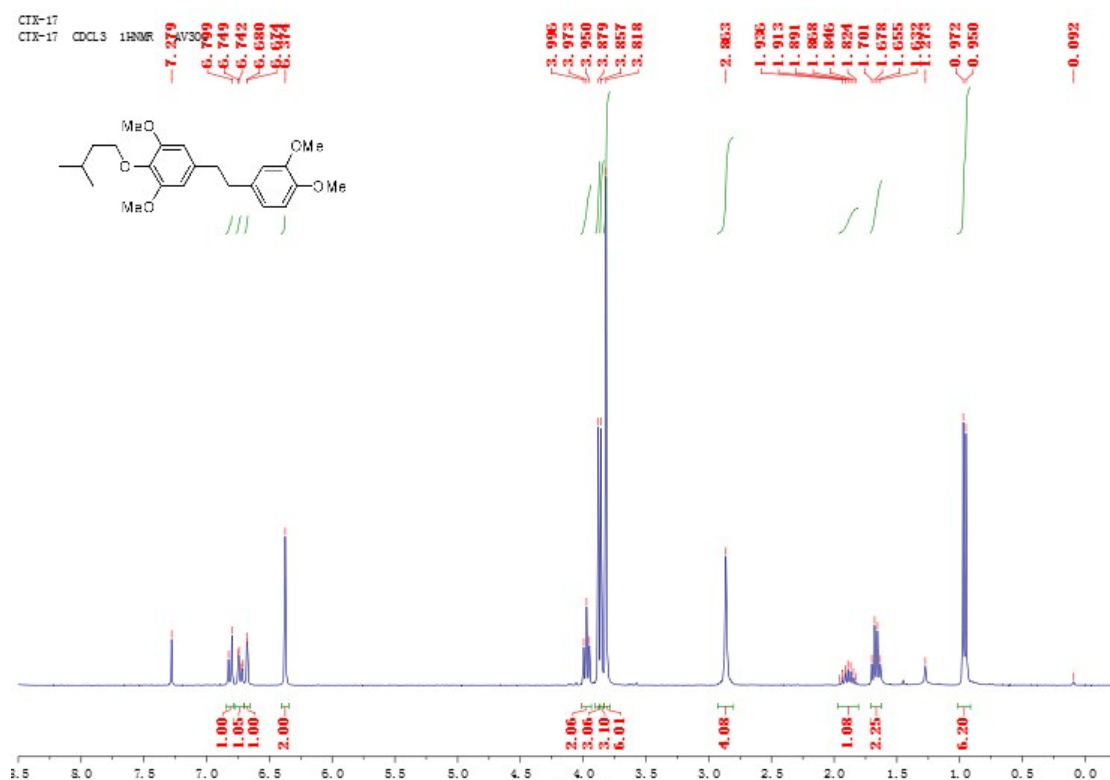


Fig S3.24.2 ¹H-NMR spectrum of compound **3f** (300MHz, CDCl₃)

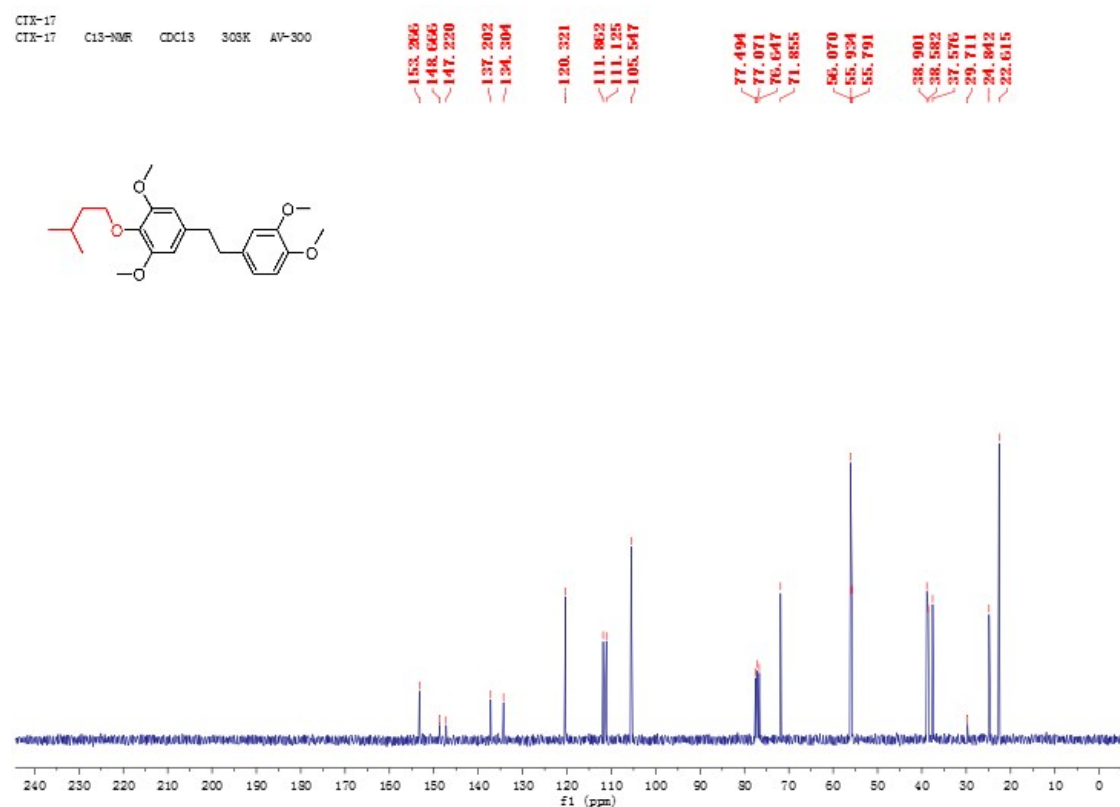


Fig S3.24.3 ¹³C-NMR spectrum of compound **3f** (75 MHz, CDCl₃)

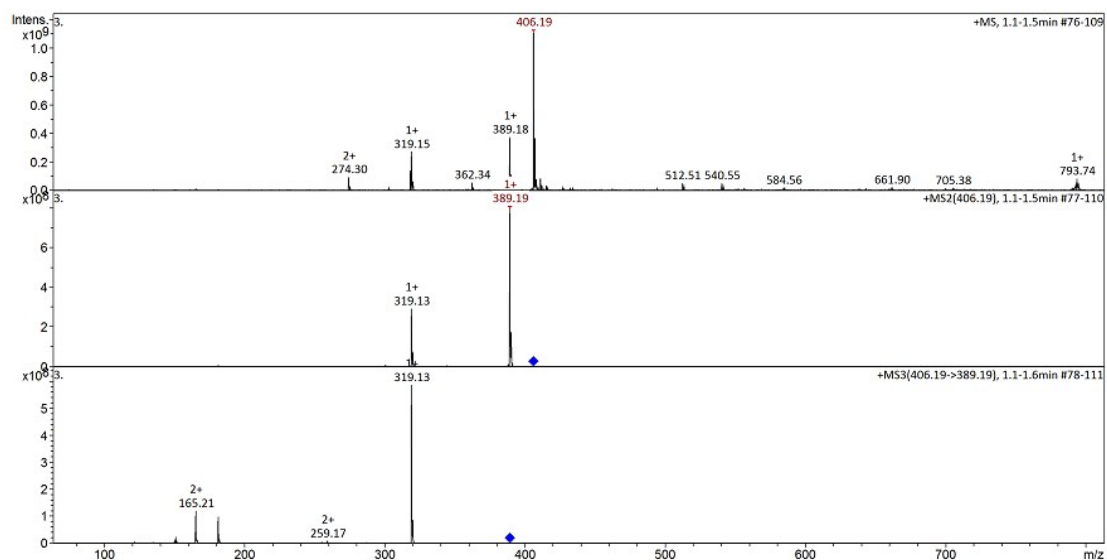


Fig S3.25.1 ESI-MS spectrum of compound **3g**

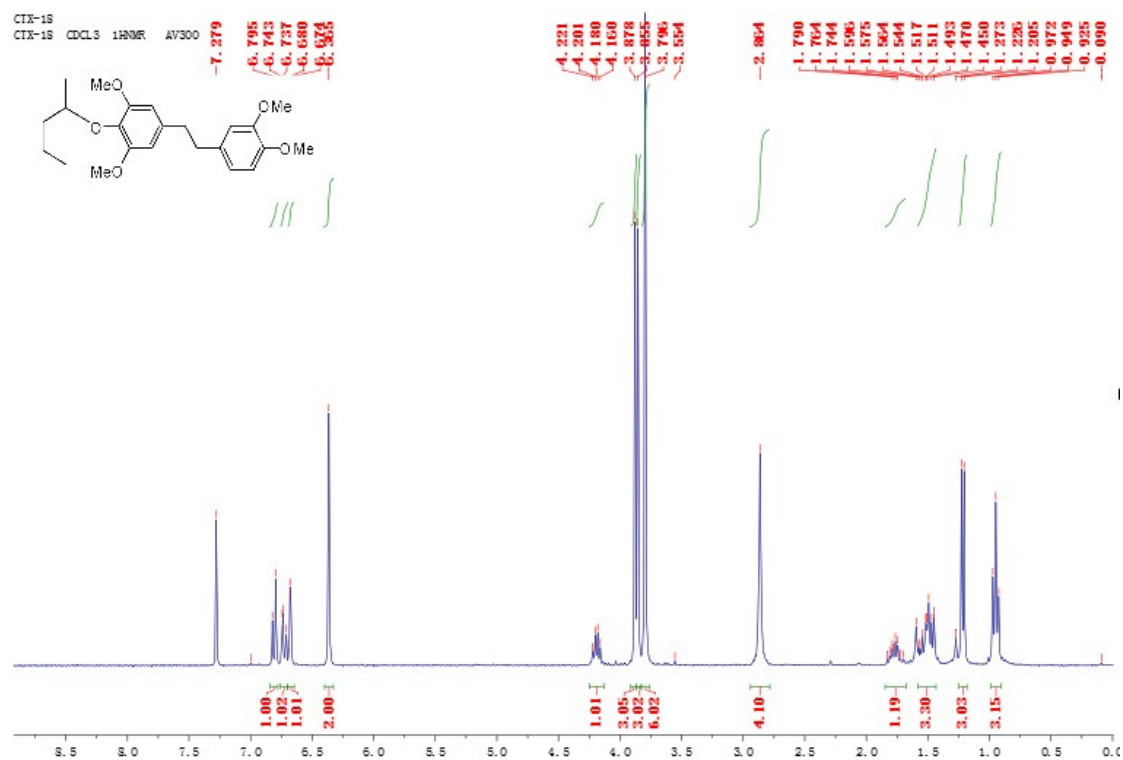


Fig S3.25.2 ¹H-NMR spectrum of compound **3g** (300MHz, CDCl₃)

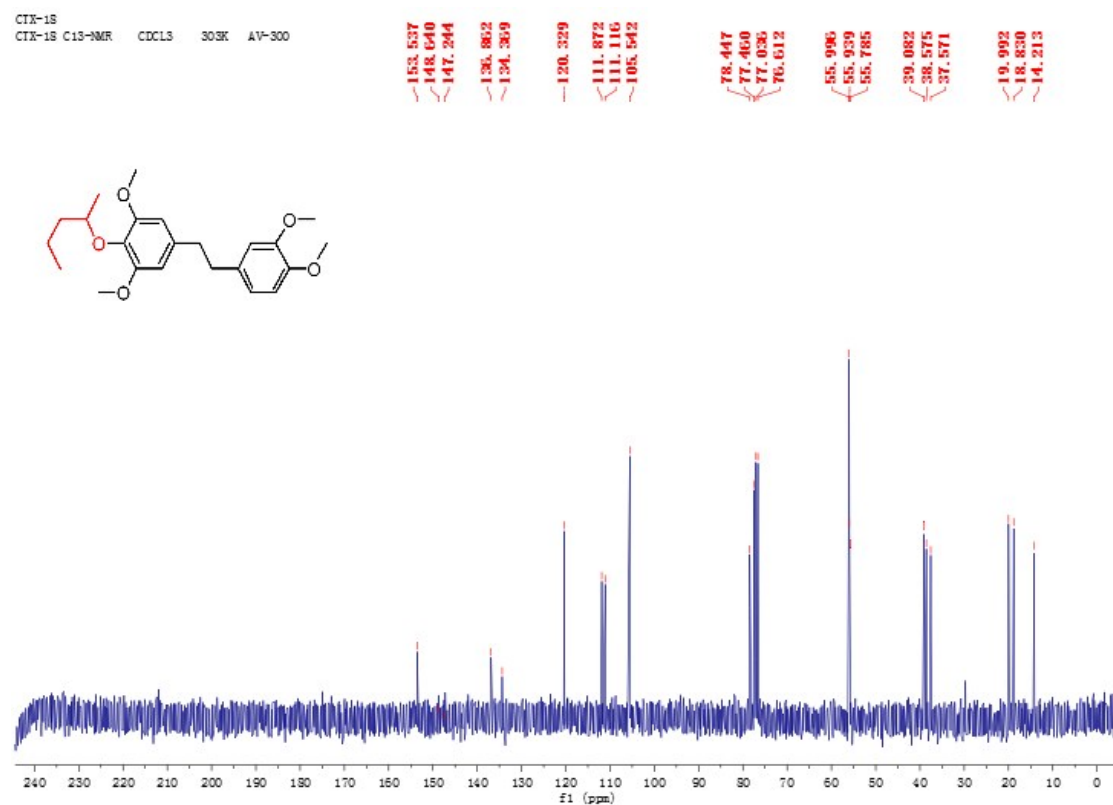


Fig S3.25.3 ¹³C-NMR spectrum of compound **3g** (75 MHz, CDCl₃)

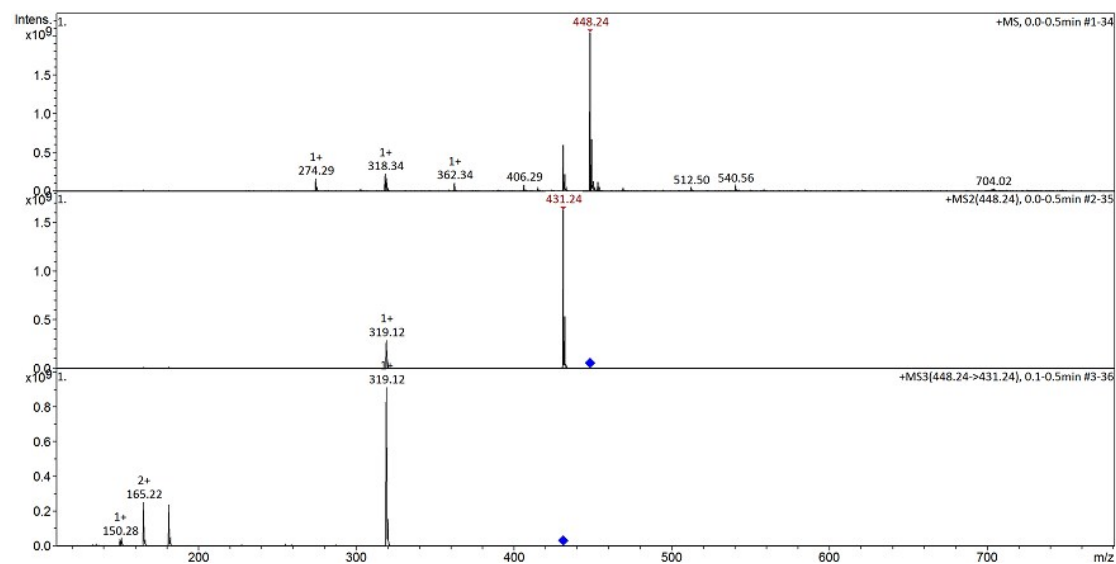


Fig S3.26.1 ESI-MS spectrum of compound **3h**

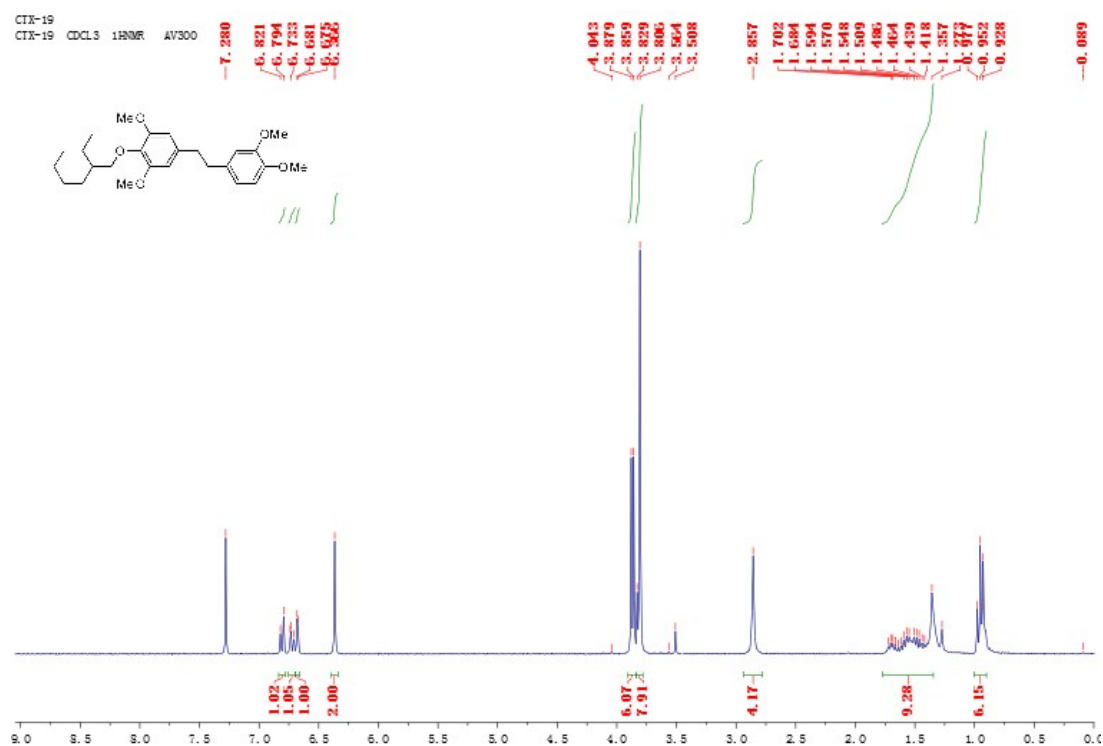


Fig S3.26.2 ¹H-NMR spectrum of compound **3h** (300MHz, CDCl₃)

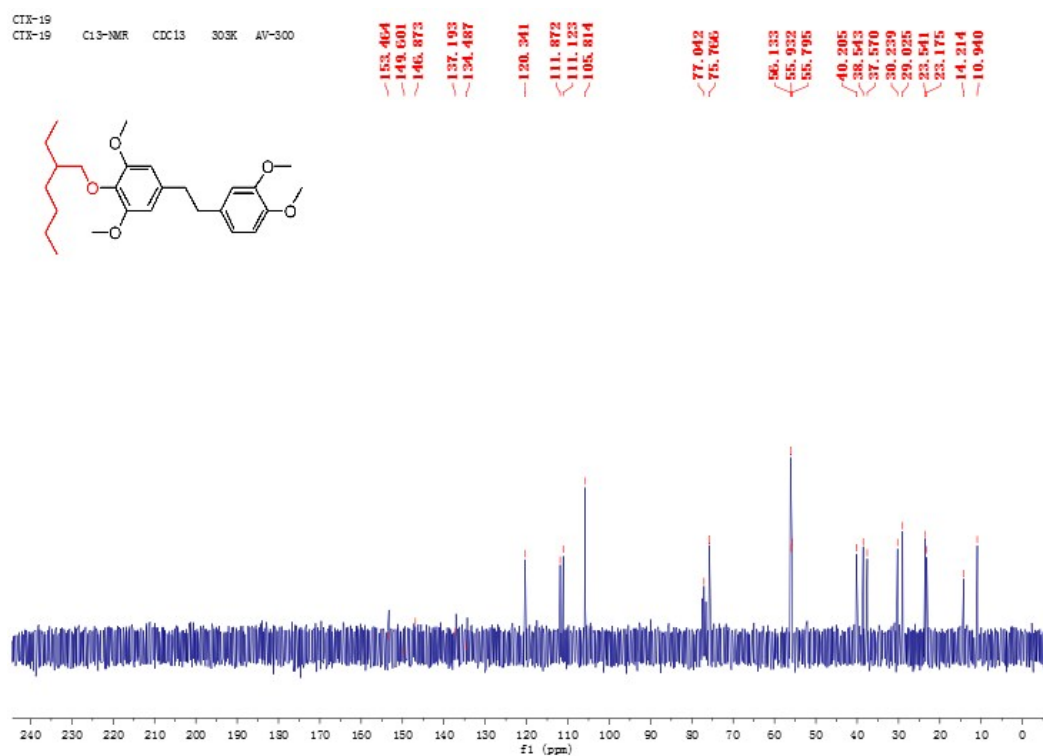


Fig S3.26.3 ¹³C-NMR spectrum of compound **3h** (75 MHz, CDCl₃)

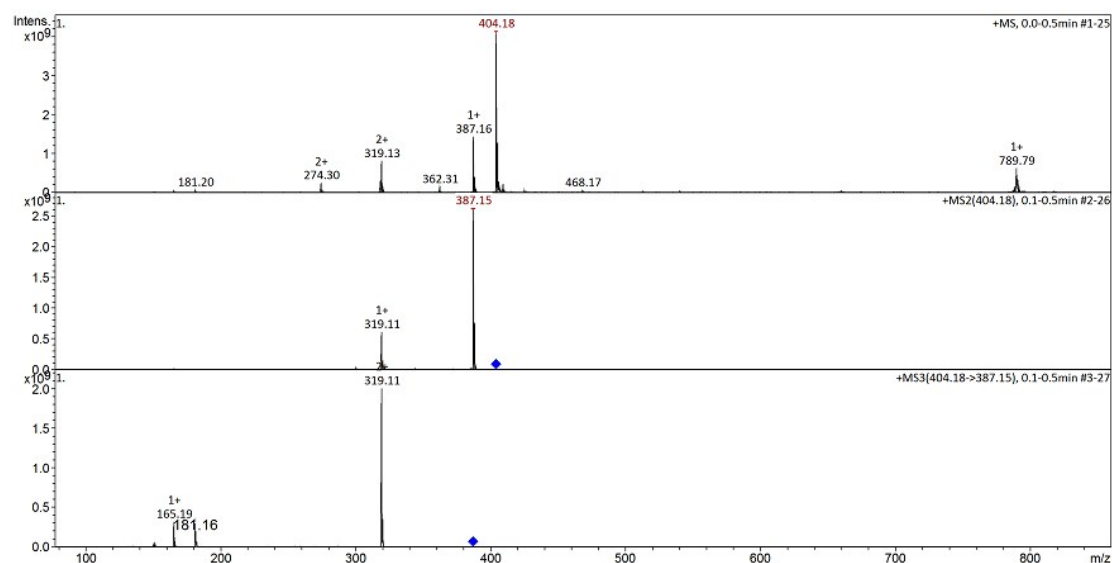


Fig S3.27.1 ESI-MS spectrum of compound **3i**

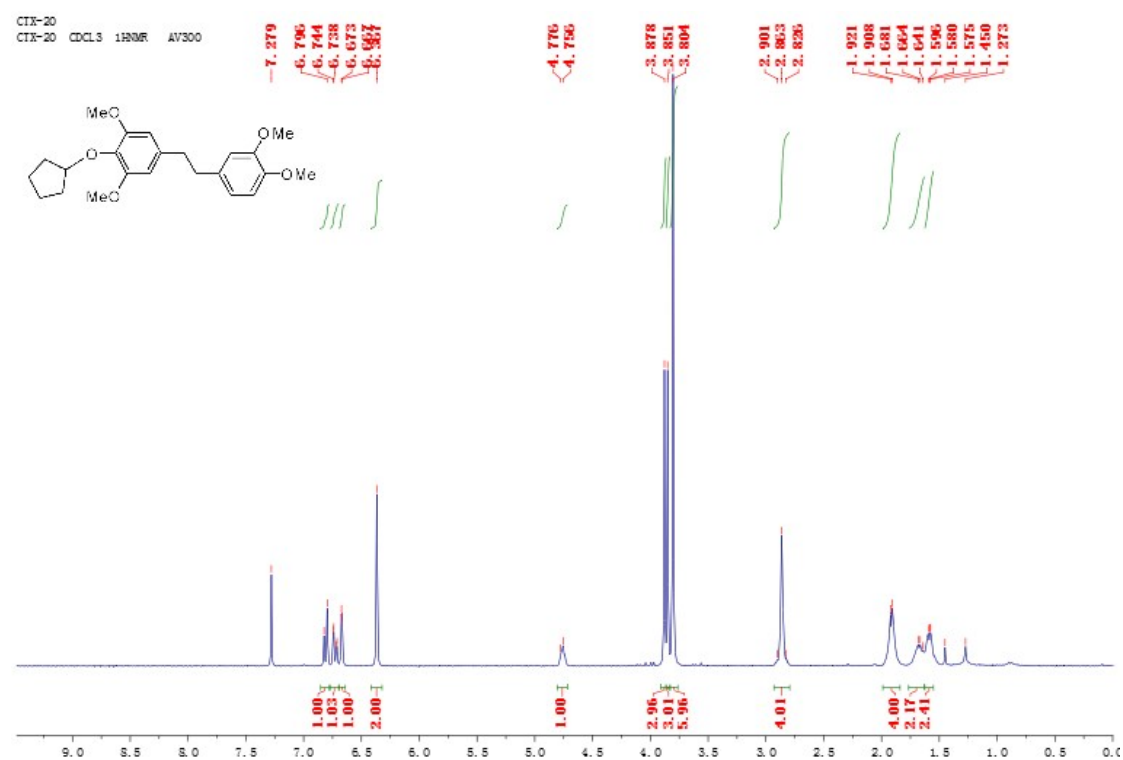


Fig S3.27.2 ^1H -NMR spectrum of compound **3i** (300MHz, CDCl_3)

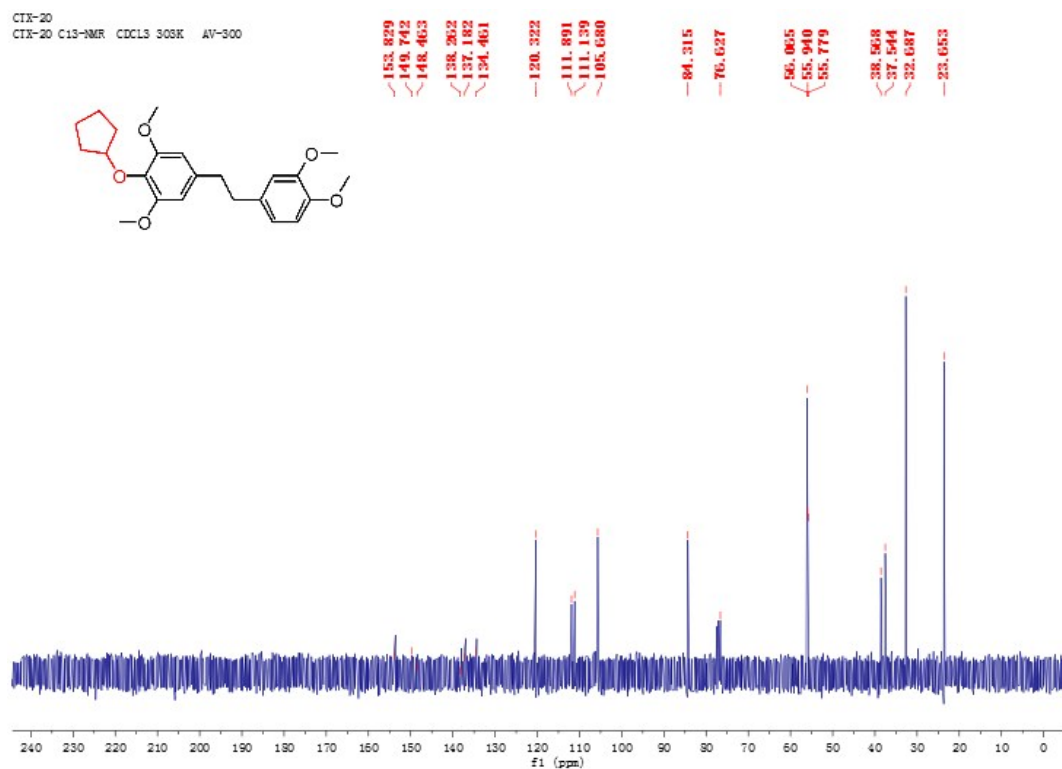


Fig S3.27.3 ^{13}C -NMR spectrum of compound **3i** (75 MHz, CDCl_3)

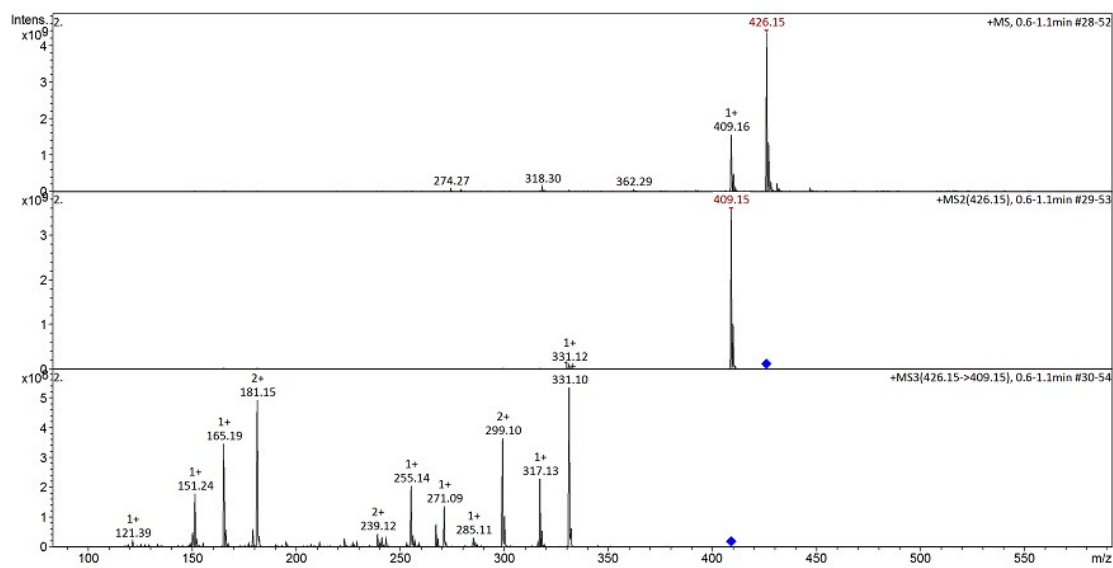


Fig S3.28.1 ESI-MS spectrum of compound **3j**

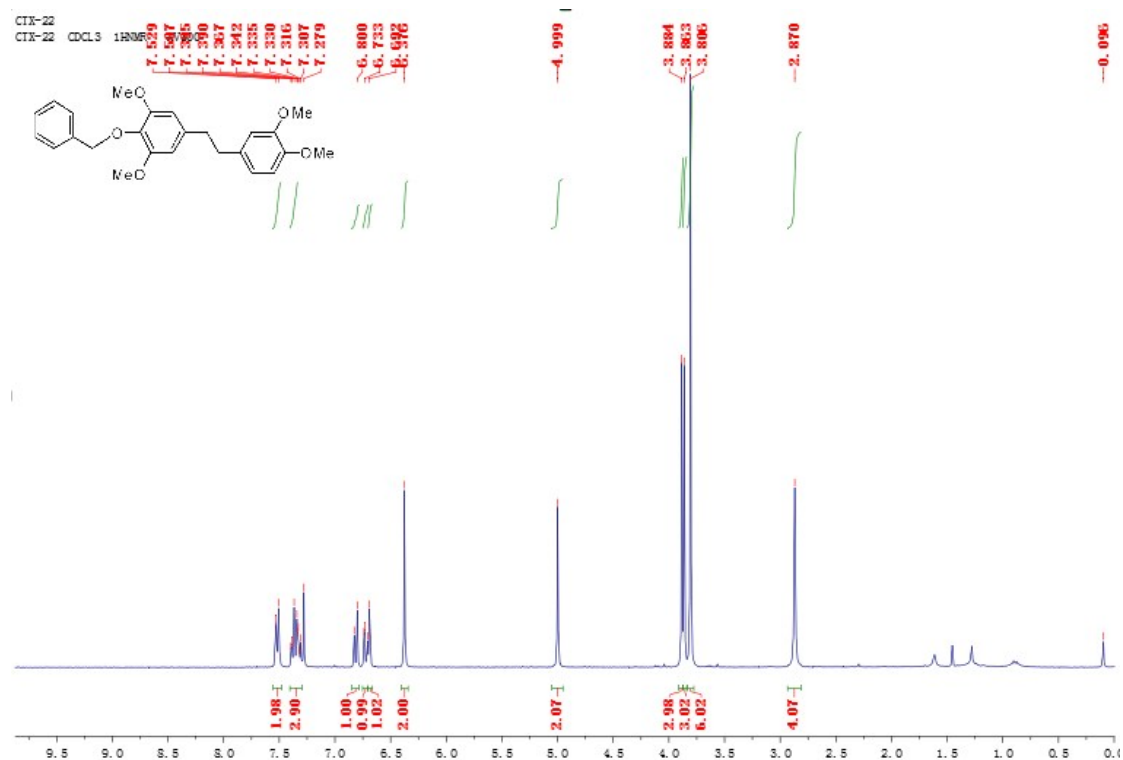


Fig S3.28.2 ¹H-NMR spectrum of compound **3j** (300MHz, CDCl₃)

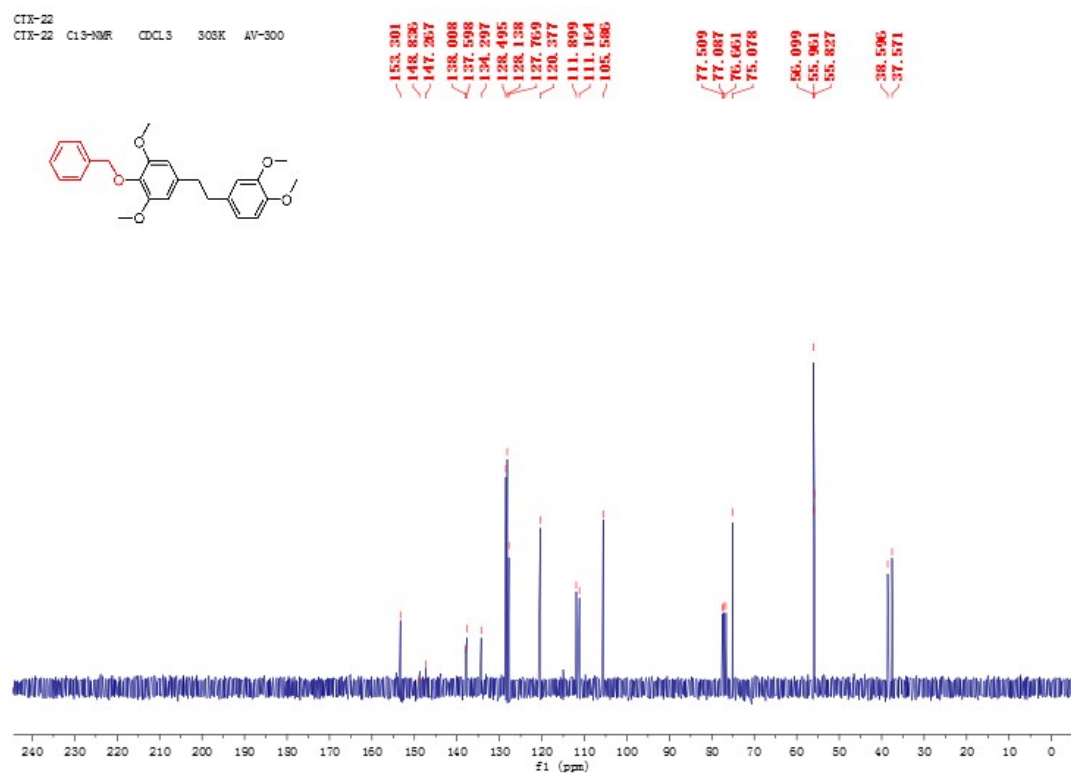


Fig S3.28.3 ¹³C-NMR spectrum of compound **3j** (75 MHz, CDCl₃)

