

Supporting Information

Title: Synthesis and preliminary biological evaluation of two fluoroolefin analogs of Largazole inspired by the structural similarity of the side chain unit in Psammoplin A

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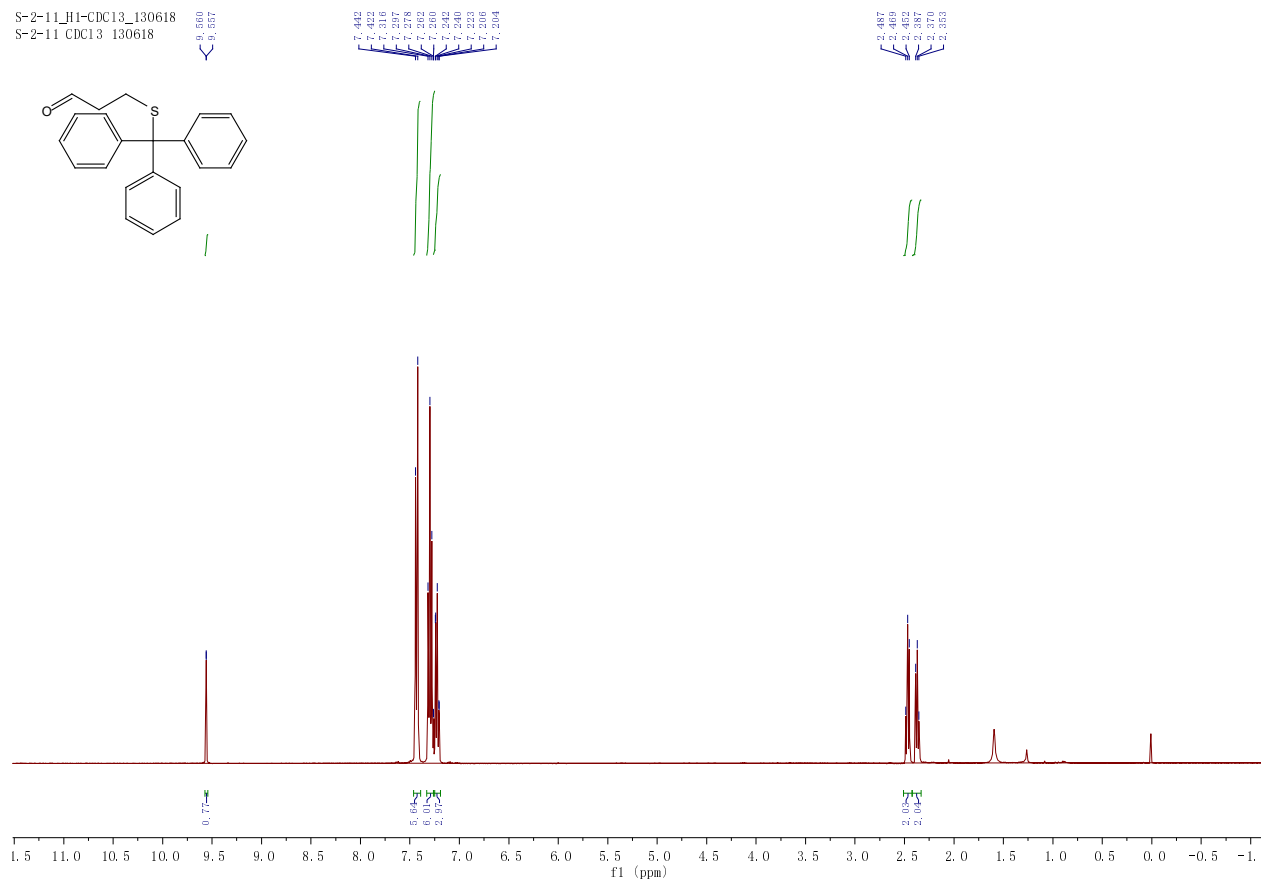
Experimental Section

General Methods. The chemicals and reagents were purchased from Acros, Alfa Aesar, and National Chemical Reagent Group Co. Ltd., P. R. China, and used without further purification. Anhydrous solvents (THF, MeOH, DMF, CH₂Cl₂, and CH₃CN) used in the reactions were dried and freshly distilled before use. All the reactions were carried out under Ar atmosphere, otherwise stated else. The progress of the reactions was monitored by TLC (silica-coated glass plates) and visualized under UV light, and by using iodine or phosphomolybdic acid. Melting points were measured on a SGW X-4 microscopy melting point apparatus without correction. ¹H NMR and ¹³C NMR spectra were recorded either on a 400 MHz Varian Instrument at 25 °C or 600 MHz Bruke Instrument at 25 °C, using TMS as an internal standard, respectively. Multiplicity is tabulated as s for singlet, d for doublet, dd for doublet of doublet, t for triplet, and m for multiplet. HRMS spectra were recorded on Finnigan-Mat-95 mass spectrometer, equipped with ESI source.

3-(tritylthio)propanal (3).

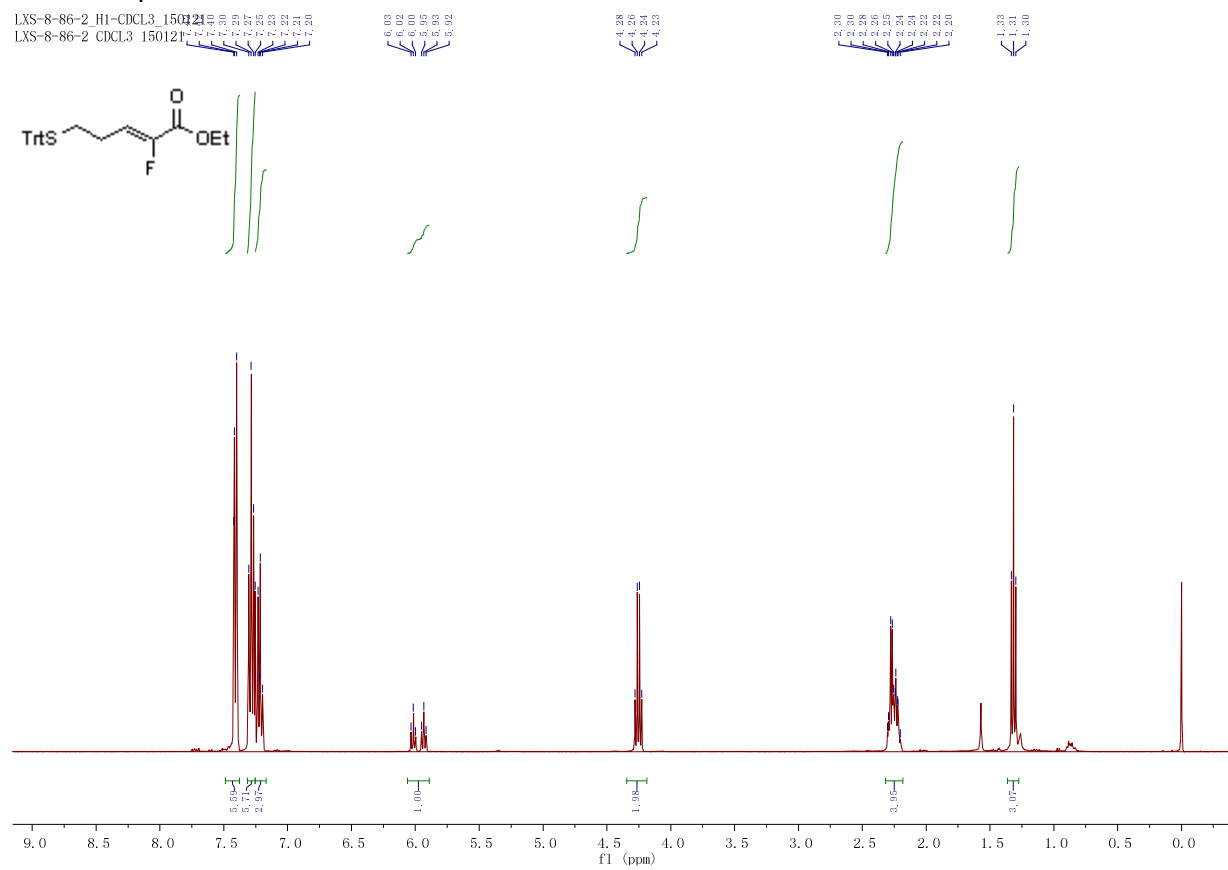
¹H NMR Spectrum of 3

S-2-11_H1-CDC13_130618
S-2-11 CDC13 130618

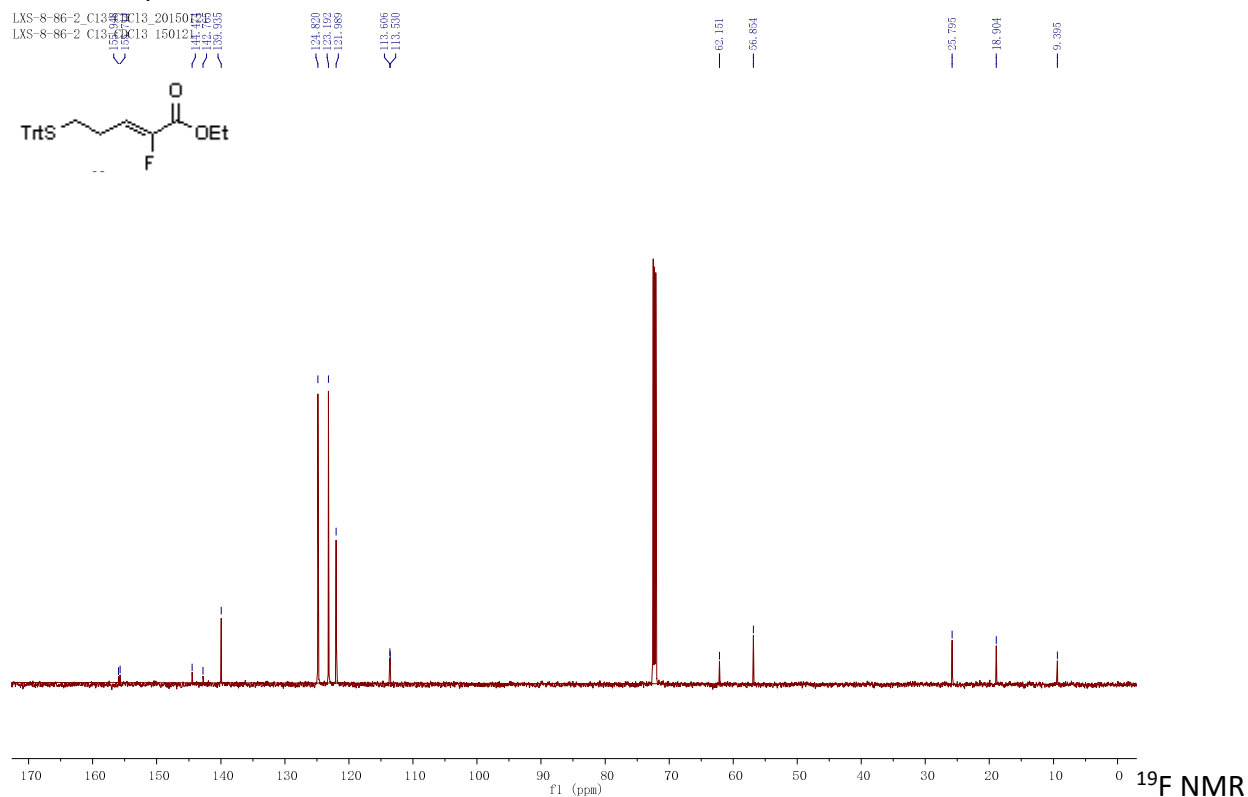


ethyl 2-fluoro-5-(tritylthio)pent-2-enoate (4).

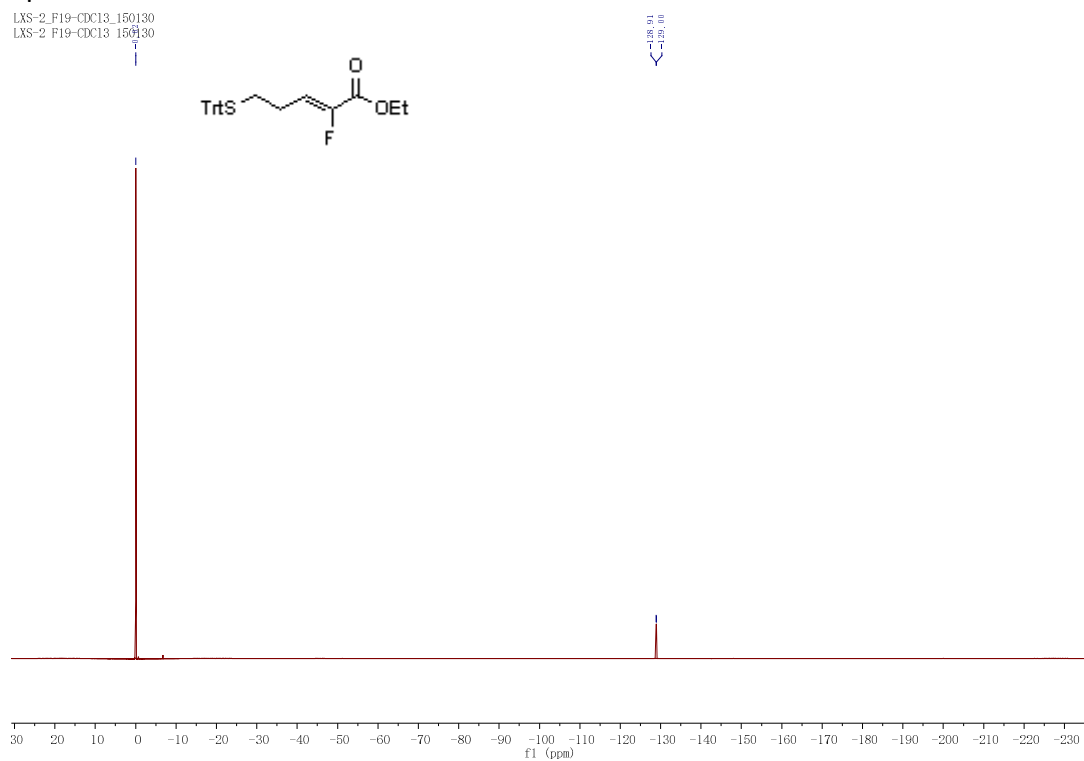
¹H NMR Spectrum of Z-isomer of 4



¹³C NMR Spectrum of Z-isomer of 4



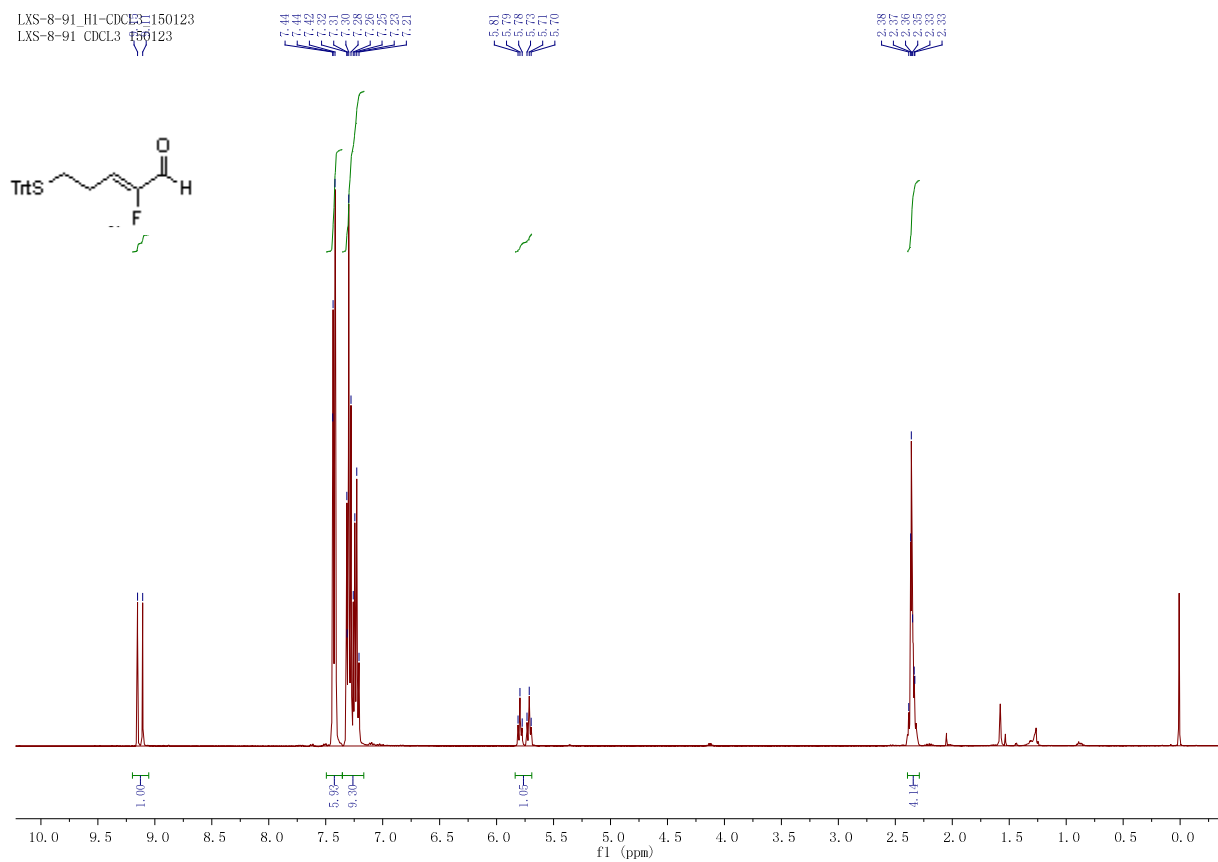
Spectrum of Z-isomer of 4



(Z)-2-fluoro-5-(tritylthio)pent-2-enal (5).

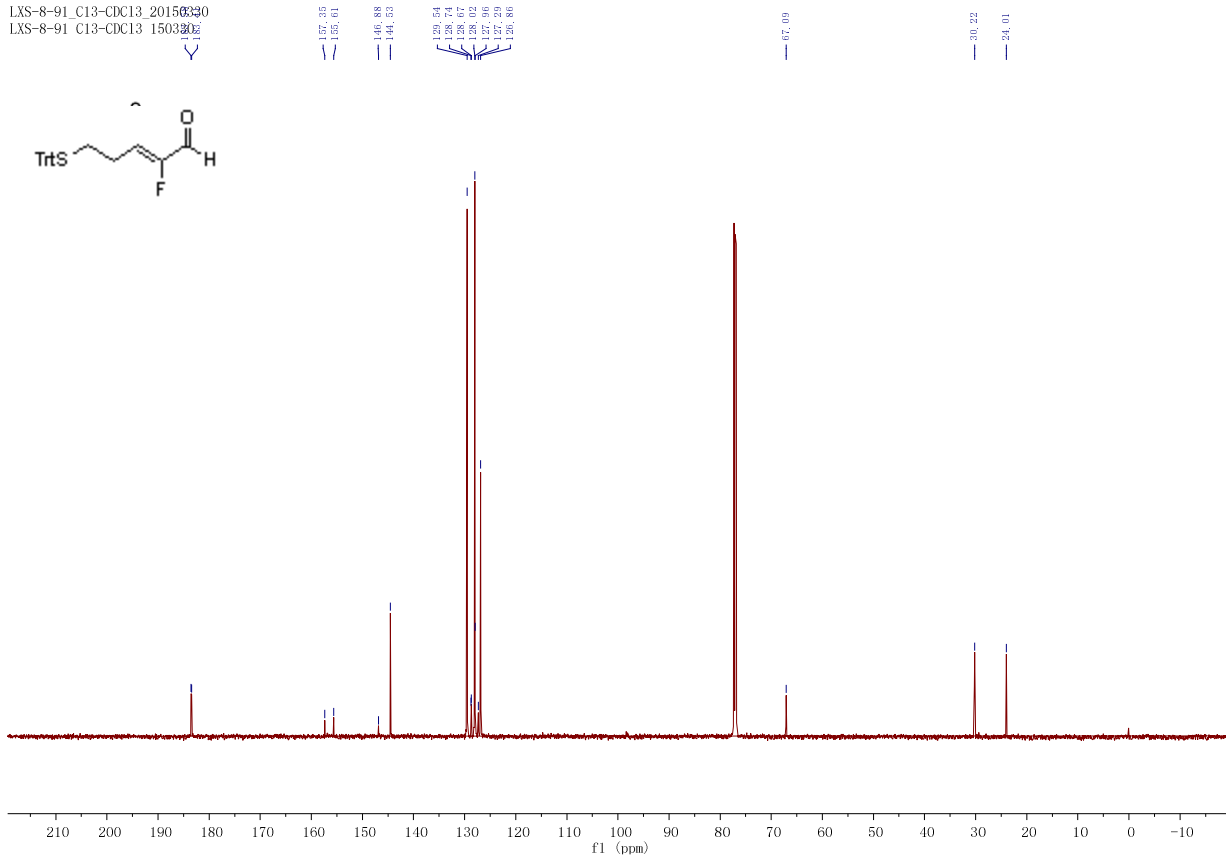
¹H NMR Spectrum of 5

LXS-8-91_H1-CDCl3=150123
LXS-8-91_CDCl3_150123



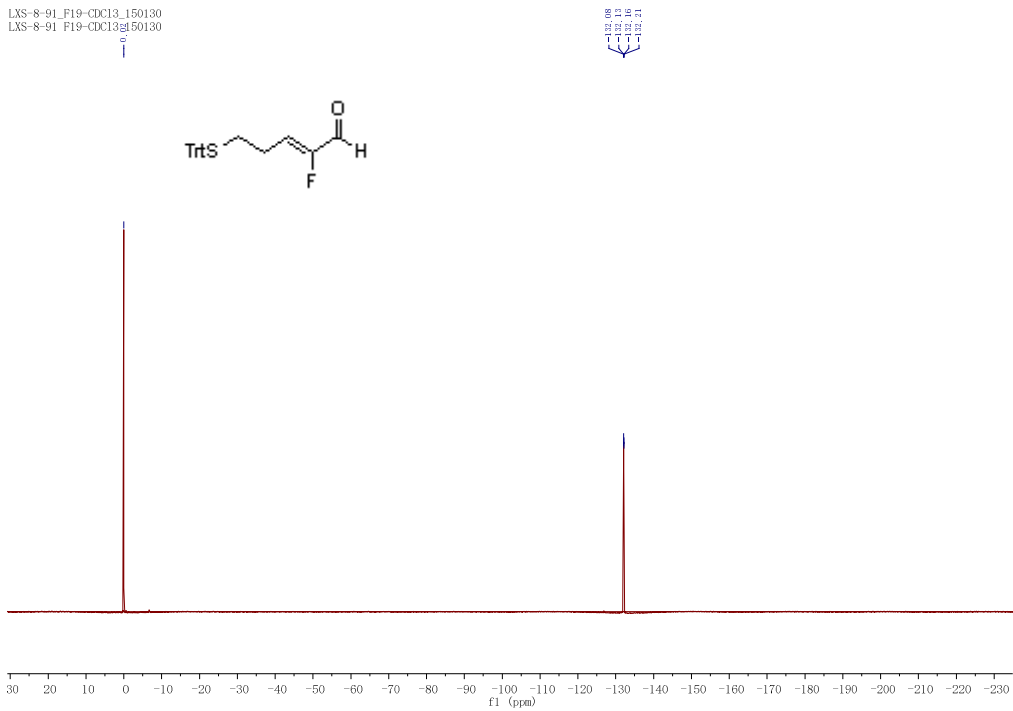
¹³C NMR Spectrum of 5

LXS-8-91_C13-CDCl3_20150330
LXS-8-91_C13-CDCl3_150330



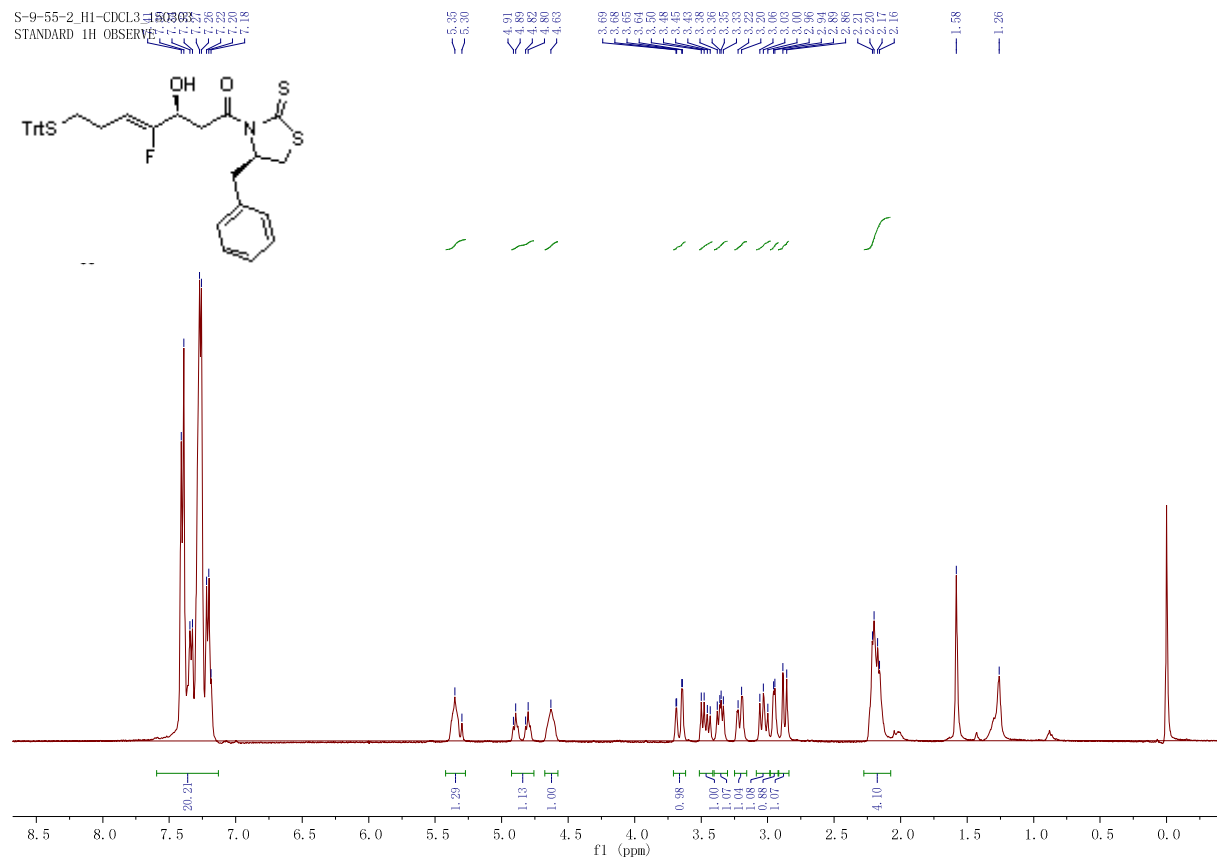
¹⁹F NMR Spectrum of 5

LXS-8-91_F19-CDCl3_150130
LXS-8-91_F19-CDCl3_50130



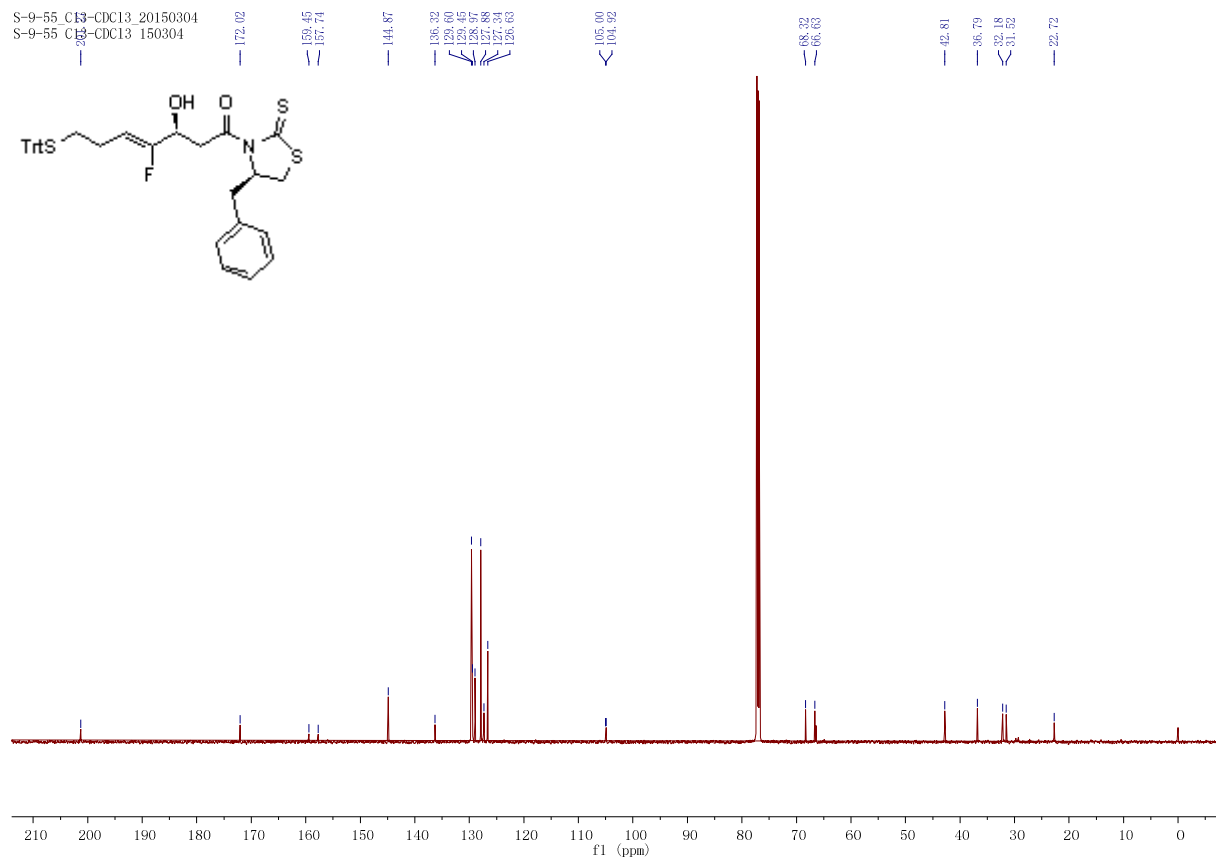
(S,Z)-1-((R)-4-benzyl-2-thioxothiazolidin-3-yl)-4-fluoro-3-hydroxy-7-(tritylthio)hept-4-en-1-one (8).

¹H NMR Spectra of 8



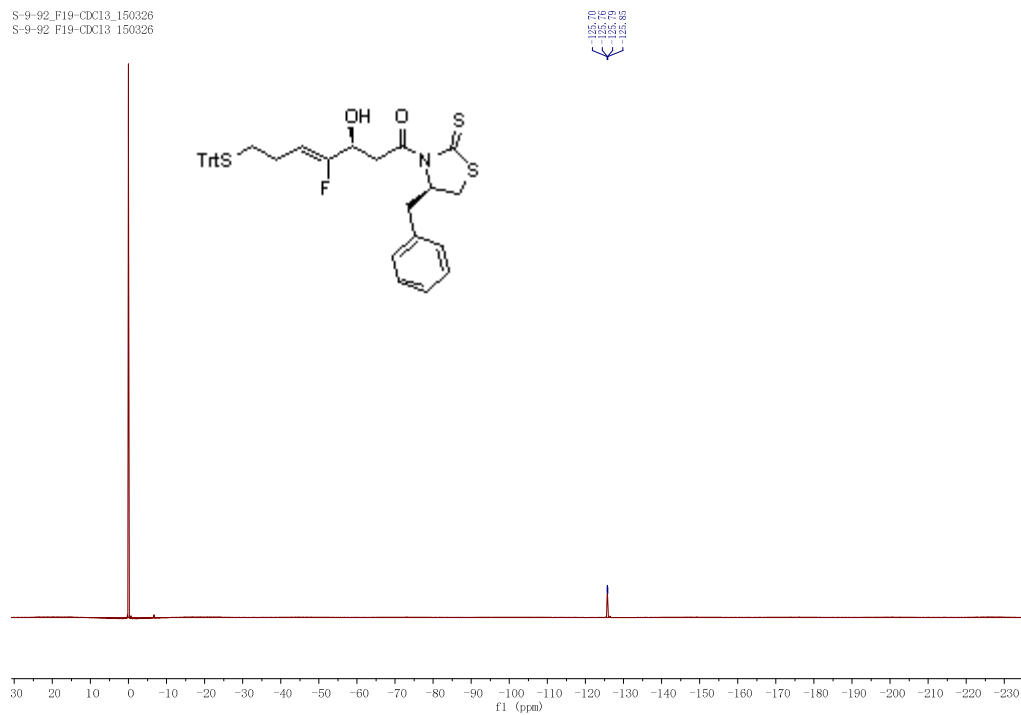
¹³C NMR Spectra of **8**

S-9-55 C13-CDC13 20150304
S-9-55 C13-CDC13 150304



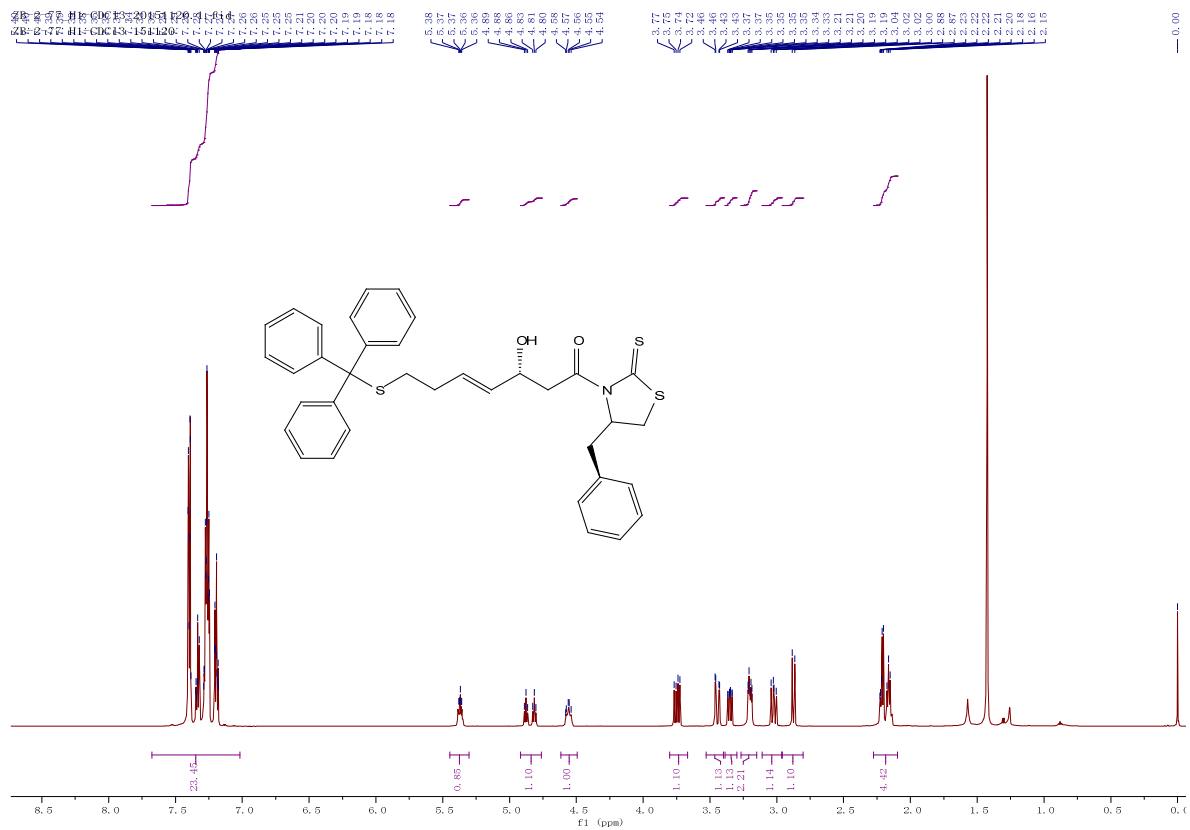
¹⁹F NMR Spectra of **8**

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S-9-92 F19-CDC13 150326

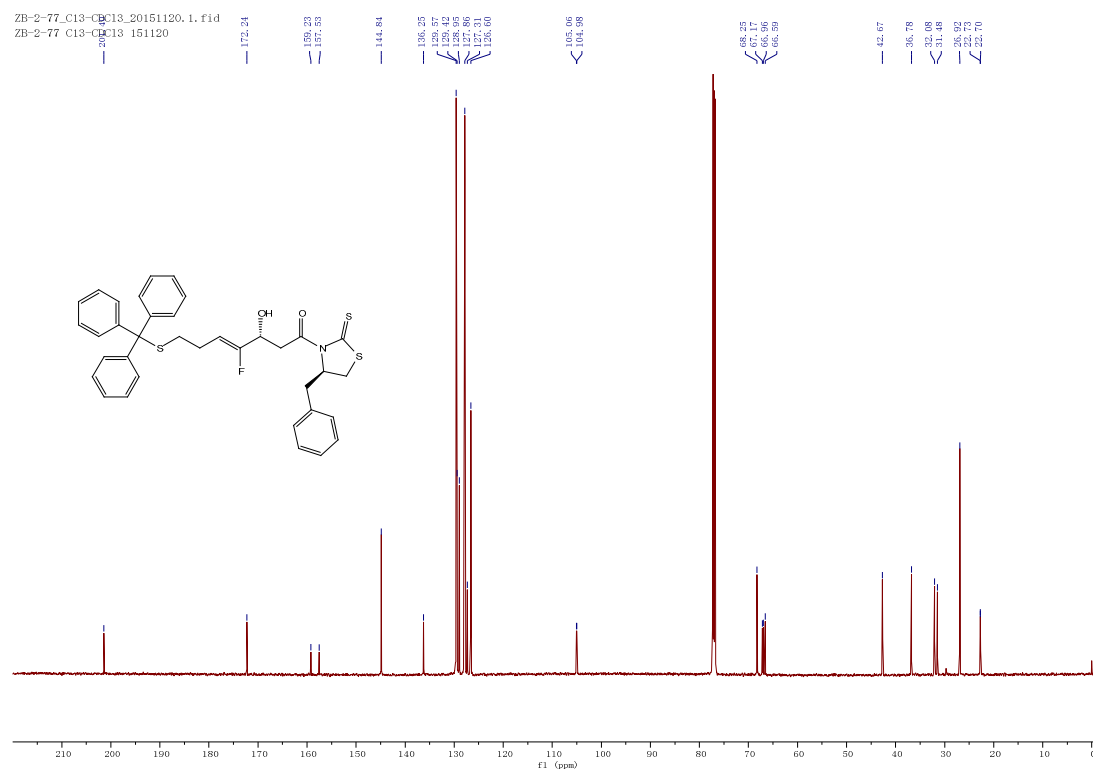


(S,Z)-1-((R)-4-benzyl-2-thioxothiazolidin-3-yl)-4-fluoro-3-hydroxy-7-(tritylthio)hept-4-en-1-one (9).

¹H NMR Spectra of 9



¹³C NMR Spectra of 9

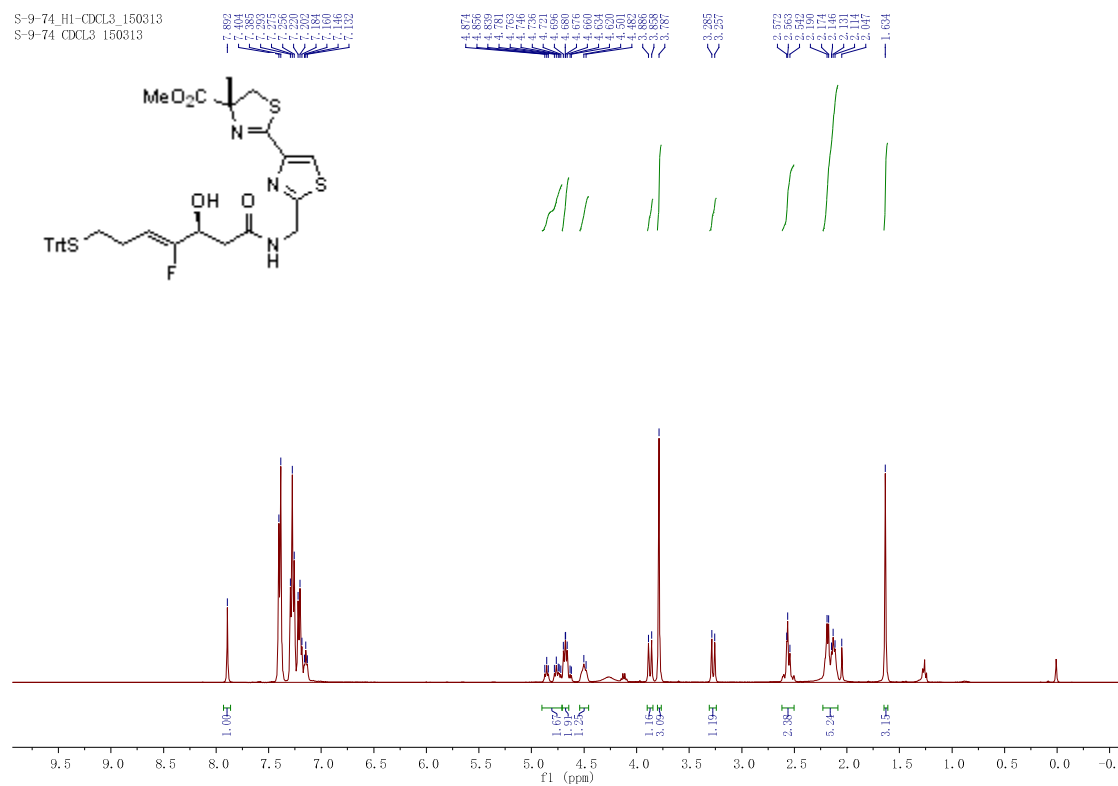


¹⁹F NMR Spectra of 9



(R)-methyl 2'-(((S,Z)-4-fluoro-3-hydroxy-7-(tritylthio)hept-4-enamido)methyl)-4-methyl-4,5-dihydro-[2,4'-bithiazole]-4-carboxylate (11)

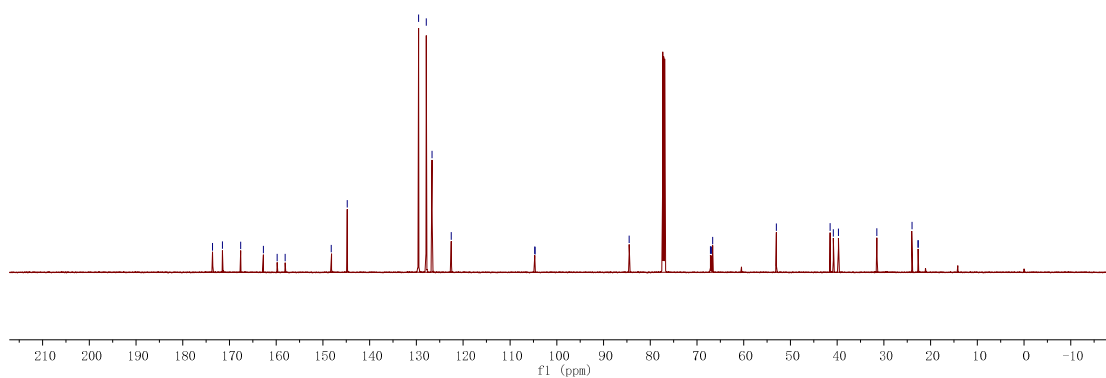
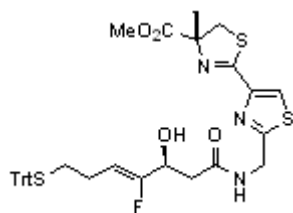
¹H NMR Spectra of 11



¹³C NMR Spectra of 11

S-9-74_C13-CDCl3_20150313
S-9-74_C13-CDCl3_150313

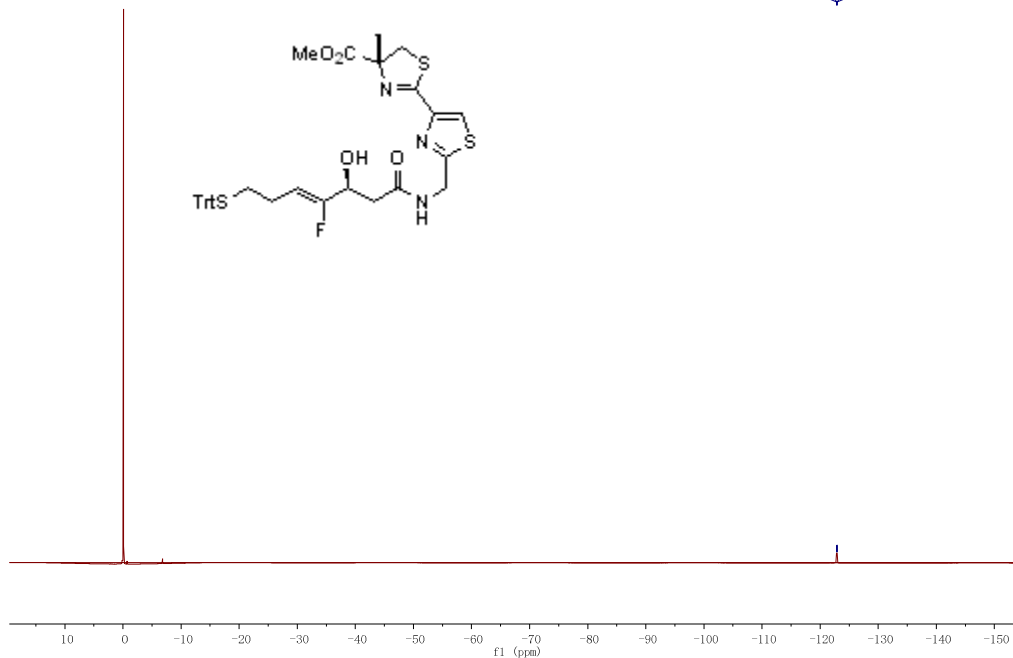
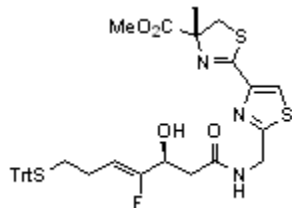
171.63
171.44
167.63
162.78
156.77
156.07
146.20
144.85
130.08
129.91
129.56
129.56
104.71
104.63
81.49
67.87
67.87
66.62
53.01
41.54
40.80
39.72
31.49
24.02
23.71
22.69



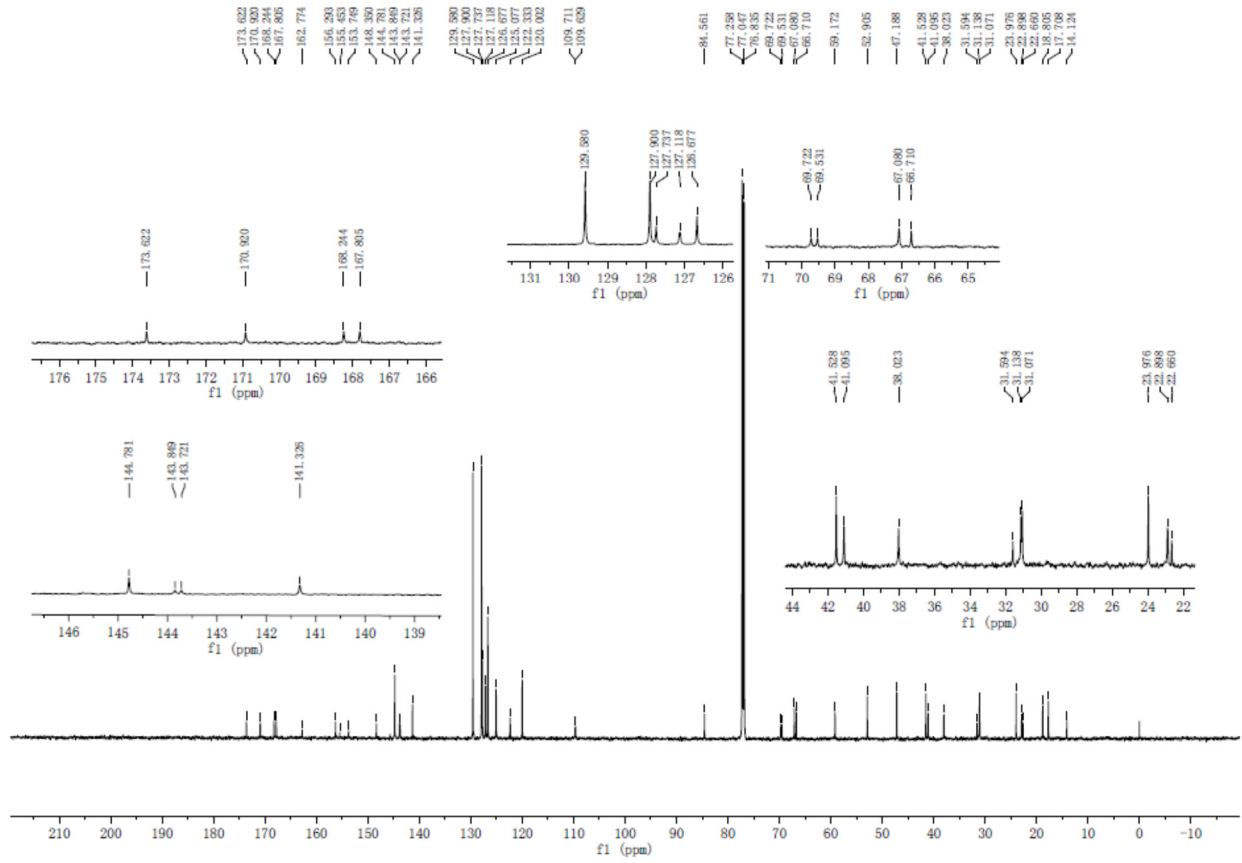
¹⁹F NMR Spectra of 11

S-9-74_F19-CDCl3_150330
S-9-74_F19-CDCl3_150330

83
-123.86
-123.55

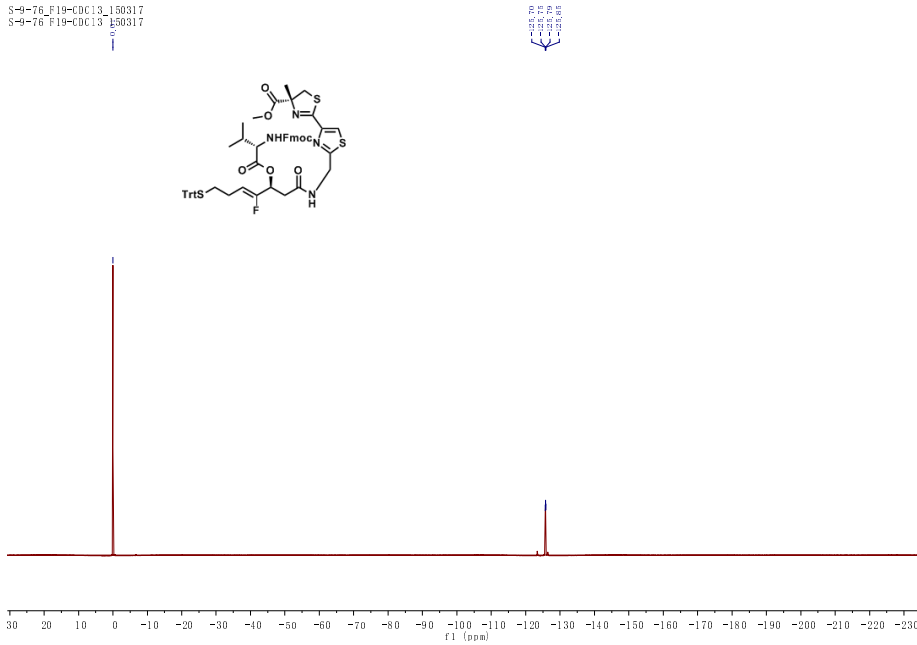
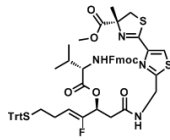


¹³C NMR Spectra of **13a**

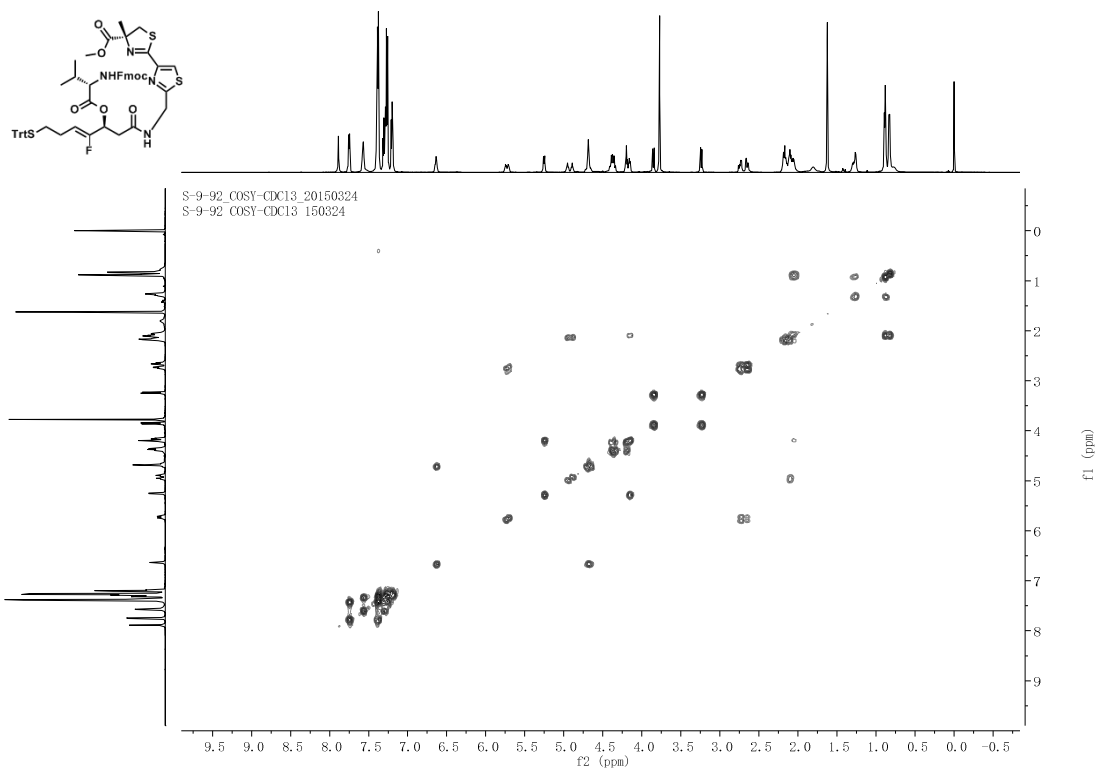


¹⁹F NMR Spectra of **13a**

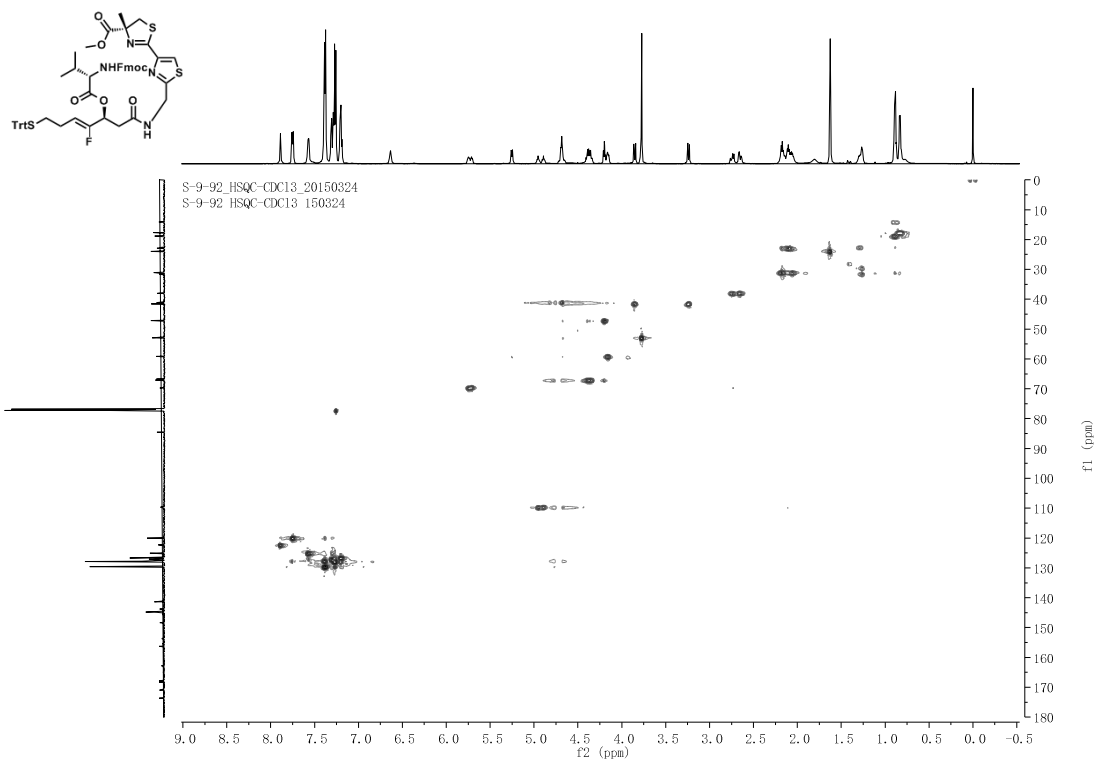
S-9-76_F19-DCI13_150317
S-9-76_F19-DCI13_150317



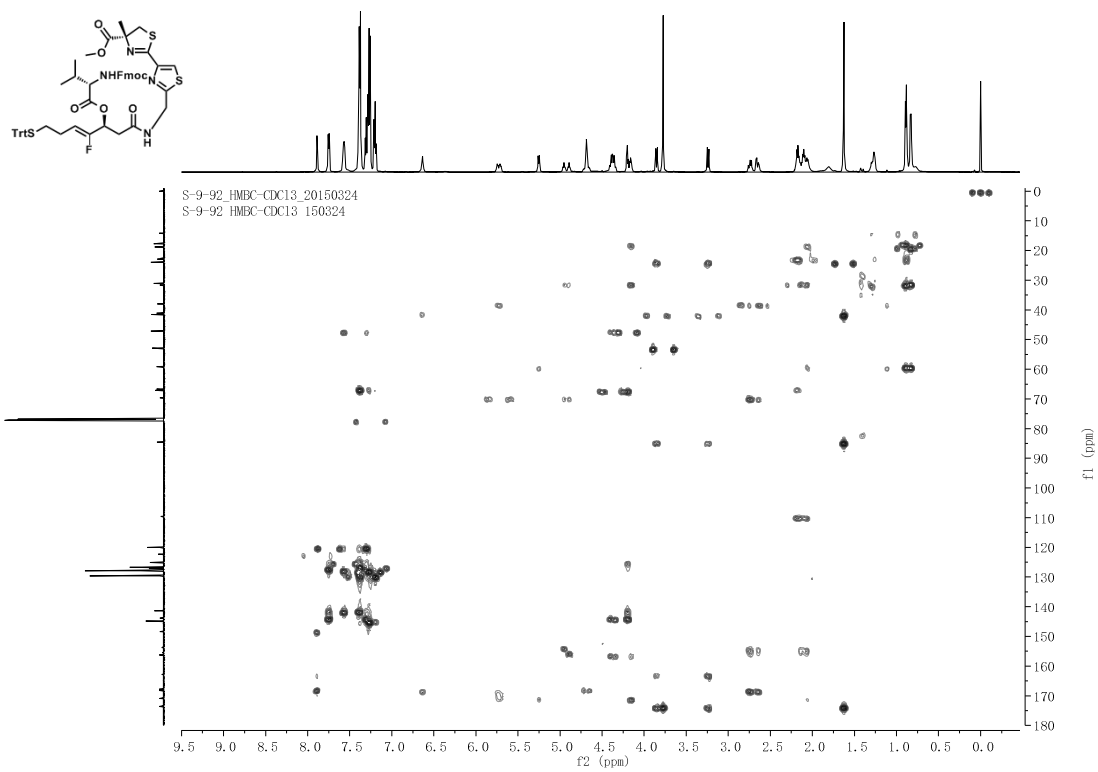
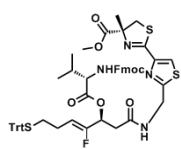
H-H COSY Spectra of 13a



H-C HMQC Spectra of 13a

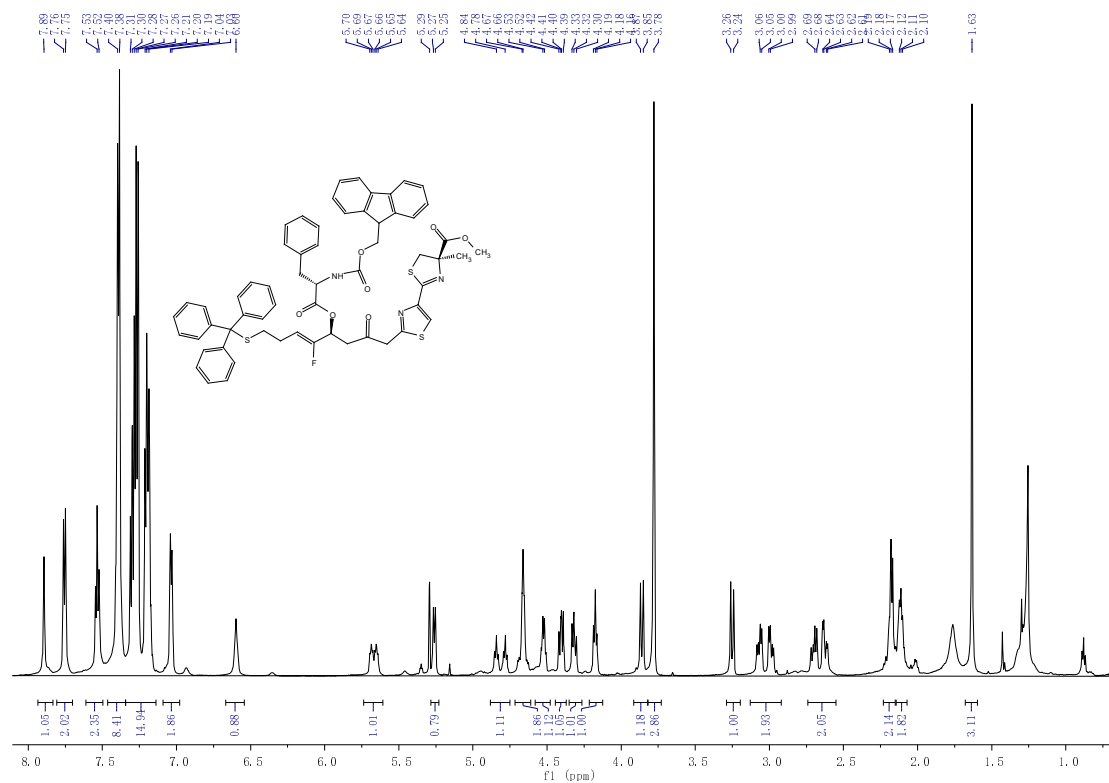


H-C HMBC Spectra of **13a**

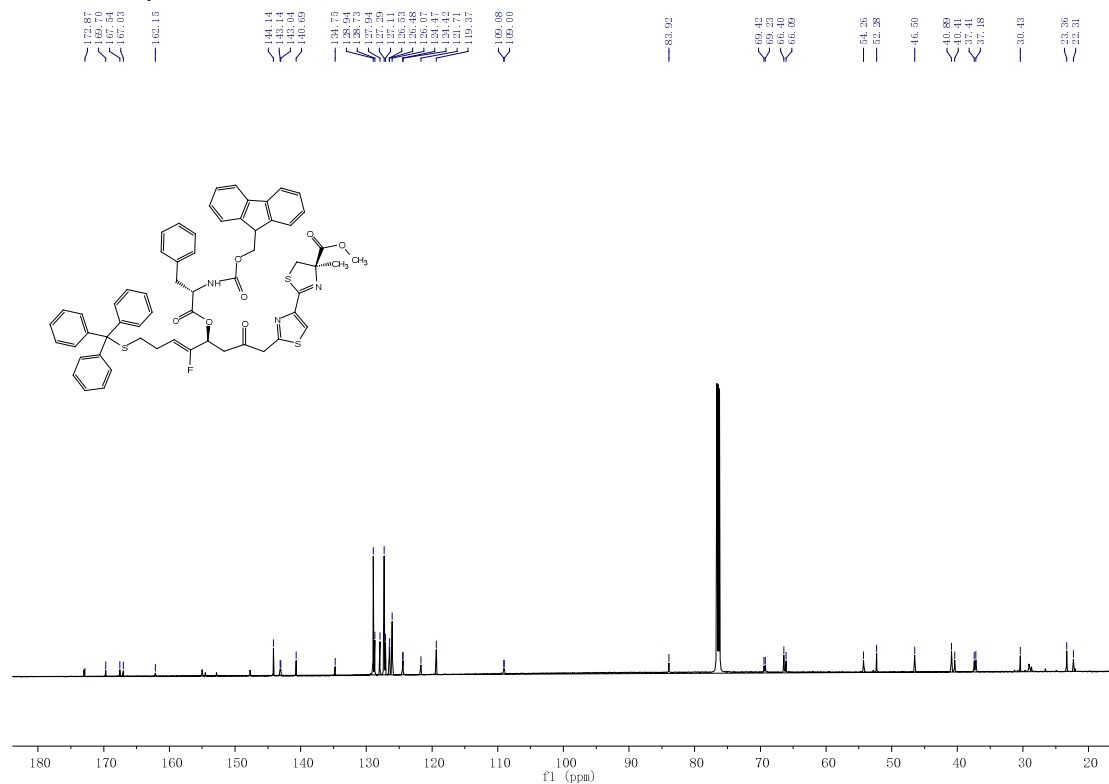


(4R)-methyl 2'-((5S)-5-benzyl-1-(9H-fluoren-9-yl)-8-((Z)-1-fluoro-4-(tritylthio)but-1-en-1-yl)-3,6,10-trioxo-2,7-dioxo-4,11-diazadodecan-12-yl)-4-methyl-4,5-dihydro-[2,4'-bithiazole]-4-carboxylate (13b)

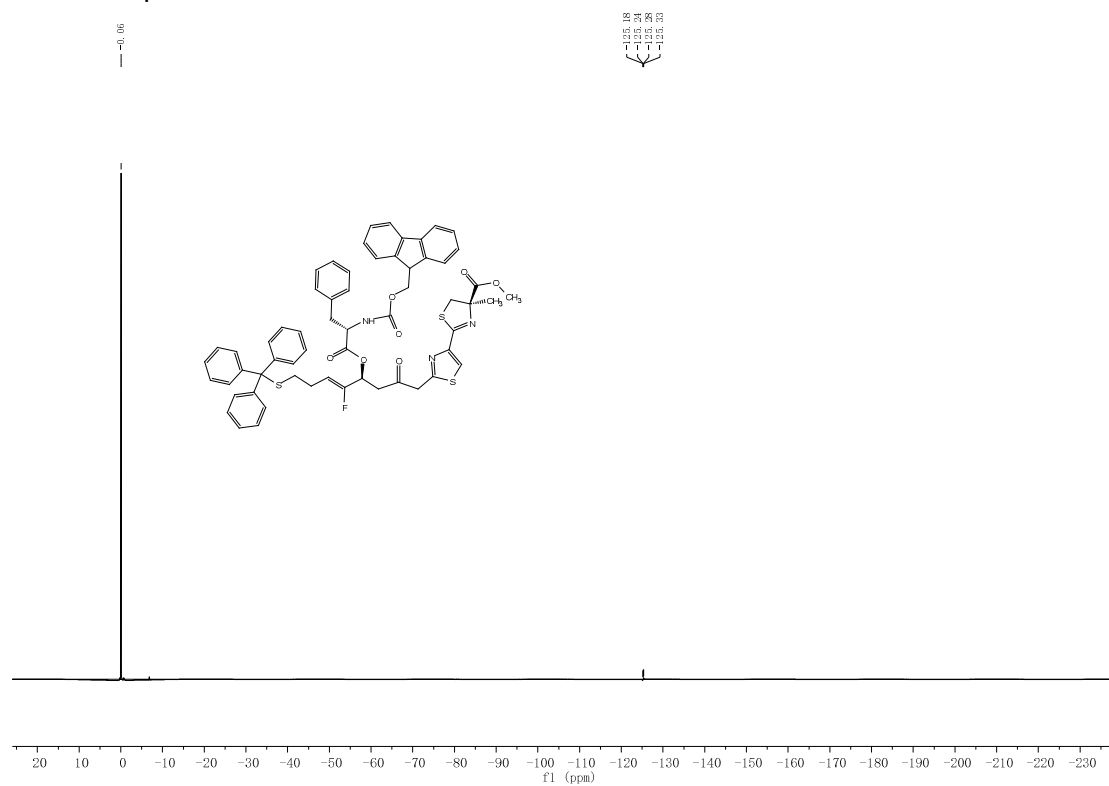
¹H NMR Spectra of 13b



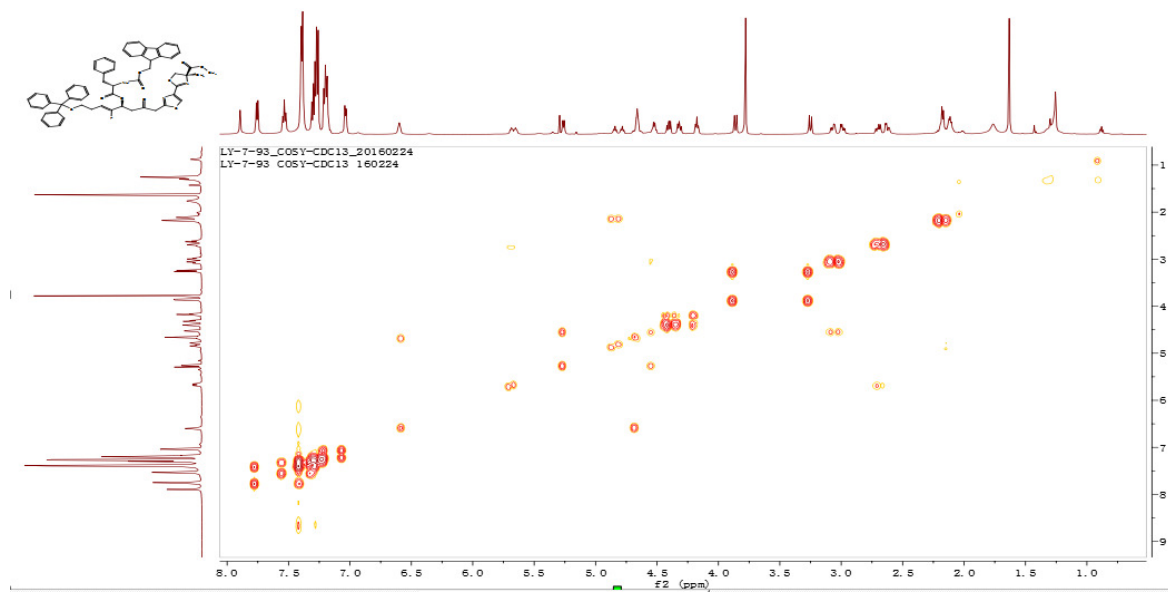
¹³C NMR Spectra of **13b**



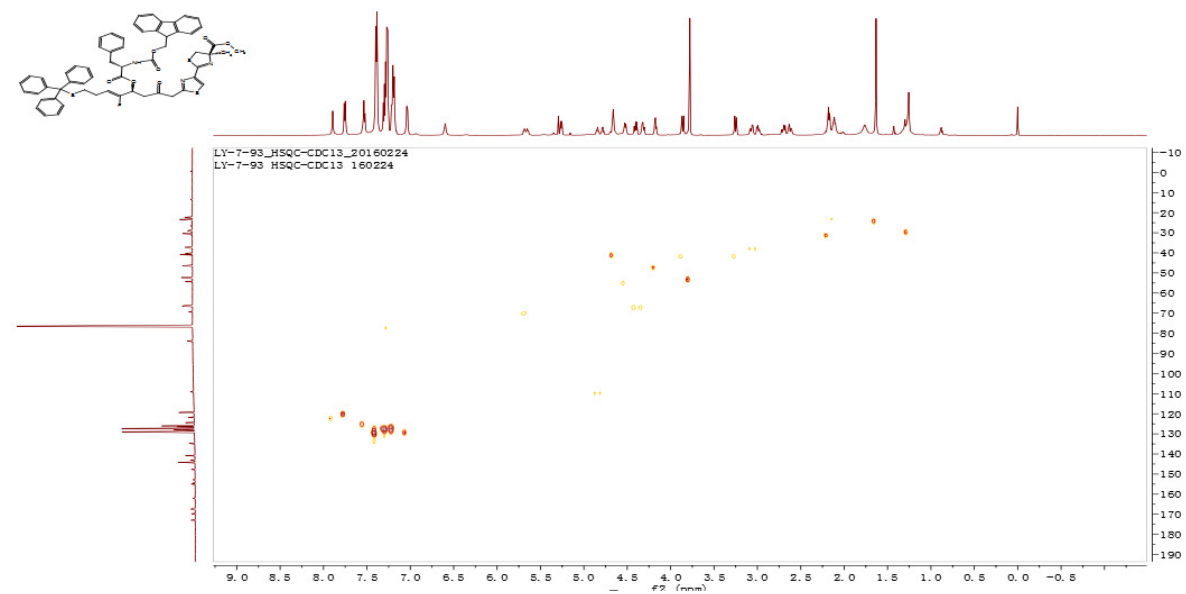
¹⁹F NMR Spectra of **13b**



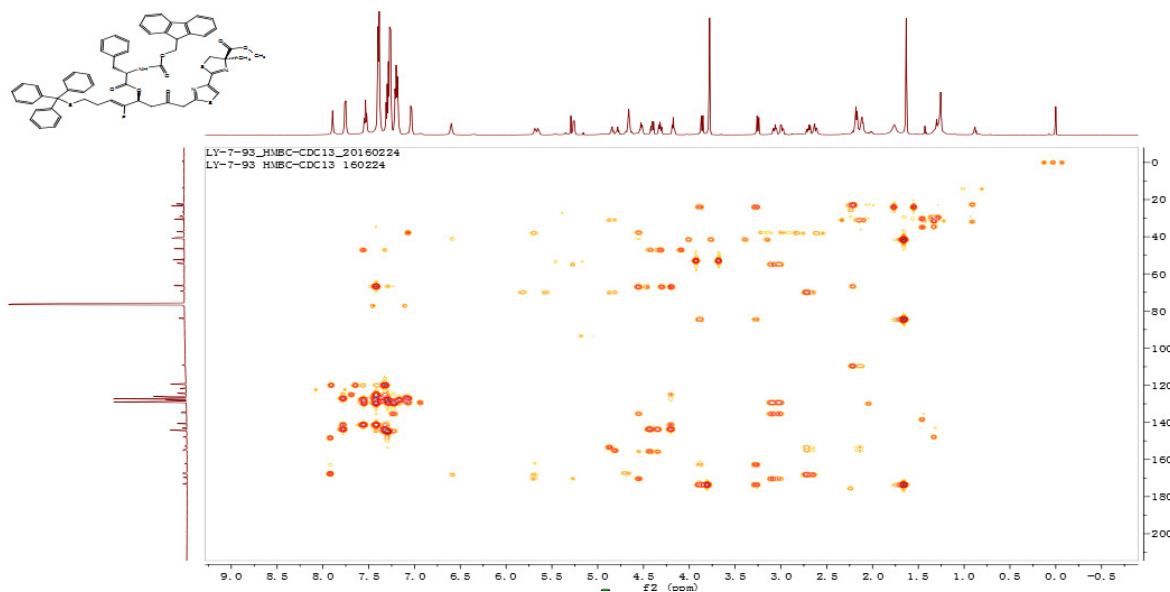
H-H COSY Spectra of **13b**



H-C HMQC Spectra of **13b**

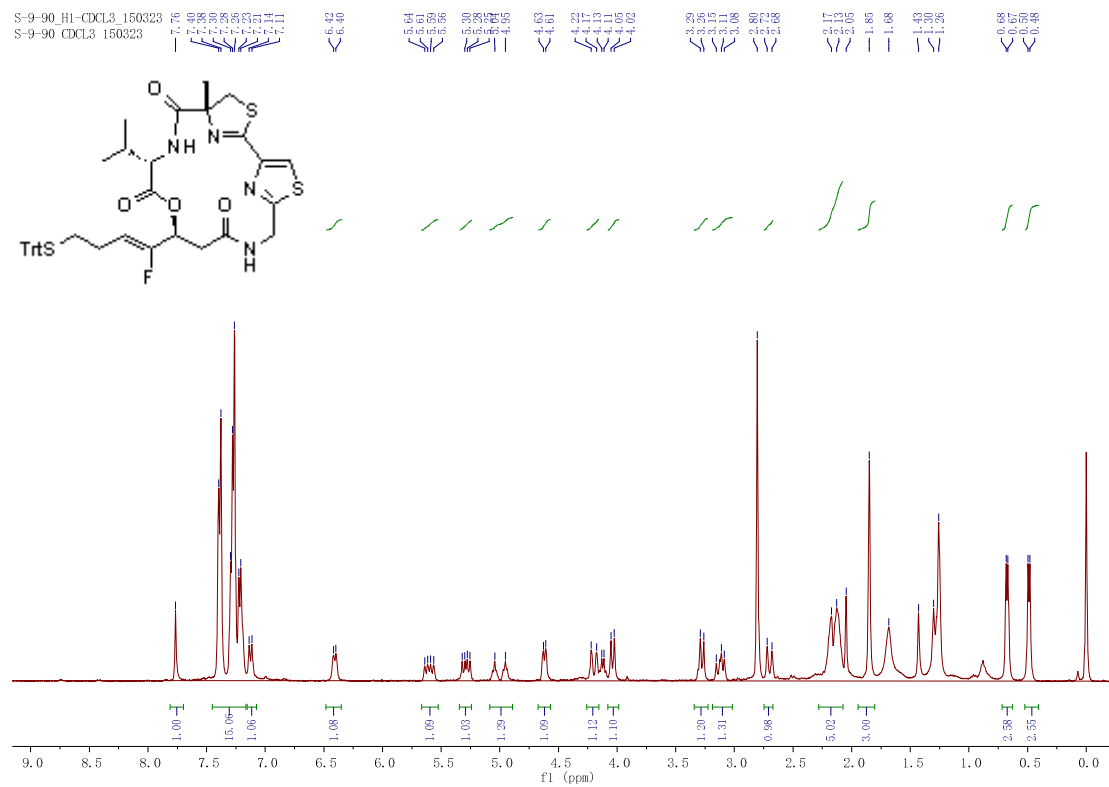


H-C HMBC Spectra of **13b**

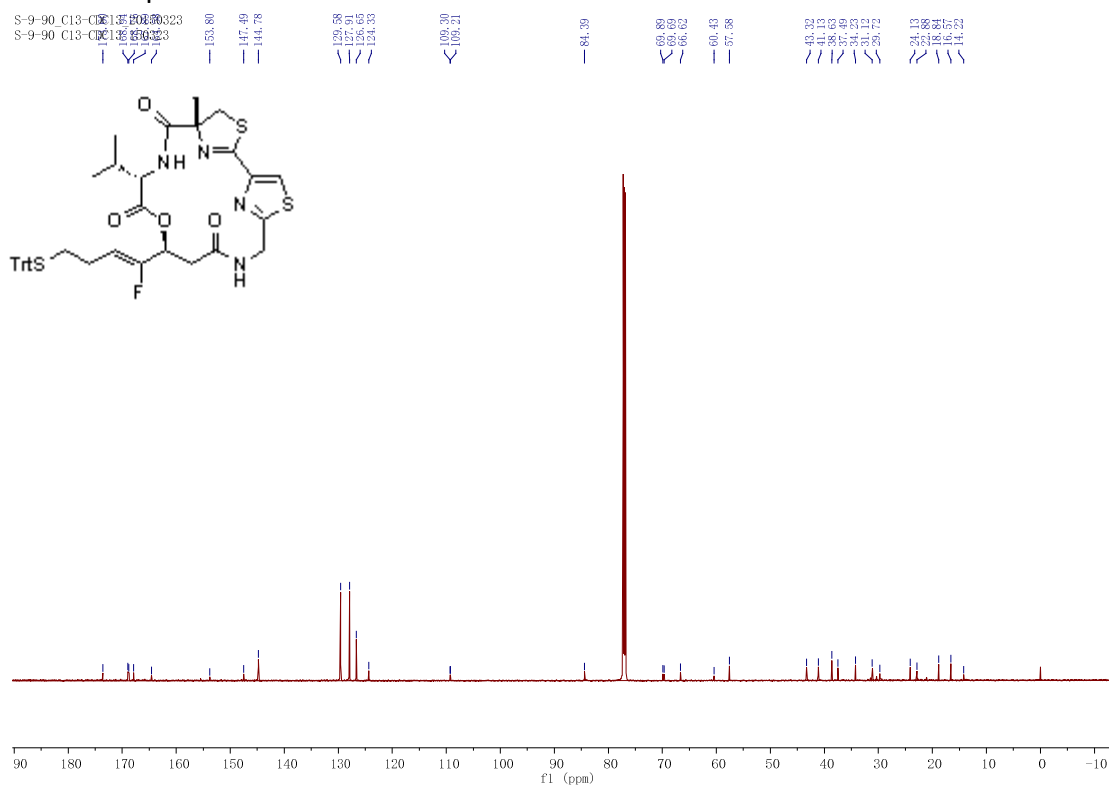


(5R,8S,11S)-11-((Z)-1-fluoro-4-(tritylthio)but-1-en-1-yl)-8-isopropyl-5-methyl-10-oxa-3,17-dithia-7,14,19,20-tetraazatricyclo[14.2.1.12,5]icosa-1(18),2(20),16(19)-triene-6,9,13-trione (14a).

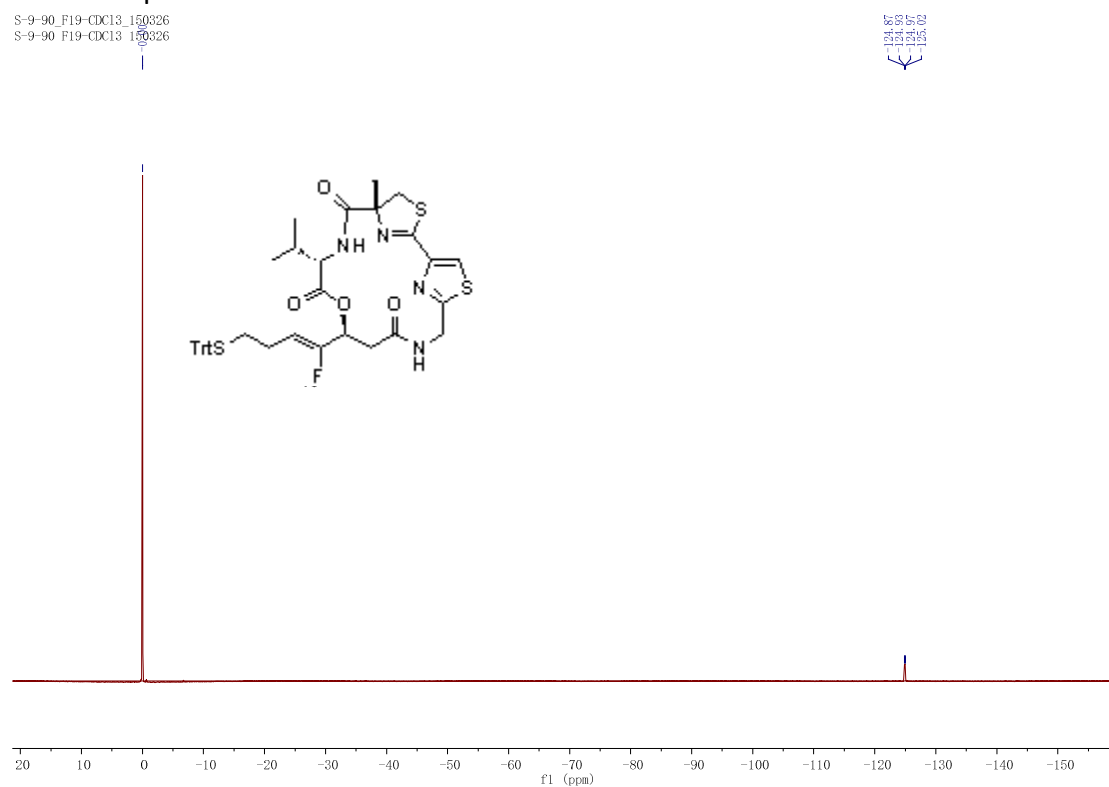
¹H NMR Spectra of 14a



¹³C NMR Spectra of 14a

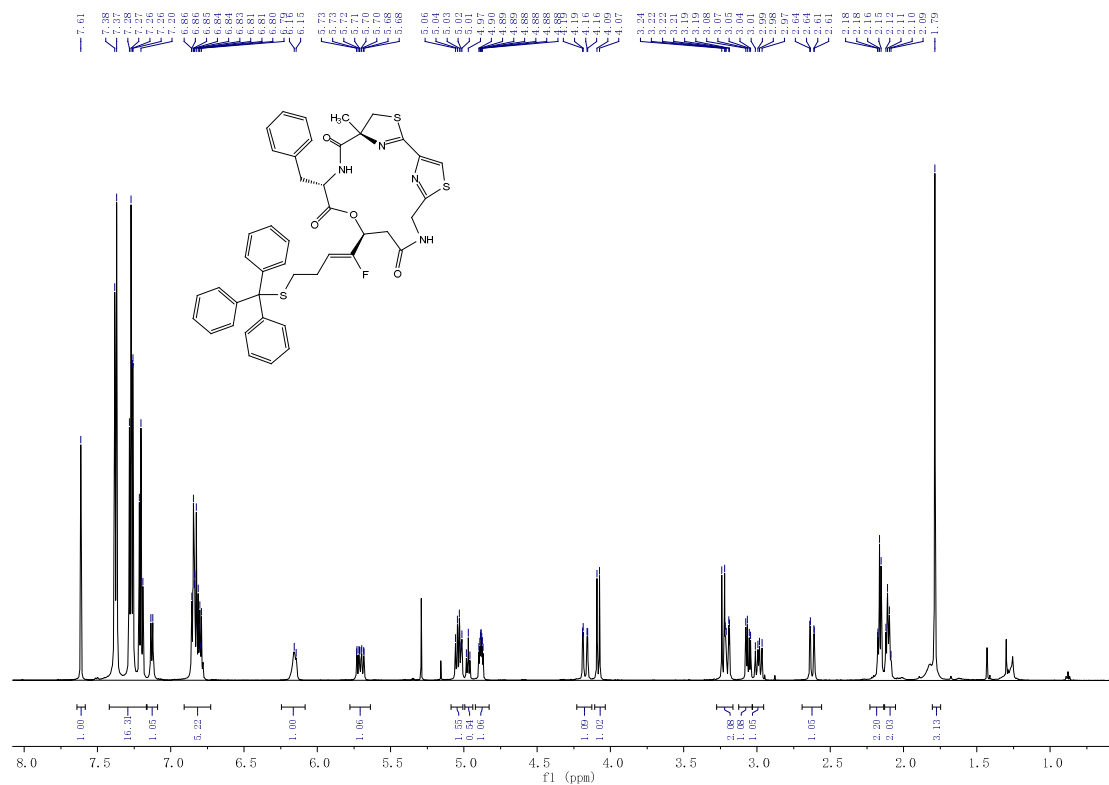


¹⁹F NMR Spectra of 14a

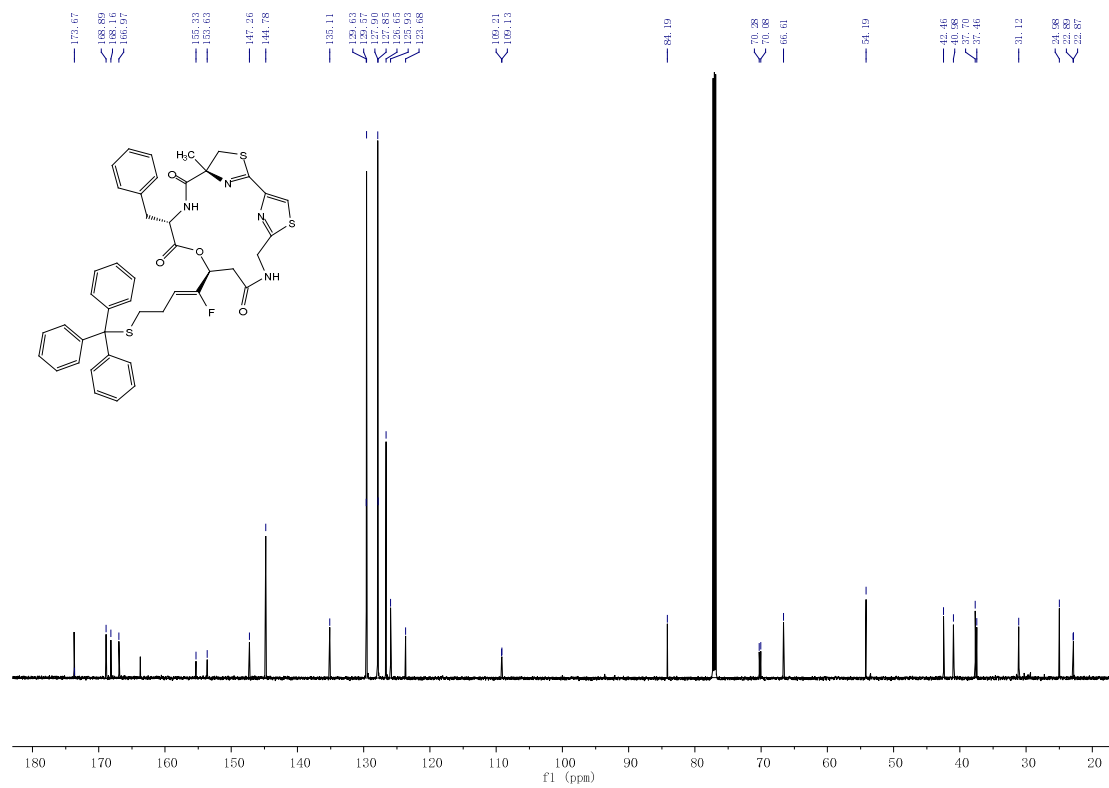


(5R,8S)-8-benzyl-11-((Z)-1-fluoro-4-(tritylthio)but-1-en-1-yl)-5-methyl-10-oxa-3,17-dithia-7,14,19,20-tetraazatricyclo[14.2.1.1^{2,5}]icosa-1(18),2(20),16(19)-triene-6,9,13-trione (14b)

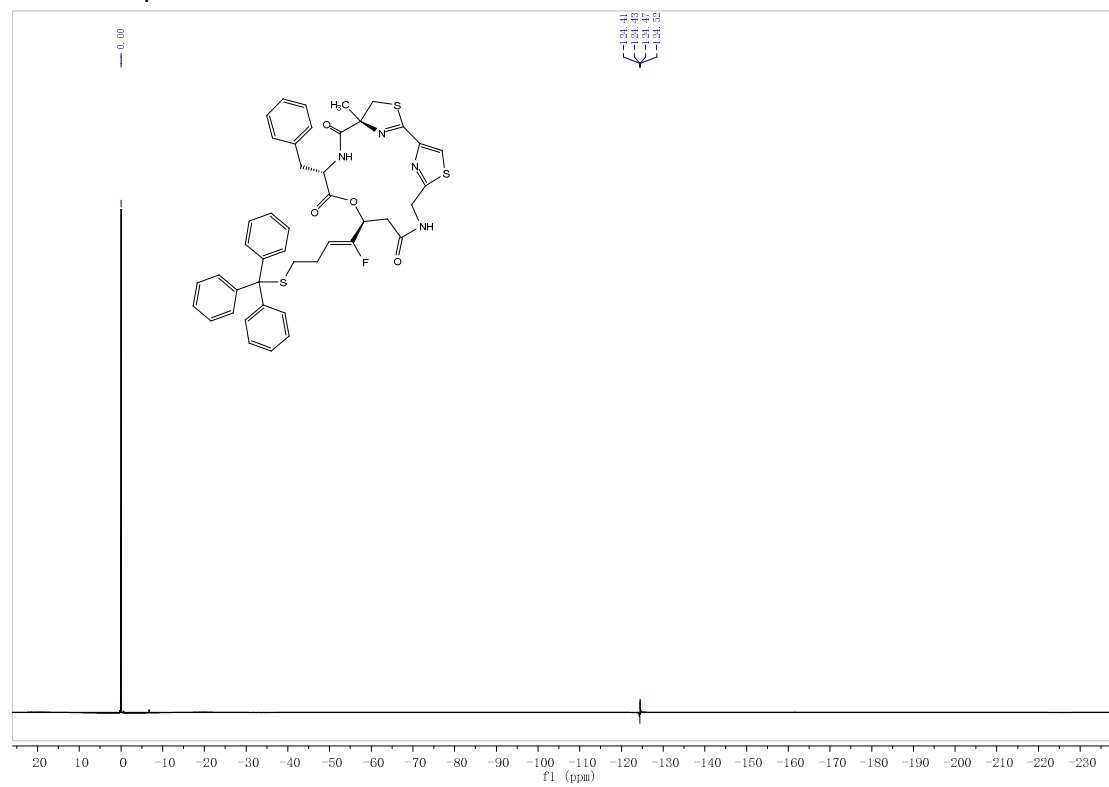
¹H NMR Spectra of 14b



¹³C NMR Spectra of **14b**

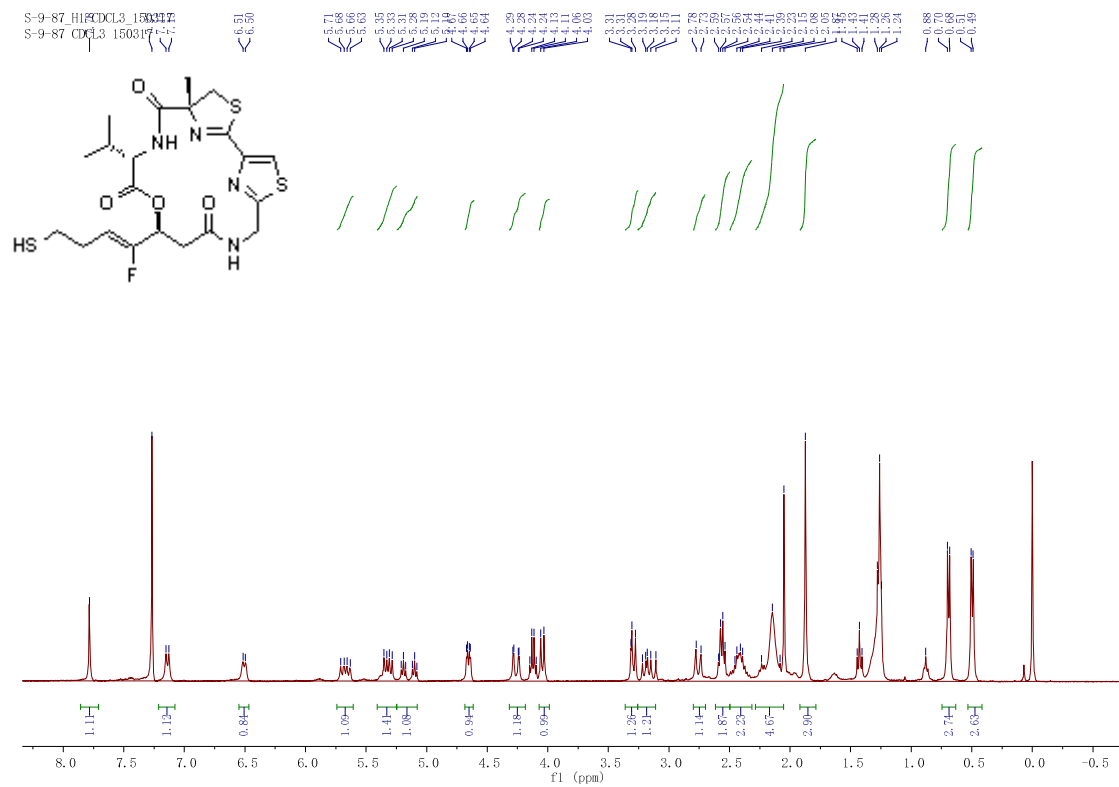


¹⁹F NMR Spectra of **14b**



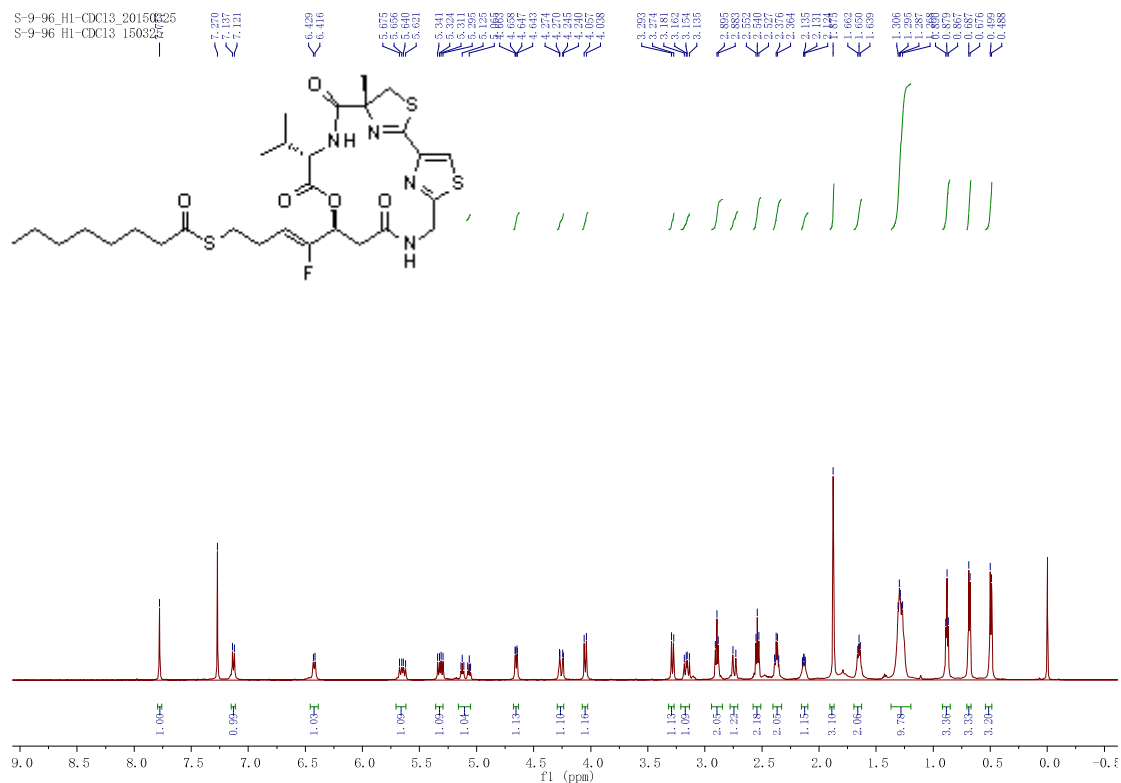
(5R,8S,11S)-11-((Z)-1-fluoro-4-mercaptobut-1-en-1-yl)-8-isopropyl-5-methyl-10-oxa-3,17-dithia-7,14,19,20-tetraazatricyclo[14.2.1.1^{2,5}]icosa-1(18),2(20),16(19)-triene-6,9,13-trione (15a).

¹H NMR Spectra of 15a



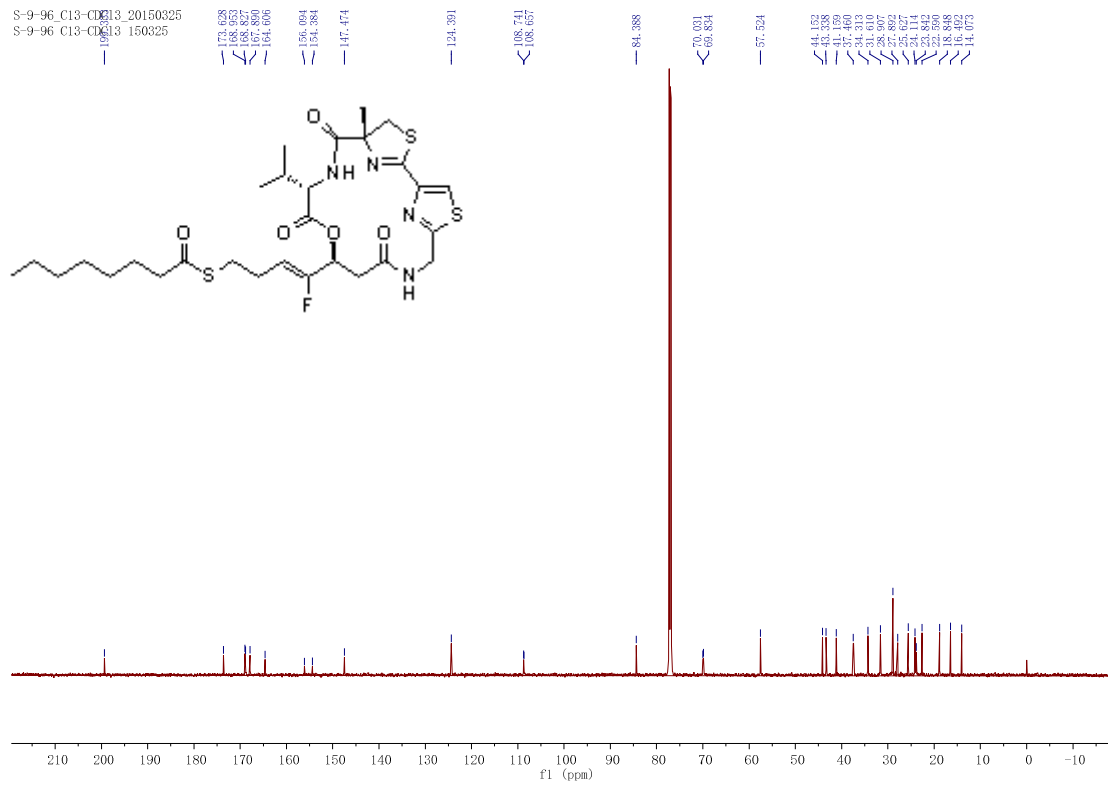
S-((Z)-4-fluoro-4-((5R,8S,11S)-8-isopropyl-5-methyl-6,9,13-trioxo-10-oxa-3,17-dithia-7,14,19,20-tetraazatricyclo[14.2.1.12,5]icosa-1(18),2(20),16(19)-trien-11-yl)but-3-en-1-yl) octanethioate (16a).

¹H NMR Spectra of 16a



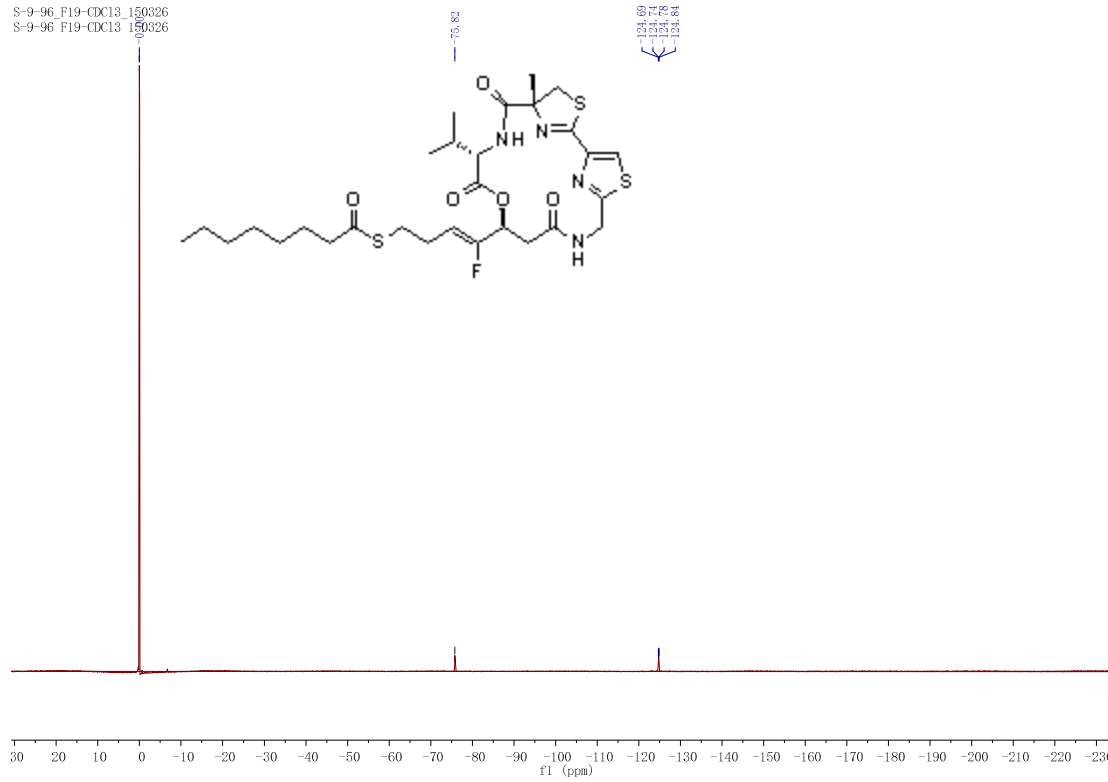
¹³C NMR Spectra of 16a

S-9-96 C13-CDCl3_20150325
S-9-96 C13-CDCl3_150325

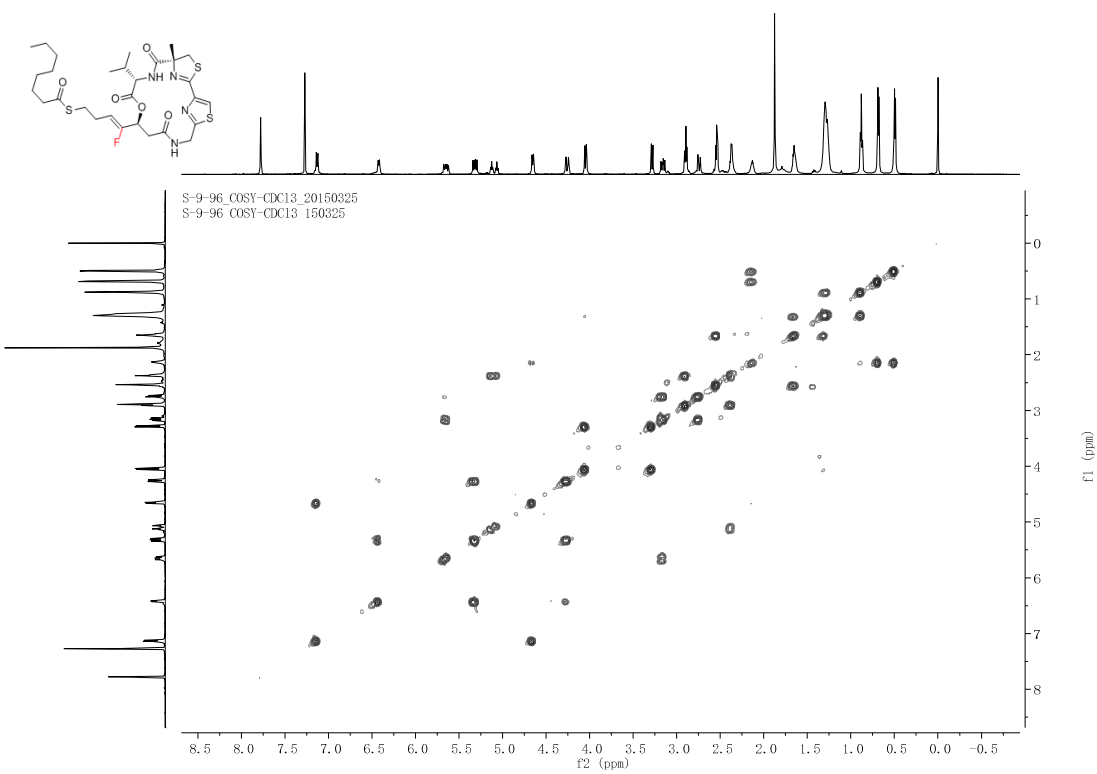


¹⁹F NMR Spectra of 16a (CF₃Cl and CF₃CO₂H as the reference)

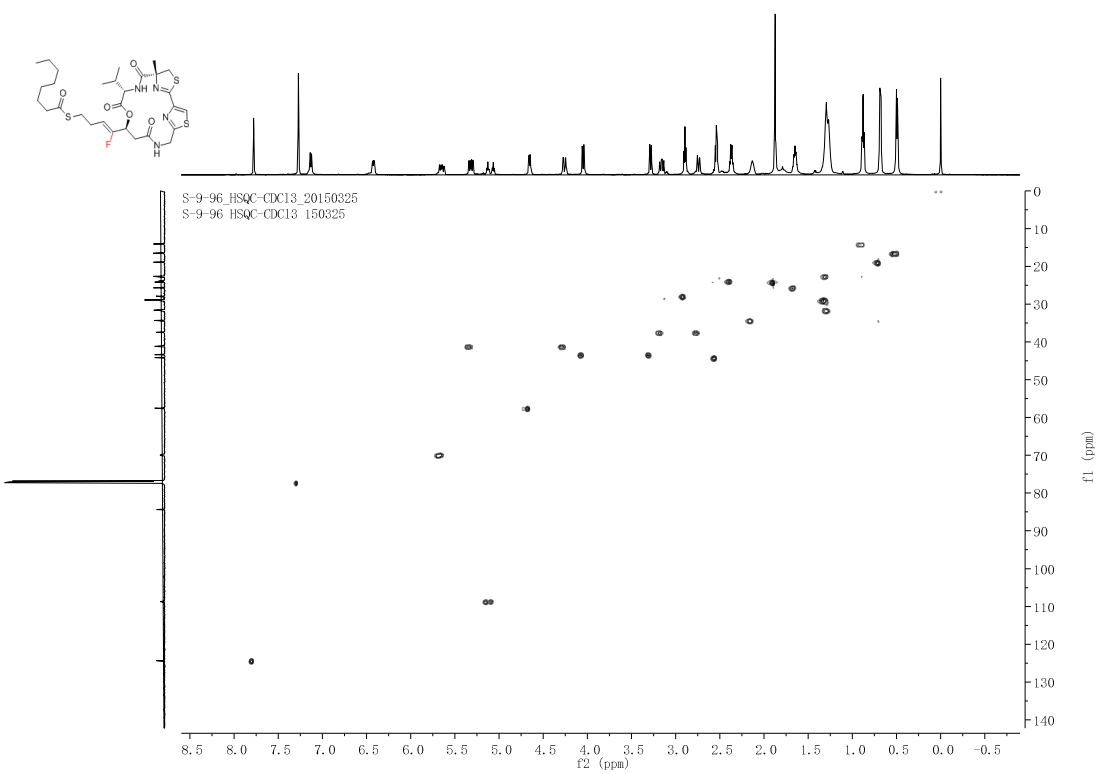
S-9-96 F19-CDCl3_150326
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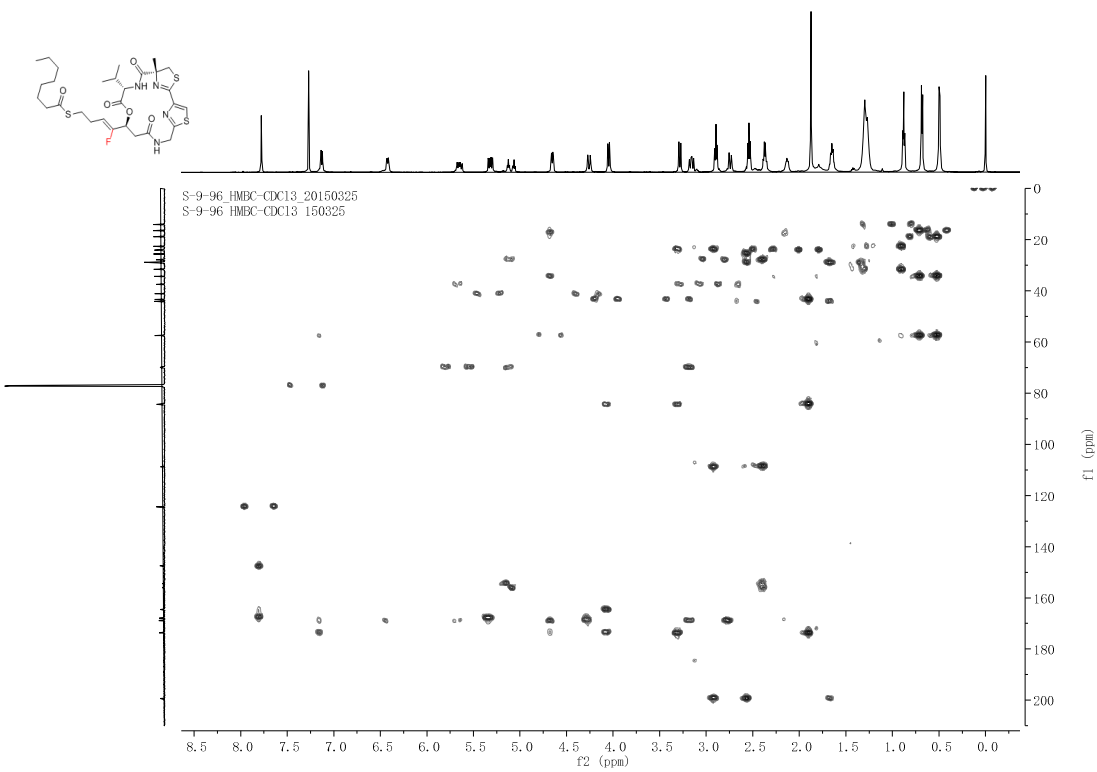
H-H COSY Spectra of 16a



H-C HMQC Spectra of 16a

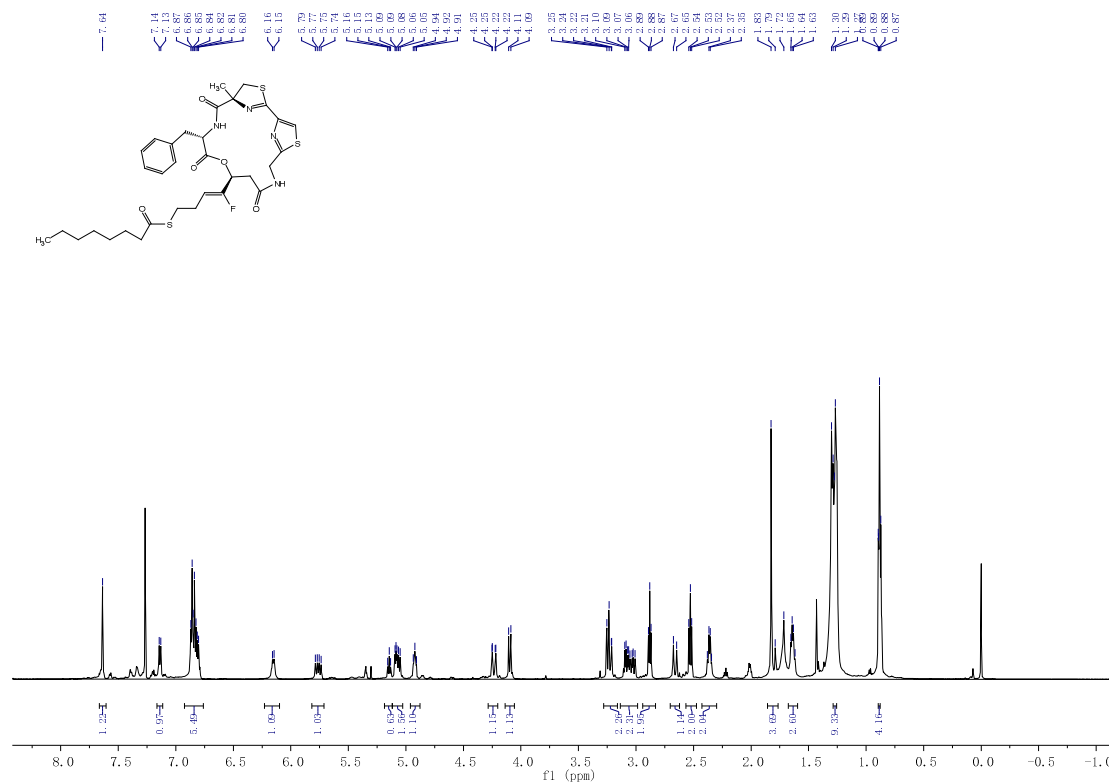


H-C HMBC Spectra of 16a

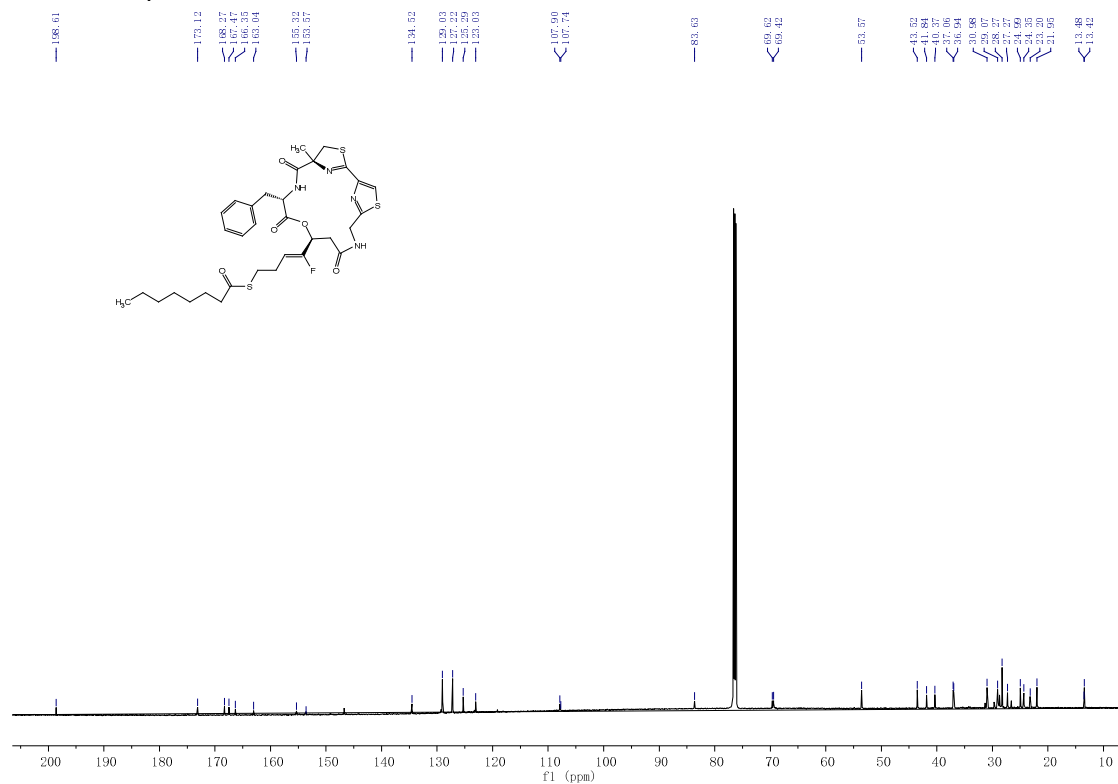


S-((Z)-4-((5R,8S)-8-benzyl-5-methyl-6,9,13-trioxo-10-oxa-3,17-dithia-7,14,19,20-tetraazatricyclo[14.2.1.1^{2,5}]icosa-1(18),2(20),16(19)-trien-11-yl)-4-fluorobut-3-en-1-yl) octanethioate (16b)

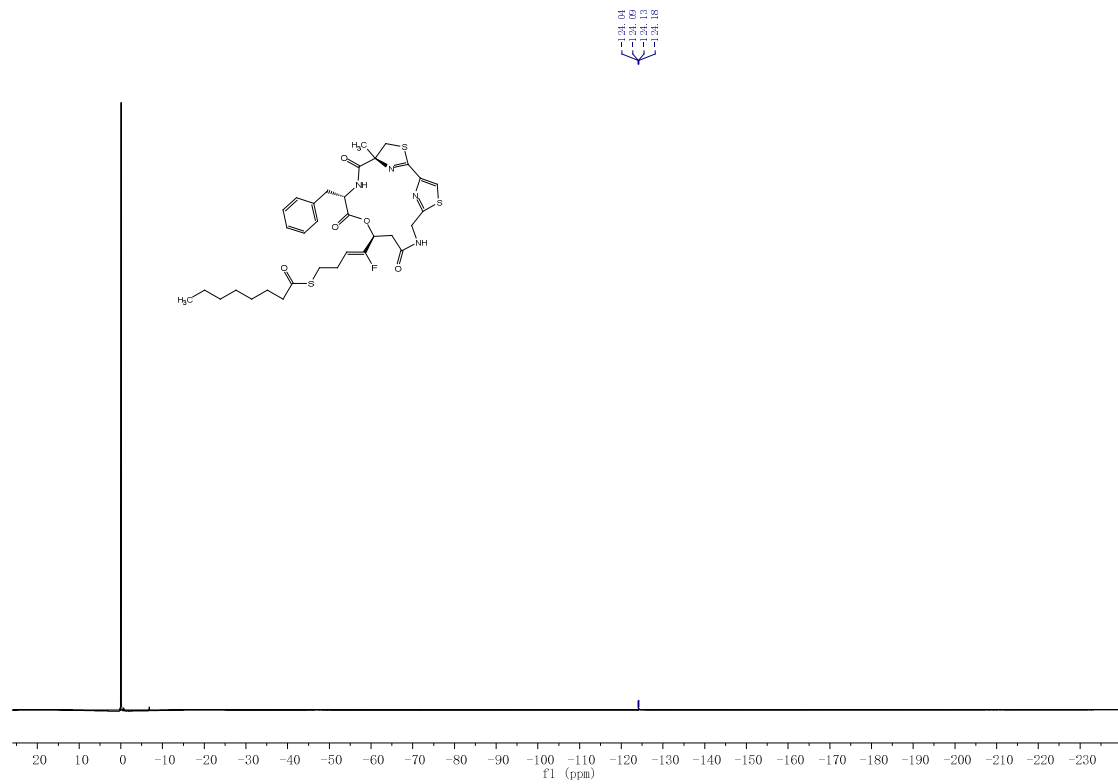
¹H NMR Spectra of 16b



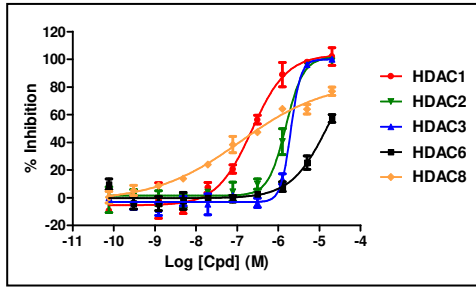
¹³C NMR Spectra of **16b**



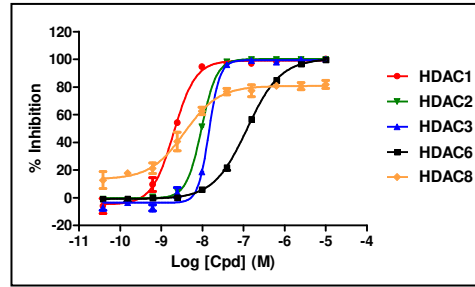
¹⁹F NMR Spectra of **16b**



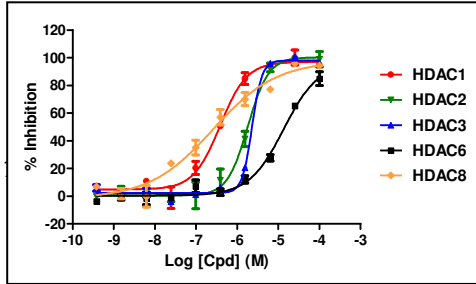
Largazole



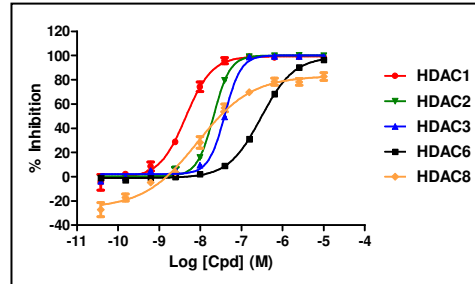
Largazole thiol



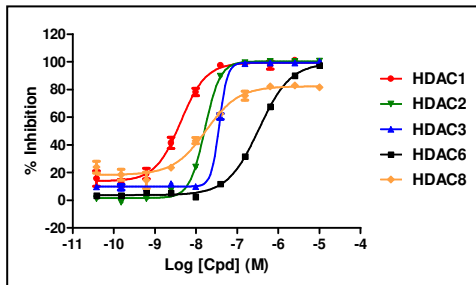
16a



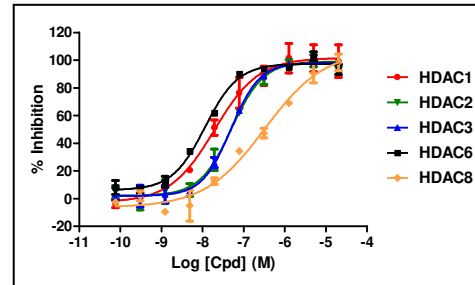
15a



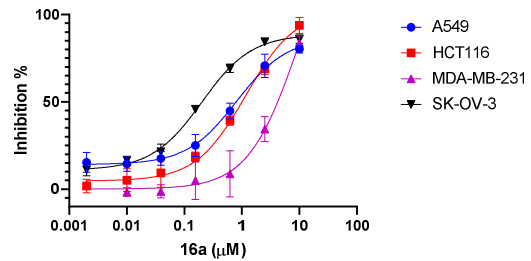
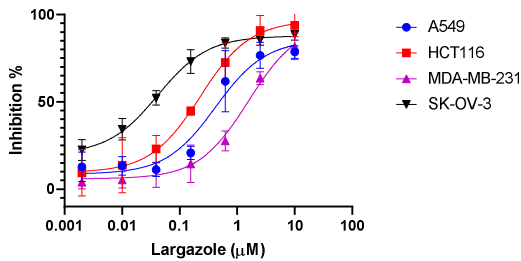
15b



SAHA



The concentration-response curves of the compounds in the enzymatic assays (HDAC 1, 2, 3, 8 and 6).



The concentration-response curves of the compounds in the cellular assays