

**Design, synthesis and antitumor activity evaluation of novel IMPDH II and HDAC1 dual inhibitor**

## Contents

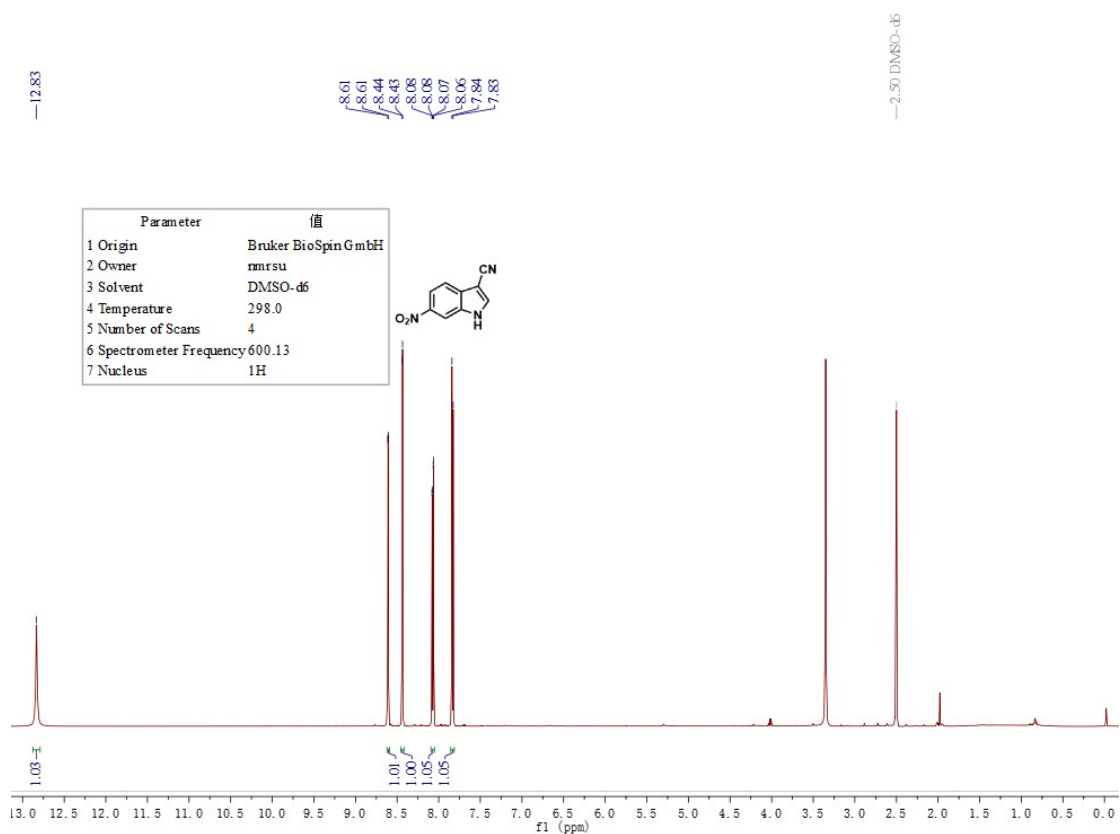
The representative  $^1\text{H}$  NMR spectra of compounds **2a~4b** and **5a~5f**.

The representative  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra of the target compounds **A1~A40**, **B1~B12** and **C1~C28**.

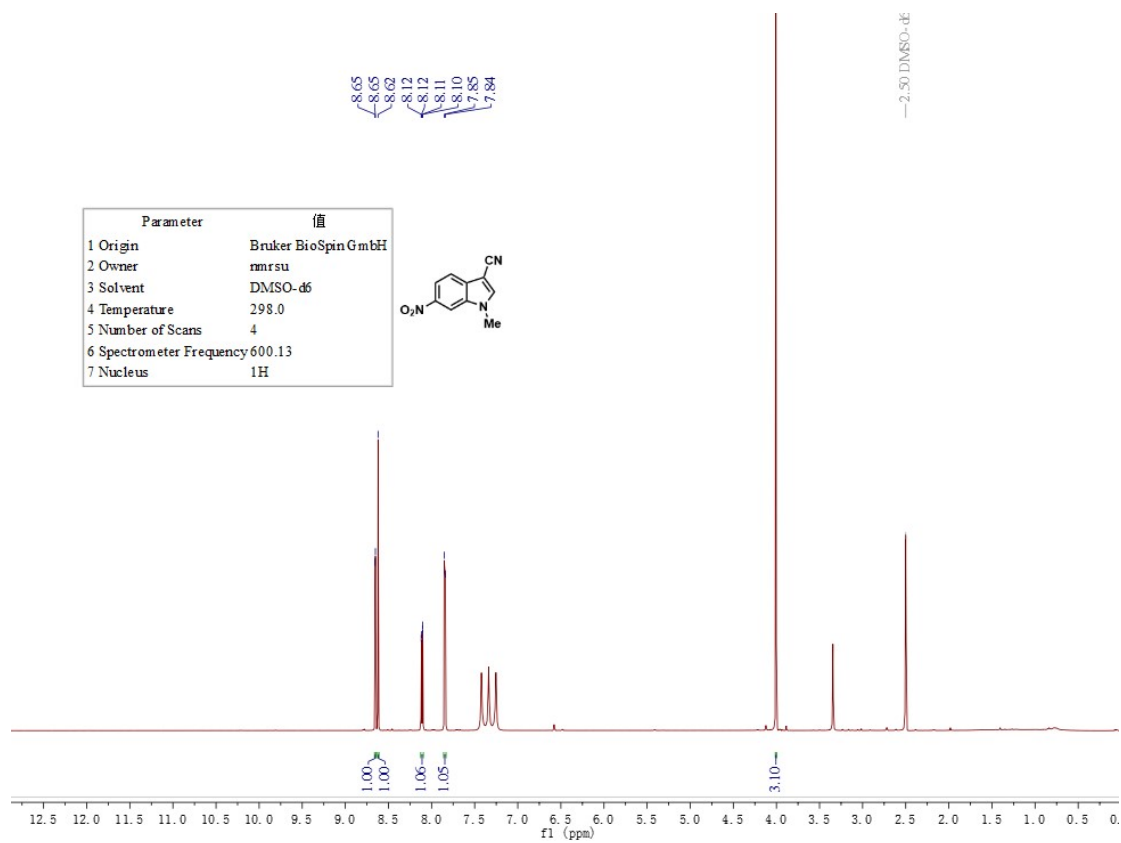
The representative HRMS (ESI) spectra of the target compounds **A1~A40**, **B1~B12** and **C1~C28**.

The representative HPLC spectra of **C12** and **C18**.

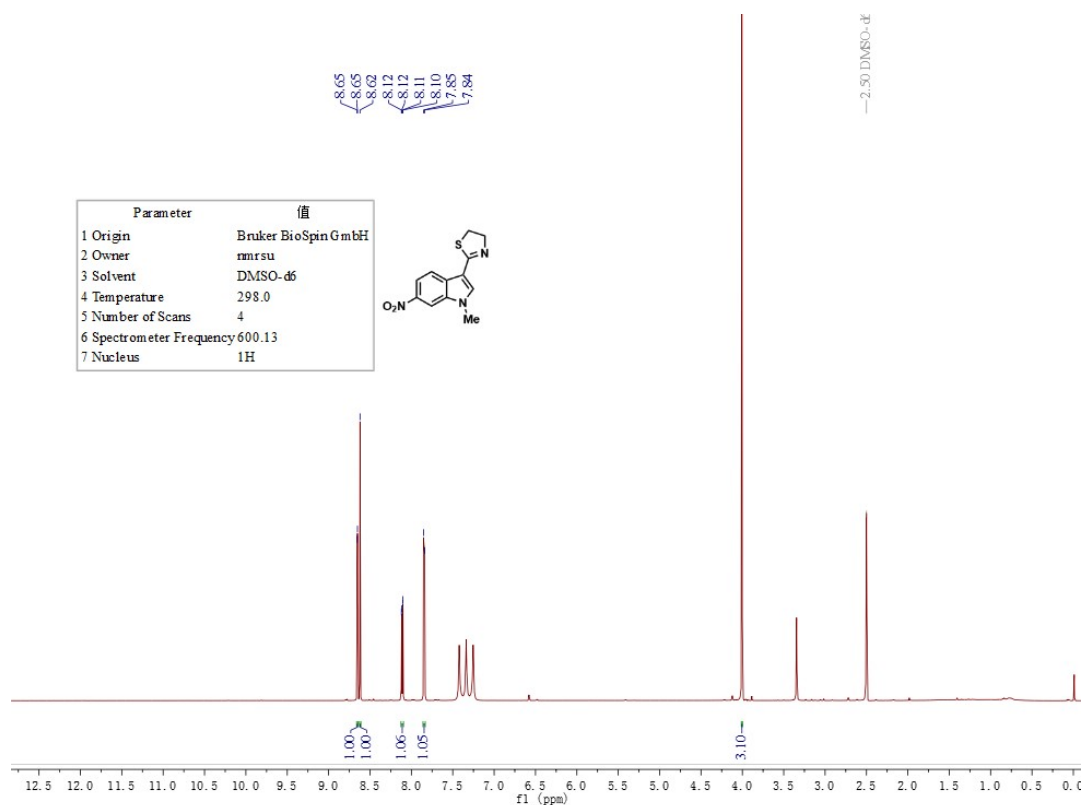
# <sup>1</sup>H-NMR spectrum of compound 2a



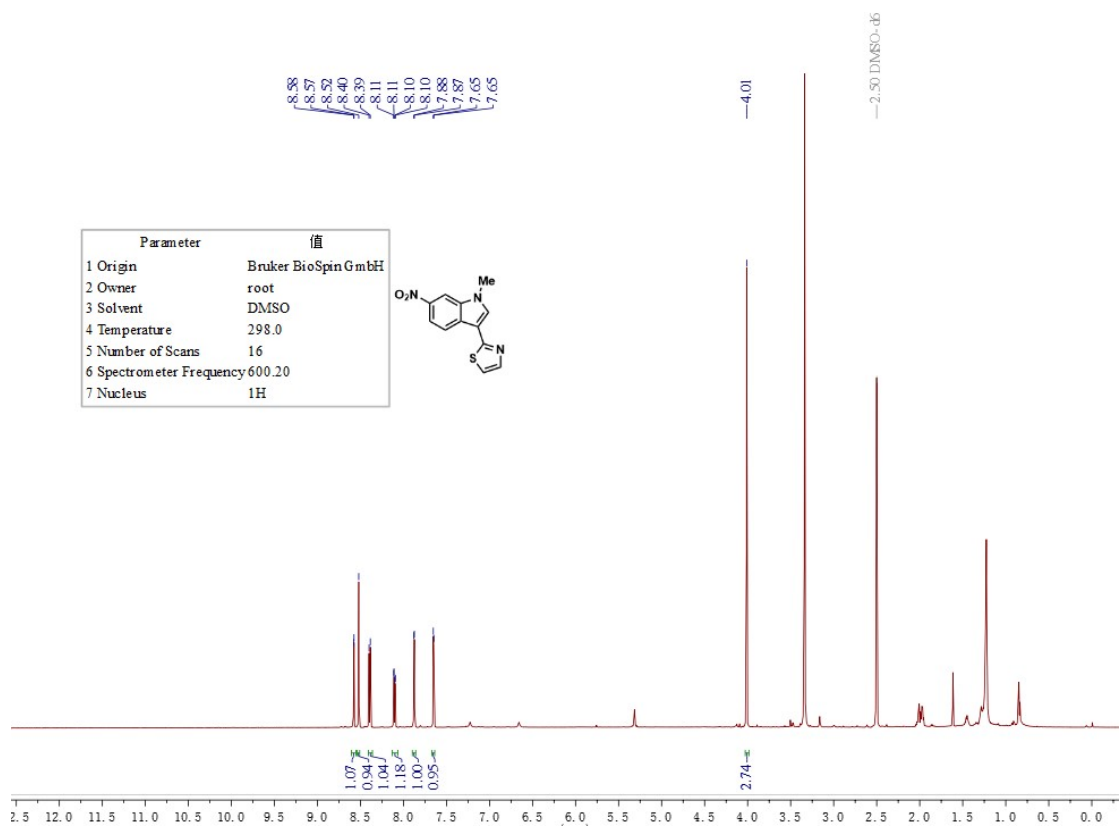
# <sup>1</sup>H-NMR spectrum of compound 2b



# <sup>1</sup>H-NMR spectrum of compound 3b

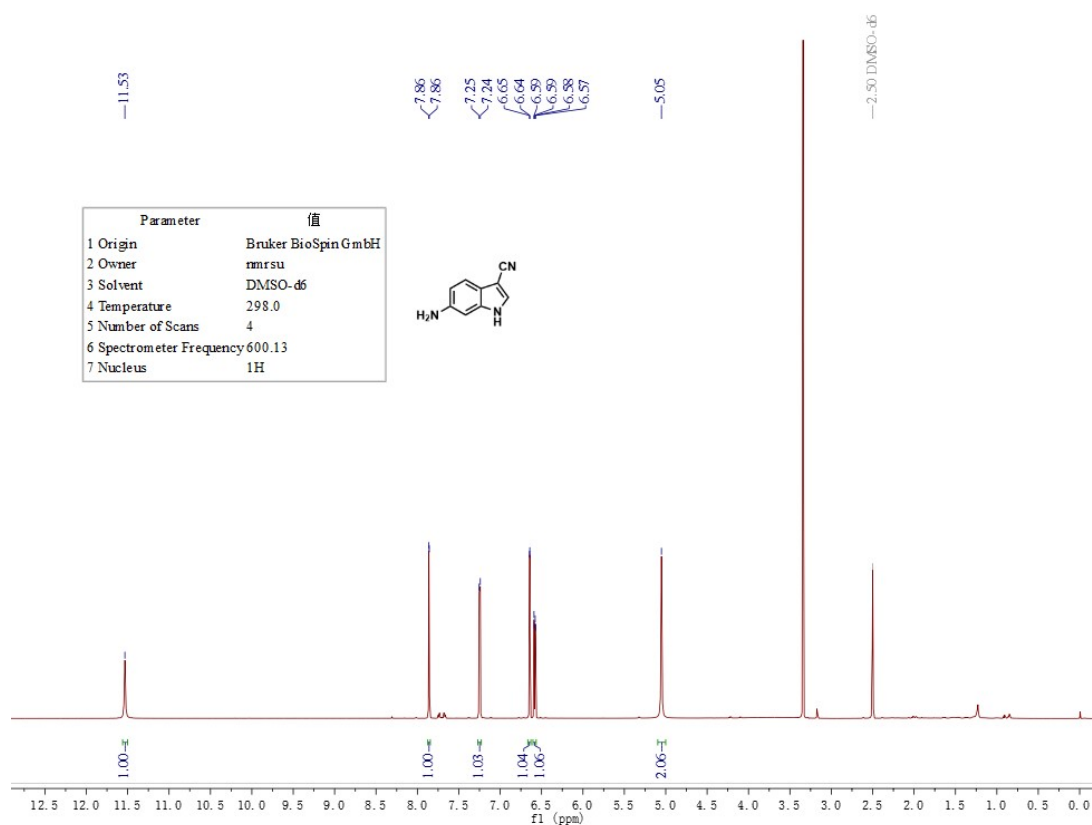


# <sup>1</sup>H-NMR spectrum of compound 4b

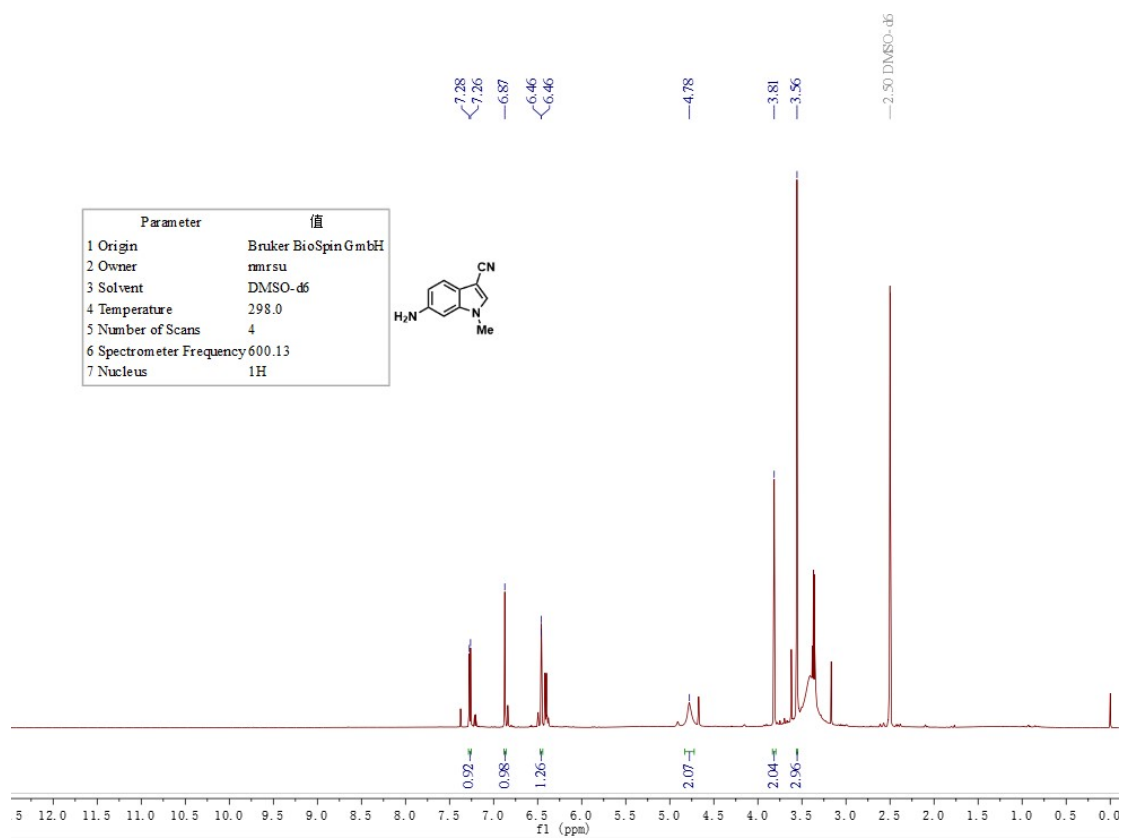




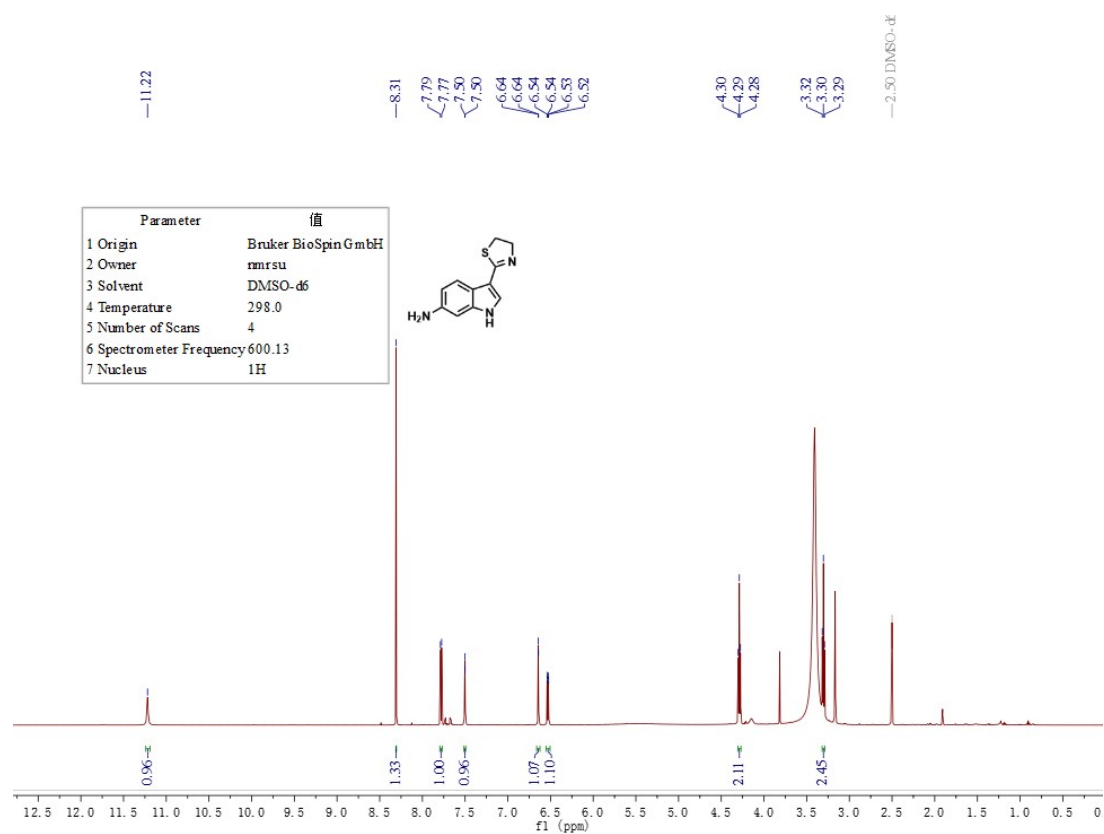
# <sup>1</sup>H-NMR spectrum of compound 5a



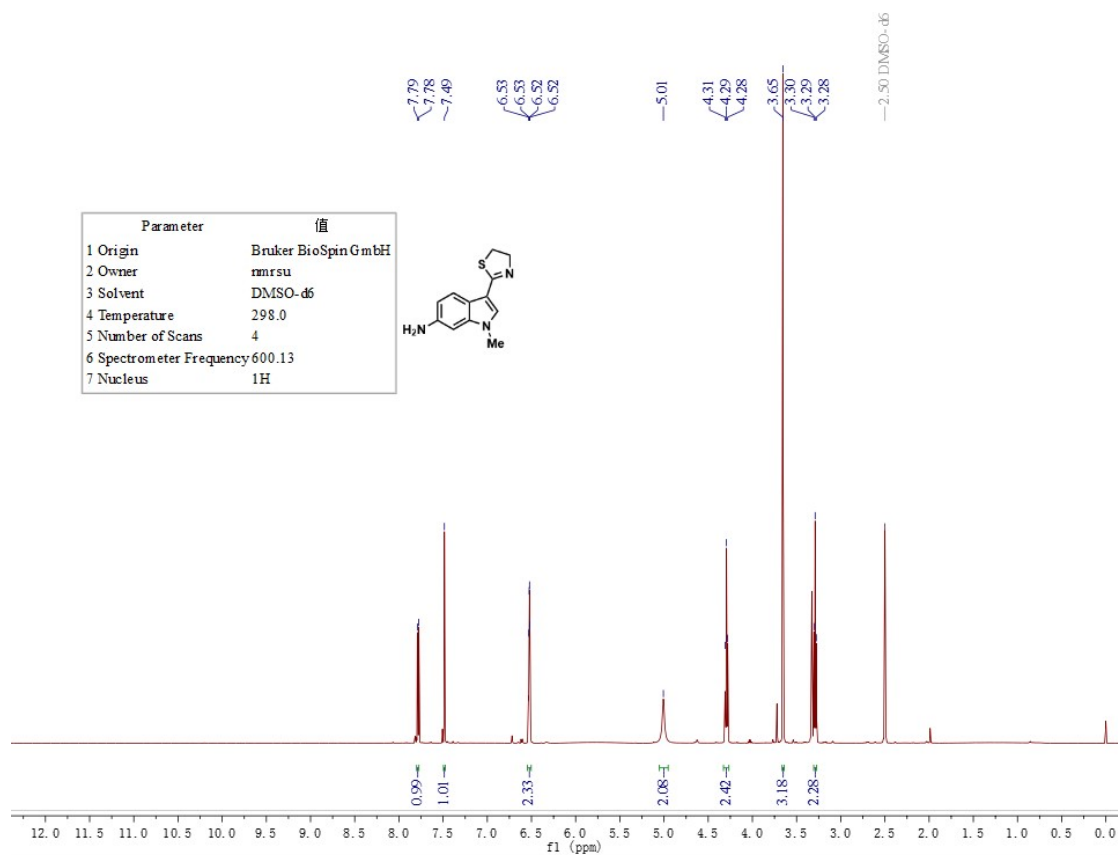
# <sup>1</sup>H-NMR spectrum of compound 5b



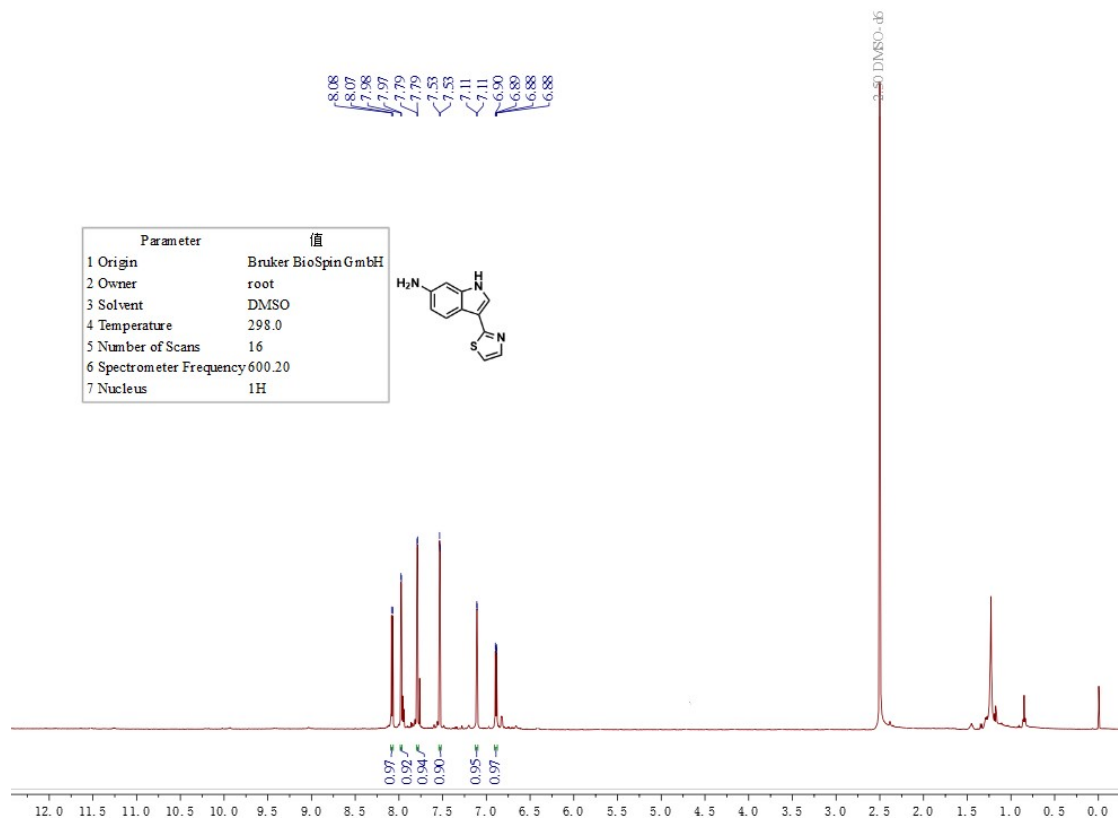
# <sup>1</sup>H-NMR spectrum of compound 5c



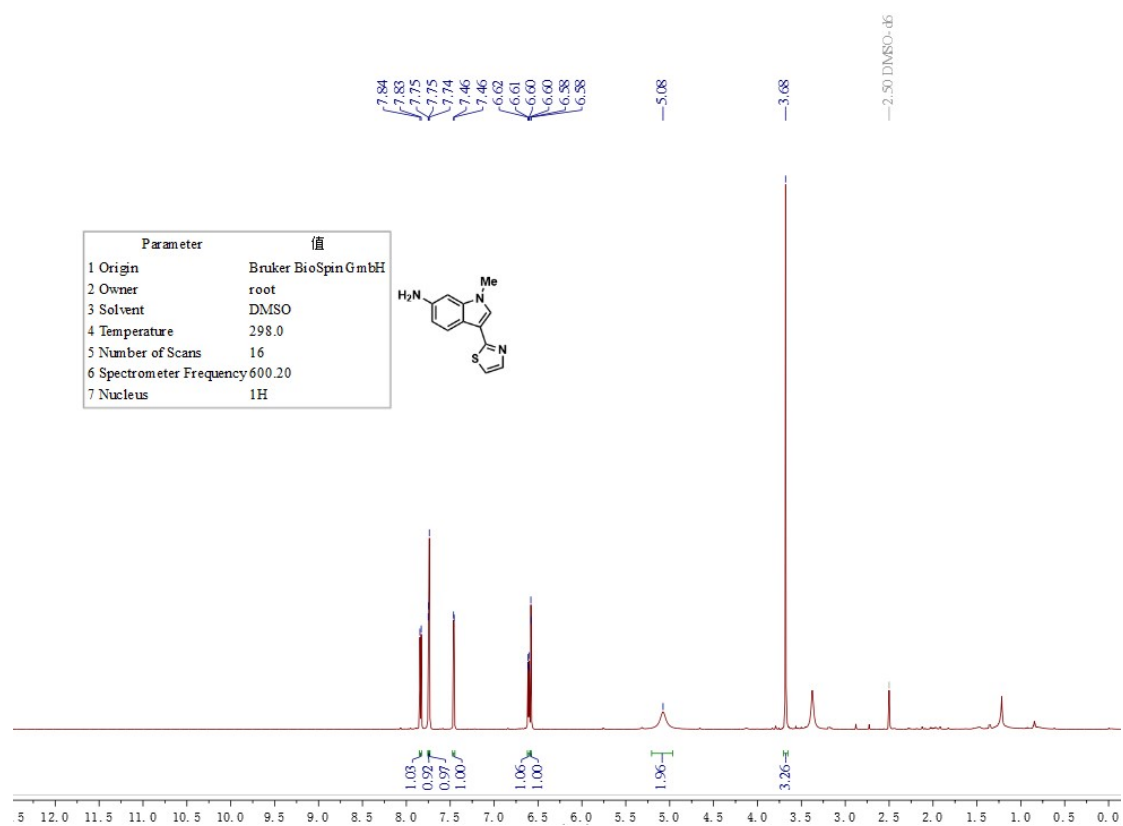
# <sup>1</sup>H-NMR spectrum of compound 5d



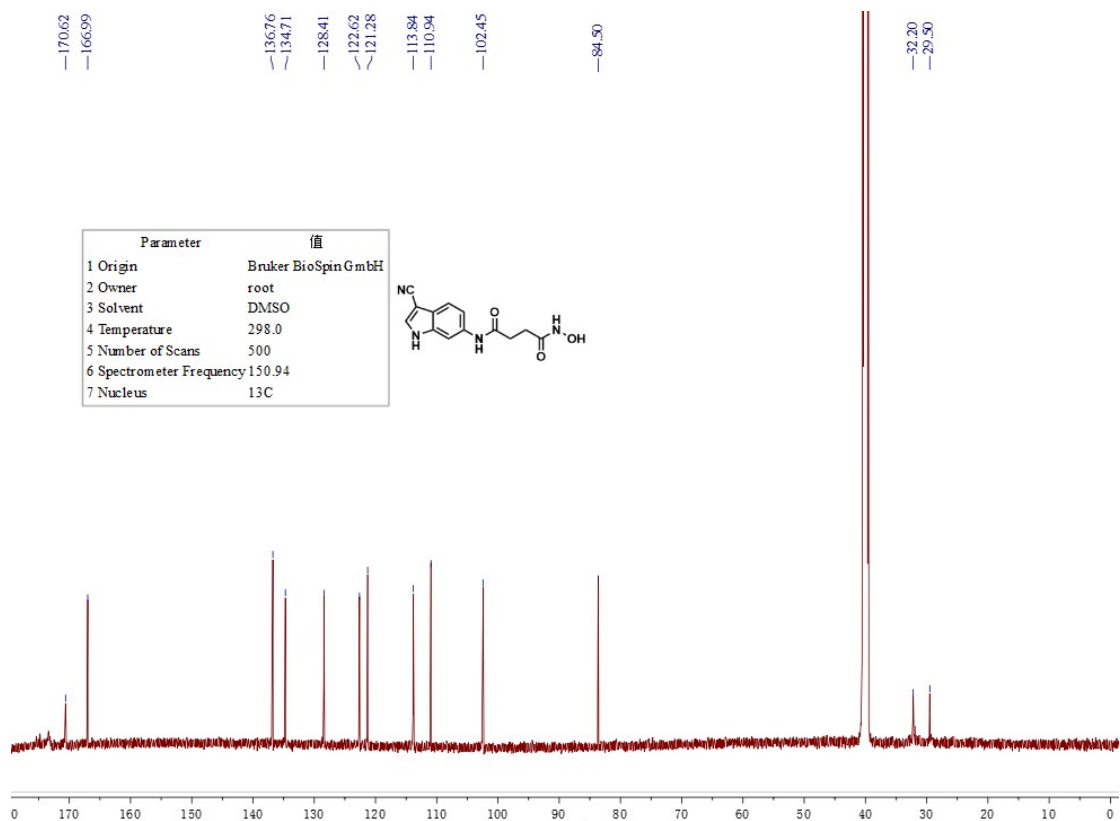
# <sup>1</sup>H-NMR spectrum of compound 5e



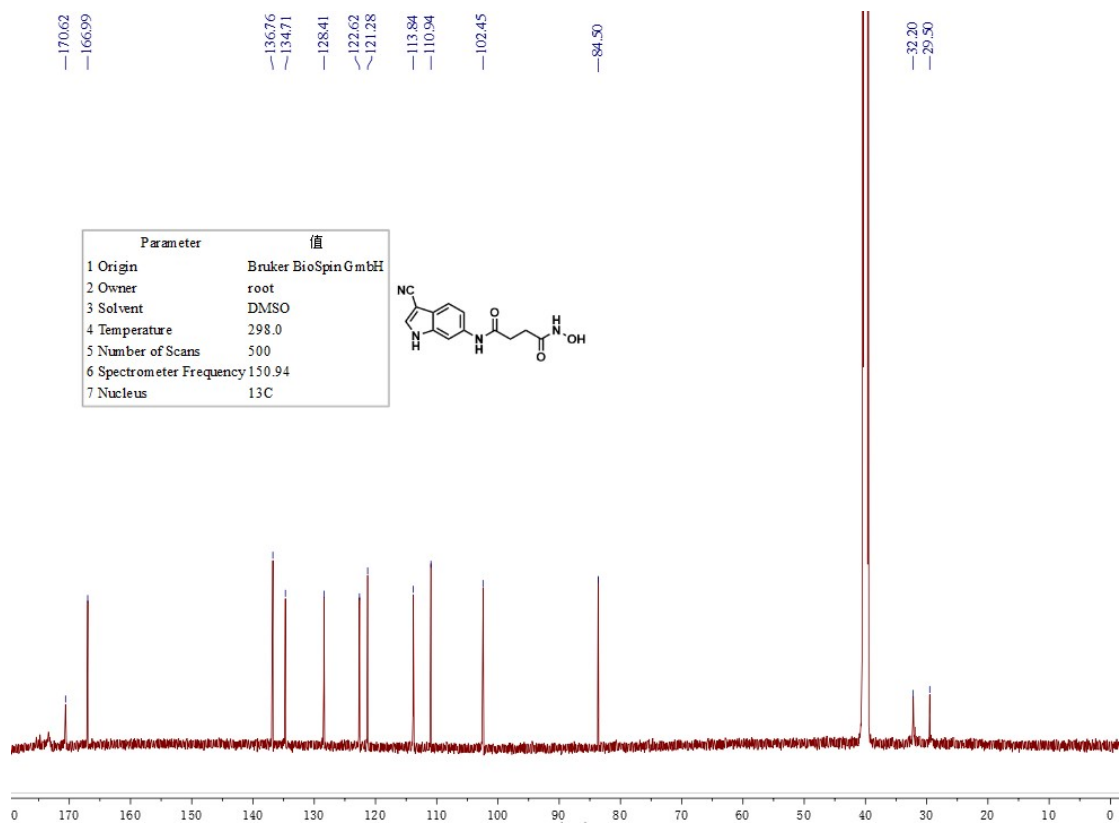
# <sup>1</sup>H-NMR spectrum of compound 5f



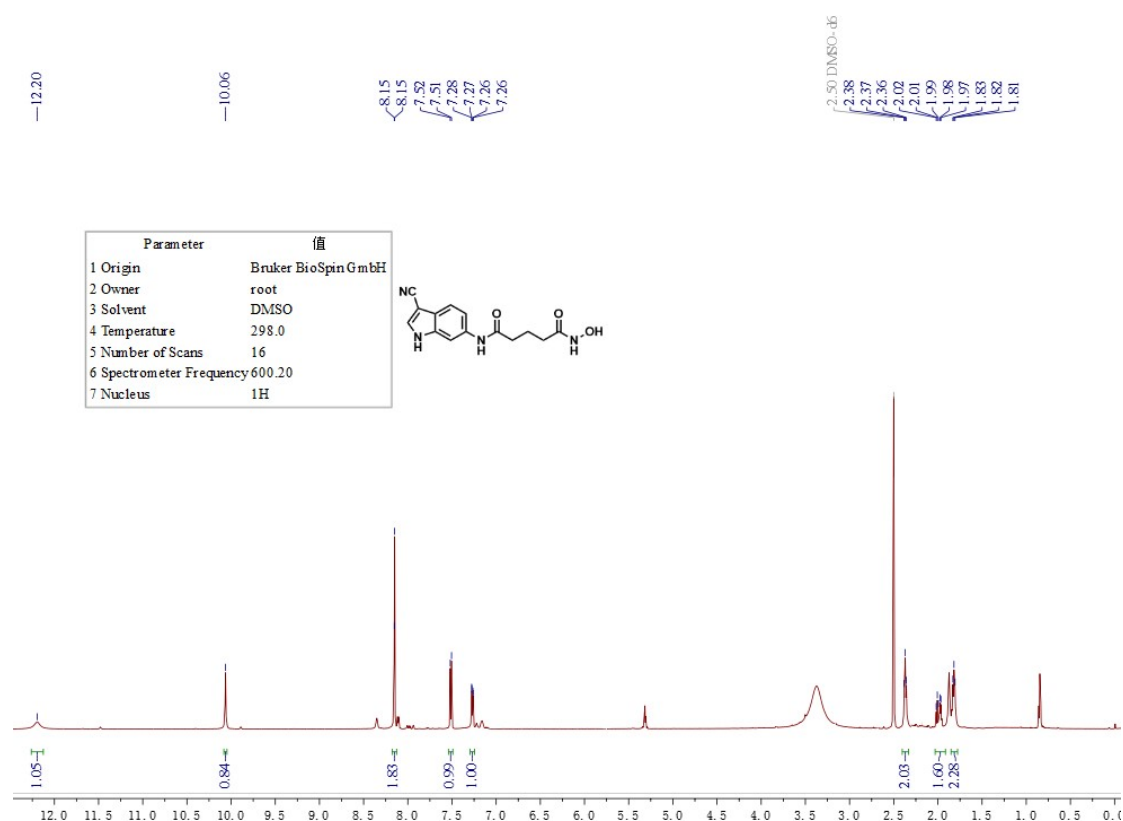
# <sup>1</sup>H-NMR spectrum of compound A1



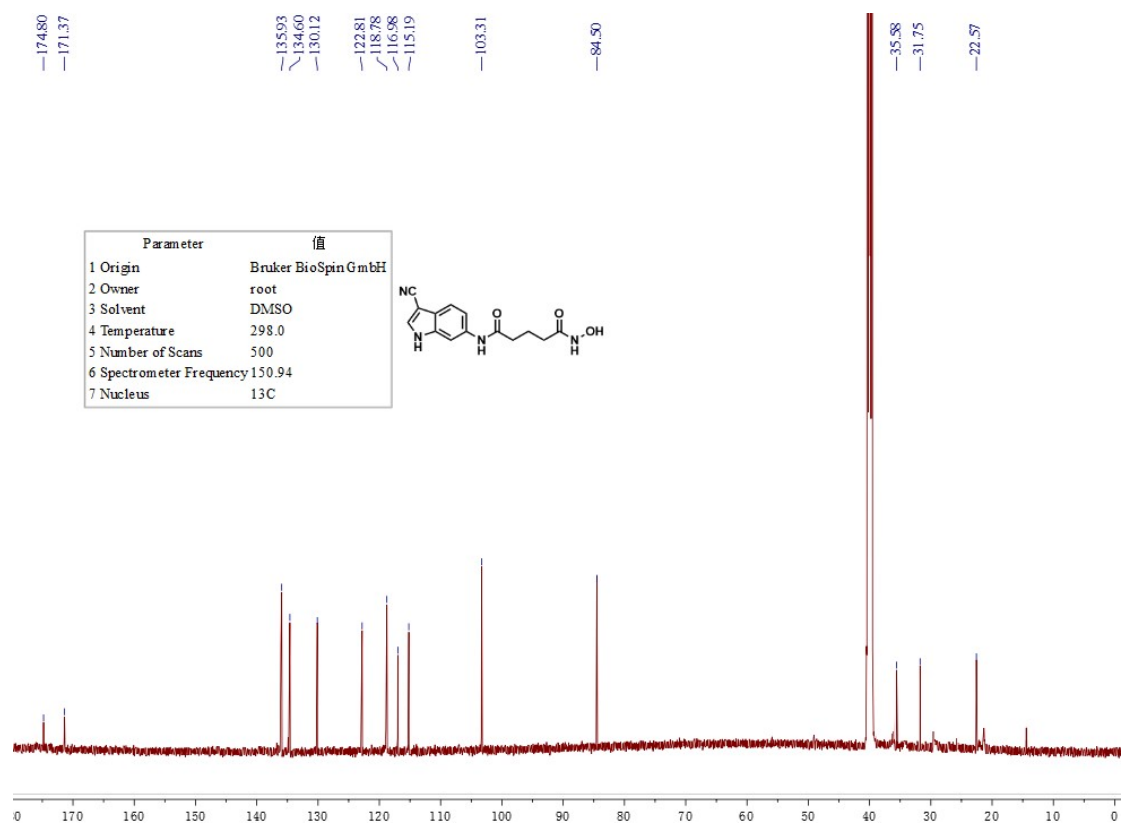
# <sup>13</sup>C-NMR spectrum of compound A1



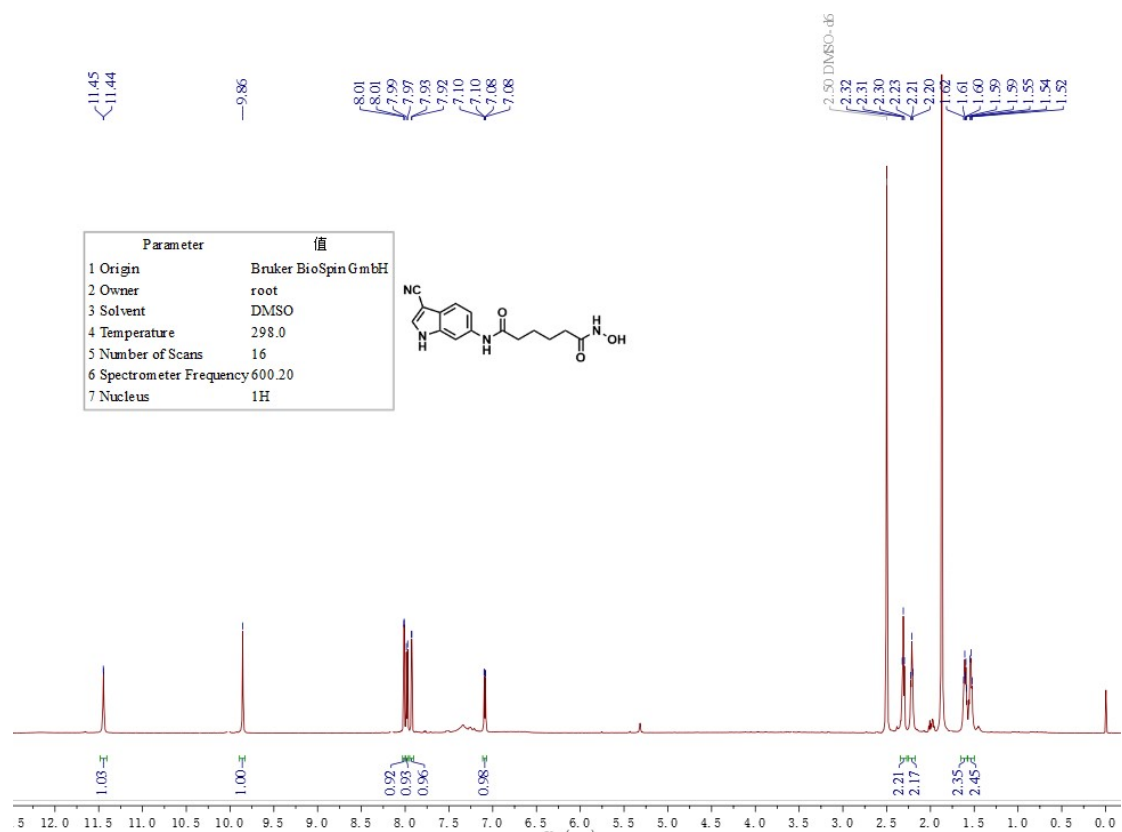
# <sup>1</sup>H-NMR spectrum of compound A2



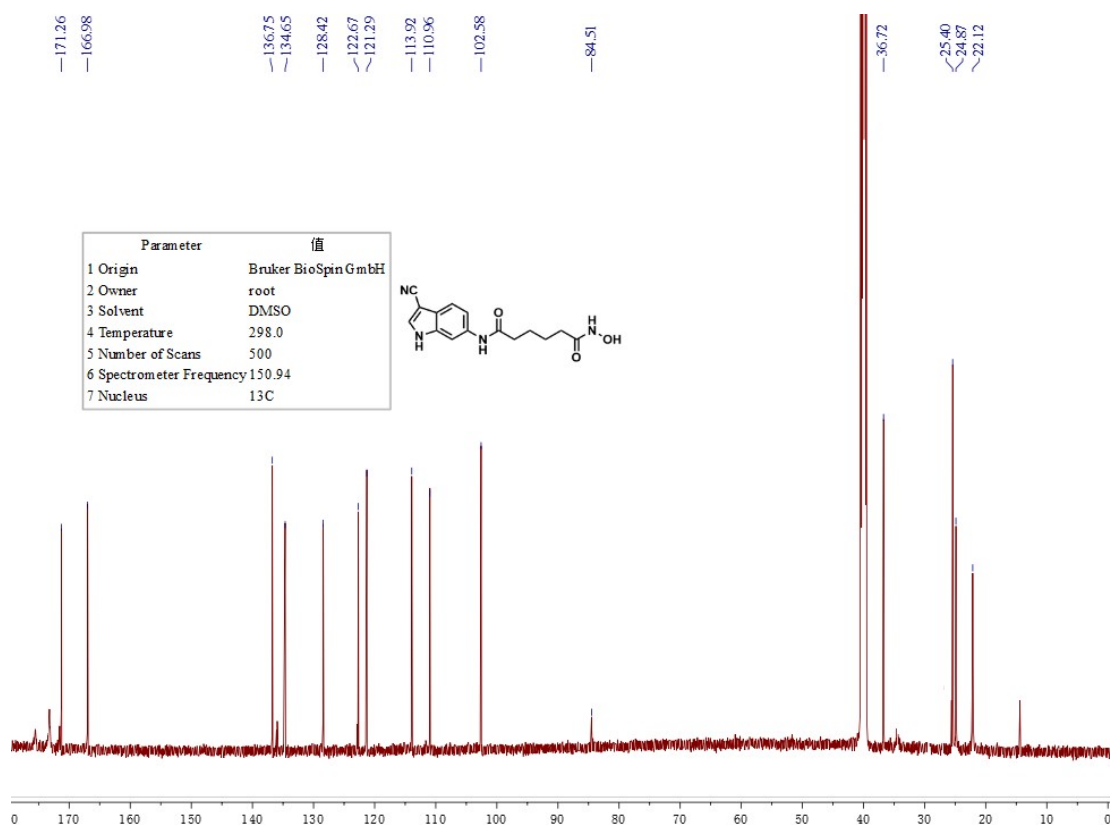
# <sup>13</sup>C-NMR spectrum of compound A2



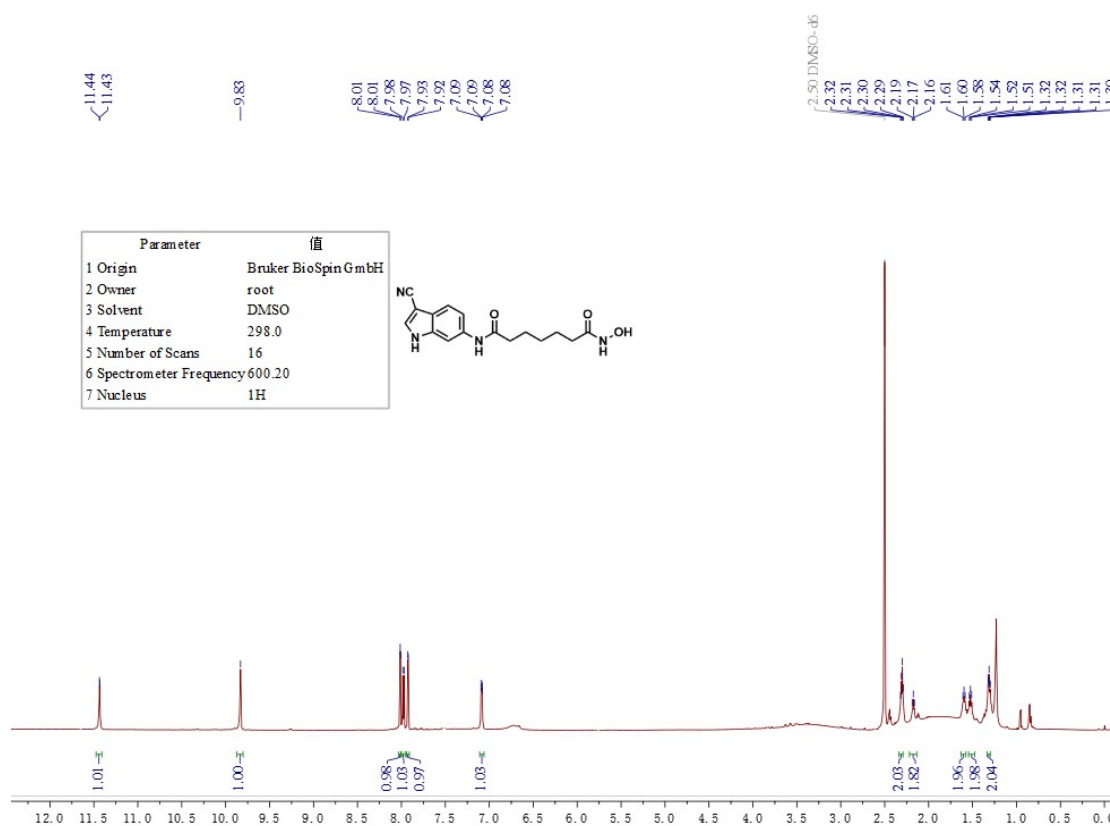
# <sup>1</sup>H-NMR spectrum of compound A3



### <sup>13</sup>C-NMR spectrum of compound A3

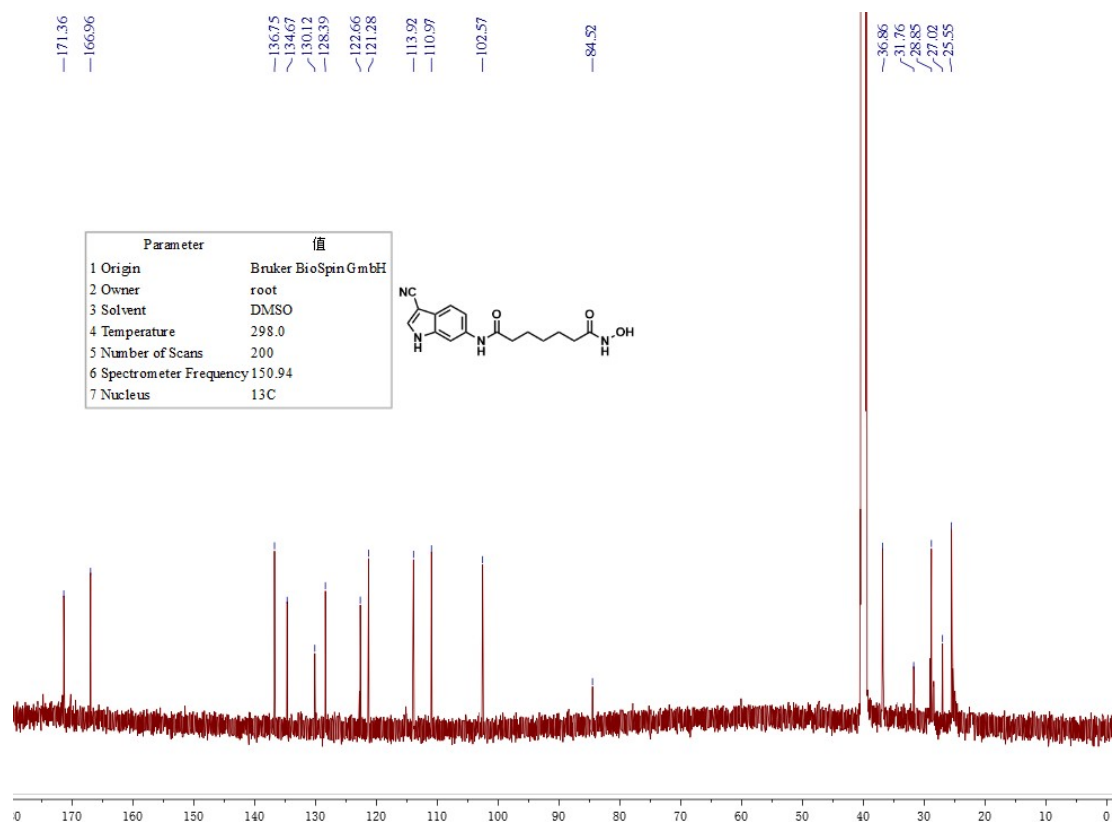


### <sup>1</sup>H-NMR spectrum of compound A4

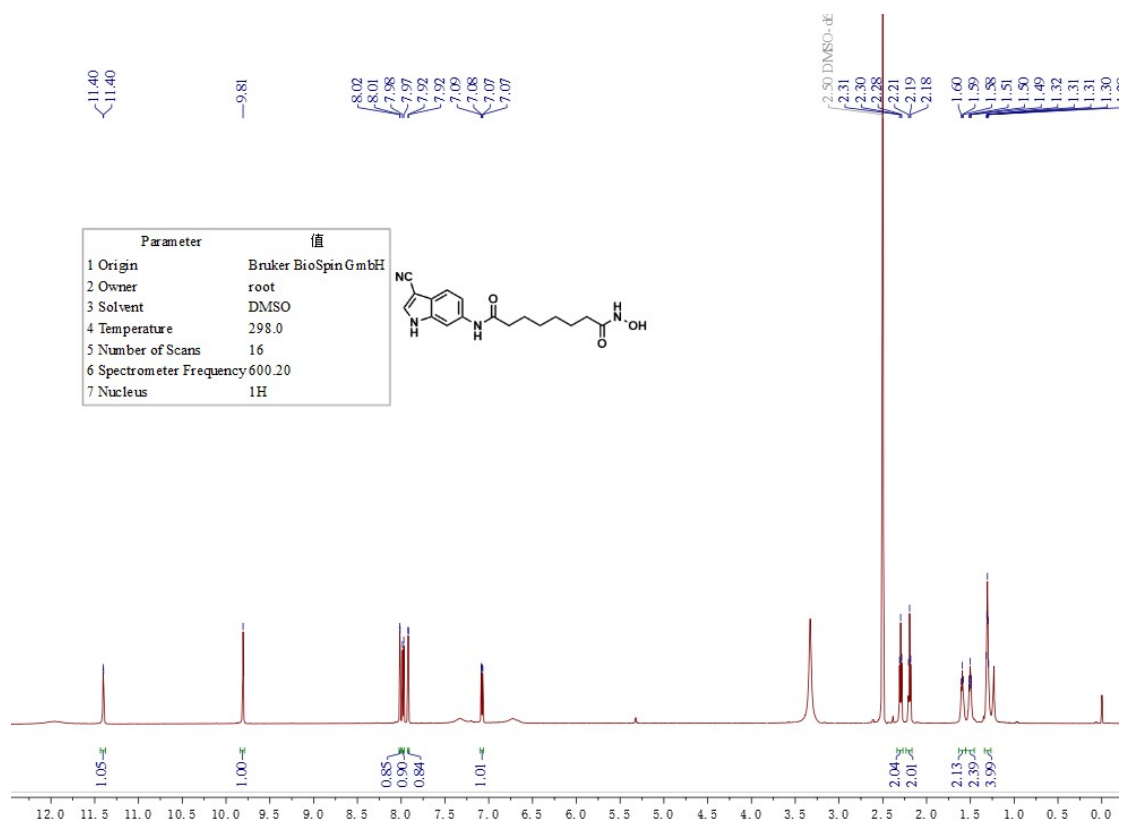




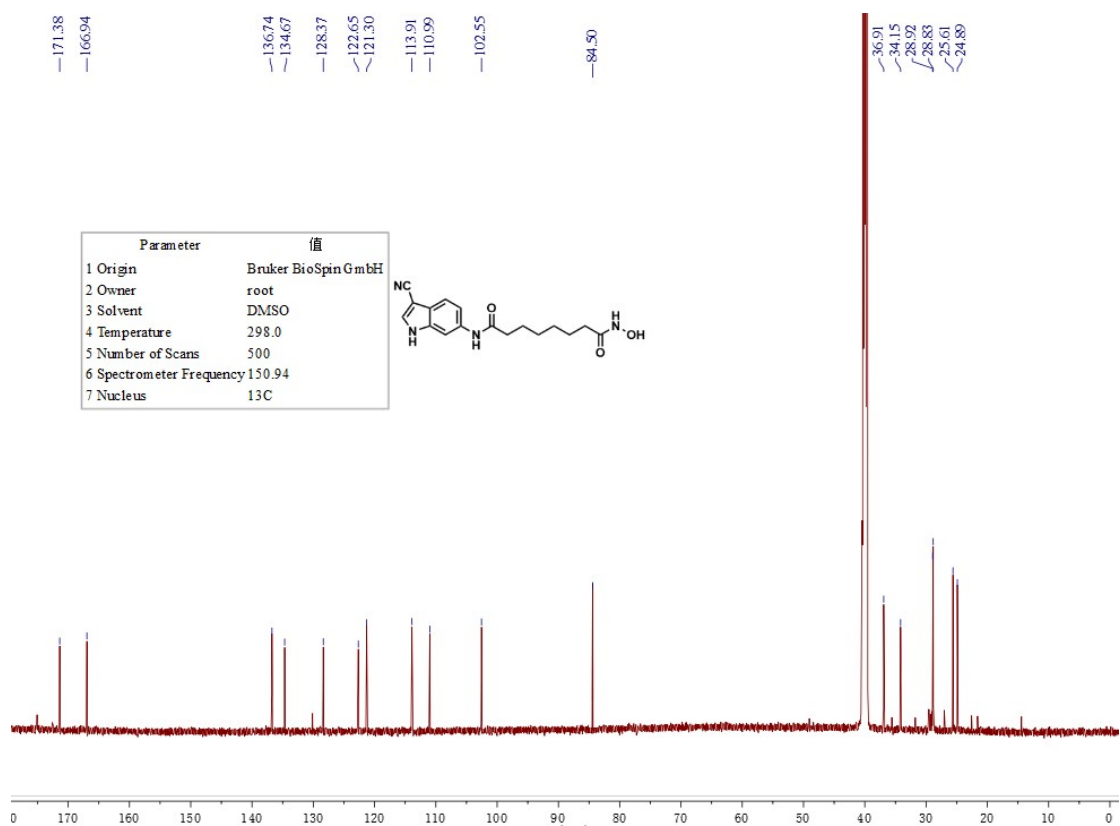
# <sup>13</sup>C-NMR spectrum of compound A4



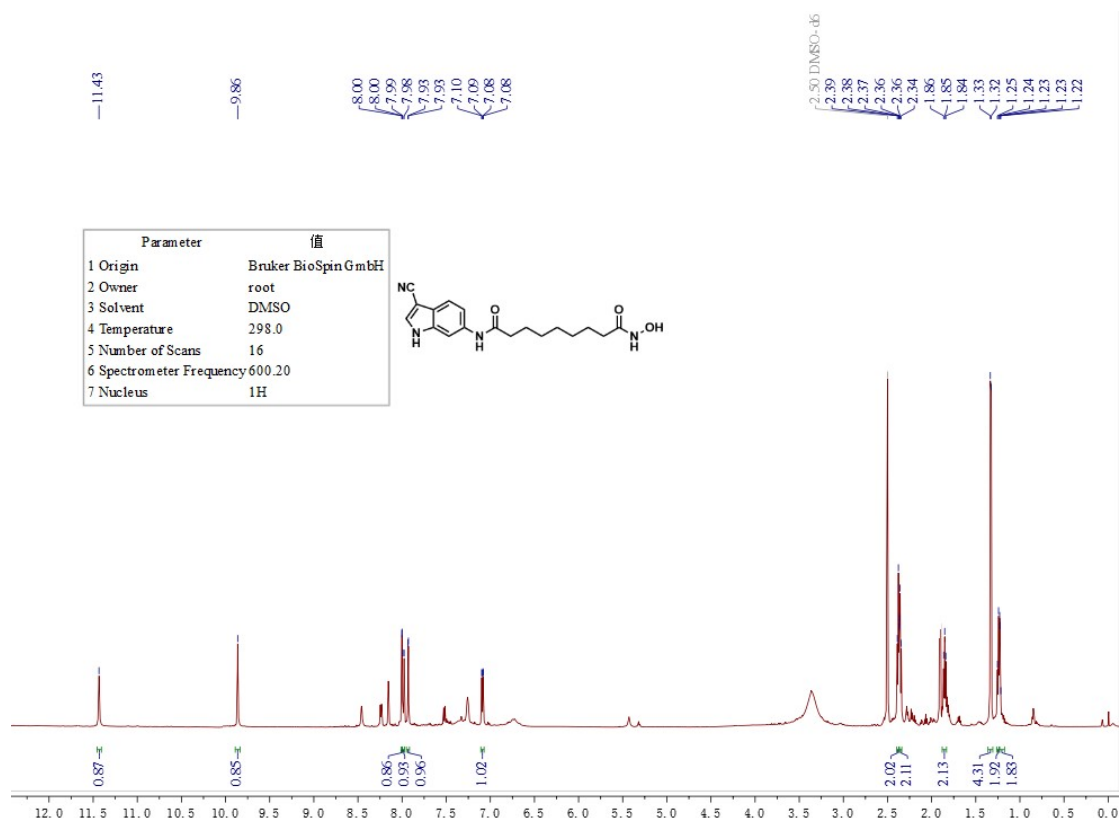
# <sup>1</sup>H-NMR spectrum of compound A5



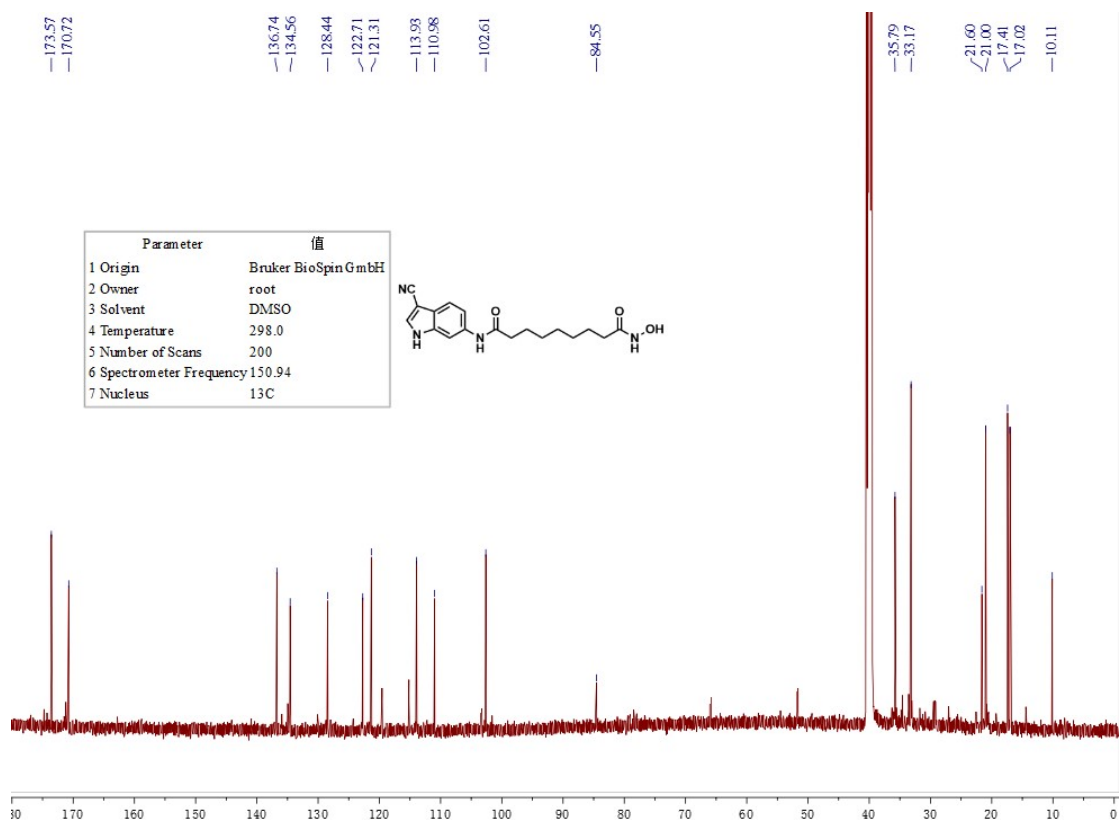
### <sup>13</sup>C-NMR spectrum of compound A5



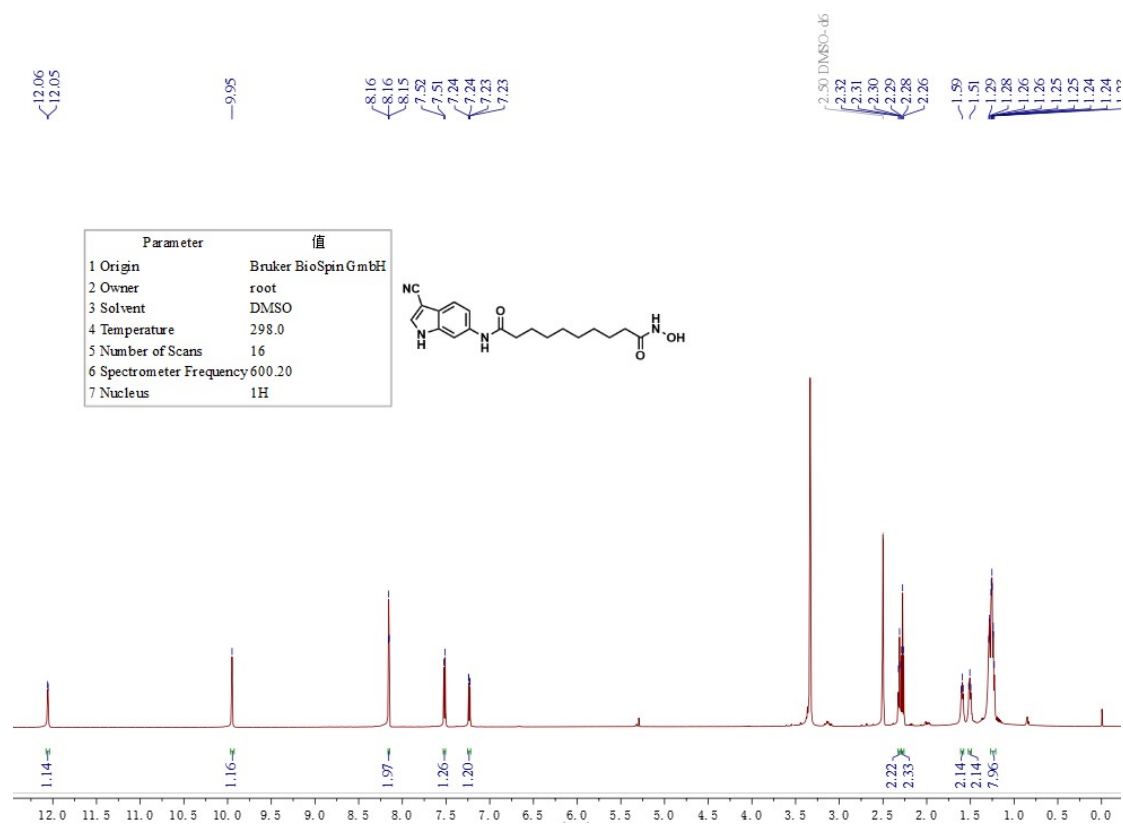
# <sup>1</sup>H-NMR spectrum of compound A6



# <sup>13</sup>C-NMR spectrum of compound A6



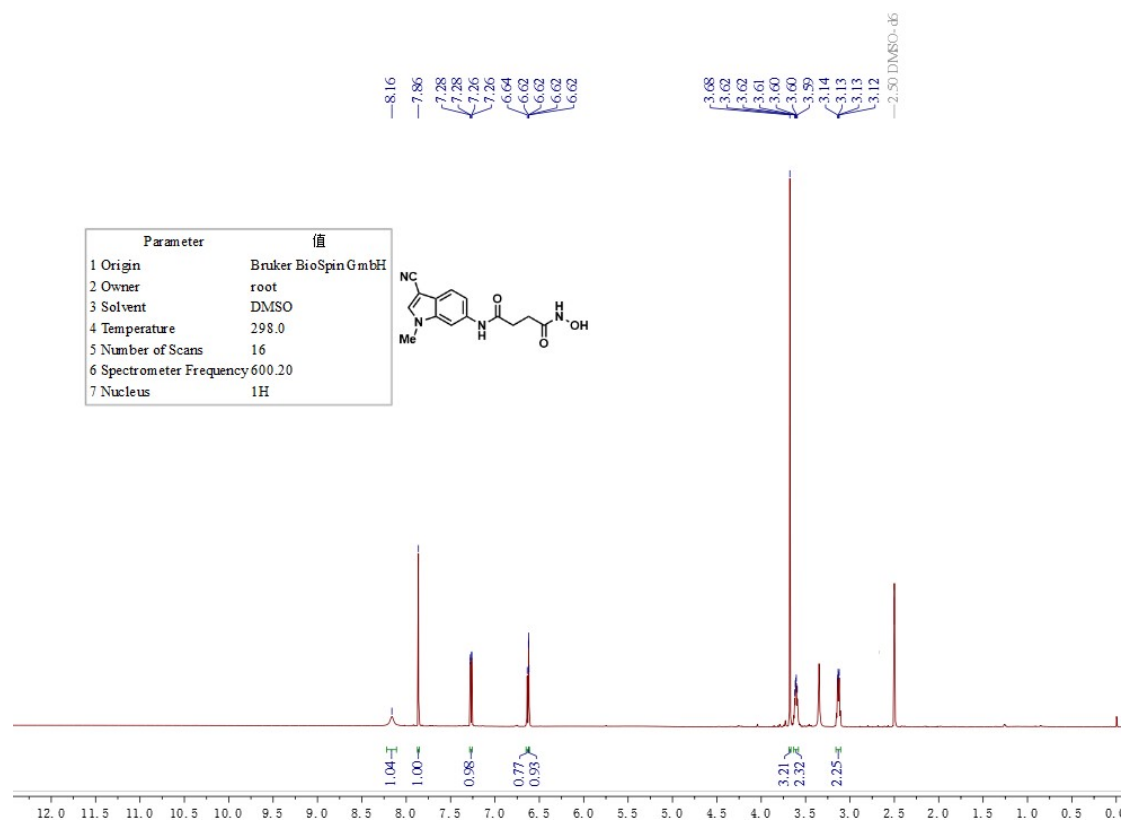
# <sup>1</sup>H-NMR spectrum of compound A7

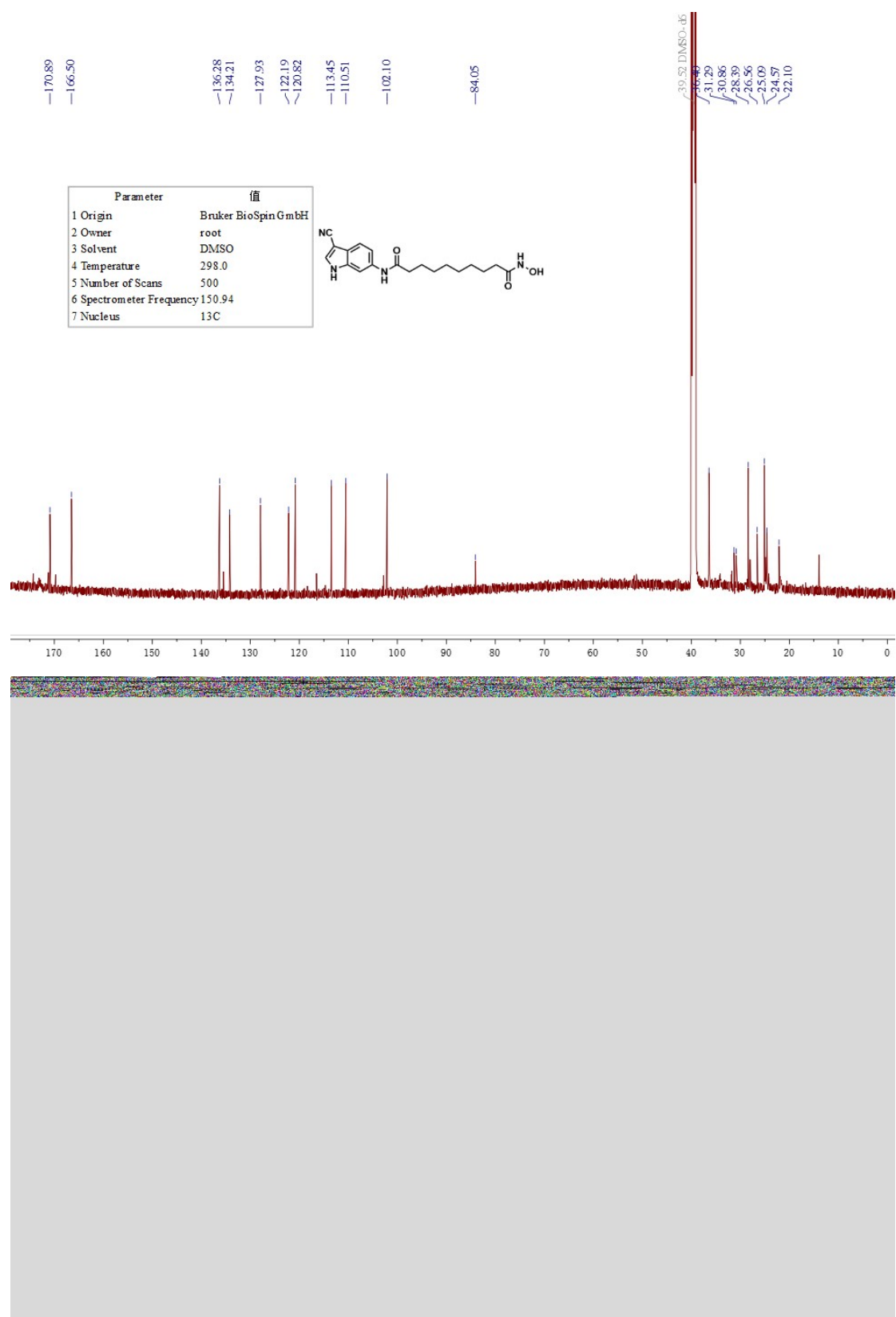


# <sup>13</sup>C-NMR spectrum of compound A7

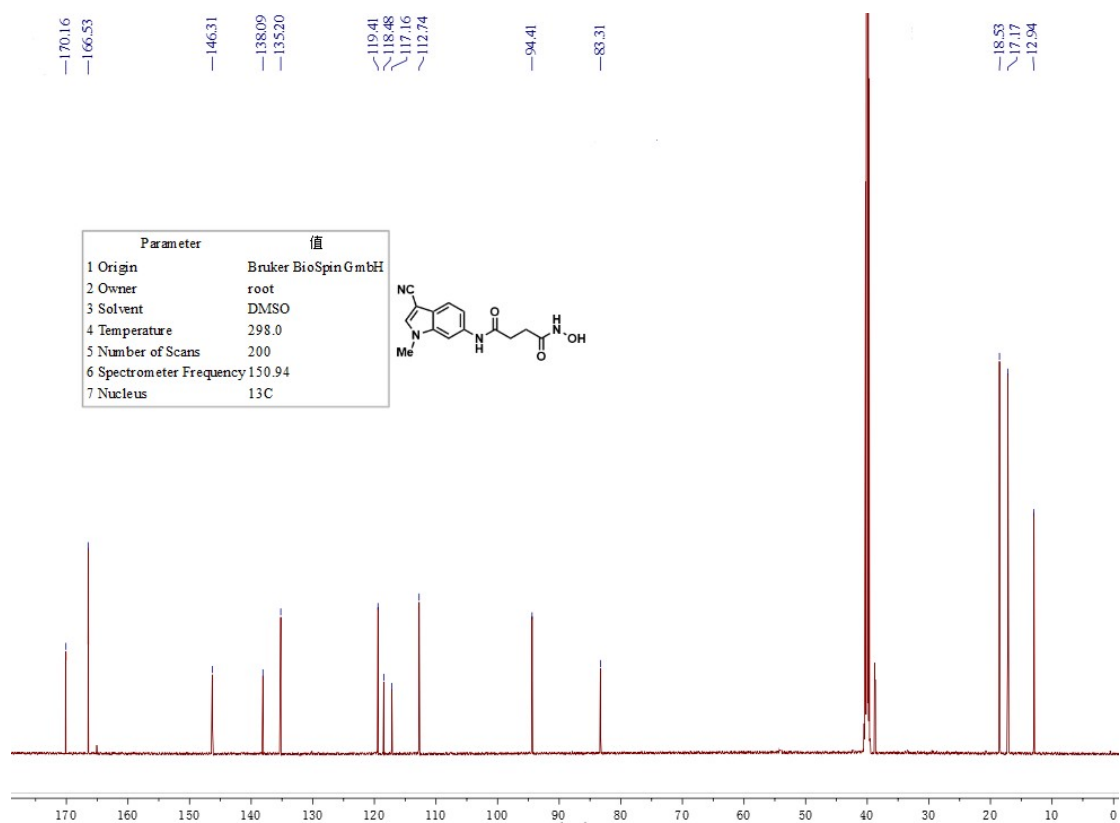


# <sup>1</sup>H-NMR spectrum of compound A8

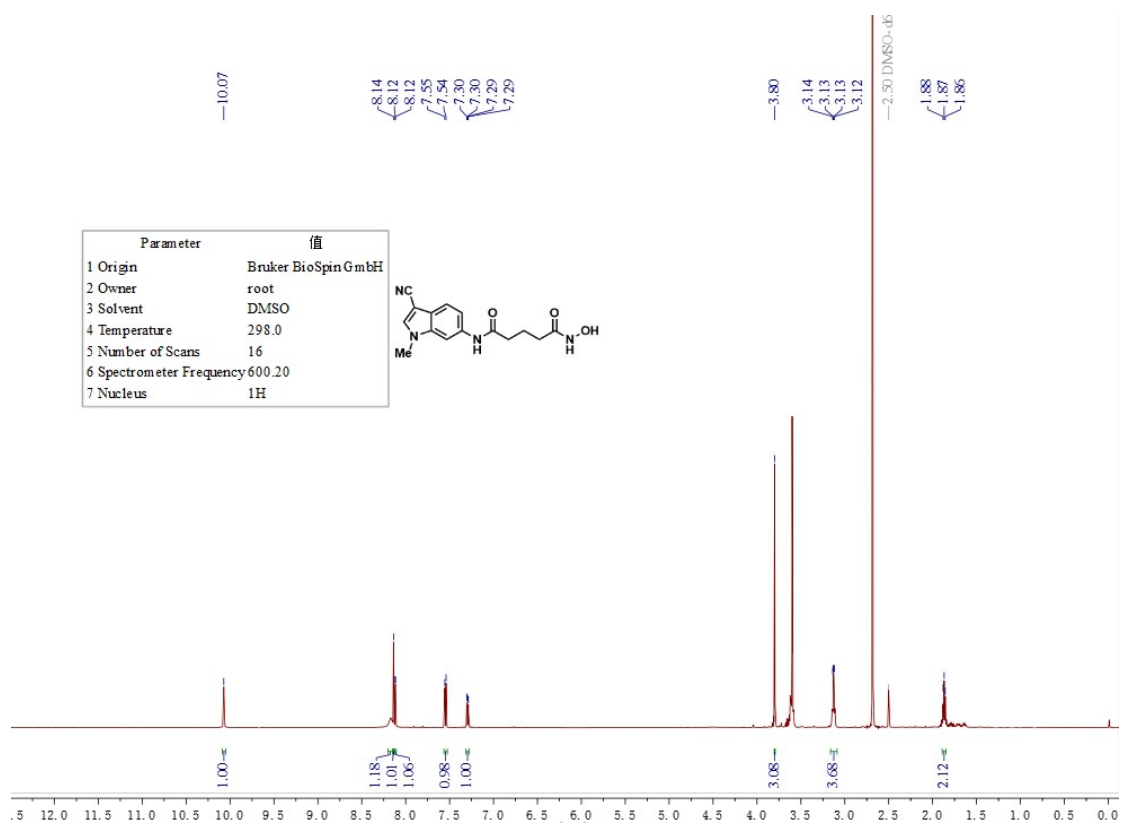




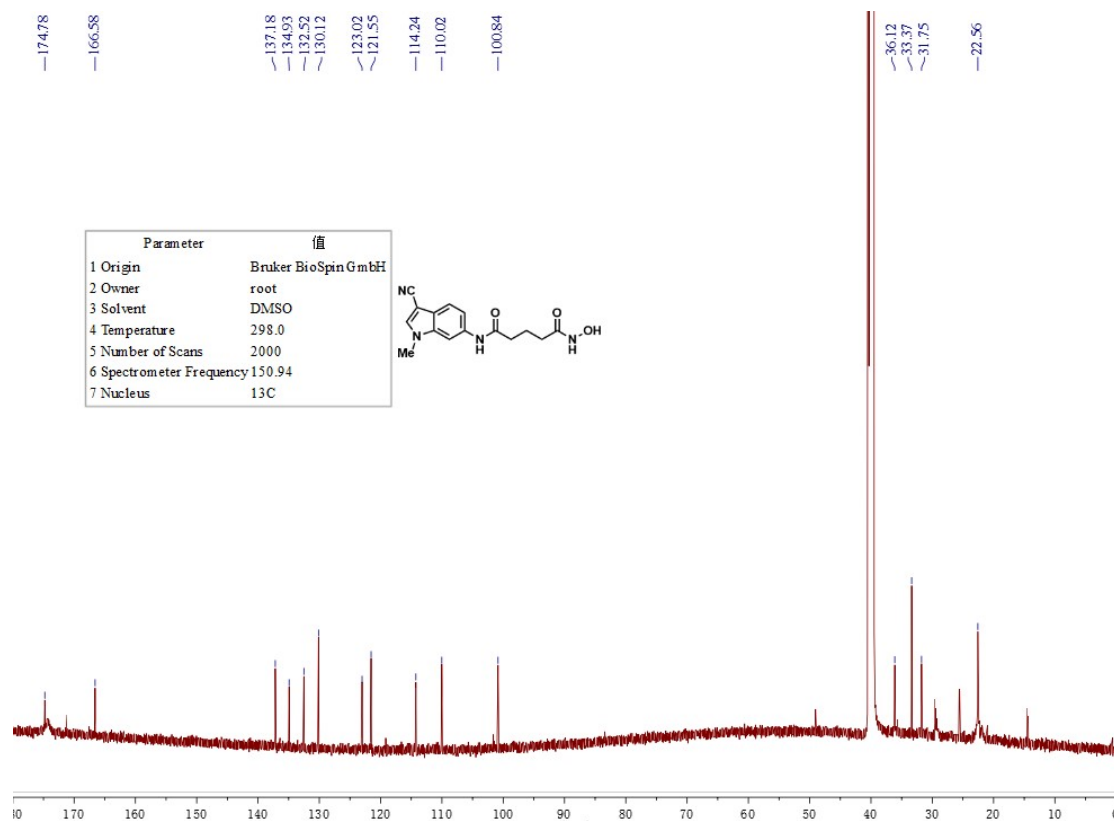
**<sup>13</sup>C-NMR spectrum of compound A8**



# **<sup>1</sup>H-NMR spectrum of compound A9**

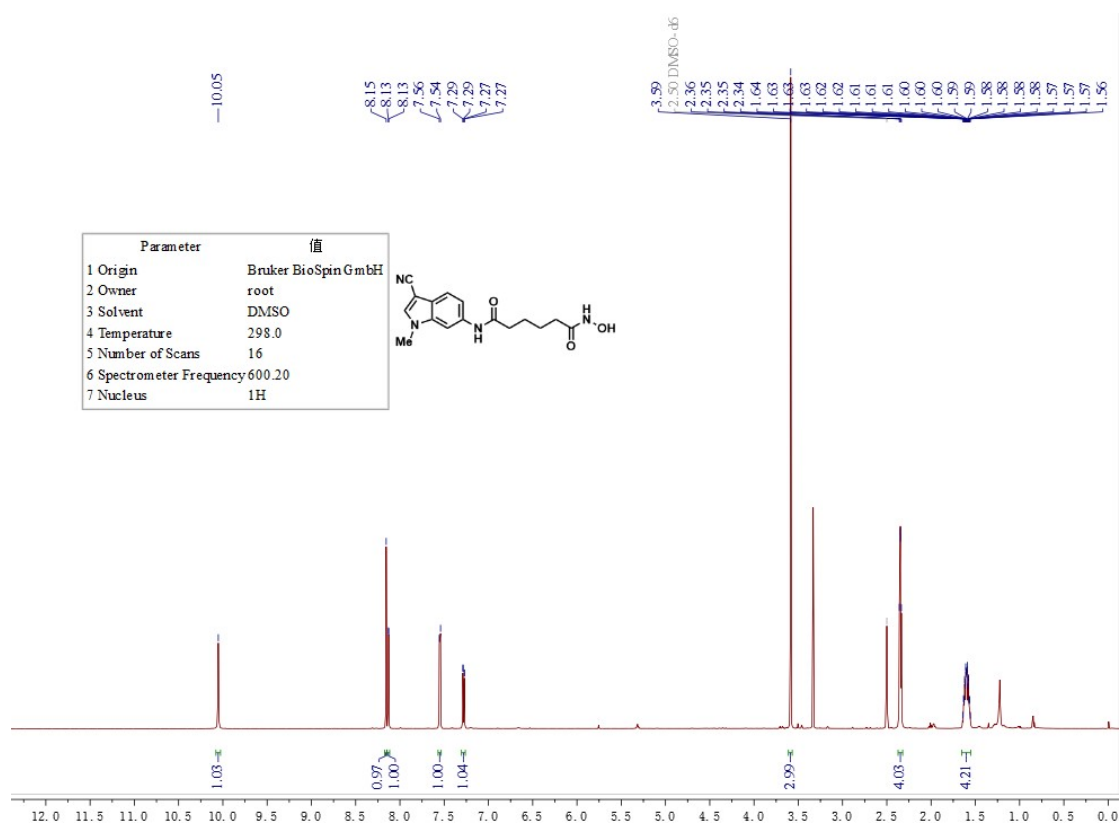


### <sup>13</sup>C-NMR spectrum of compound A9

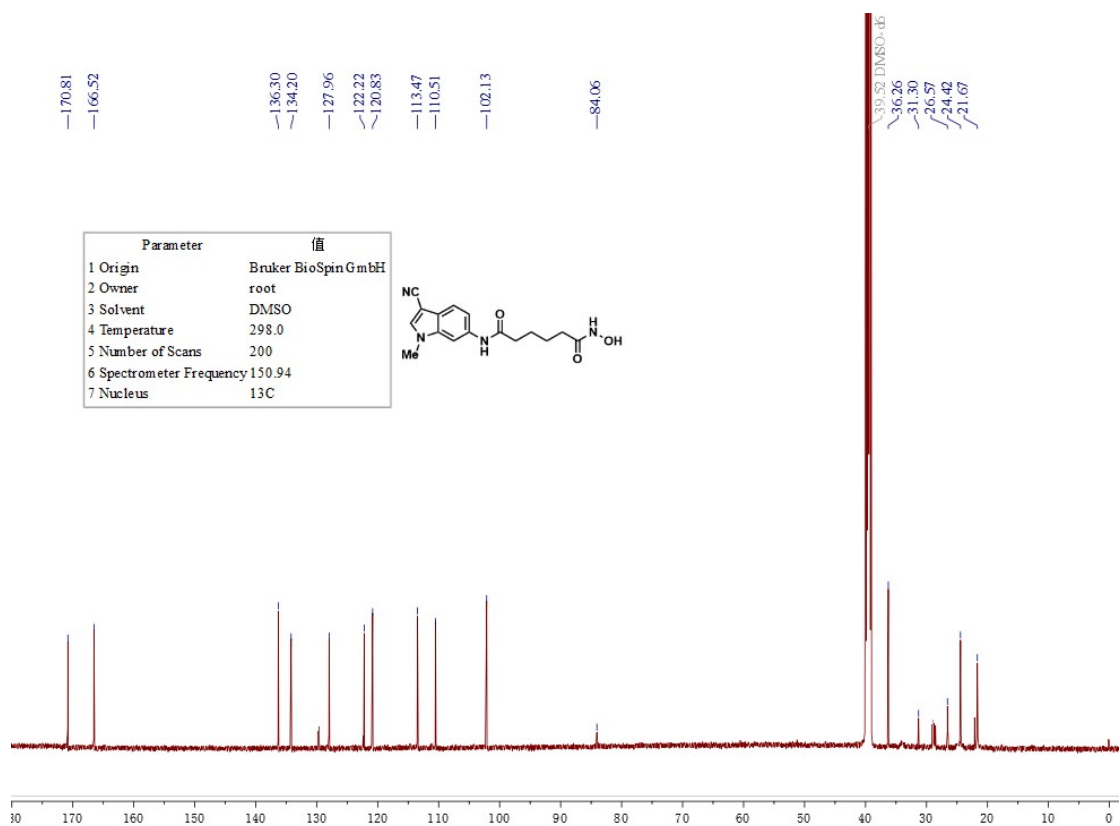


### <sup>1</sup>H-NMR spectrum of compound A10

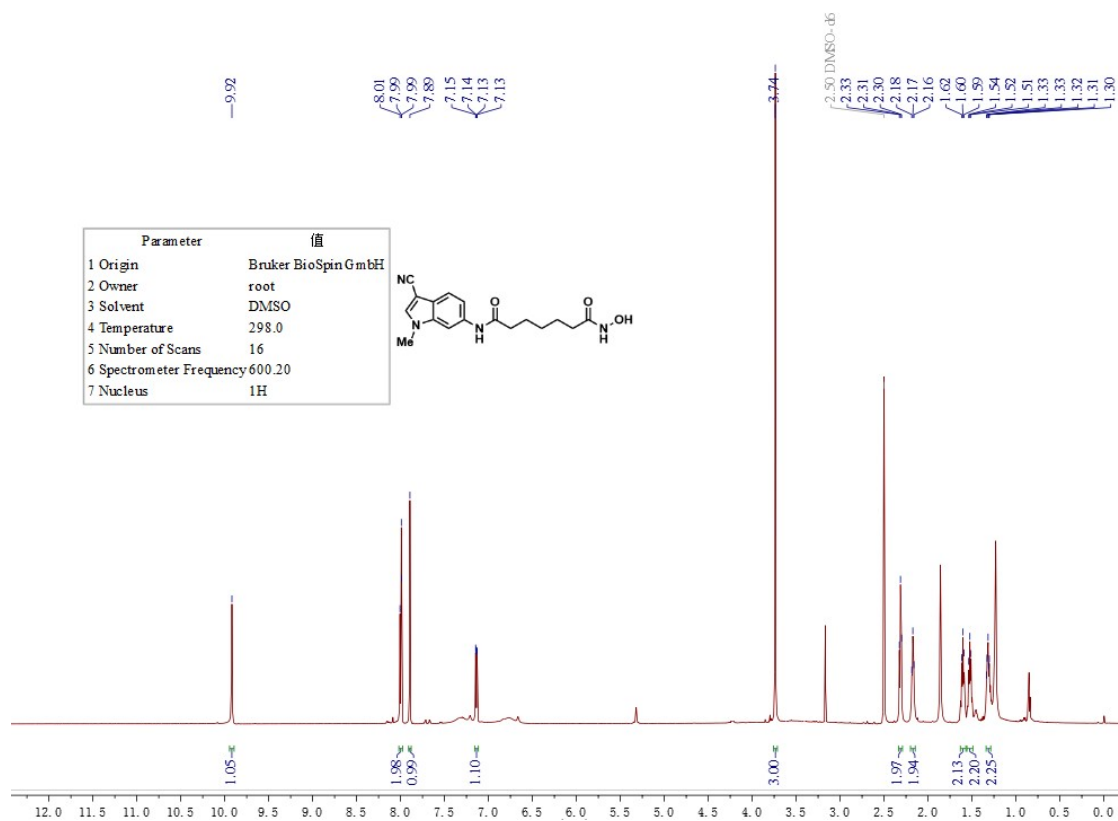




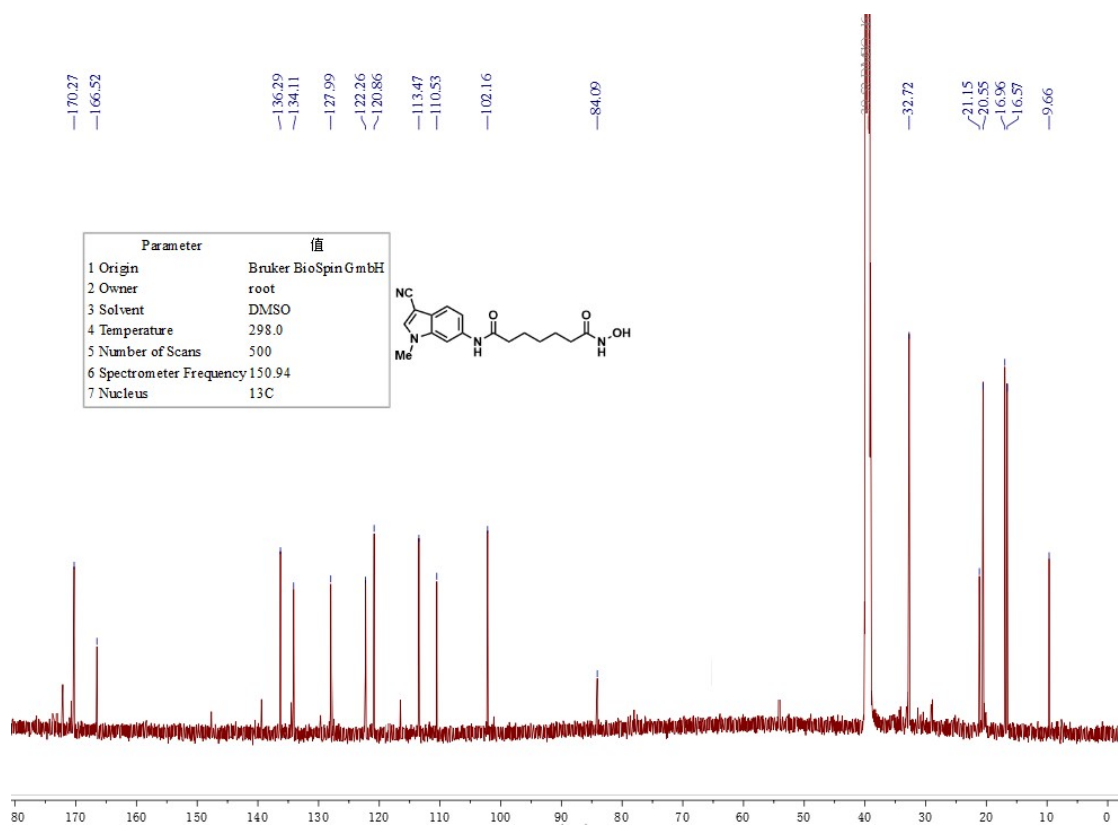
<sup>13</sup>C-NMR spectrum of compound A10



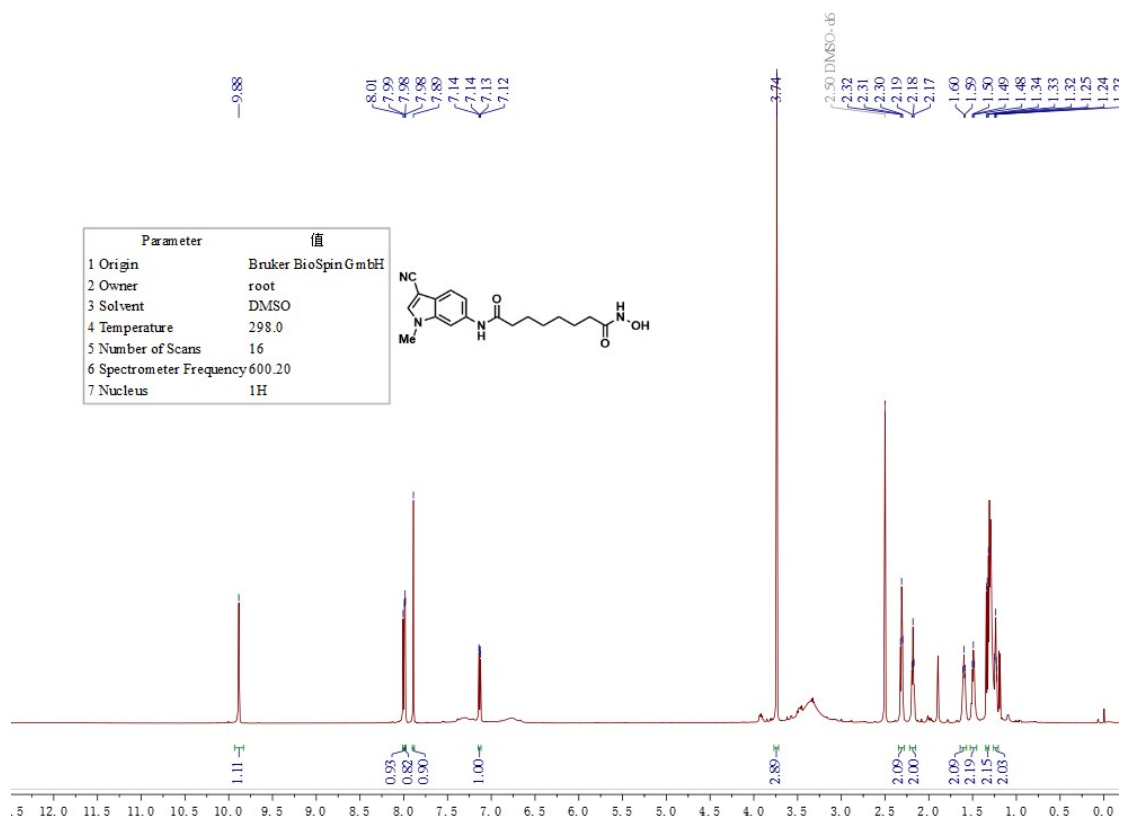
<sup>1</sup>H-NMR spectrum of compound A11



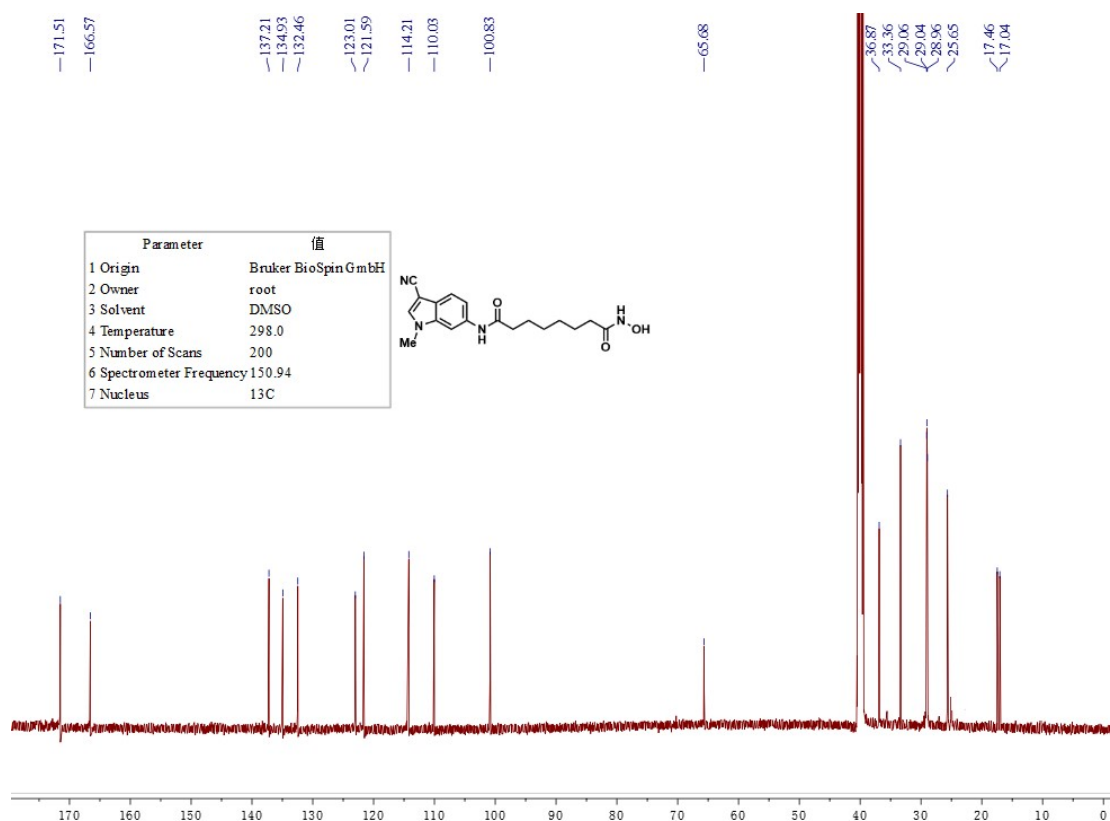
<sup>13</sup>C-NMR spectrum of compound A11



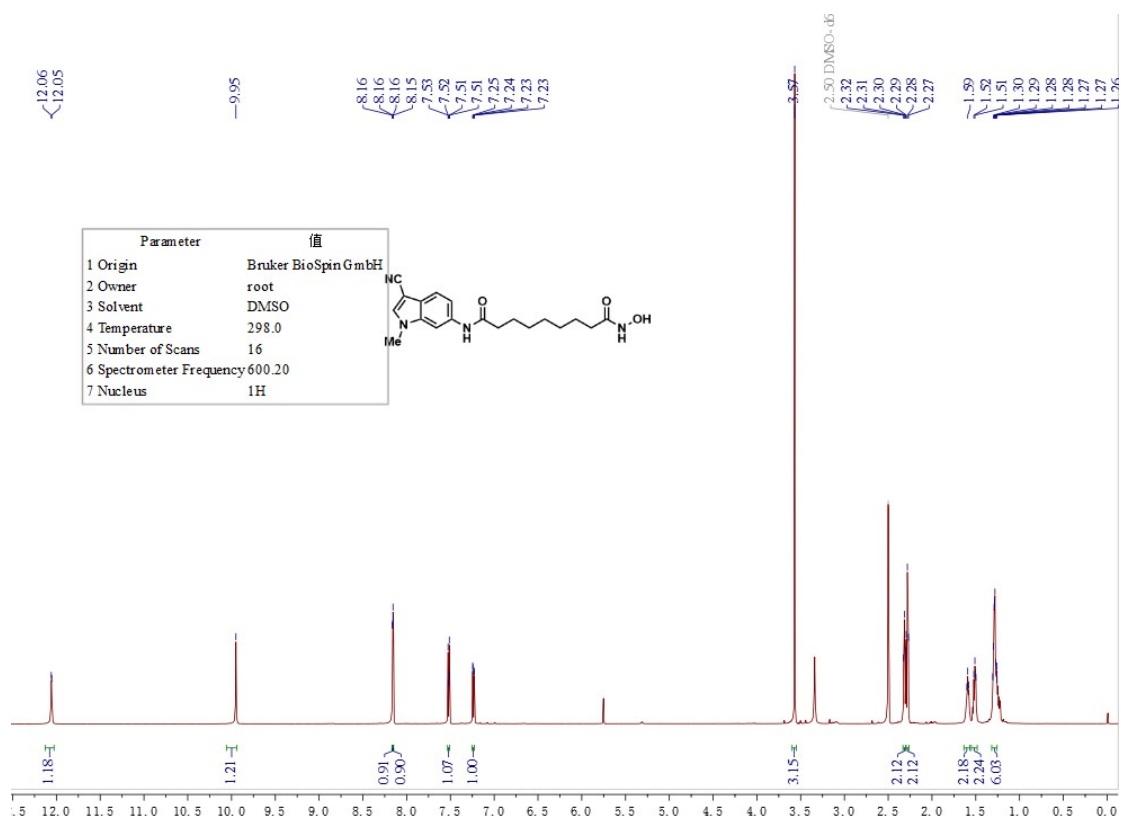
<sup>1</sup>H-NMR spectrum of compound A12



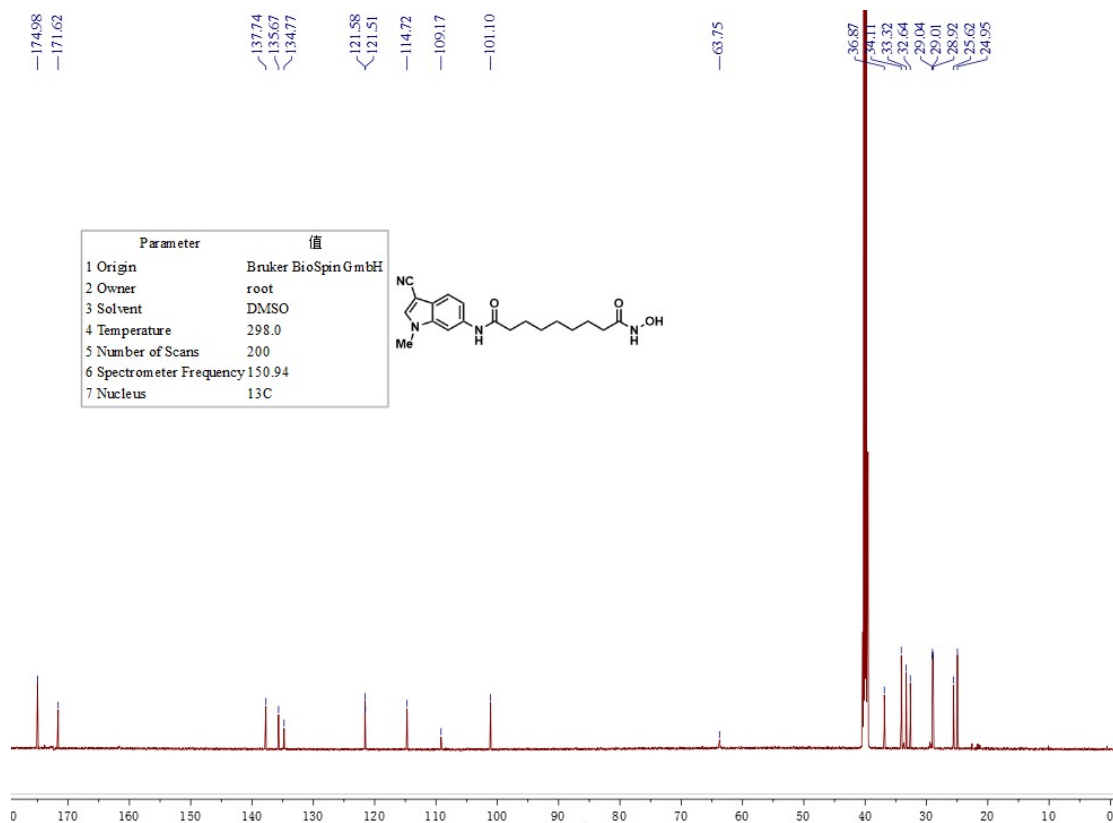
### <sup>13</sup>C-NMR spectrum of compound A12



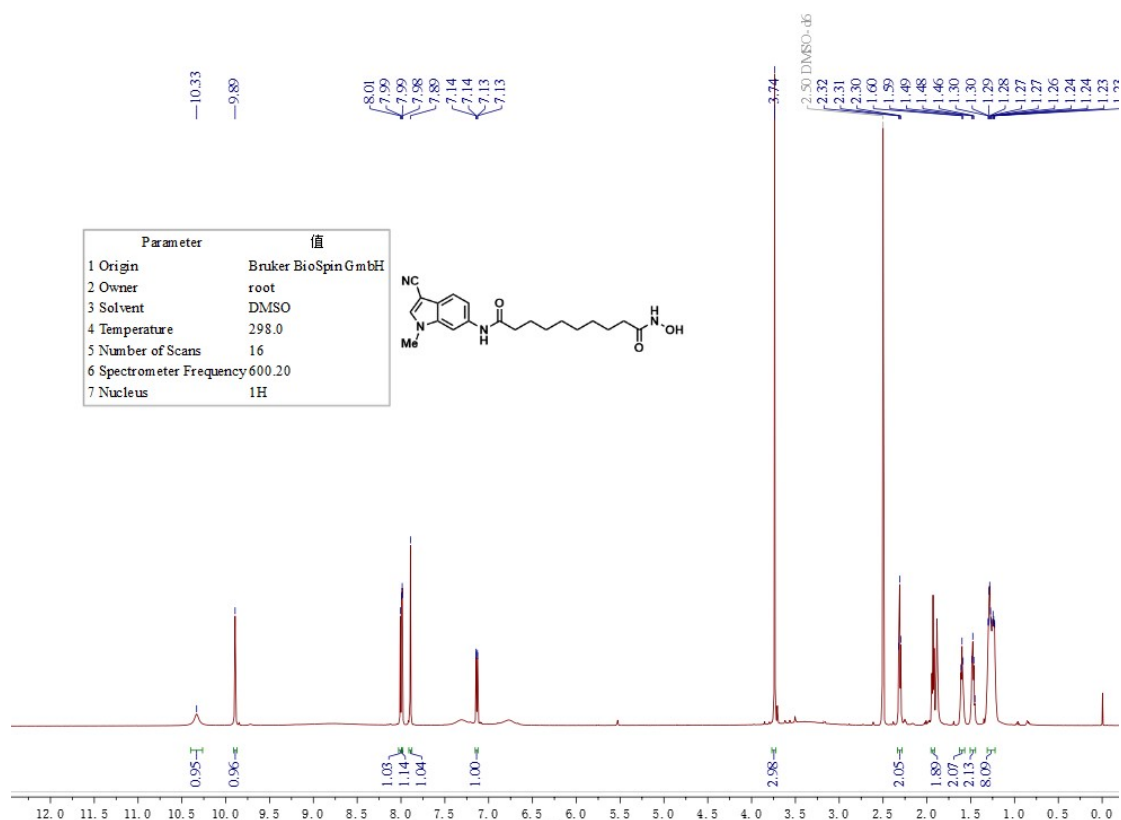
### <sup>1</sup>H-NMR spectrum of compound A13



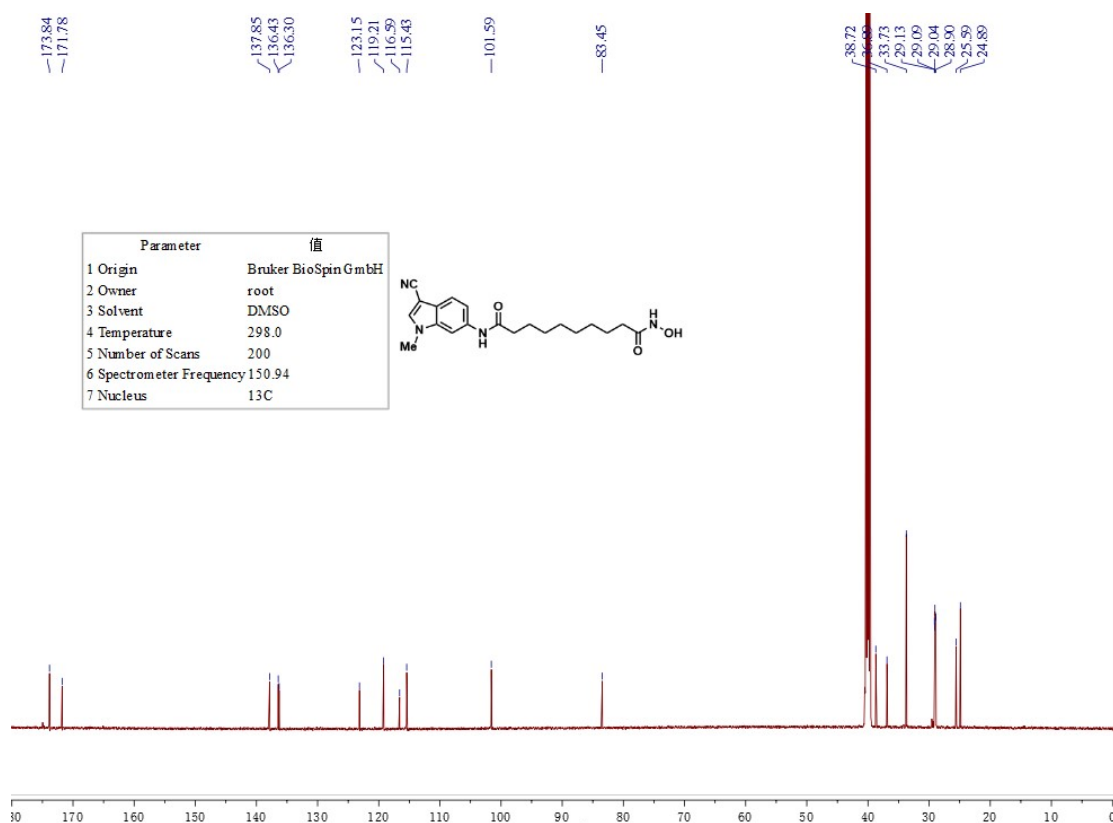
### <sup>13</sup>C-NMR spectrum of compound A13



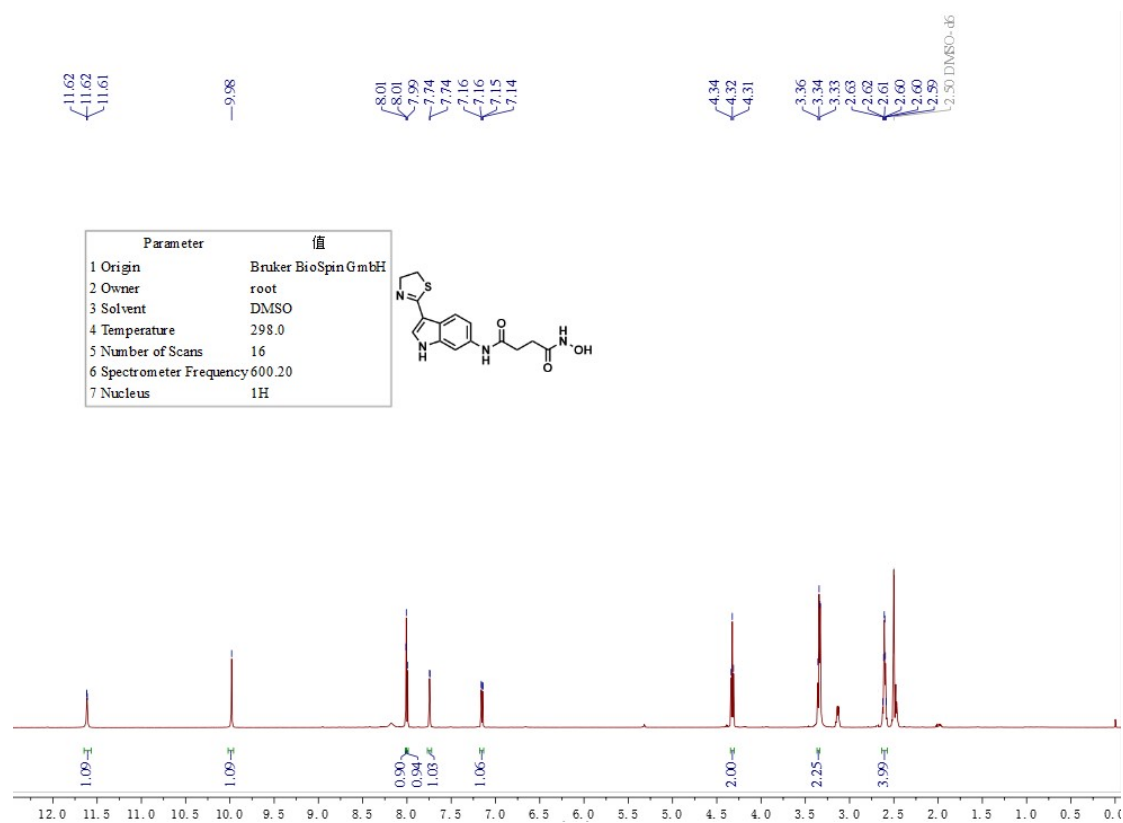
# <sup>1</sup>H-NMR spectrum of compound A14



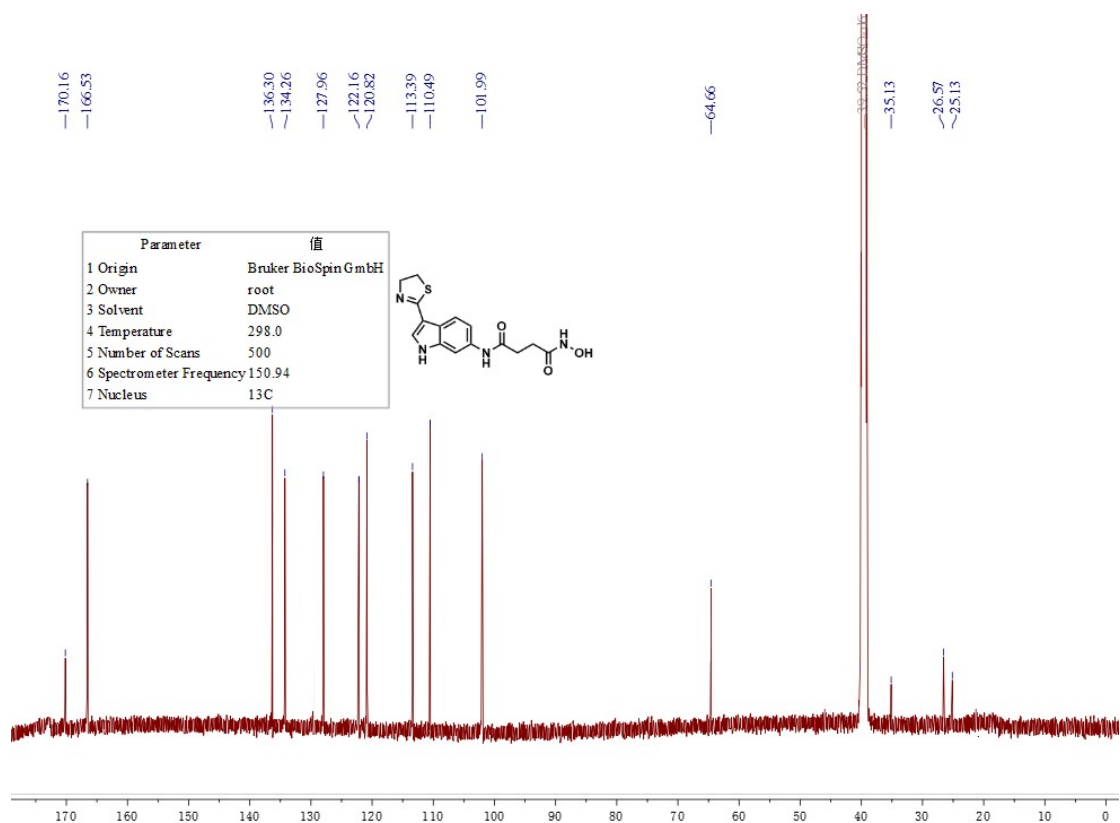
# <sup>13</sup>C-NMR spectrum of compound A14



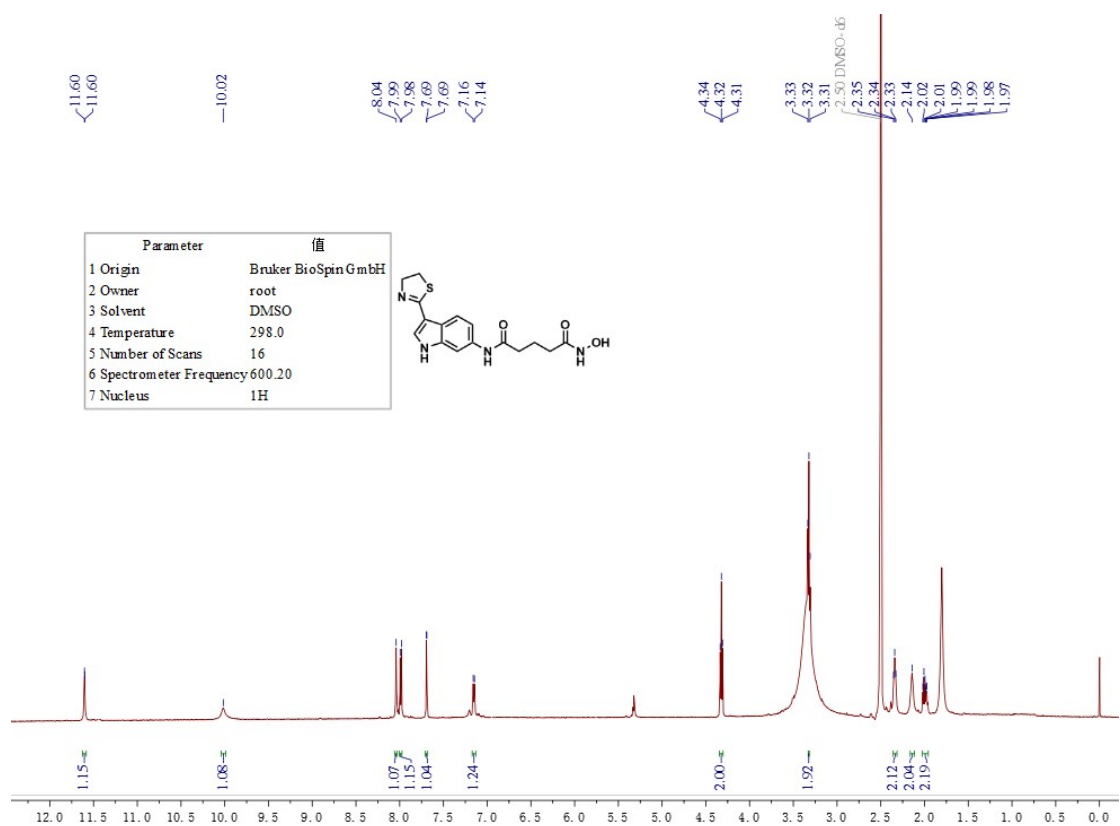
## <sup>1</sup>H-NMR spectrum of compound A15



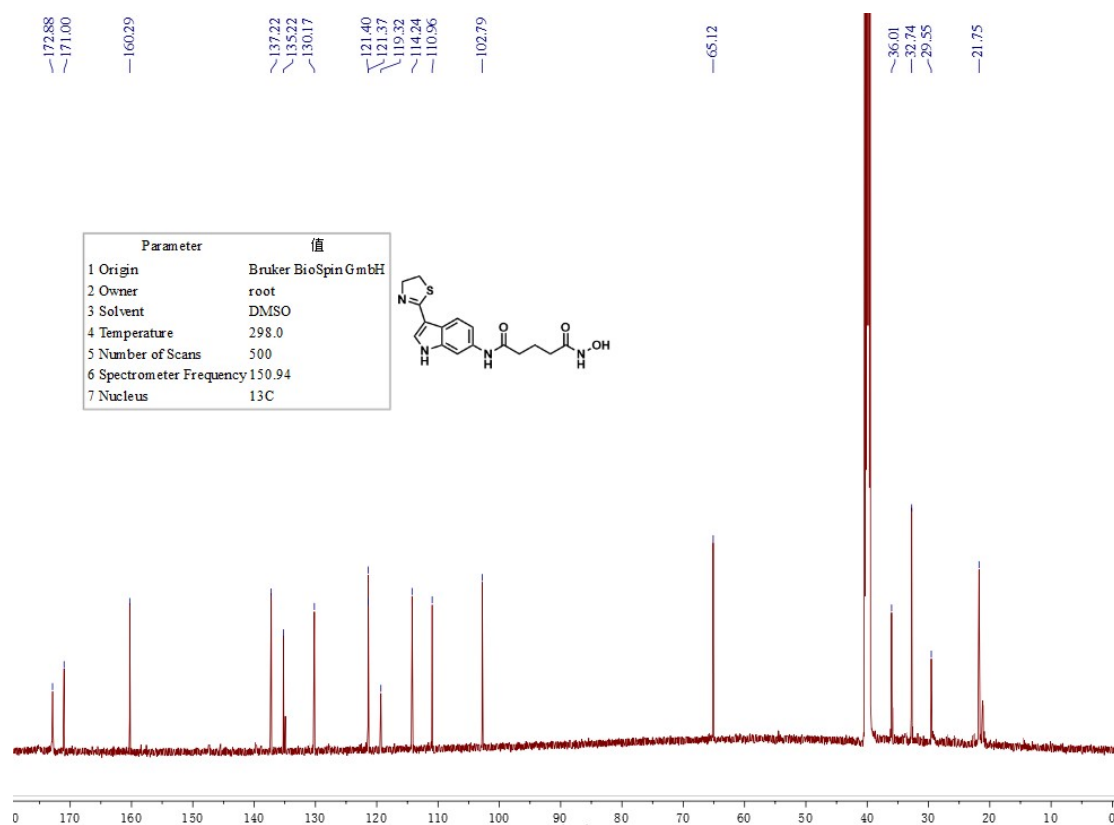
## <sup>13</sup>C-NMR spectrum of compound A15



**<sup>1</sup>H-NMR spectrum of compound A16**

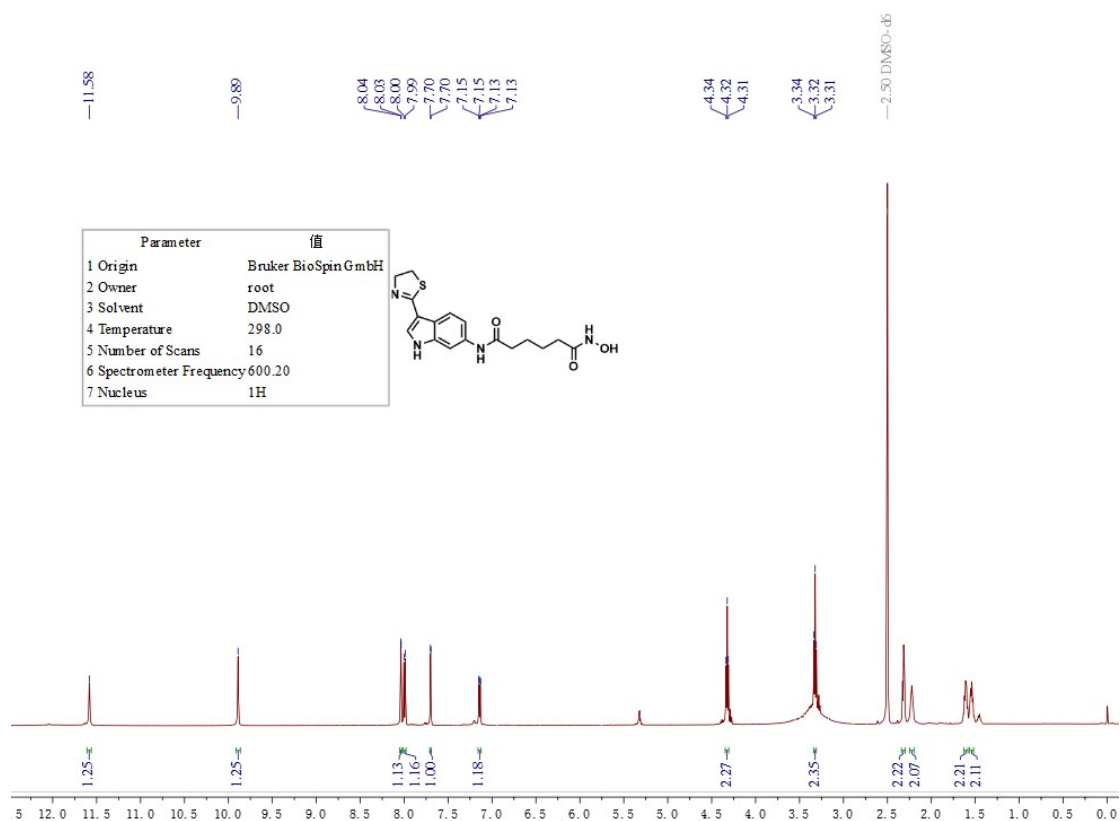


### <sup>13</sup>C-NMR spectrum of compound A16

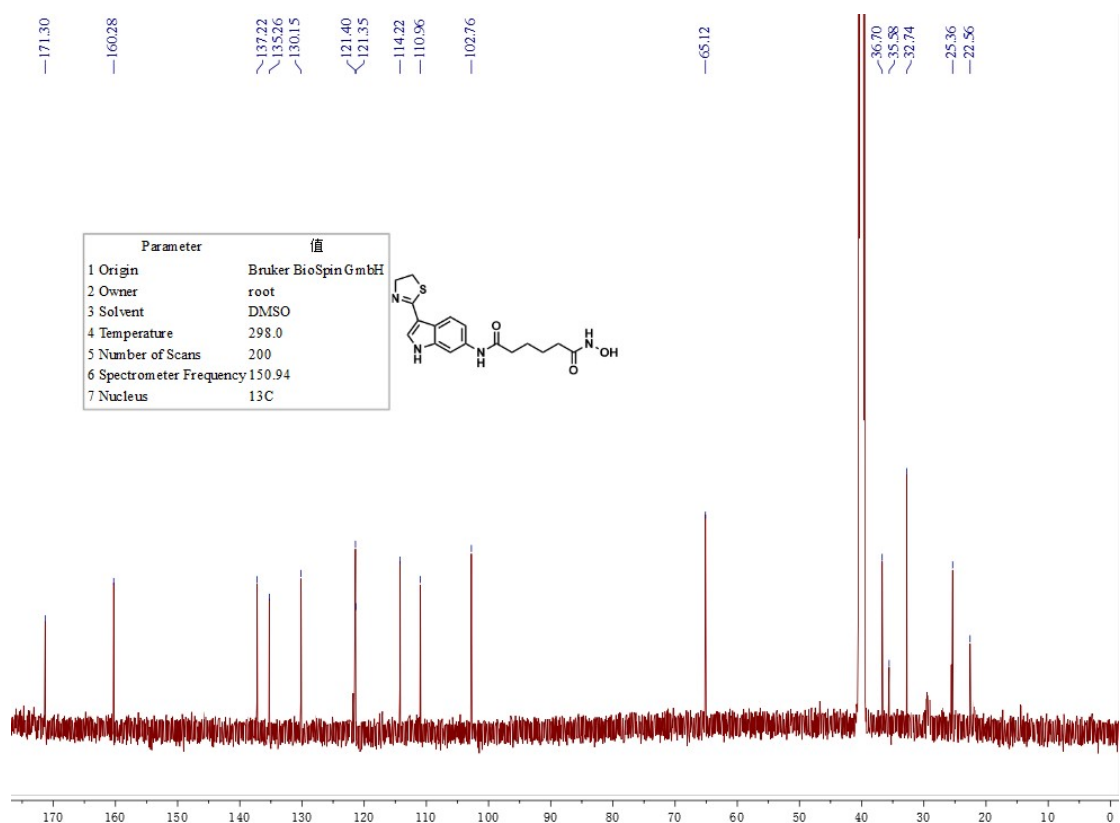


### <sup>1</sup>H-NMR spectrum of compound A17

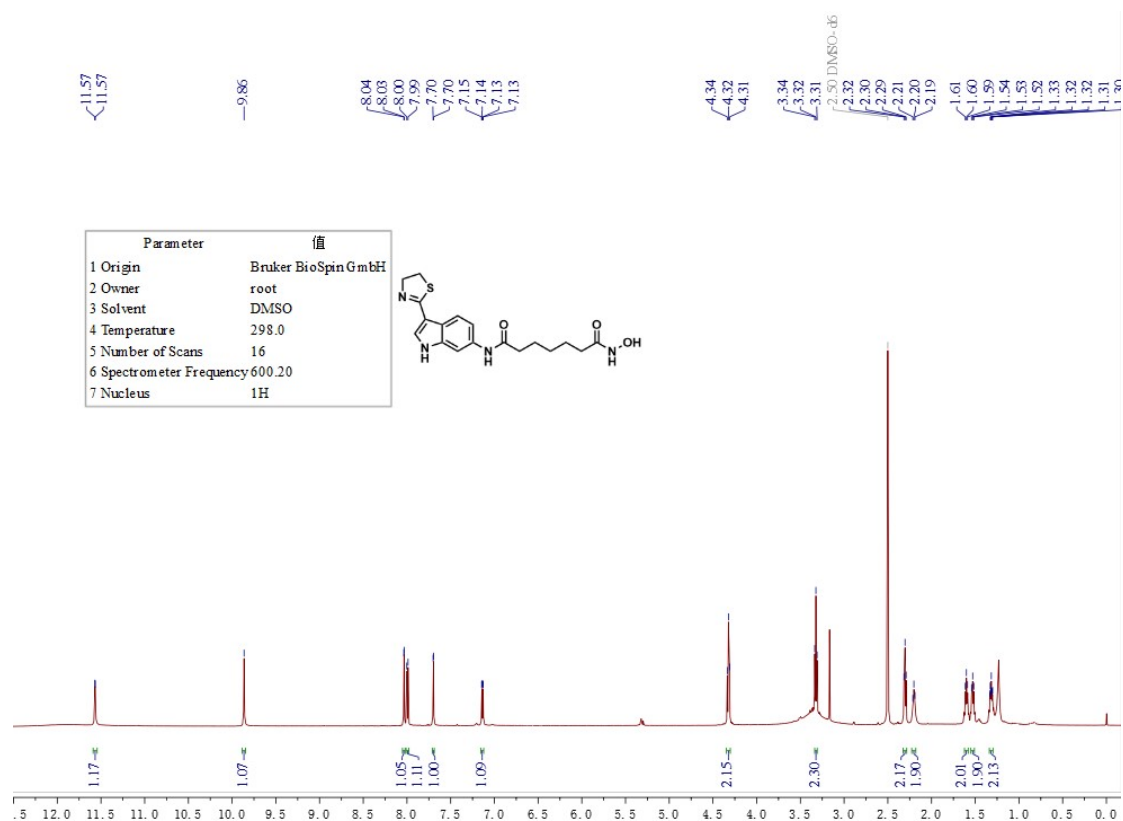




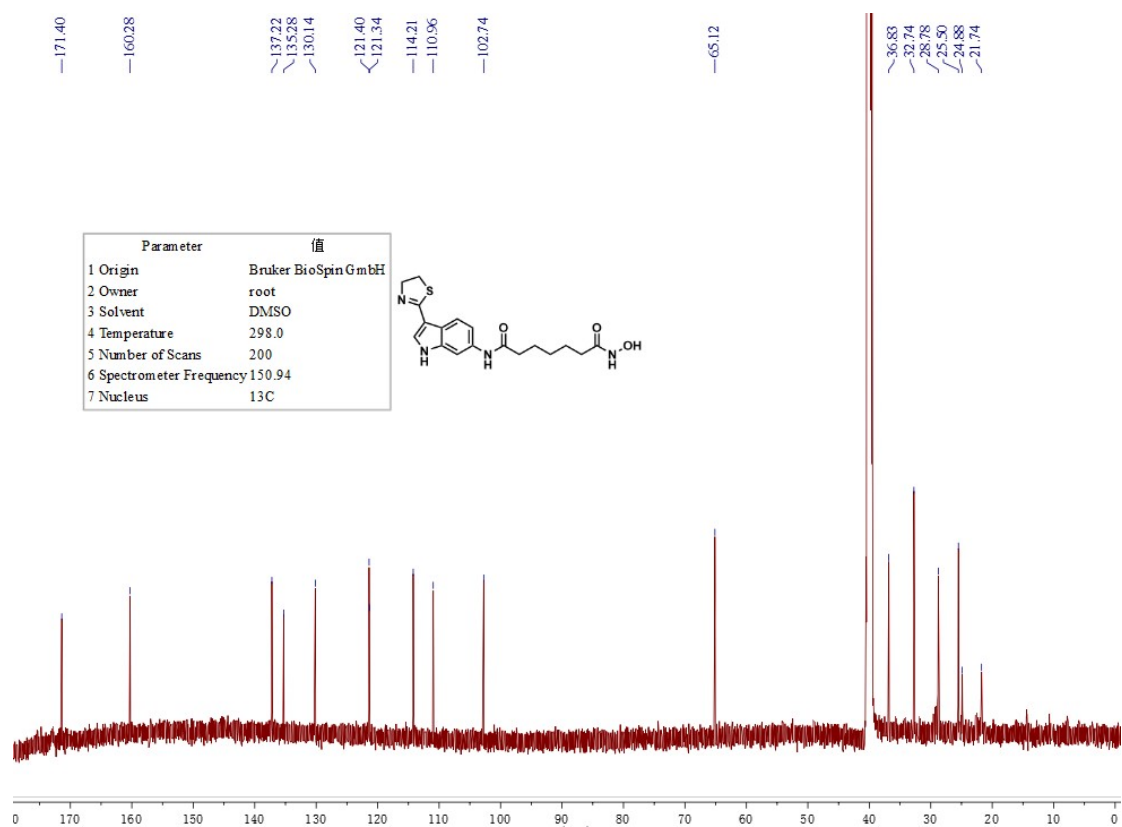
### <sup>13</sup>C-NMR spectrum of compound A17



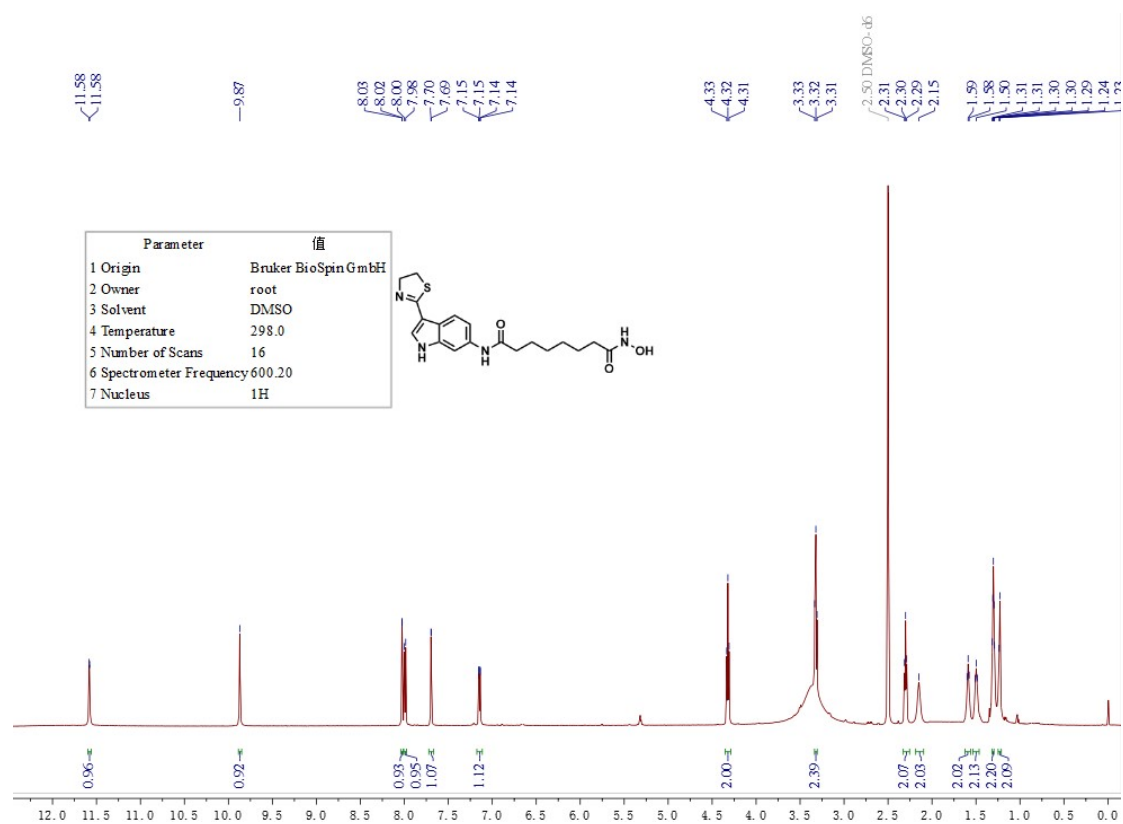
# <sup>1</sup>H-NMR spectrum of compound A18



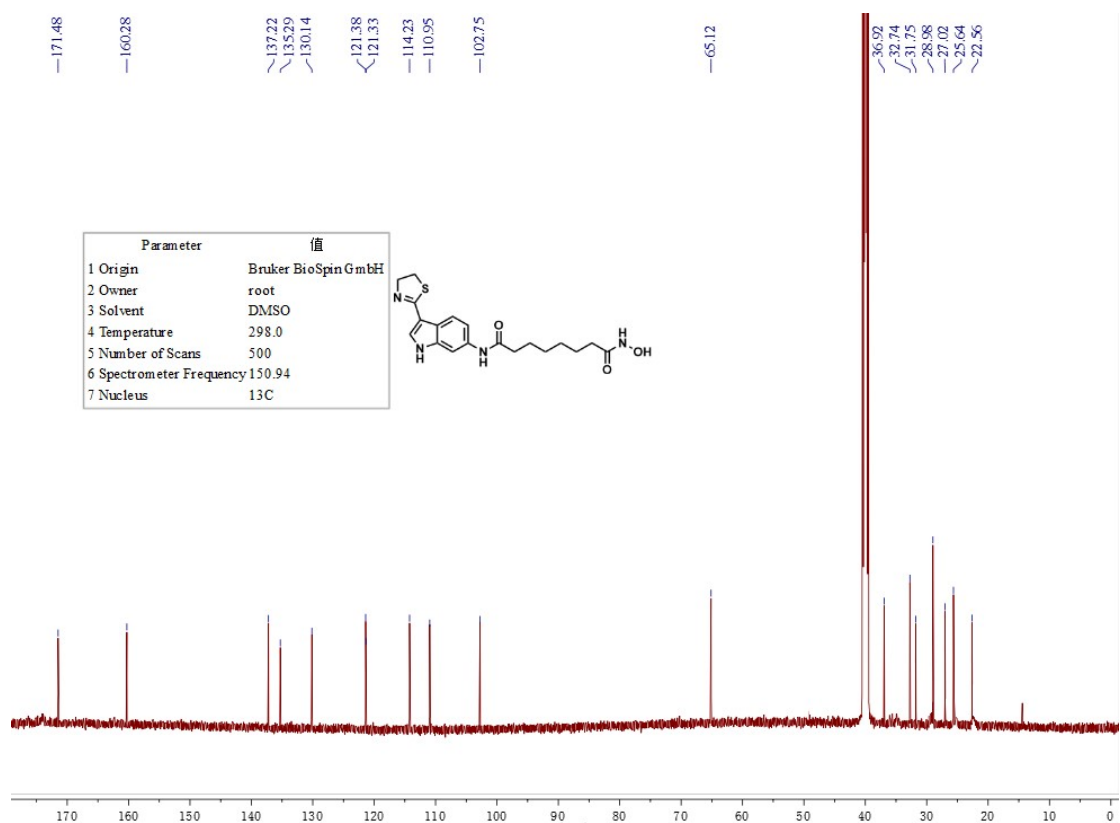
# <sup>13</sup>C-NMR spectrum of compound A18



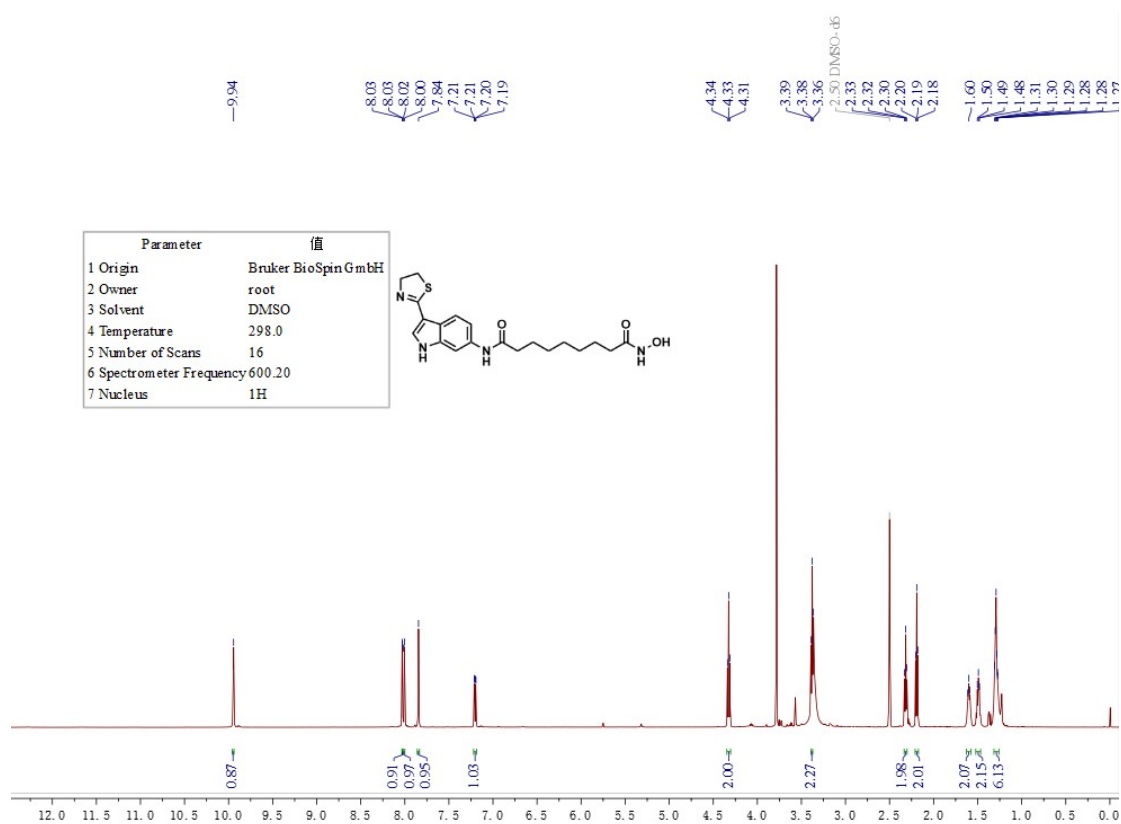
**<sup>1</sup>H-NMR spectrum of compound A19**



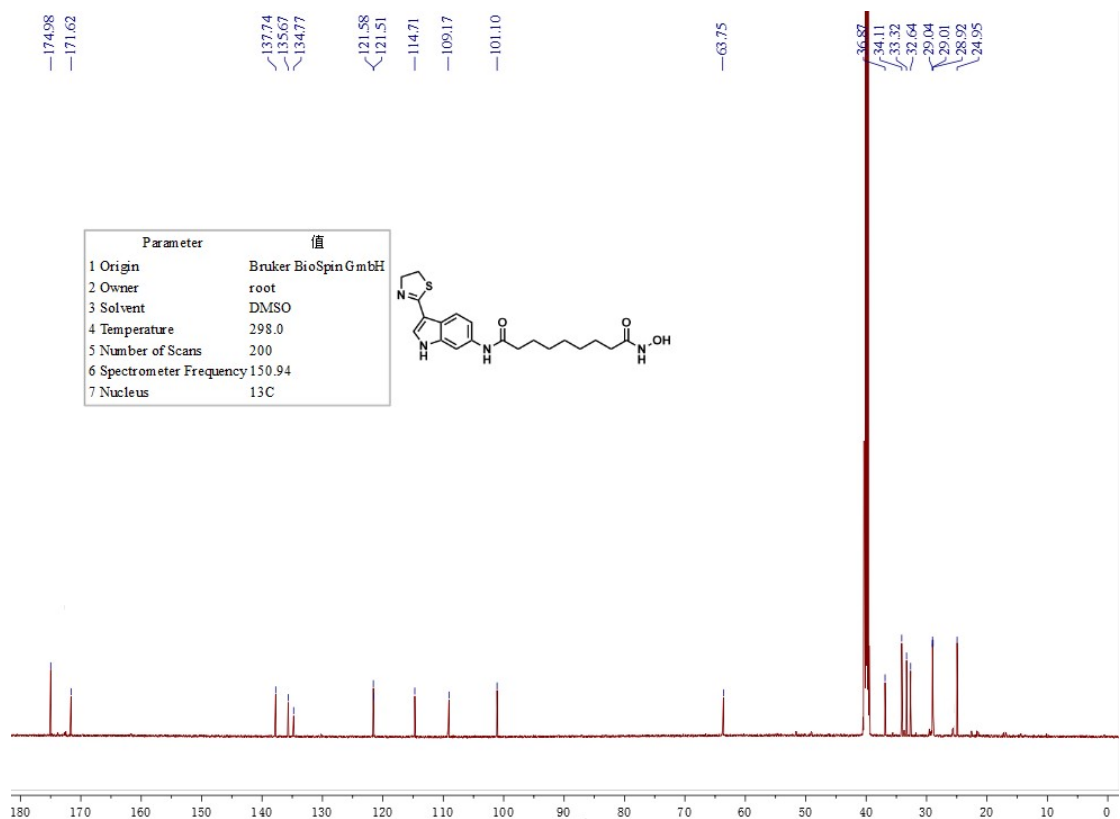
**<sup>13</sup>C-NMR spectrum of compound A20**



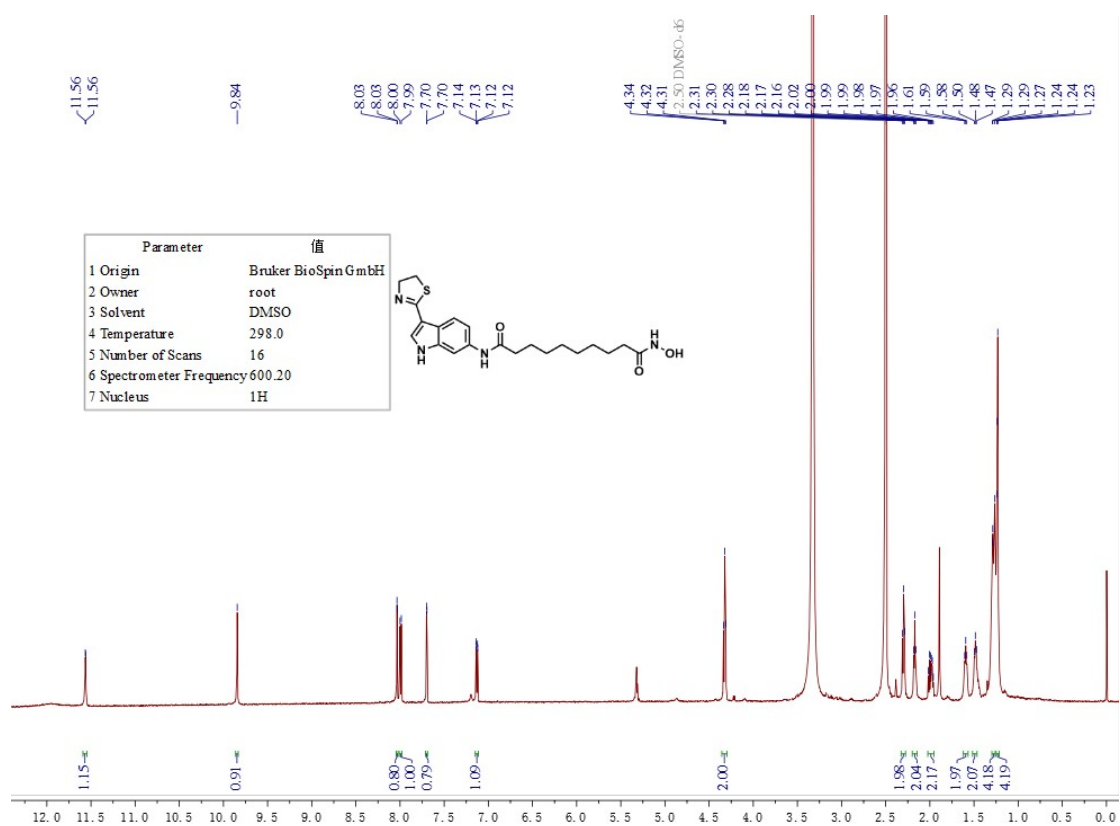
**<sup>1</sup>H-NMR spectrum of compound A21**



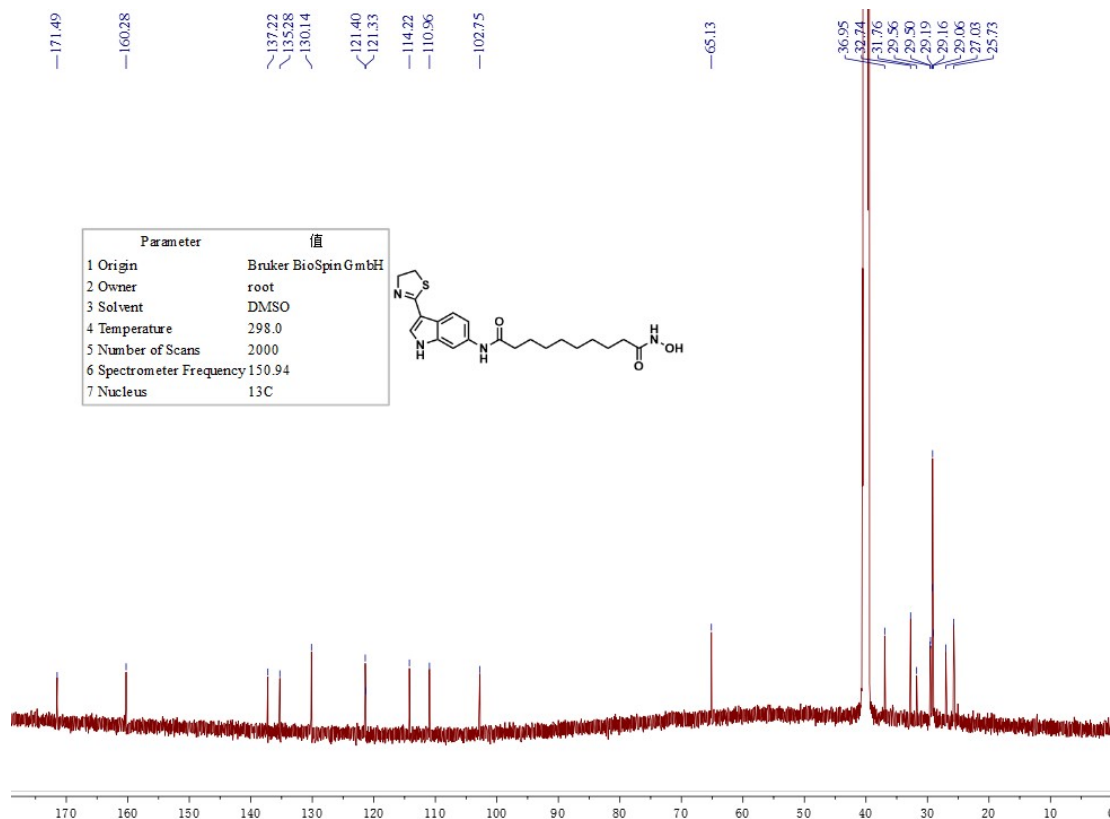
**<sup>13</sup>C-NMR spectrum of compound A21**



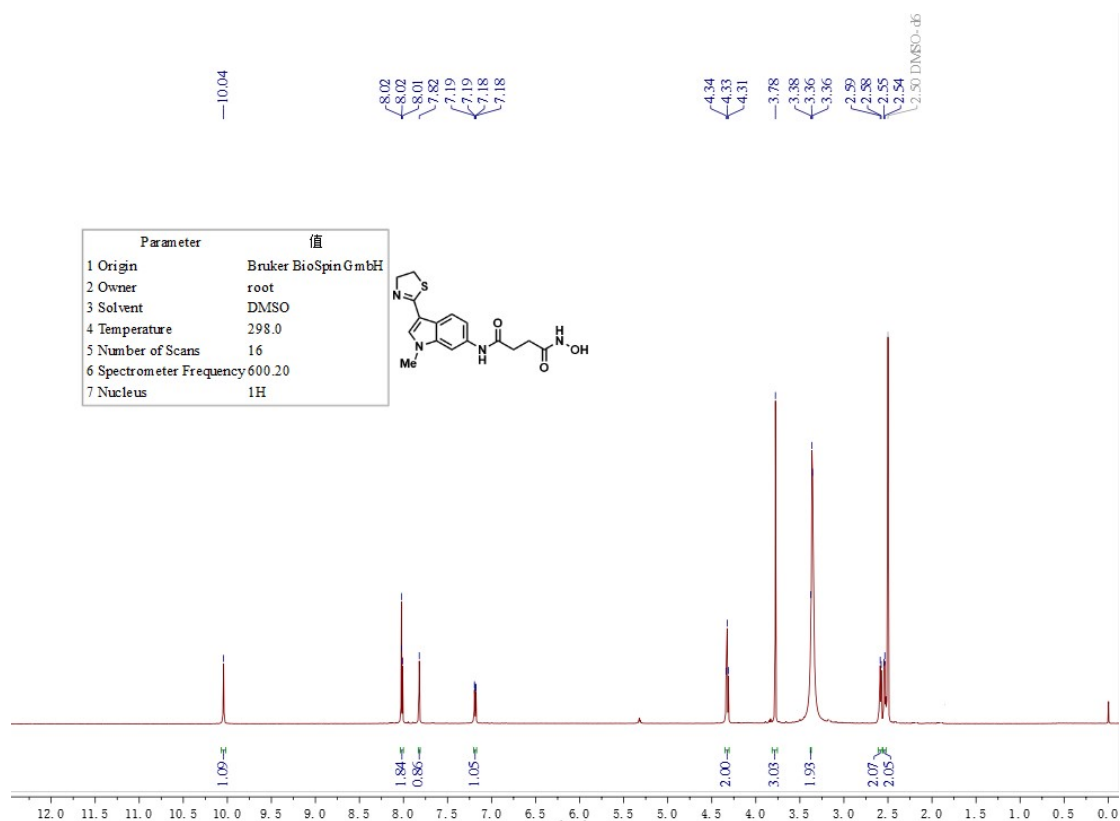
# **<sup>1</sup>H-NMR spectrum of compound A22**



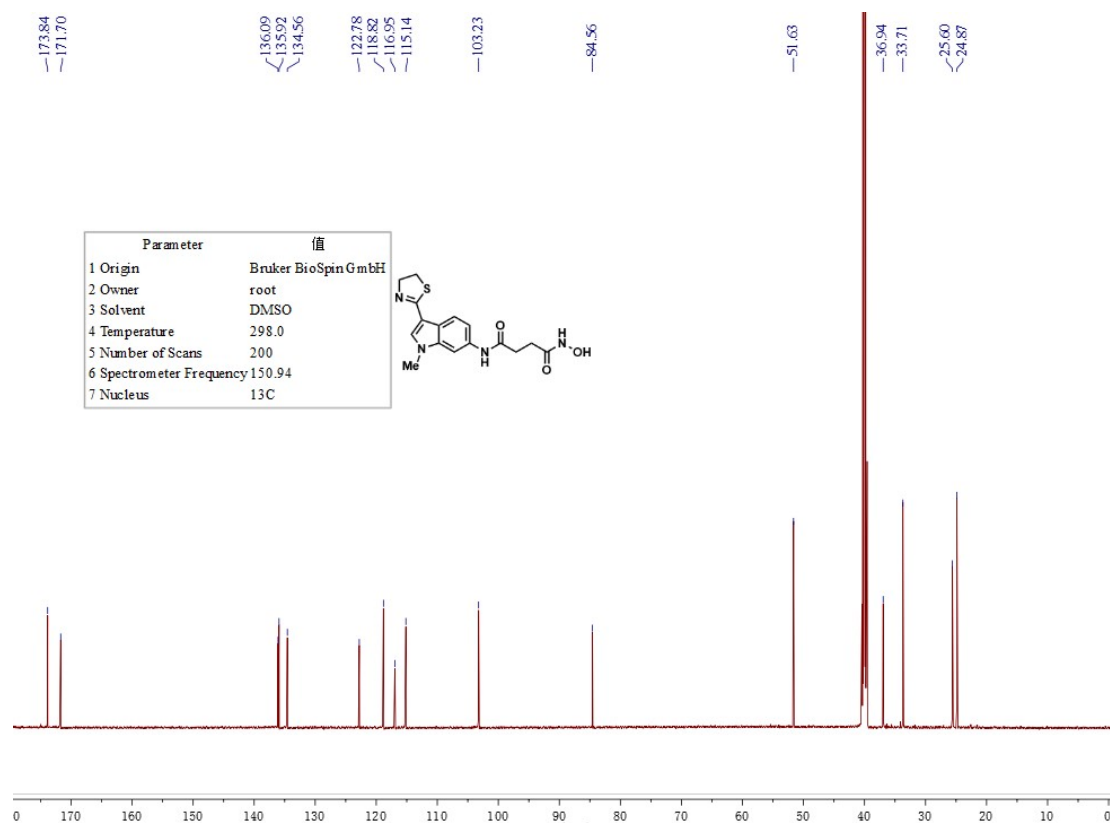
## <sup>13</sup>C-NMR spectrum of compound A23



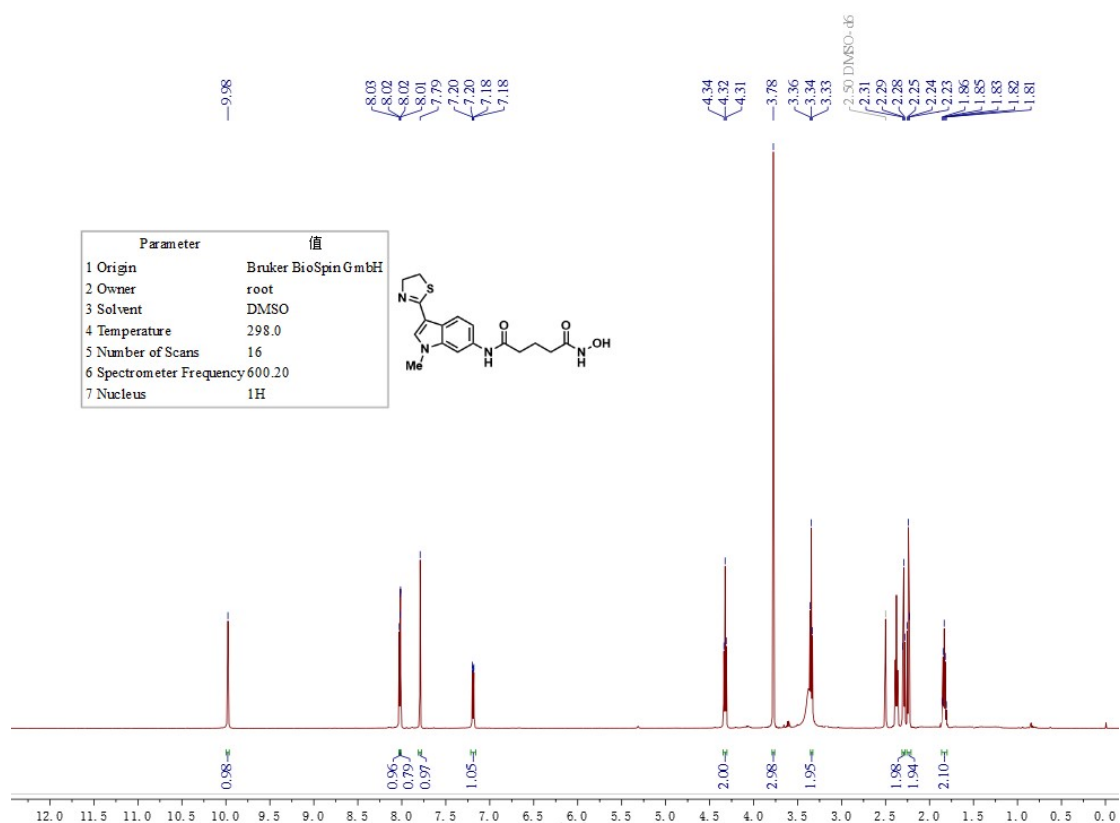
## <sup>1</sup>H-NMR spectrum of compound A24



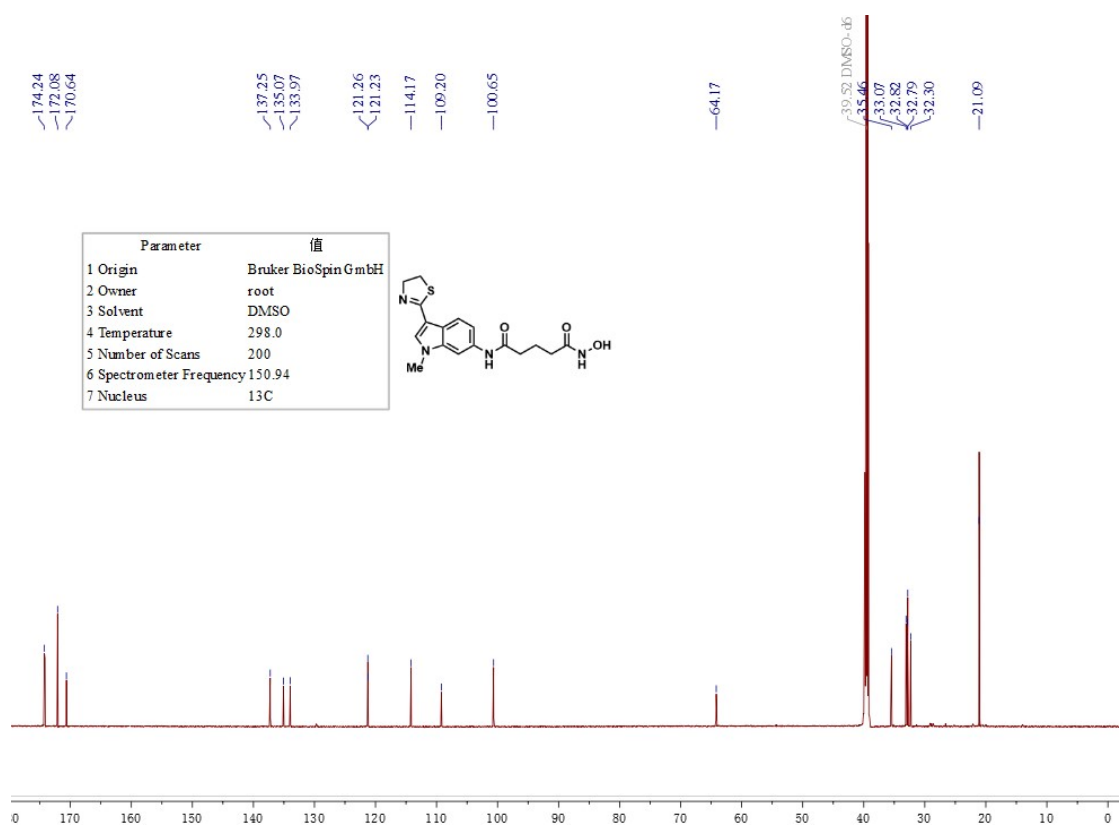
# <sup>13</sup>C-NMR spectrum of compound A24



# <sup>1</sup>H-NMR spectrum of compound A25

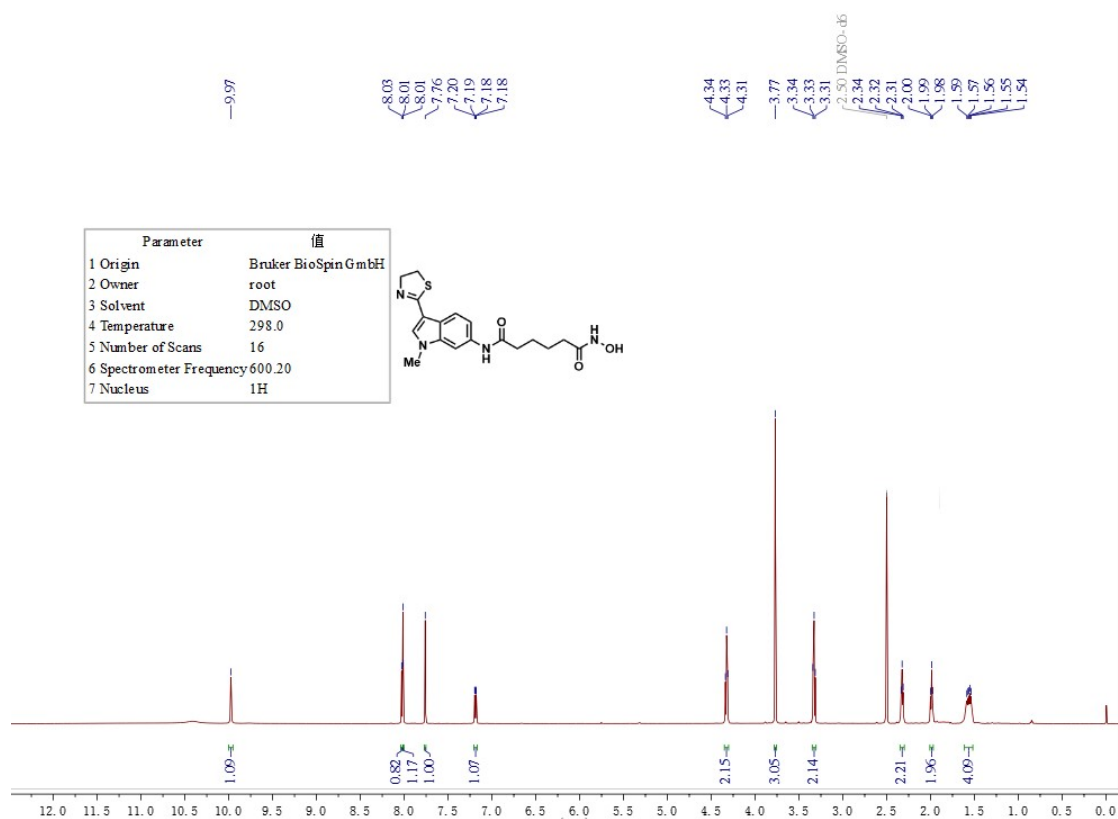


<sup>13</sup>C-NMR spectrum of compound A25

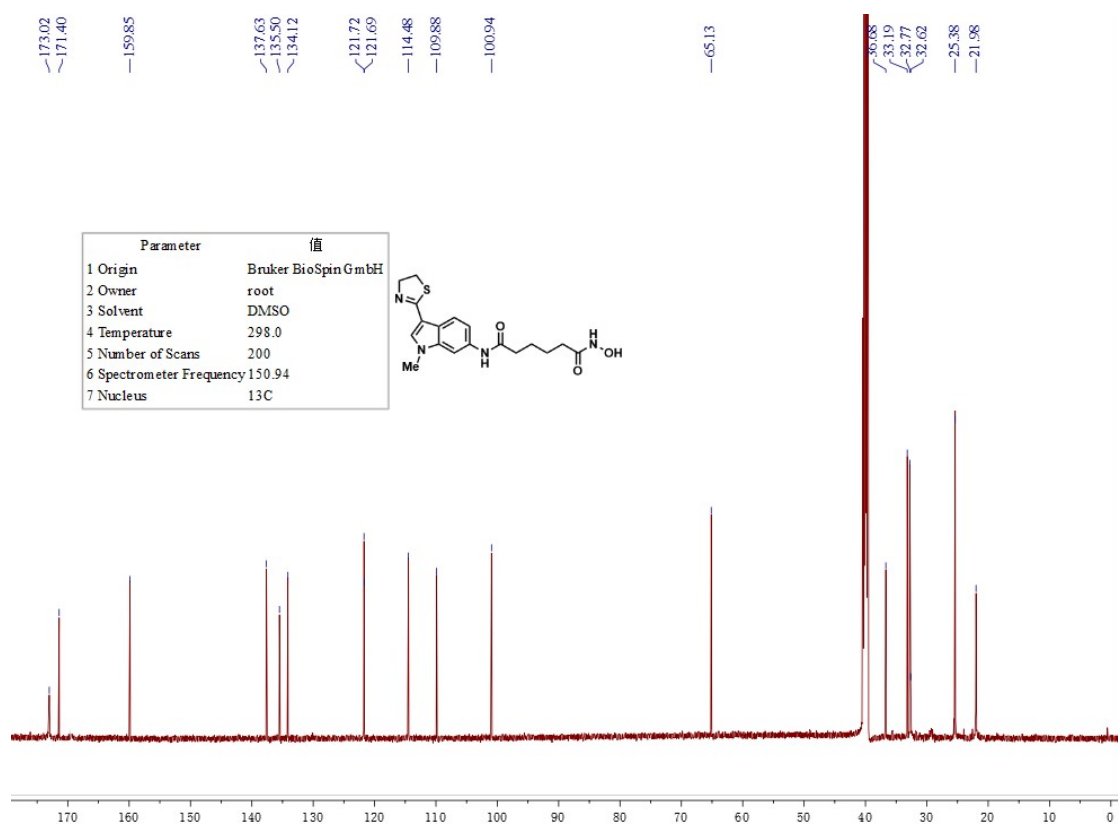


<sup>1</sup>H-NMR spectrum of compound A26

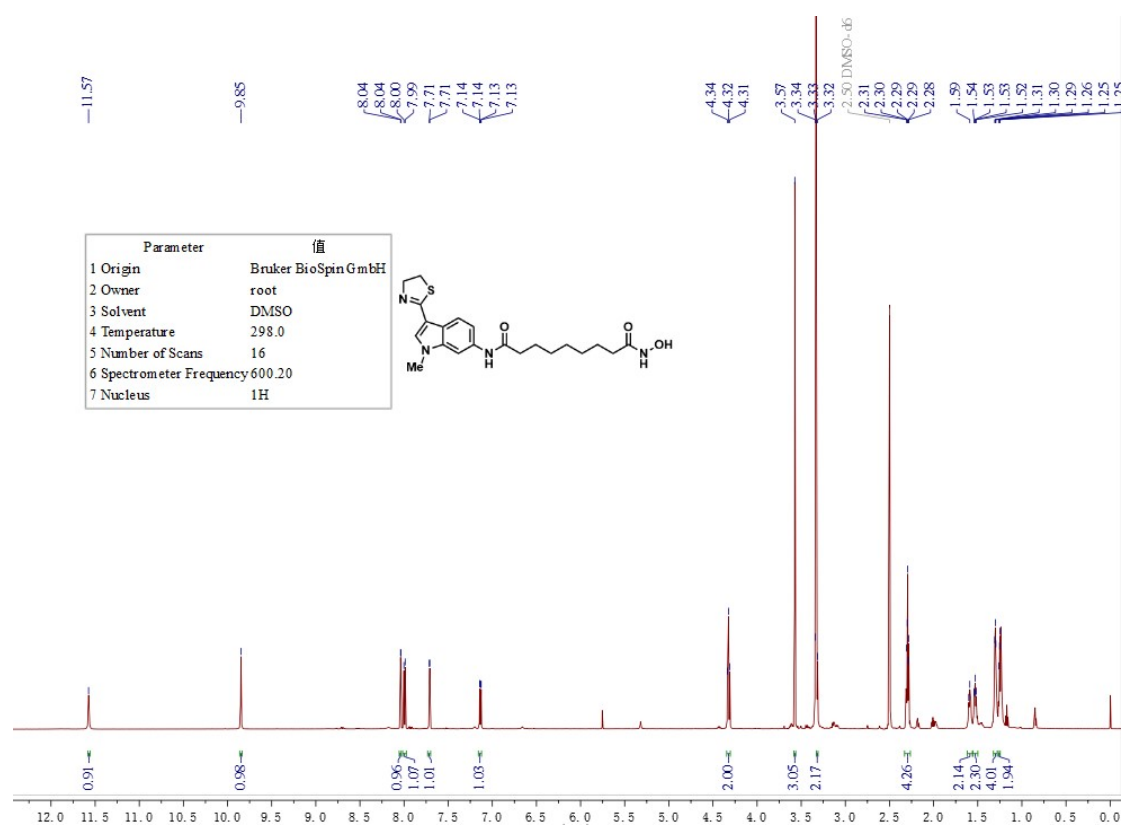




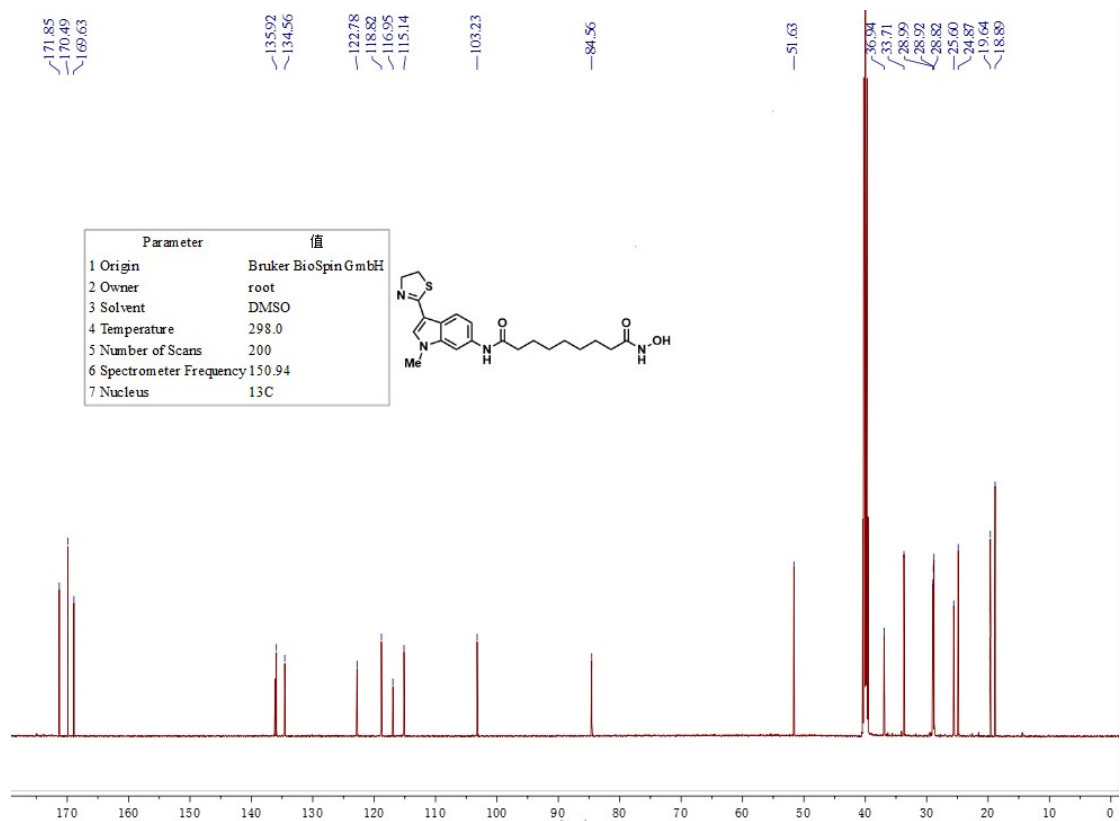
### <sup>13</sup>C-NMR spectrum of compound A26



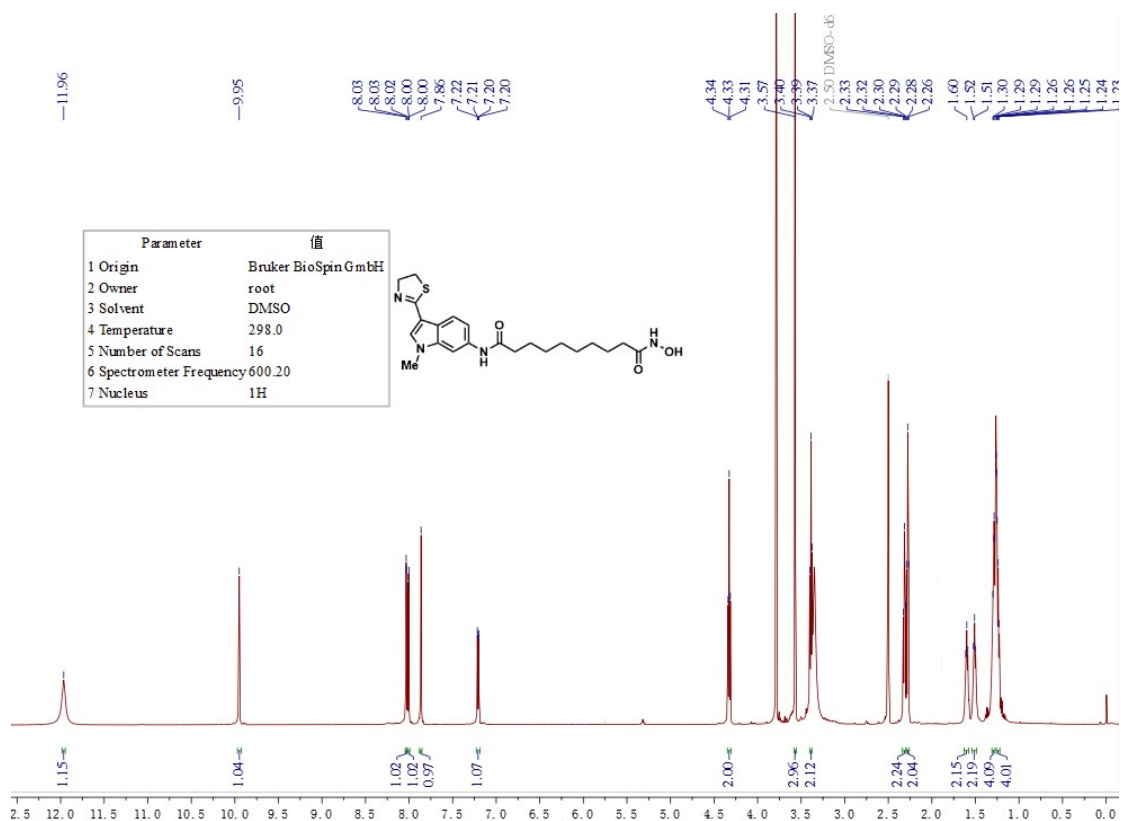
## <sup>1</sup>H-NMR spectrum of compound A27



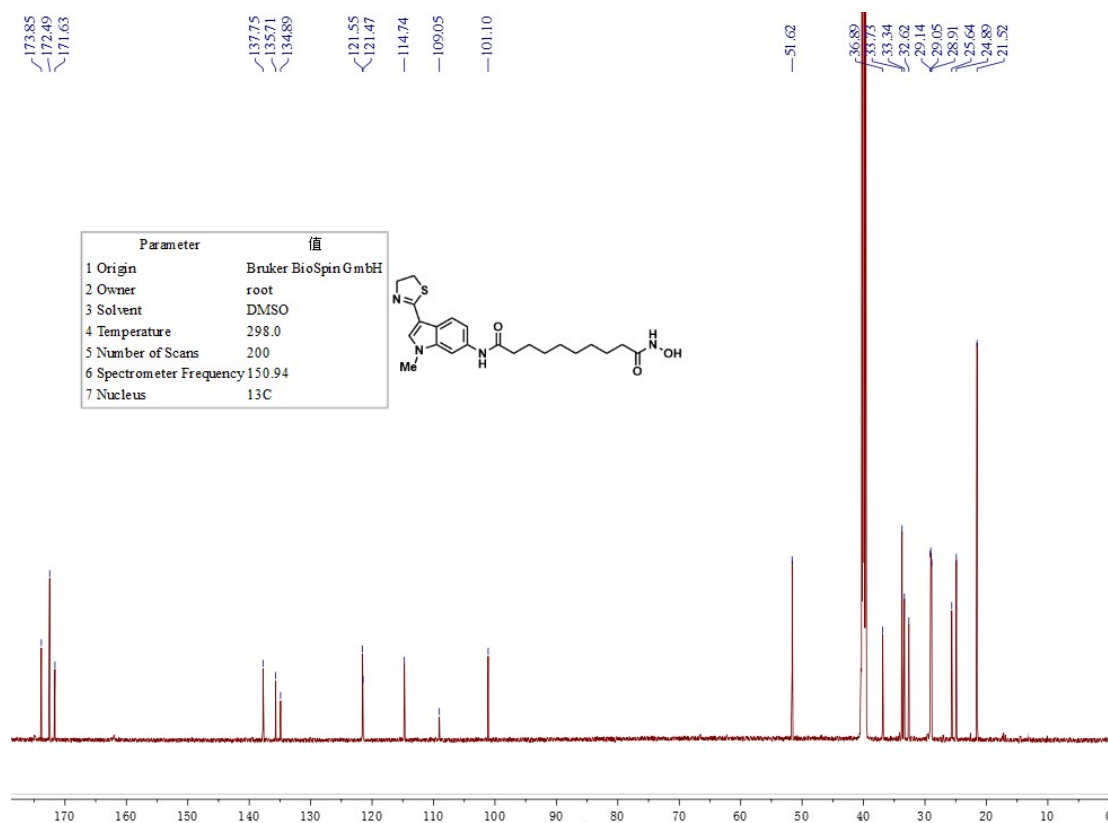
## <sup>13</sup>C-NMR spectrum of compound A27



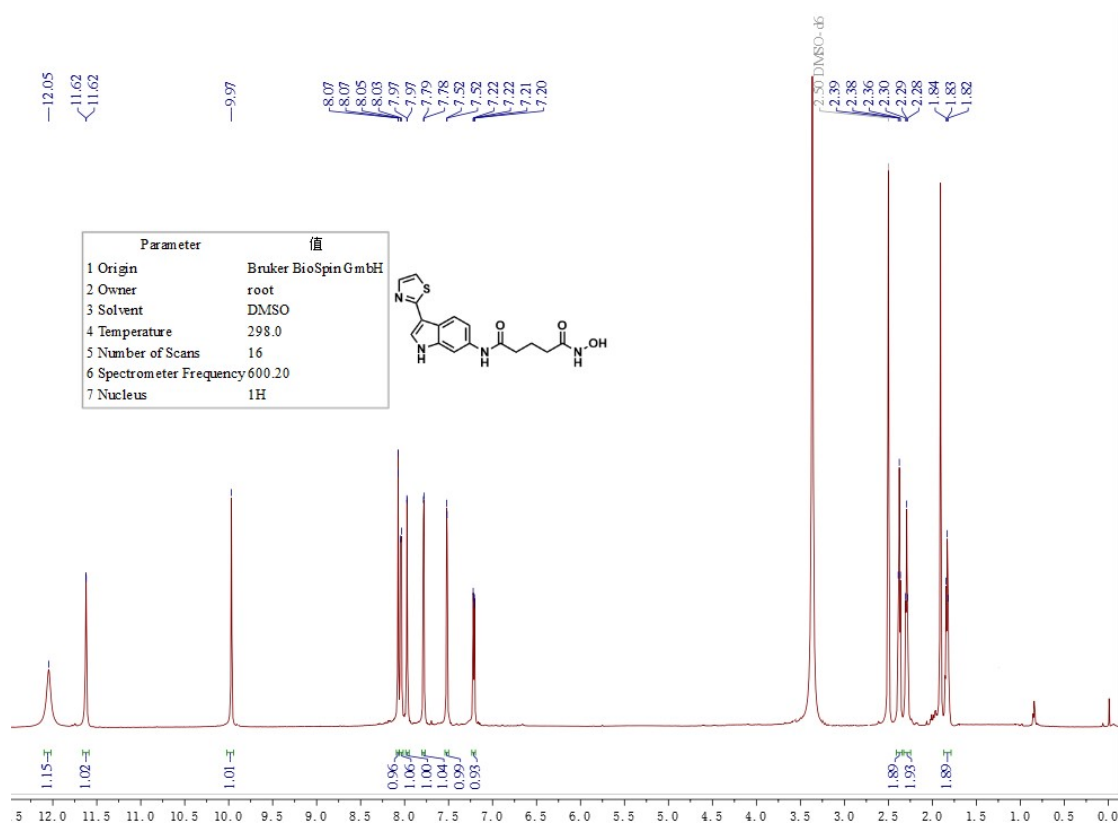
**<sup>1</sup>H-NMR spectrum of compound A28**



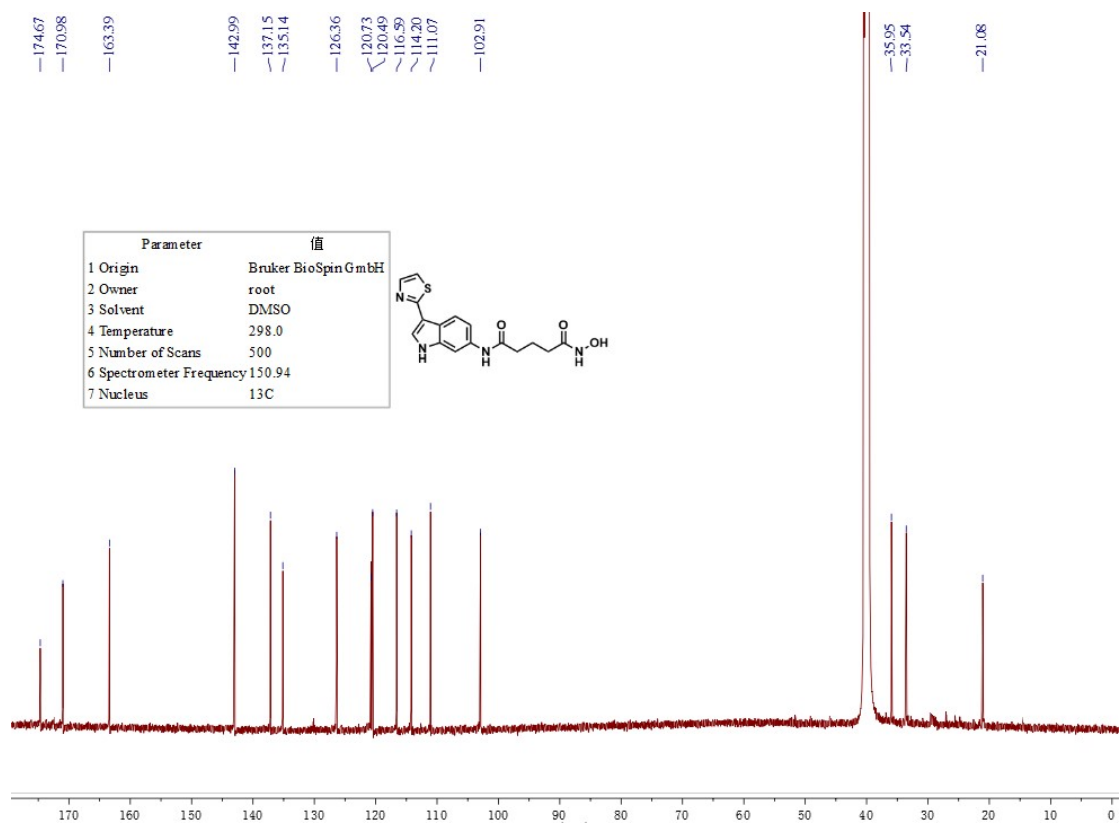
**<sup>13</sup>C-NMR spectrum of compound A28**



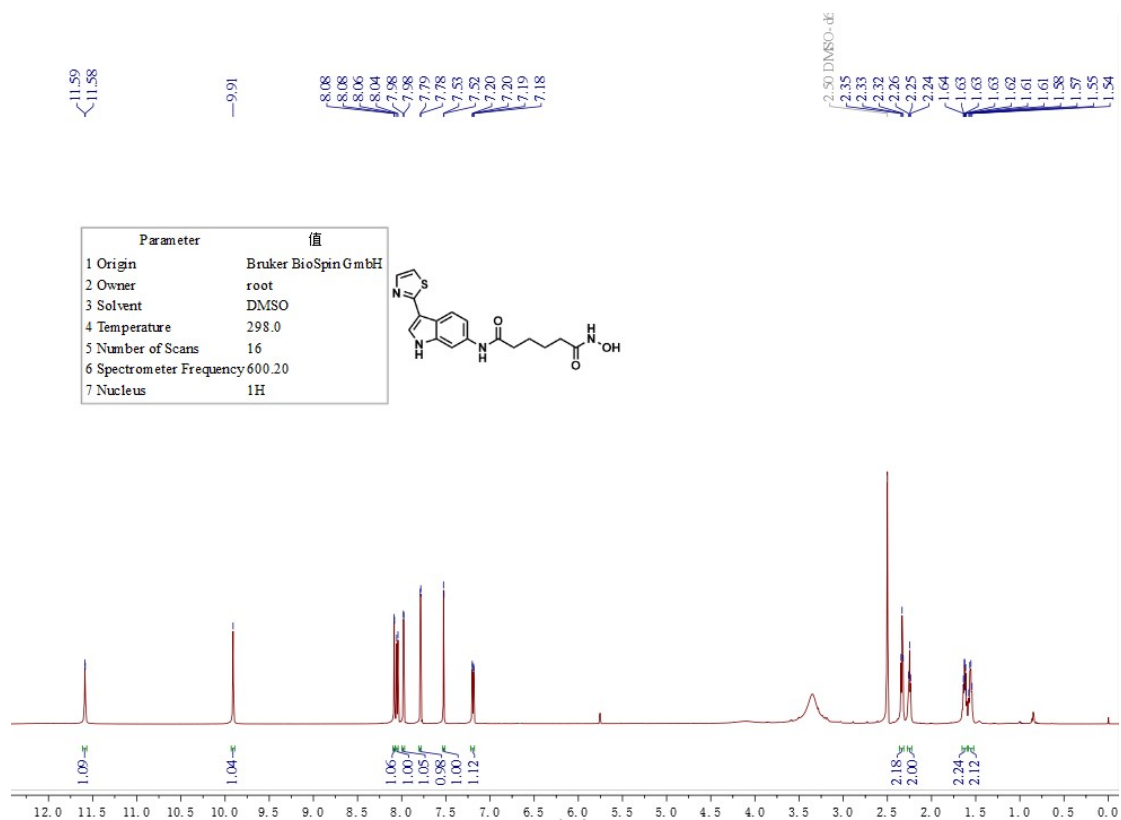
**<sup>1</sup>H-NMR spectrum of compound A29**



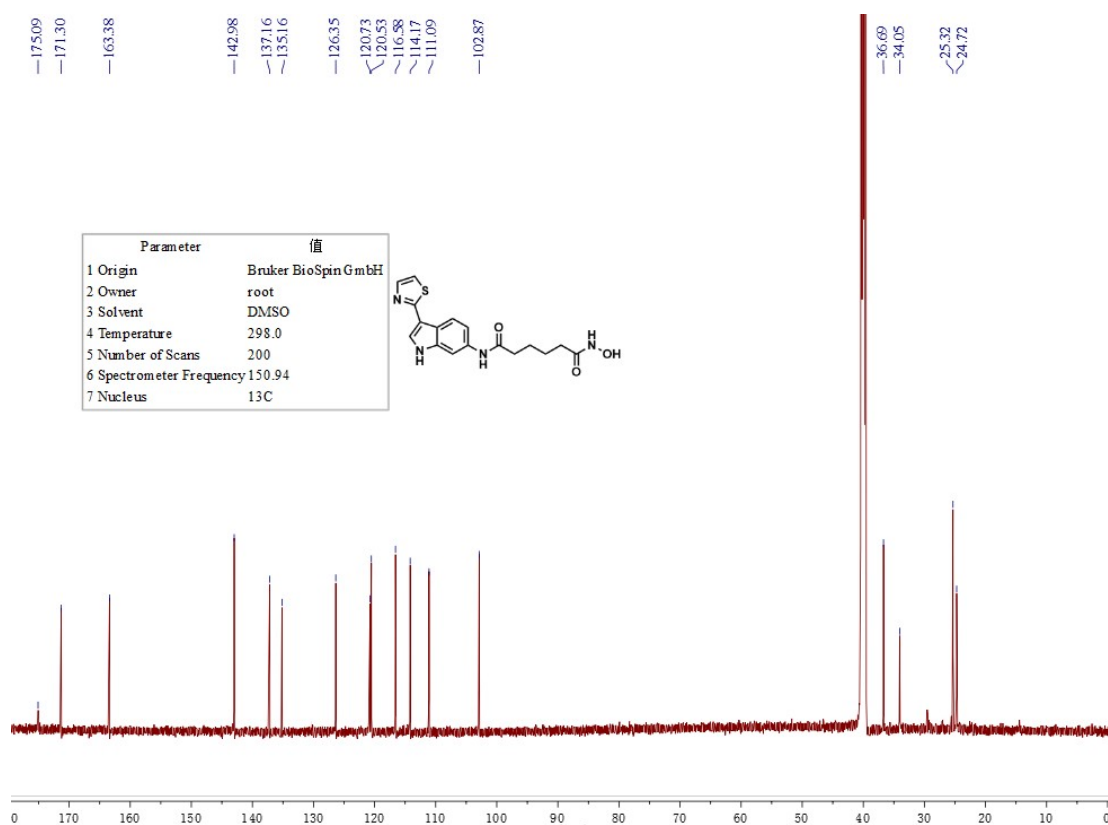
**<sup>13</sup>C-NMR spectrum of compound A29**



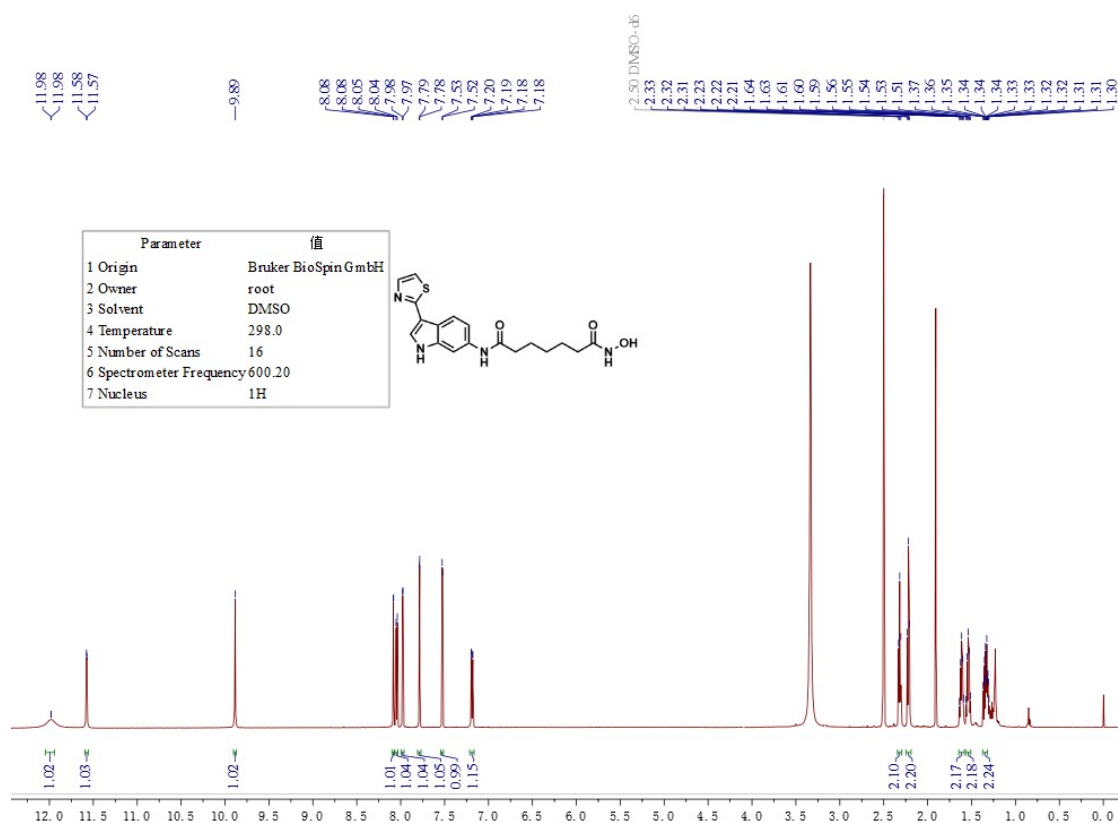
# <sup>1</sup>H-NMR spectrum of compound A30



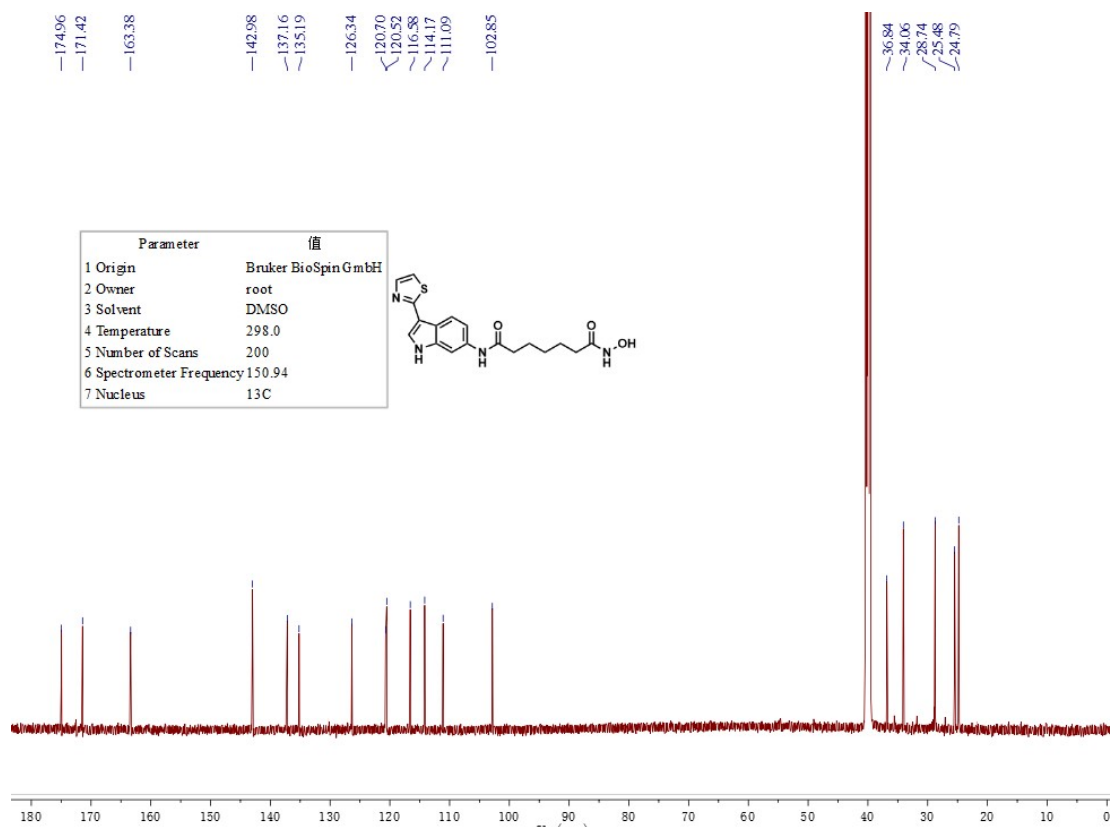
### <sup>13</sup>C-NMR spectrum of compound A30



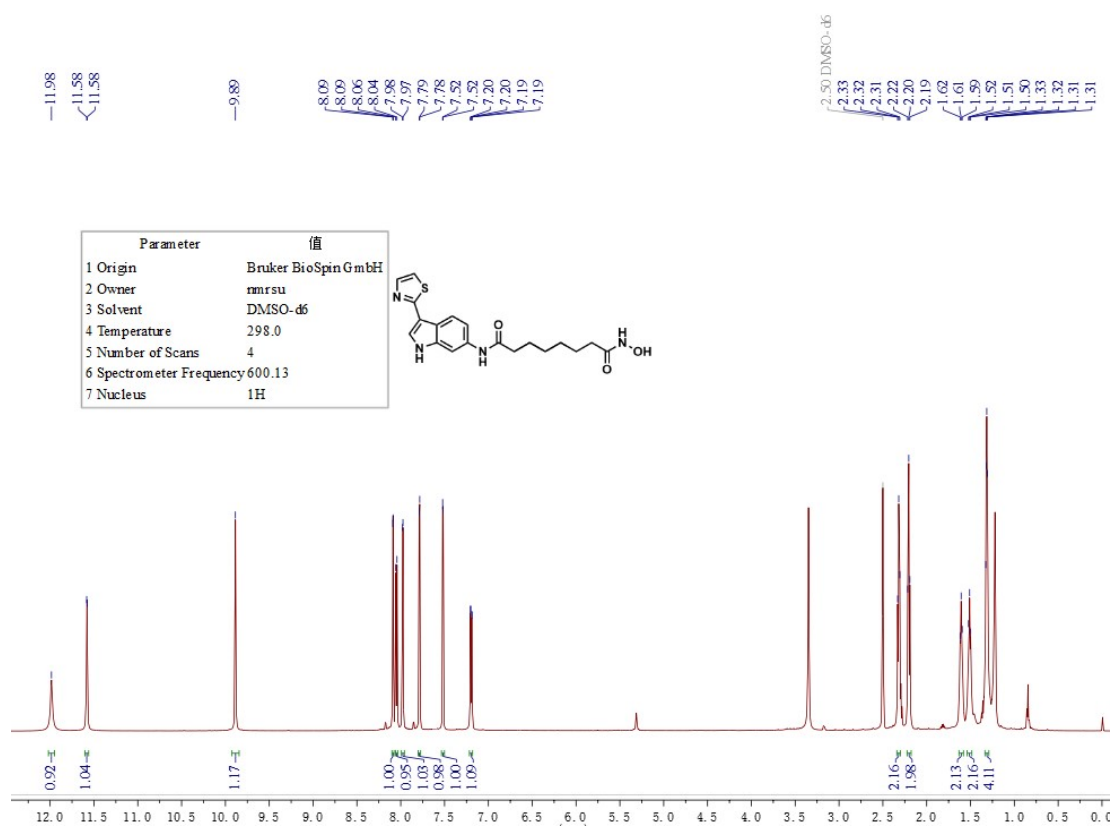
### <sup>1</sup>H-NMR spectrum of compound A31



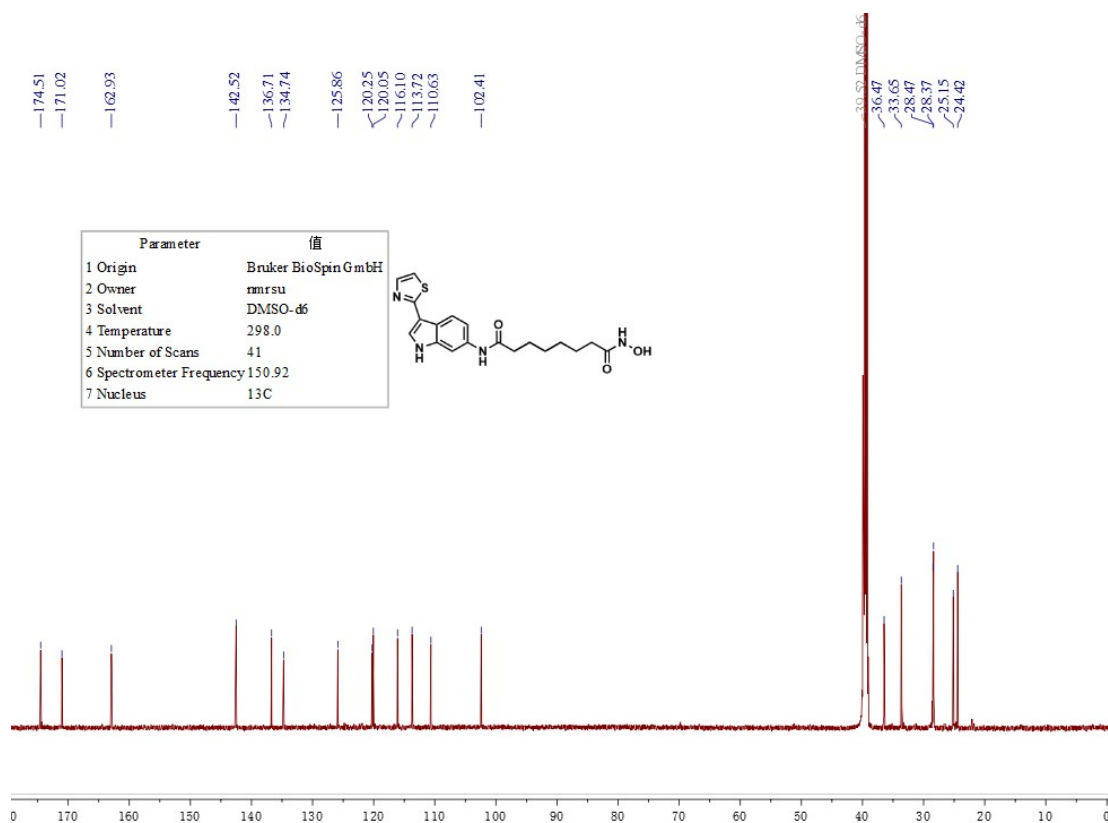
### <sup>13</sup>C-NMR spectrum of compound A31



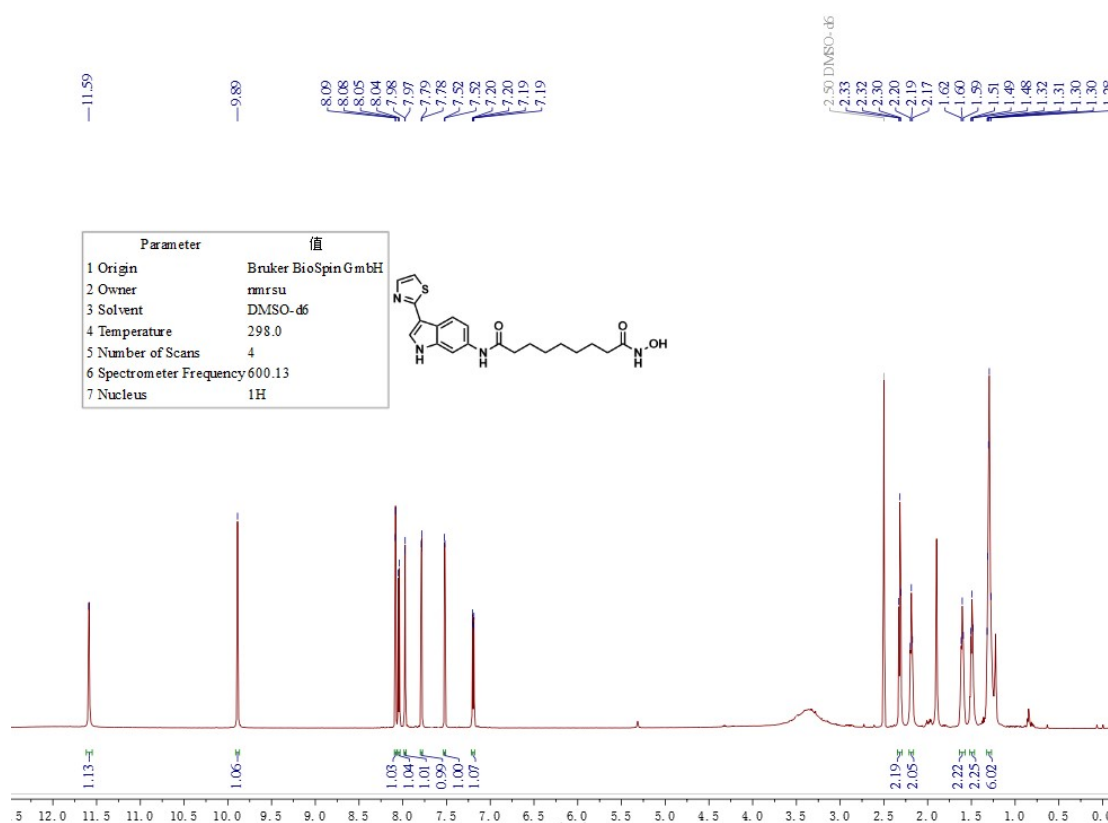
### <sup>1</sup>H-NMR spectrum of compound A32



# **<sup>13</sup>C-NMR spectrum of compound A32**

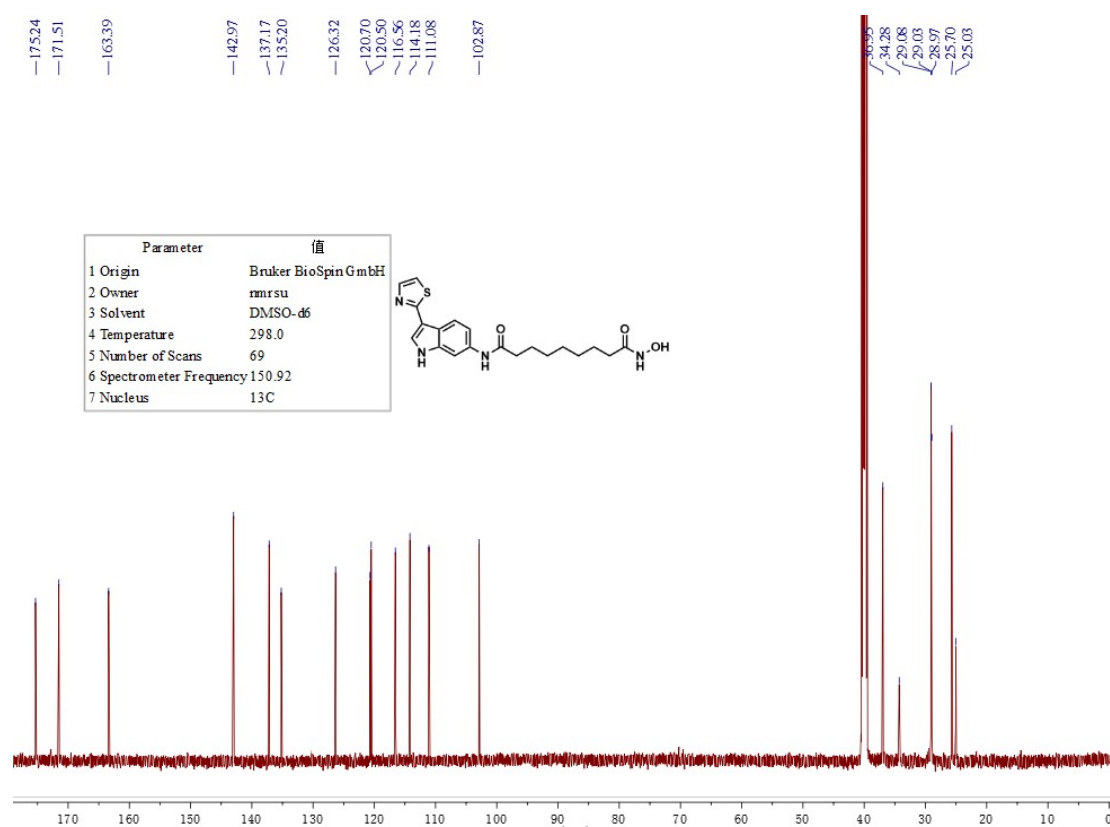


# **<sup>1</sup>H-NMR spectrum of compound A33**

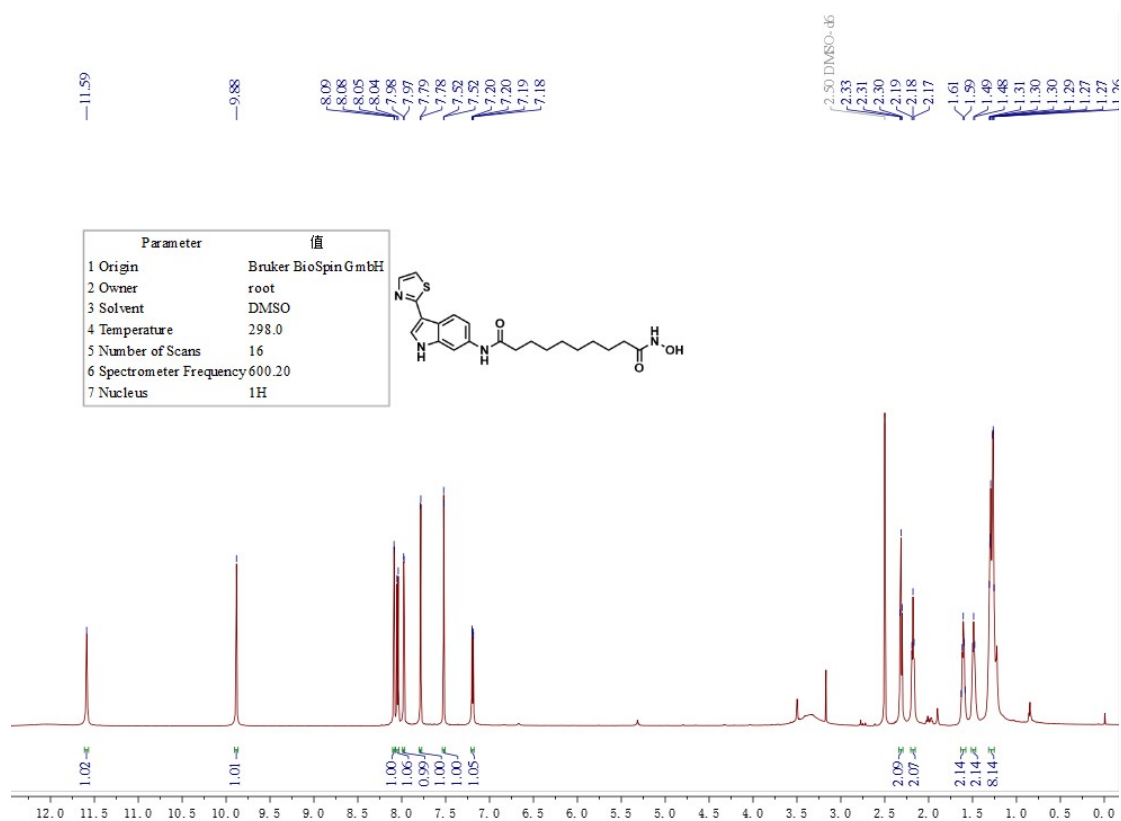




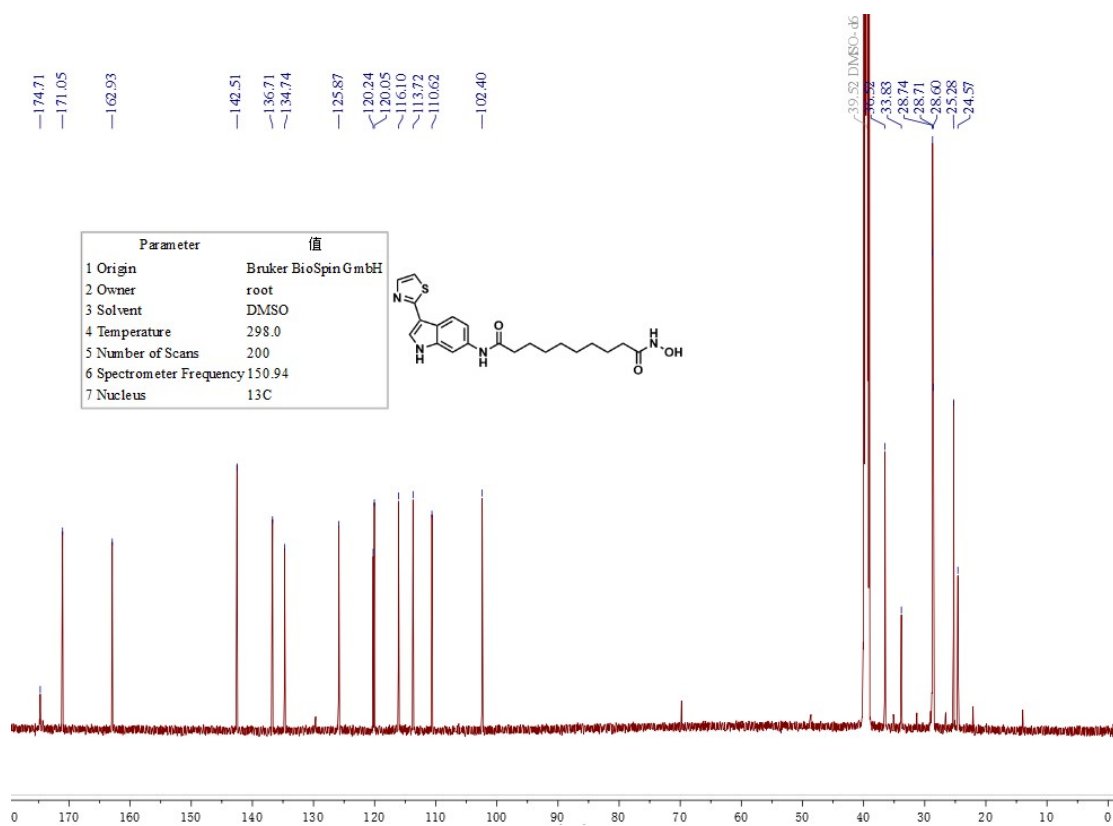
### <sup>13</sup>C-NMR spectrum of compound A33



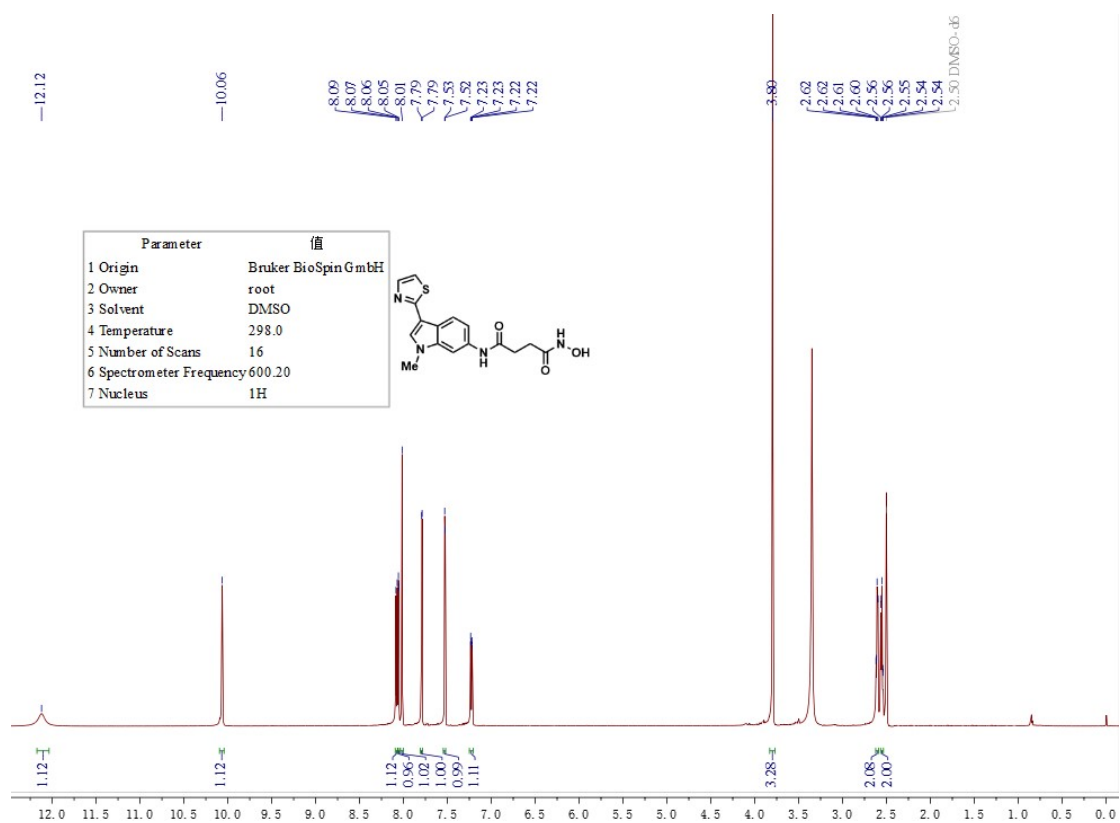
### <sup>1</sup>H-NMR spectrum of compound A34



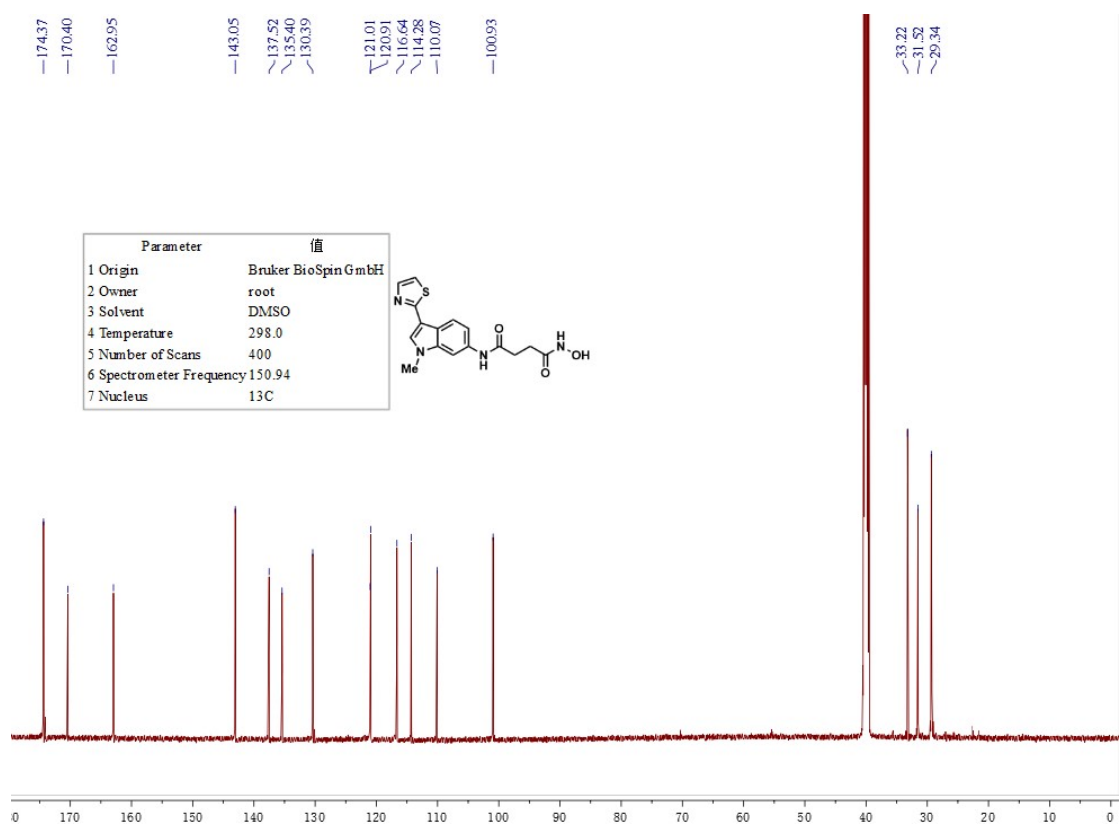
### <sup>13</sup>C-NMR spectrum of compound A34



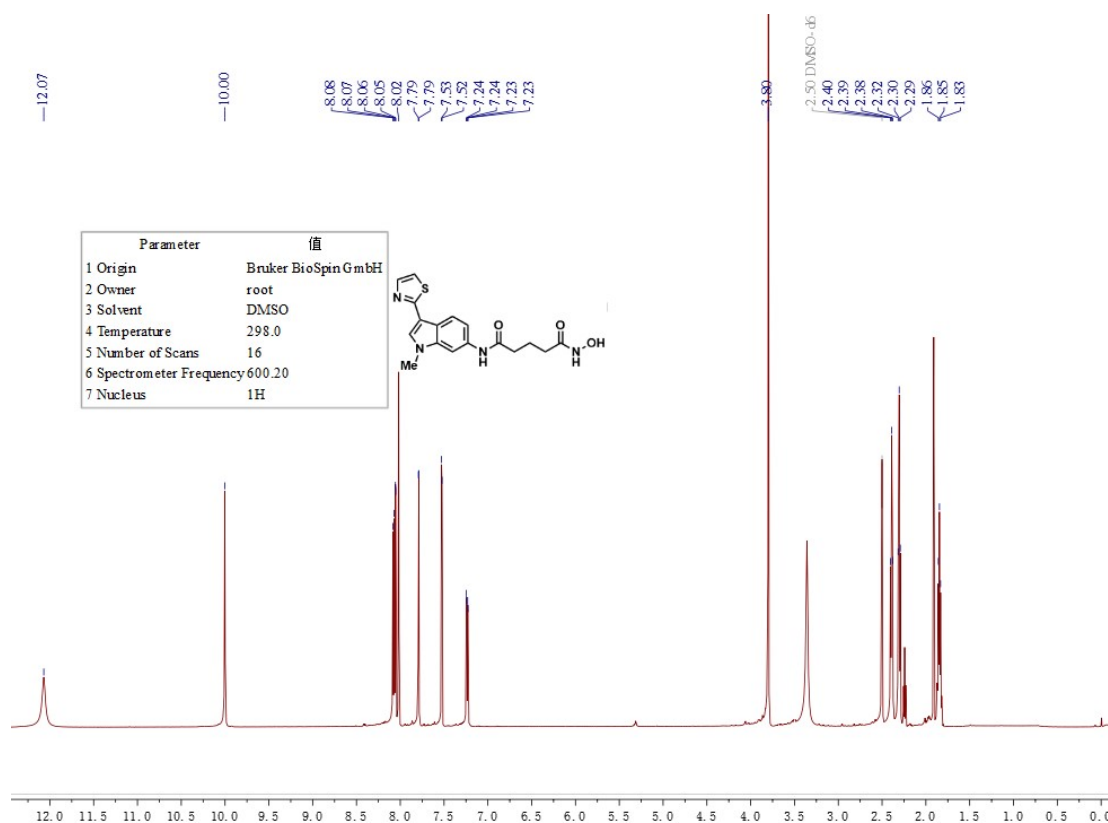
### <sup>1</sup>H-NMR spectrum of compound A35



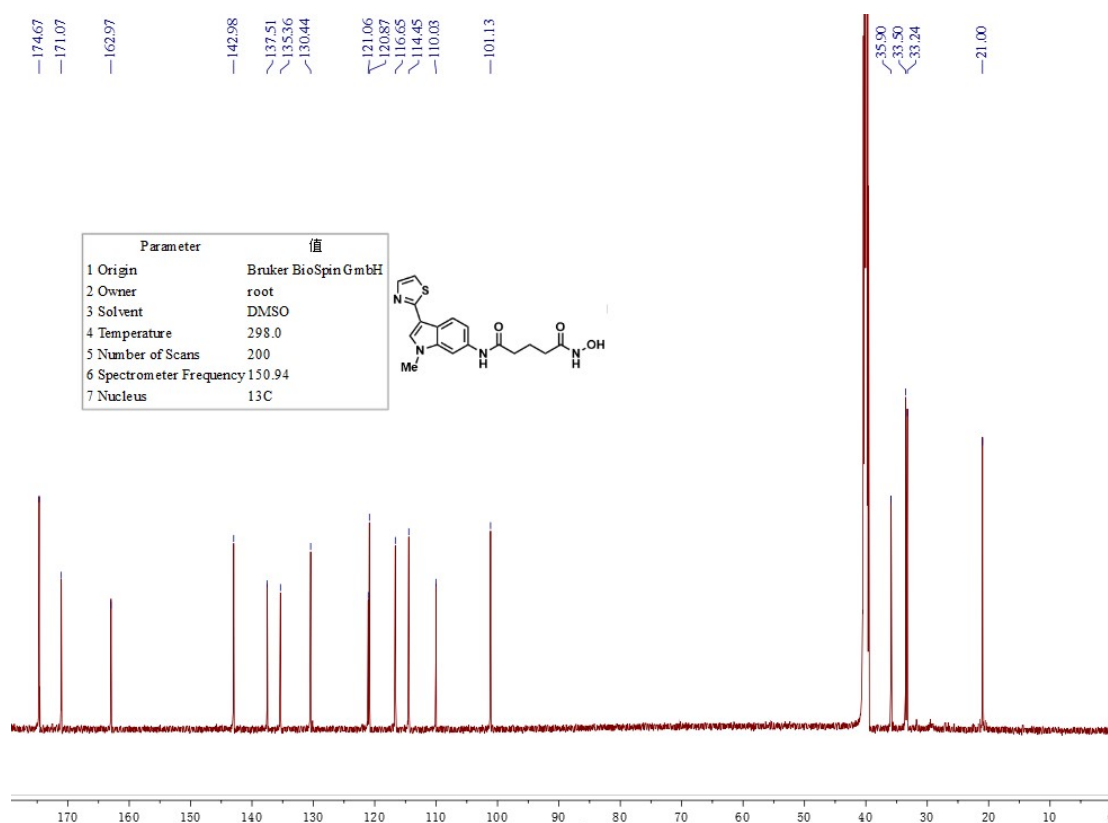
**<sup>13</sup>C-NMR spectrum of compound A35**



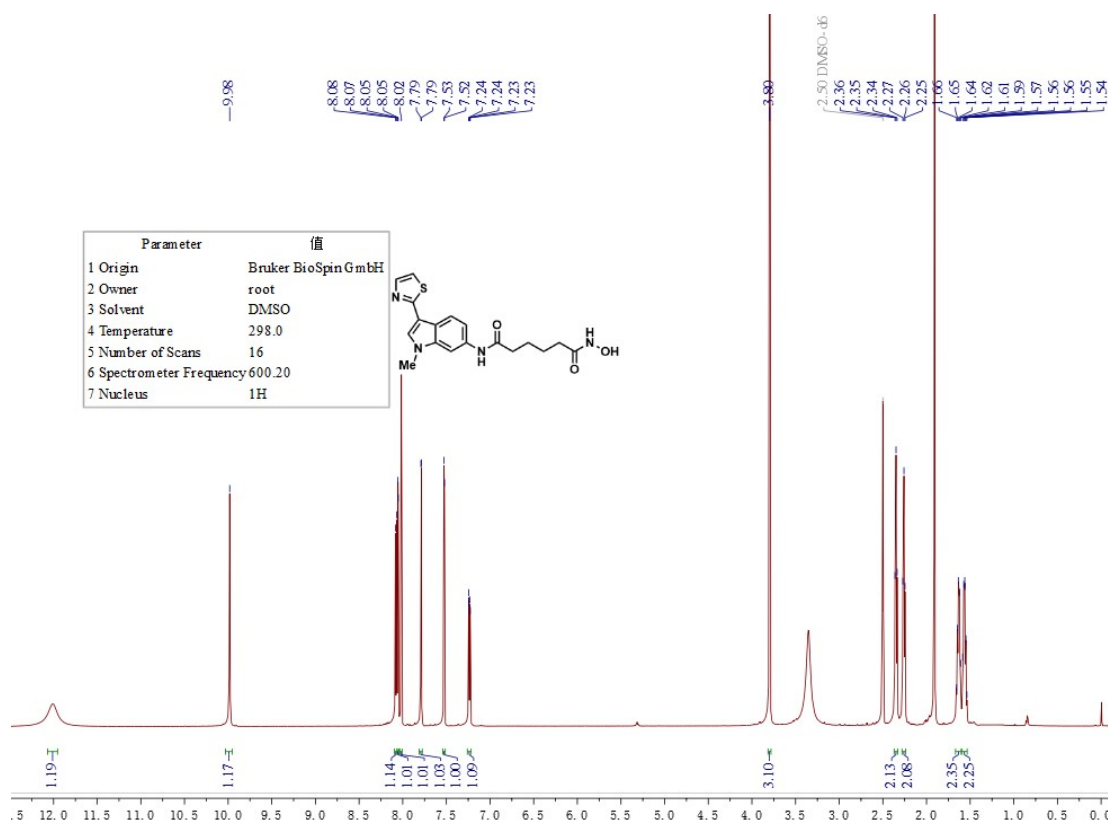
**<sup>1</sup>H-NMR spectrum of compound A36**



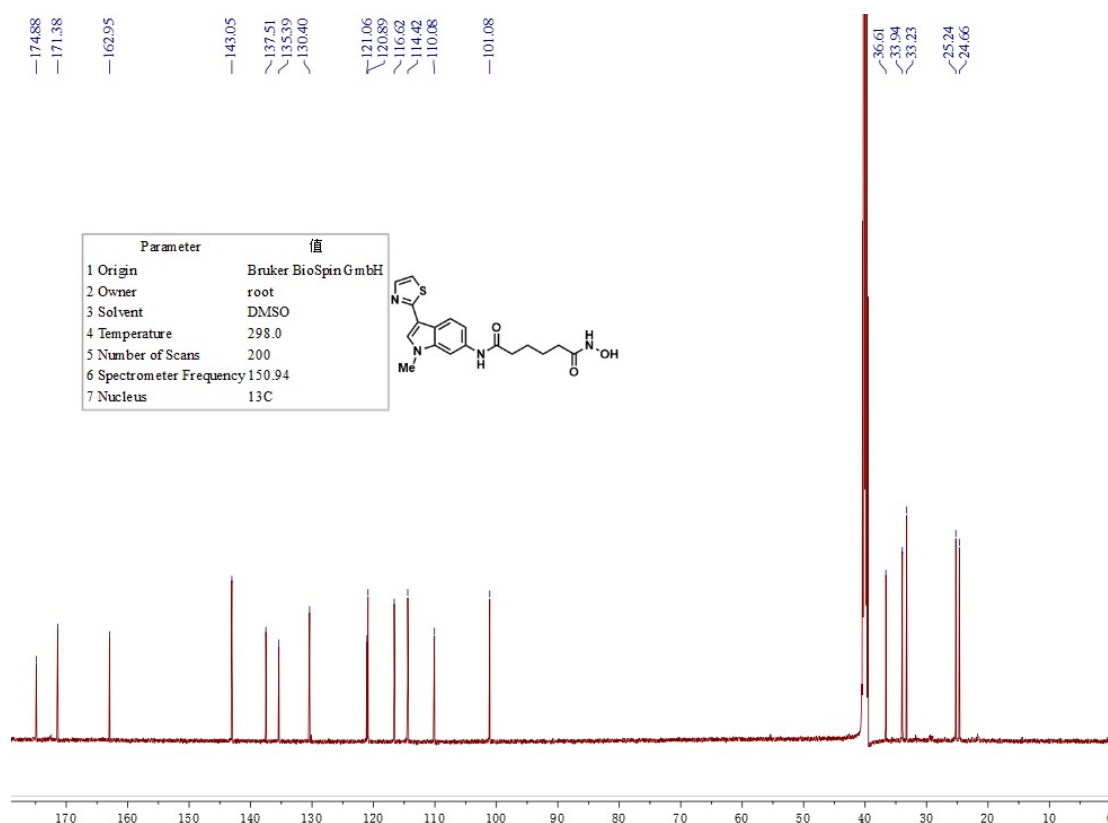
### <sup>13</sup>C-NMR spectrum of compound A36



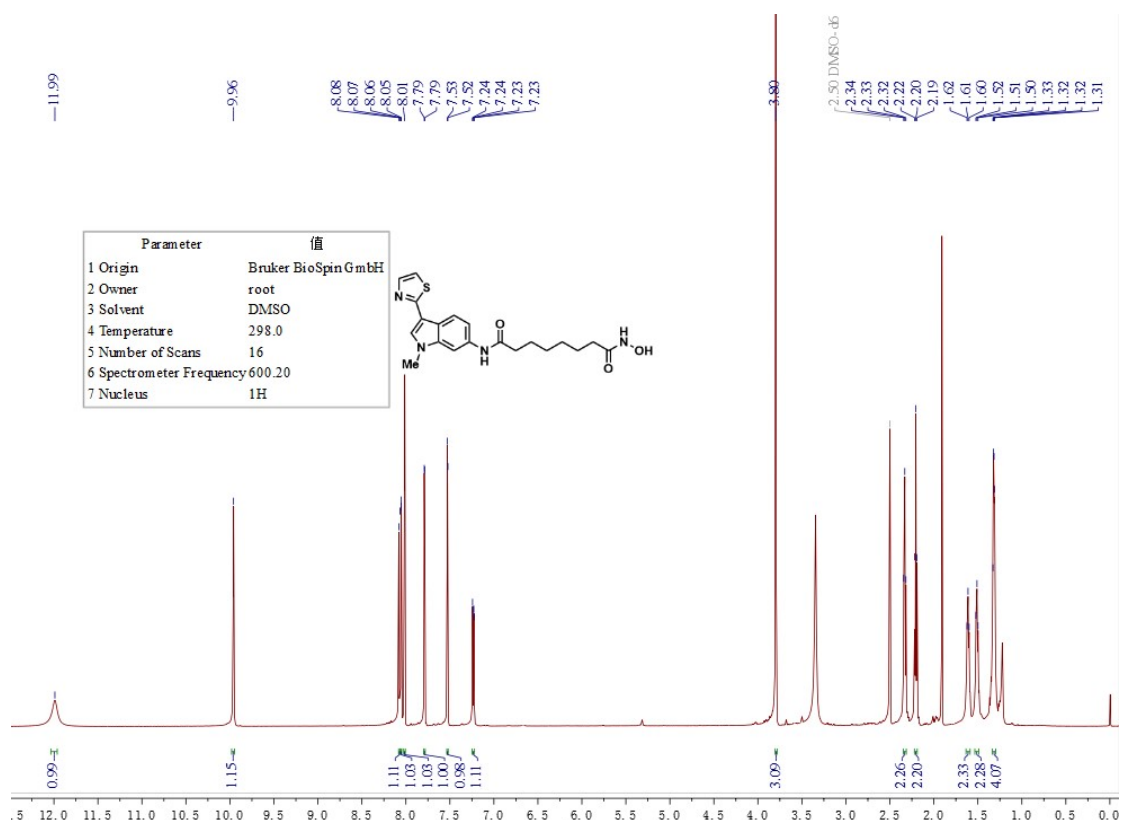
# <sup>1</sup>H-NMR spectrum of compound A37



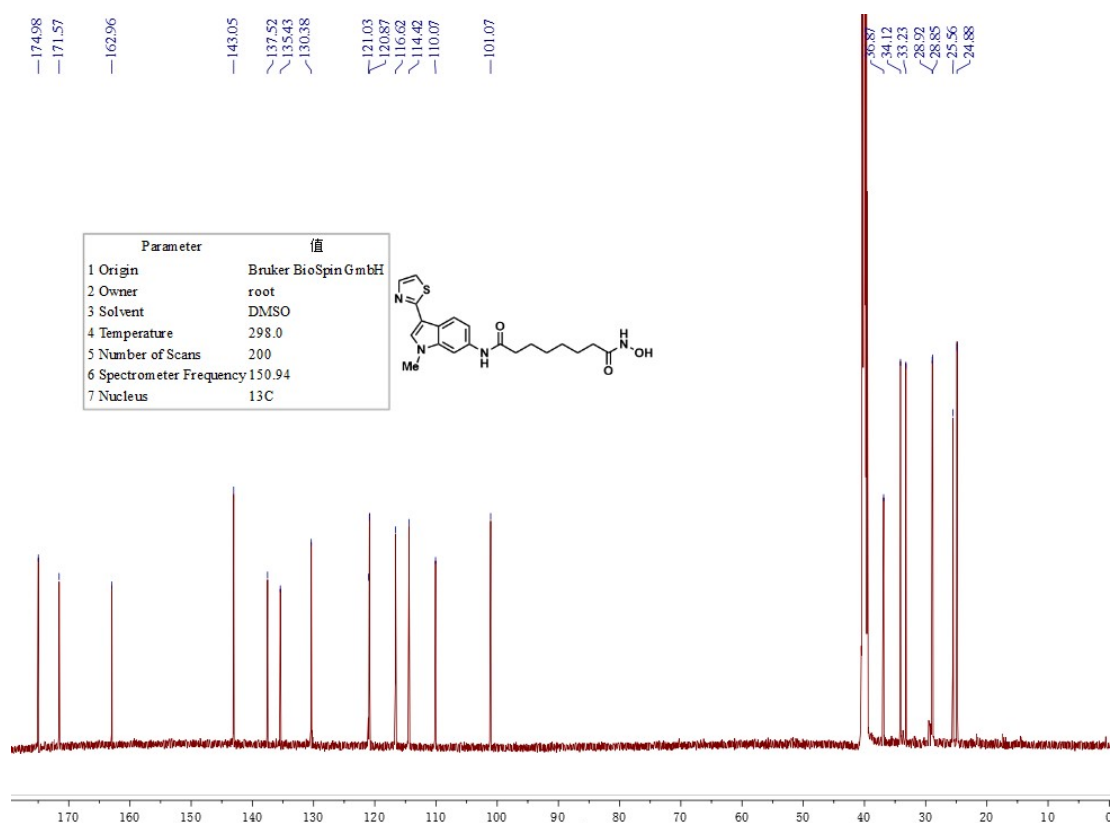
# <sup>13</sup>C-NMR spectrum of compound A37



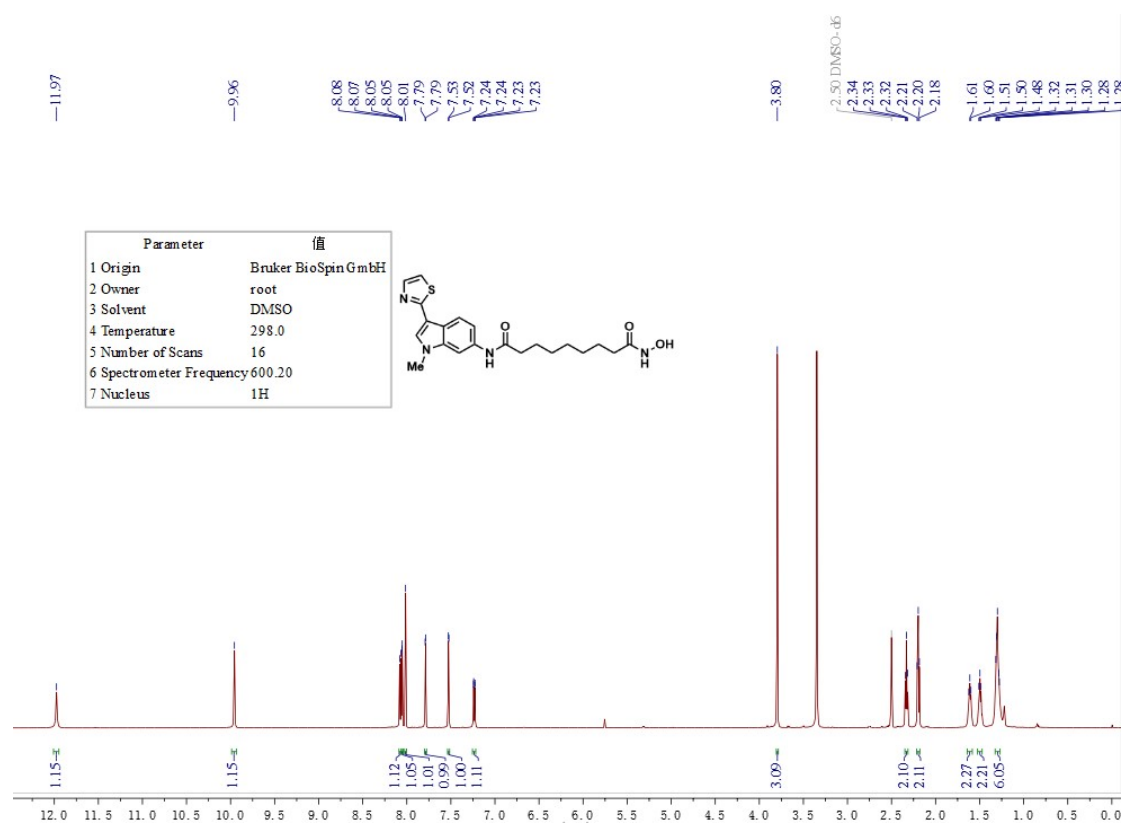
# <sup>1</sup>H-NMR spectrum of compound A38



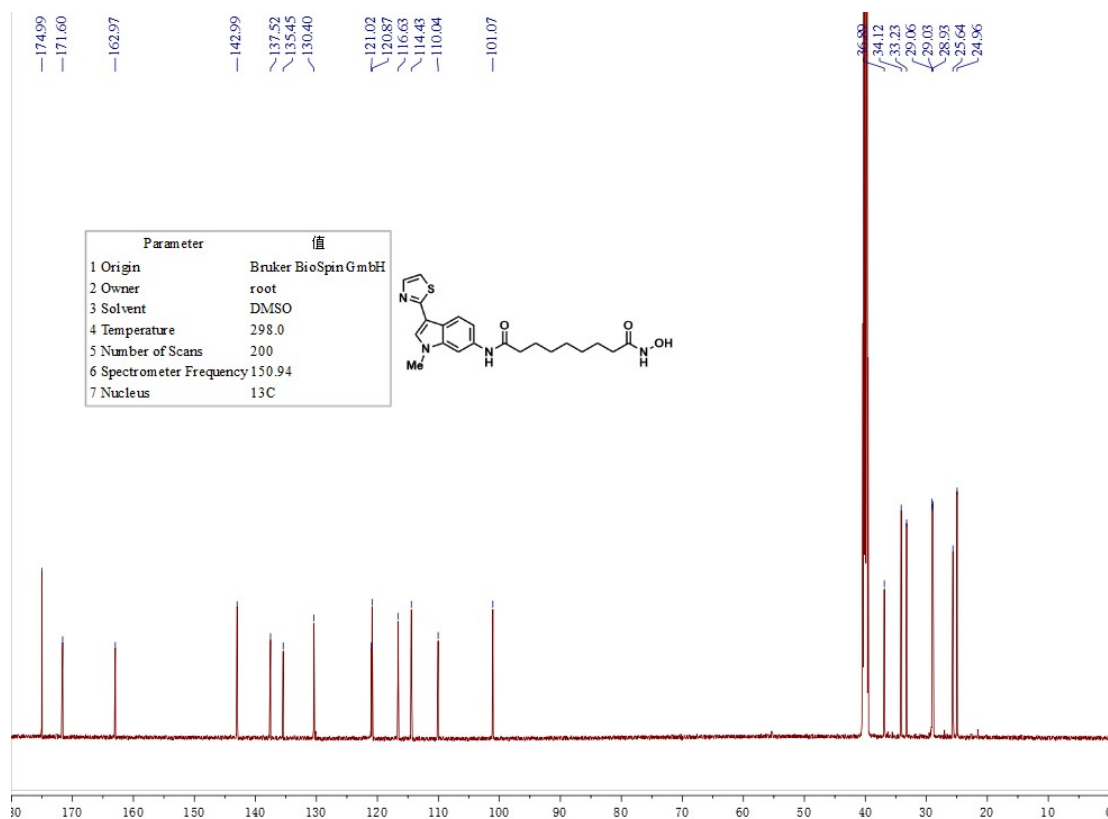
# <sup>13</sup>C-NMR spectrum of compound A38



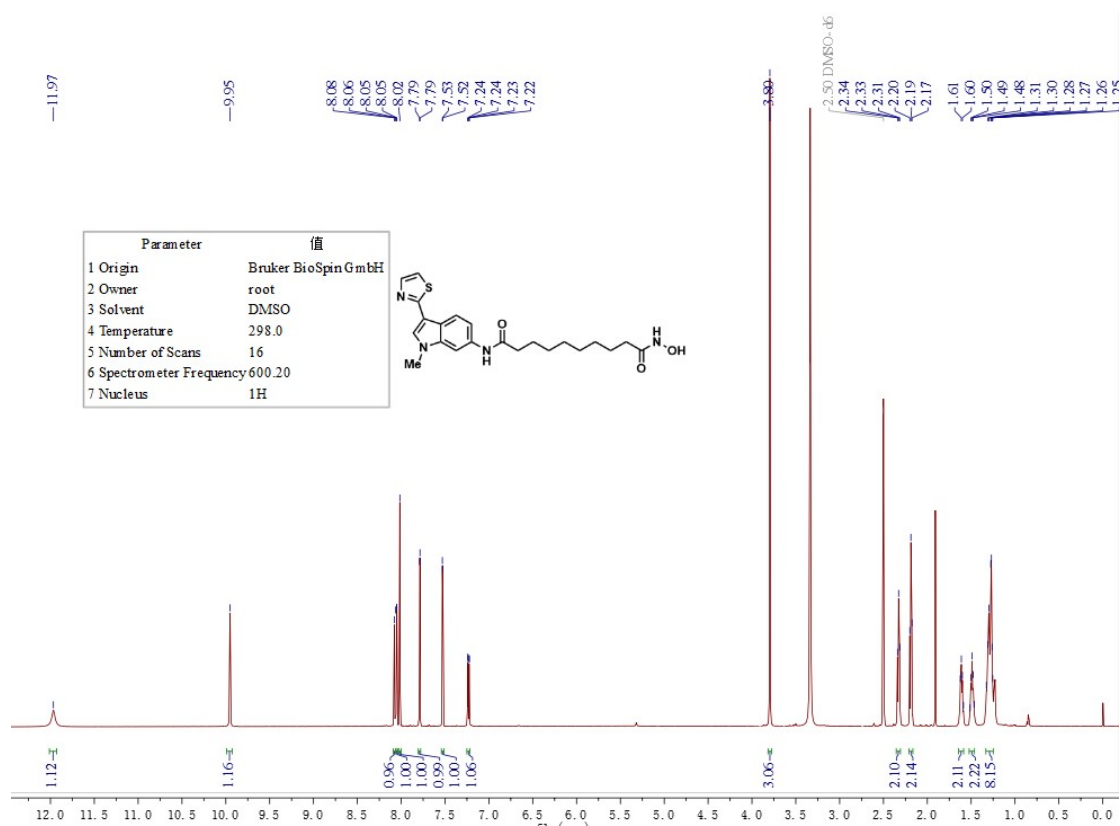
# <sup>1</sup>H-NMR spectrum of compound A39



# <sup>13</sup>C-NMR spectrum of compound A39

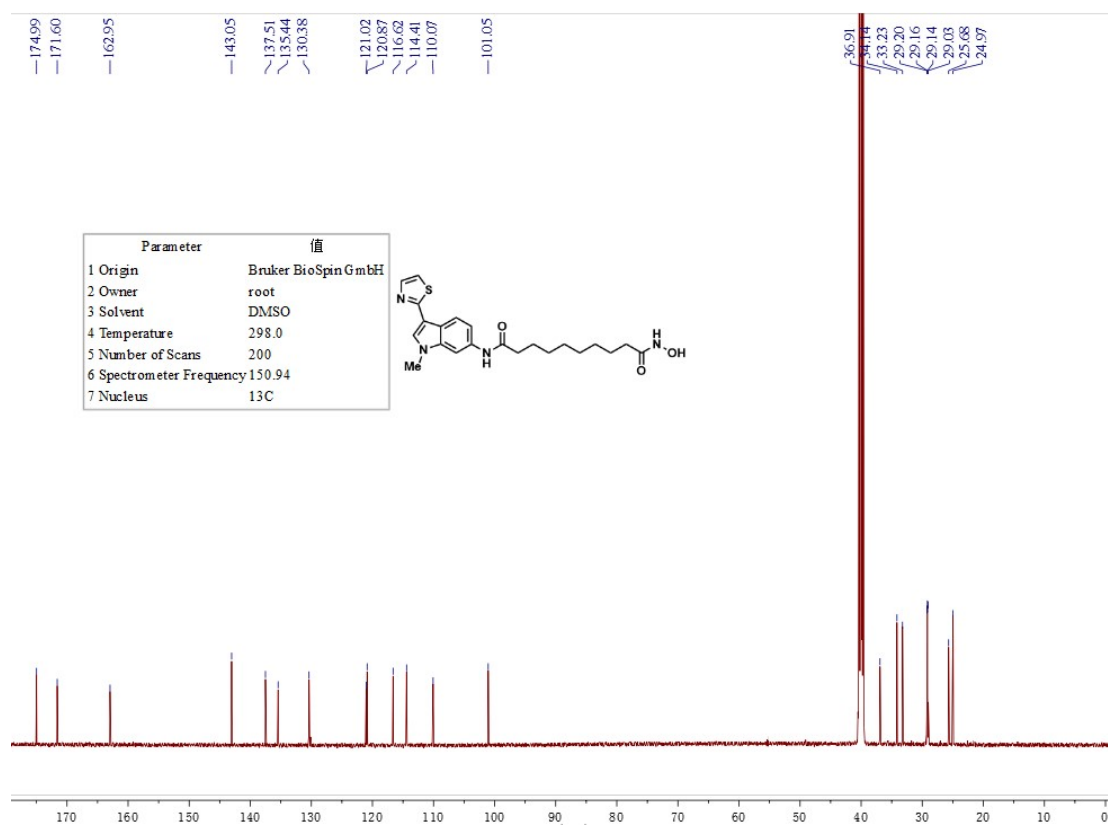


**<sup>1</sup>H-NMR spectrum of compound A 40**

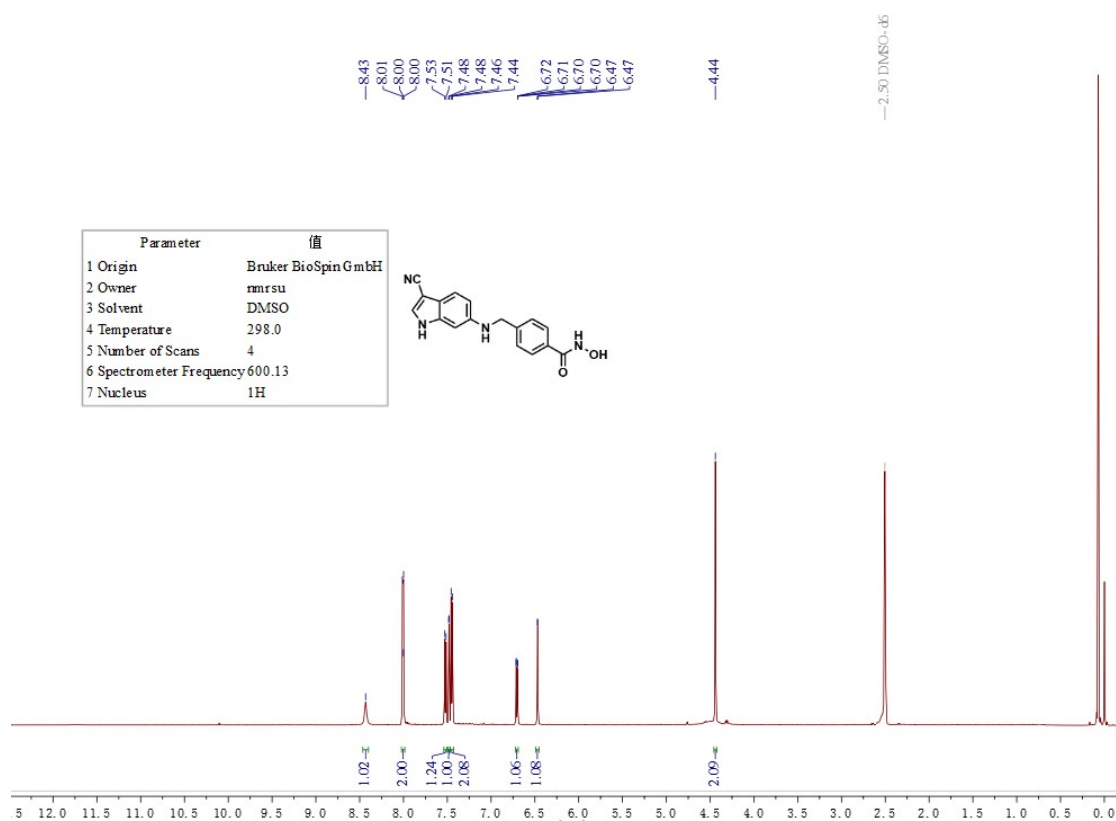


**<sup>13</sup>C-NMR spectrum of compound A40**

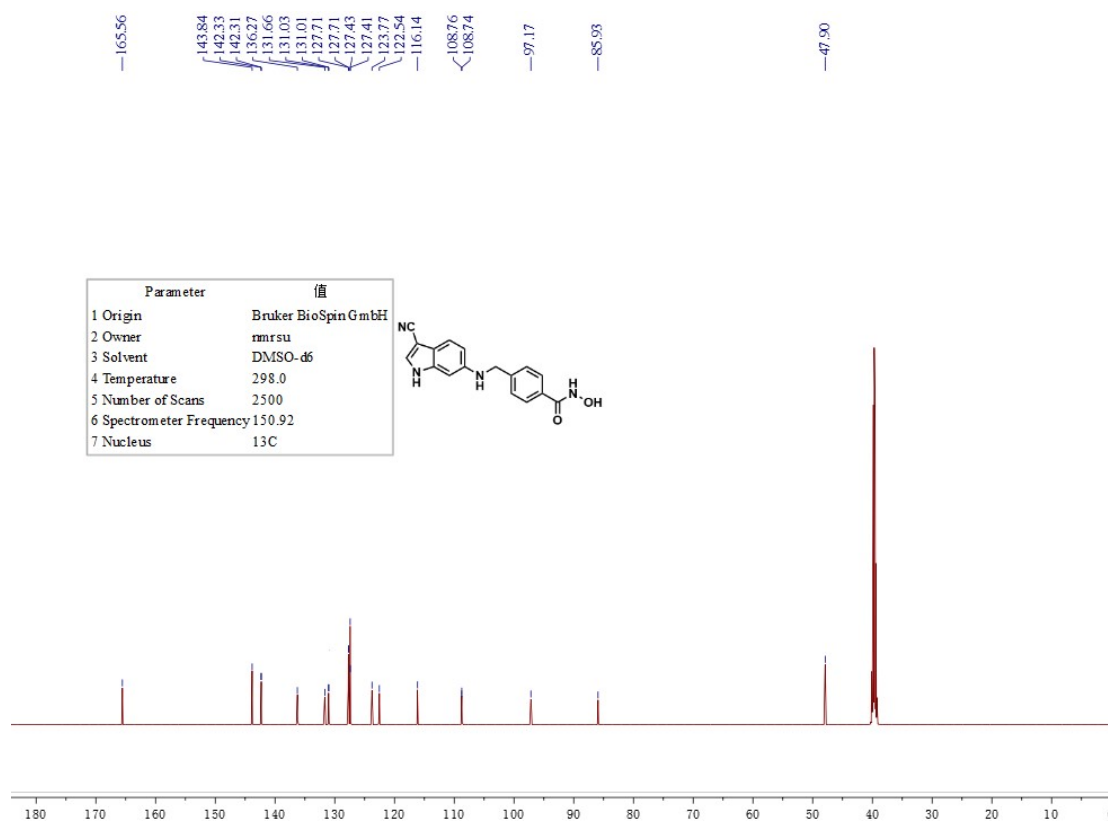




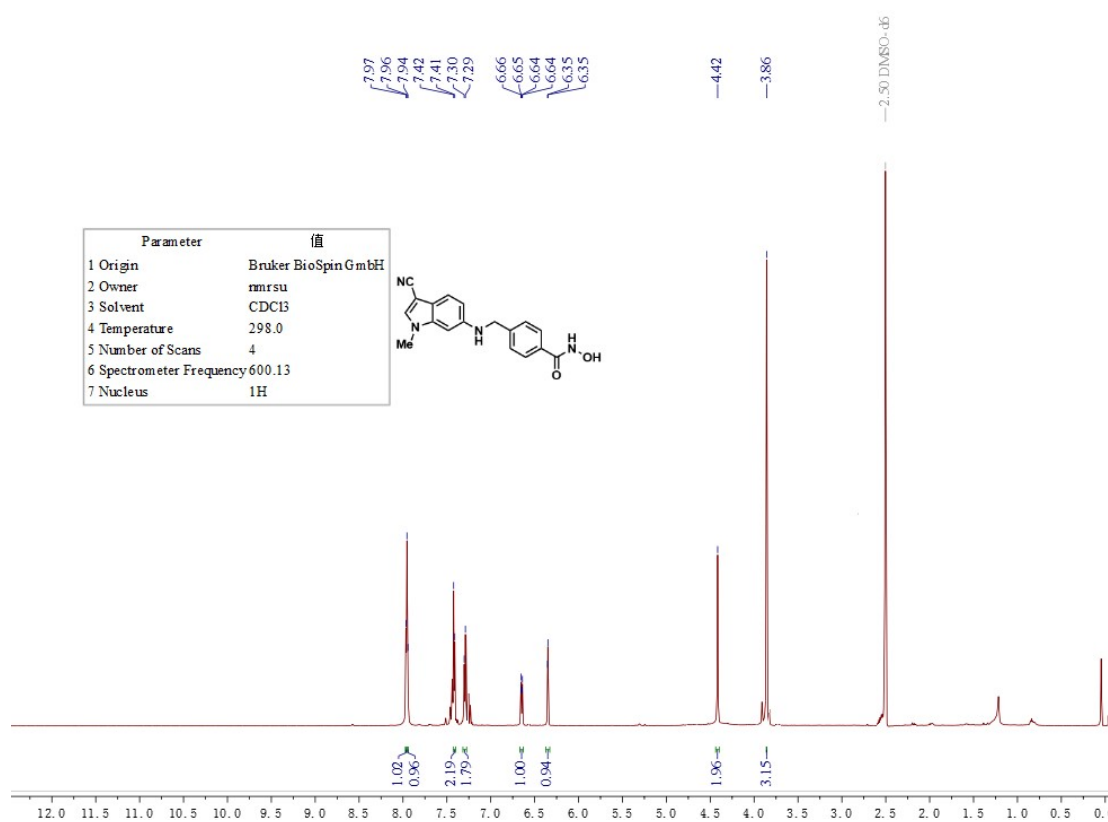
<sup>1</sup>H-NMR spectrum of compound B1



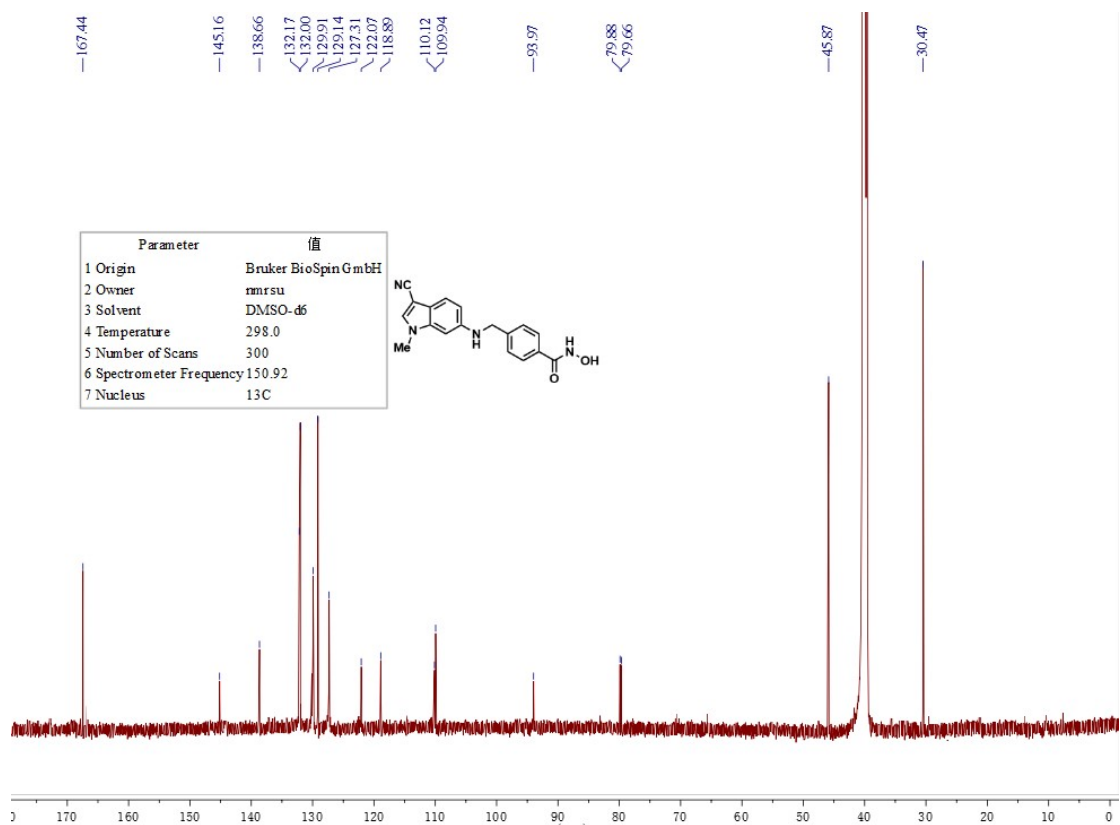
<sup>13</sup>C-NMR spectrum of compound B1



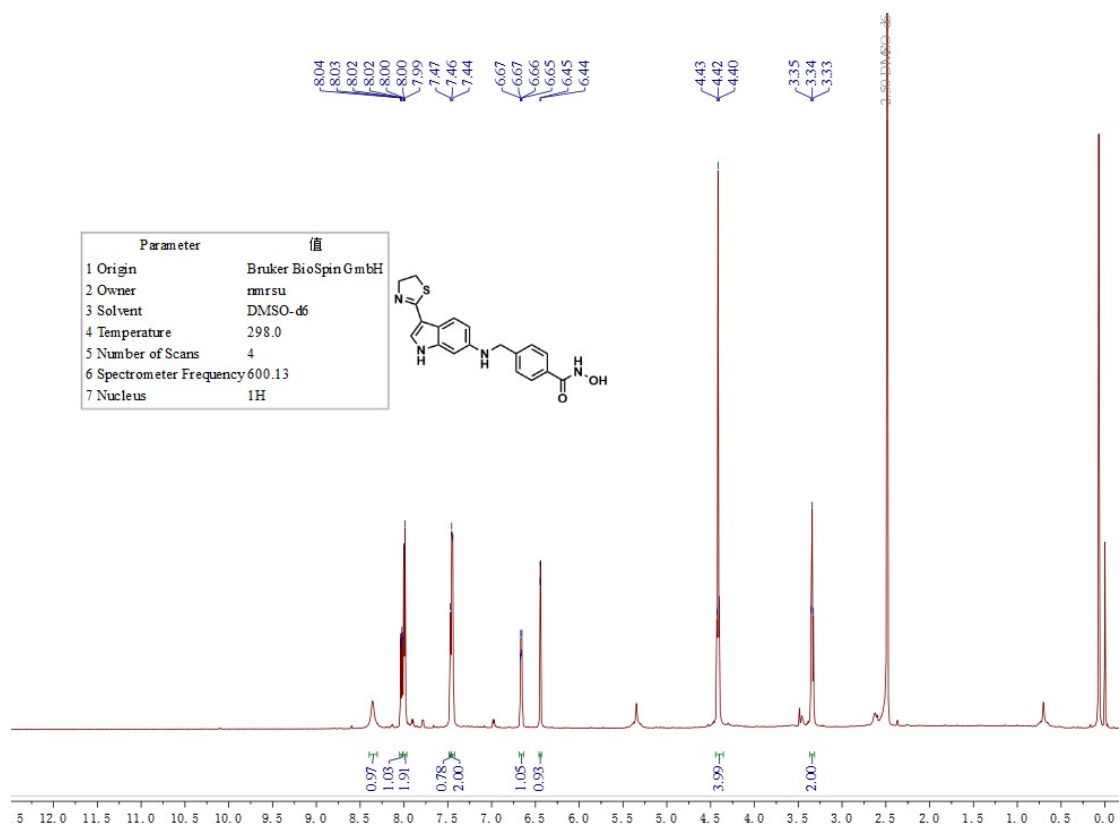
<sup>1</sup>H-NMR spectrum of compound B2



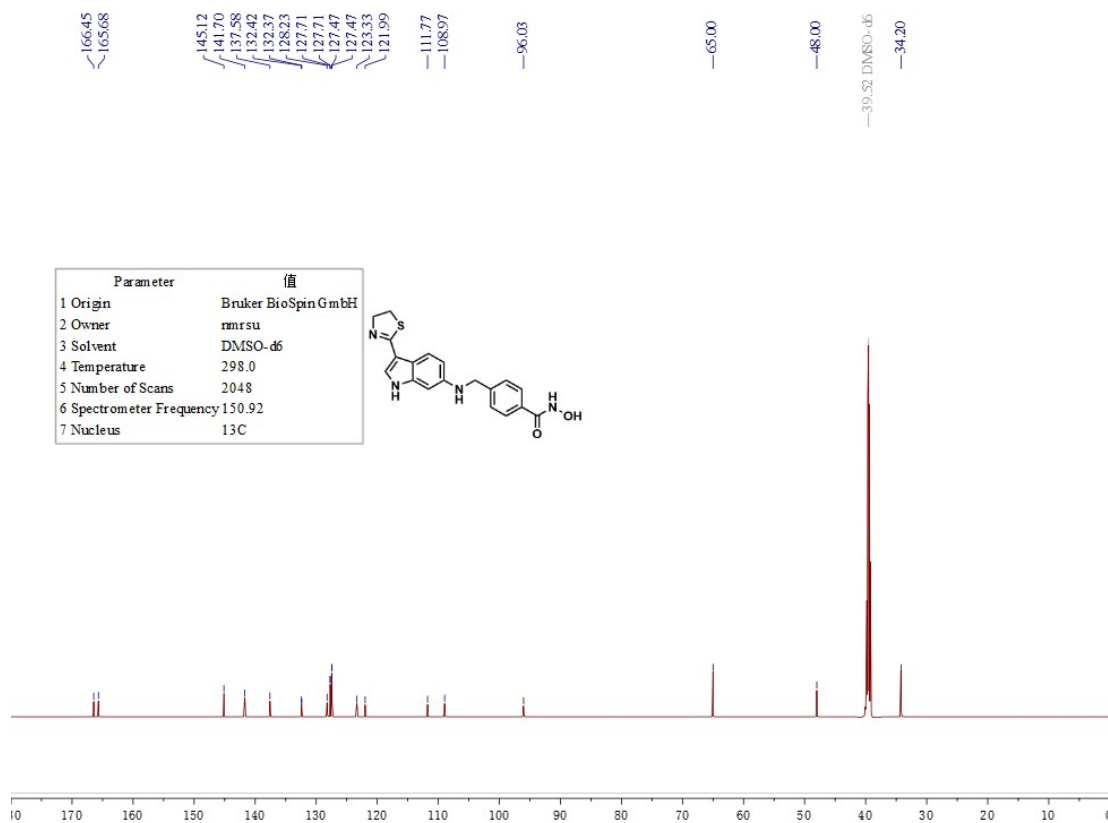
<sup>13</sup>C-NMR spectrum of compound B2



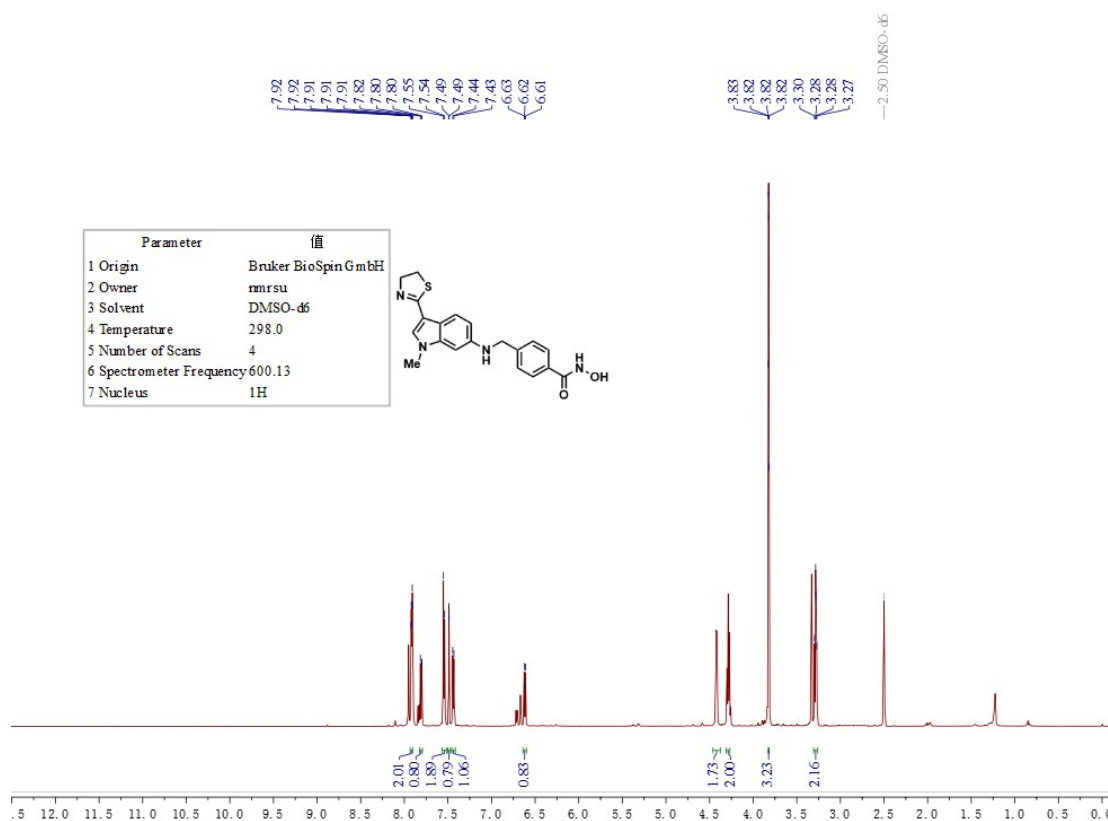
**<sup>1</sup>H-NMR spectrum of compound B3**



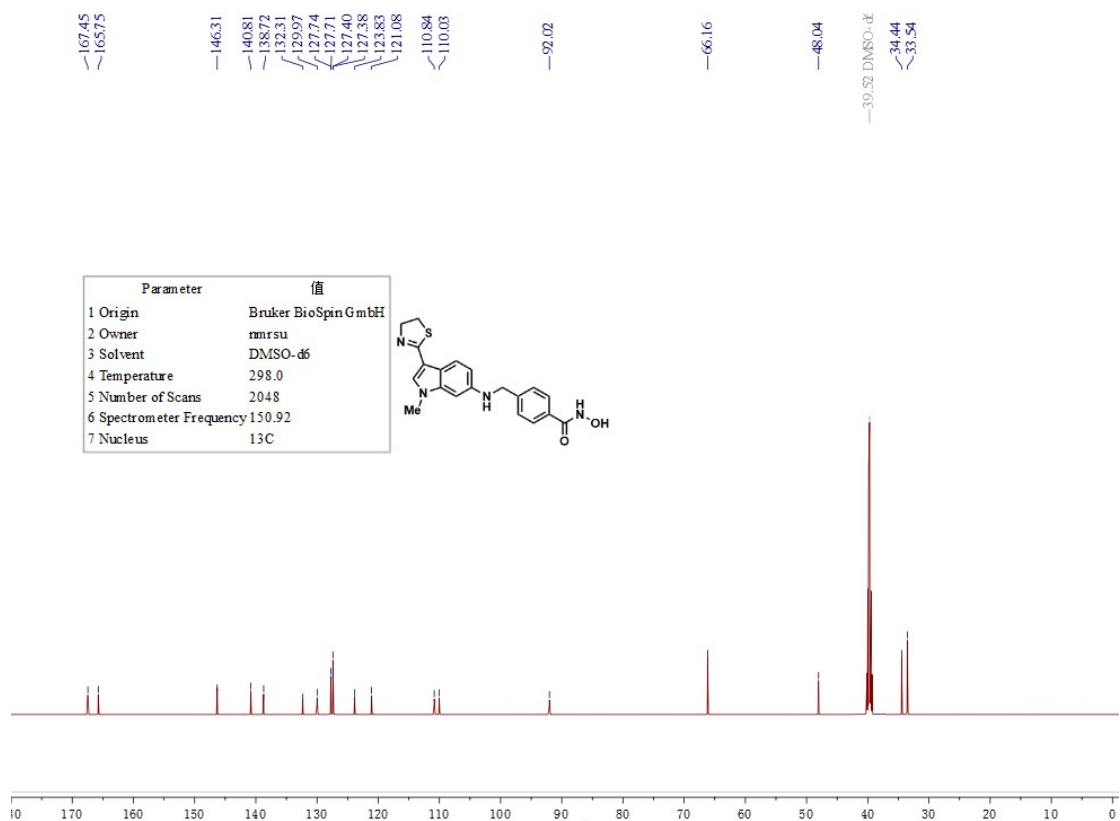
**<sup>13</sup>C-NMR spectrum of compound B3**



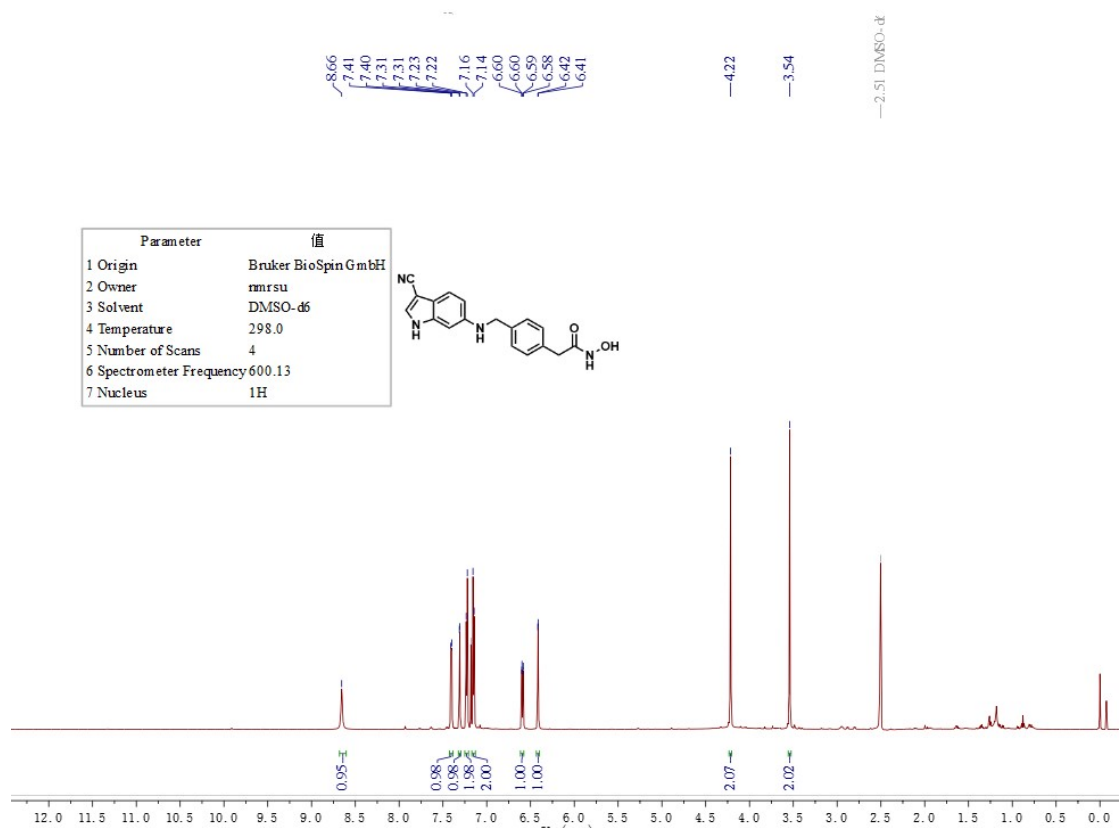
<sup>1</sup>H-NMR spectrum of compound B4



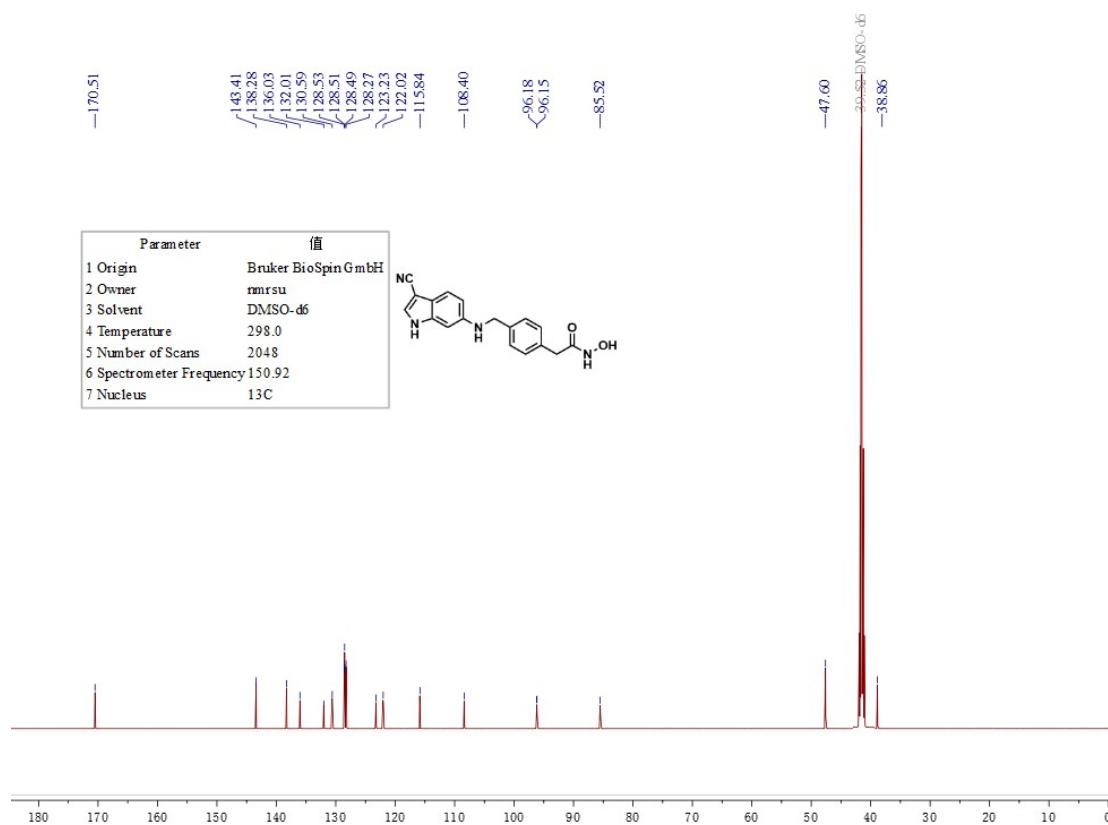
<sup>13</sup>C-NMR spectrum of compound B4



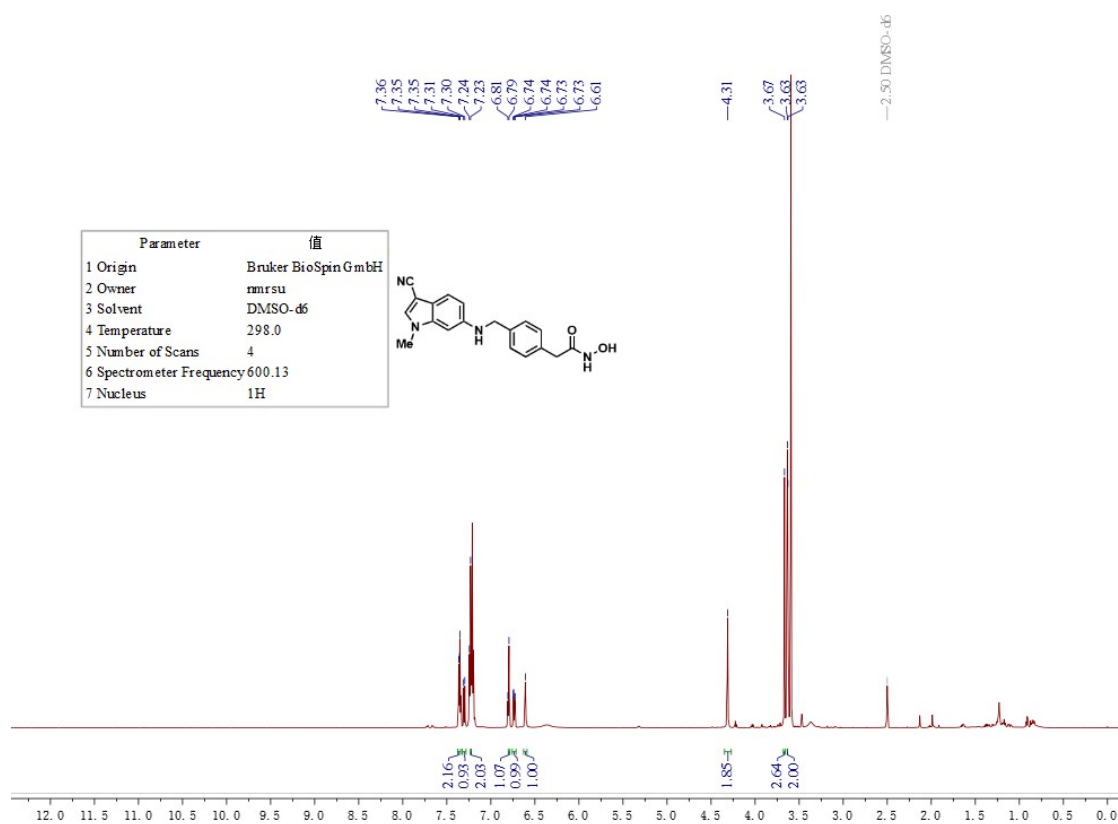
<sup>1</sup>H-NMR spectrum of compound B5



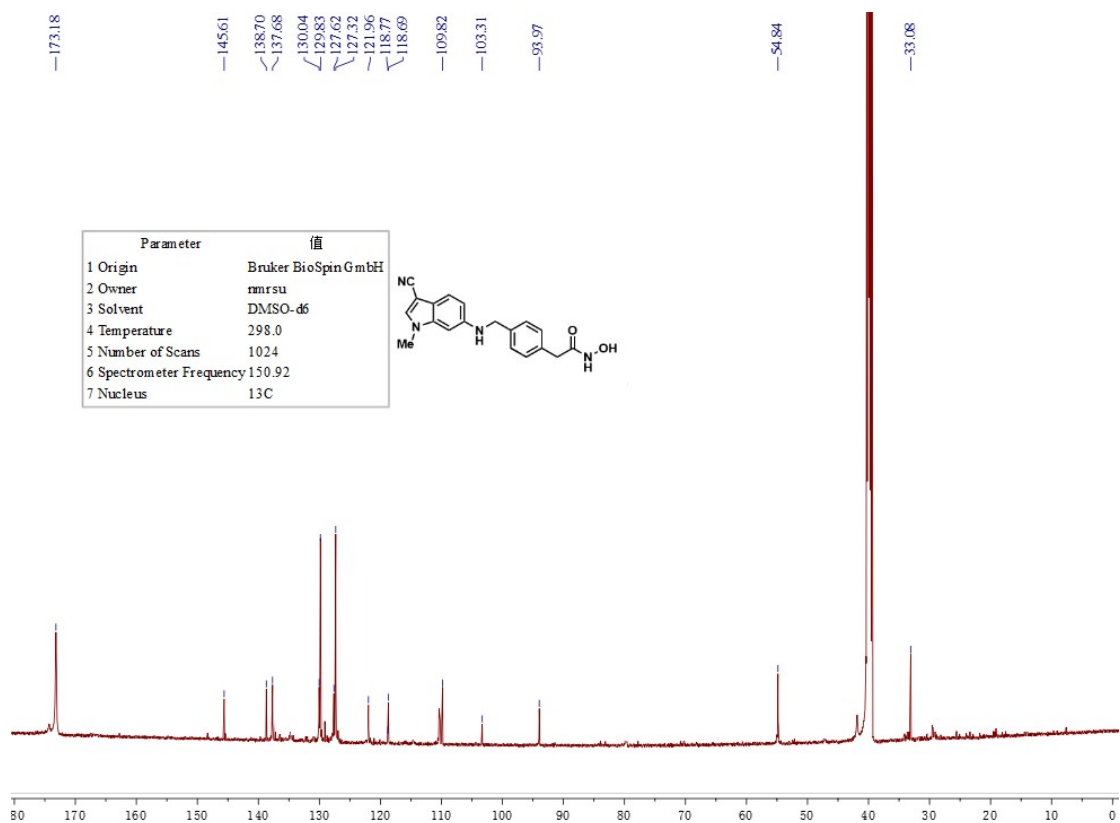
<sup>13</sup>C-NMR spectrum of compound B5



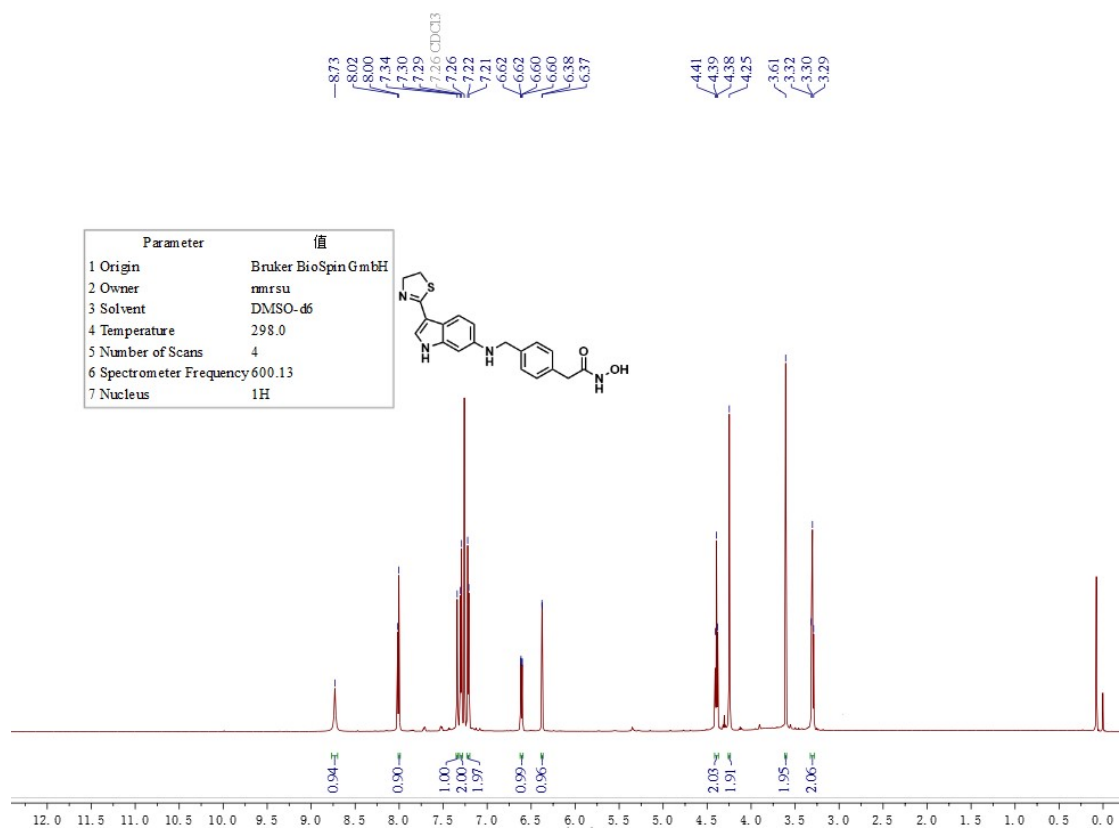
**<sup>1</sup>H-NMR spectrum of compound B6**



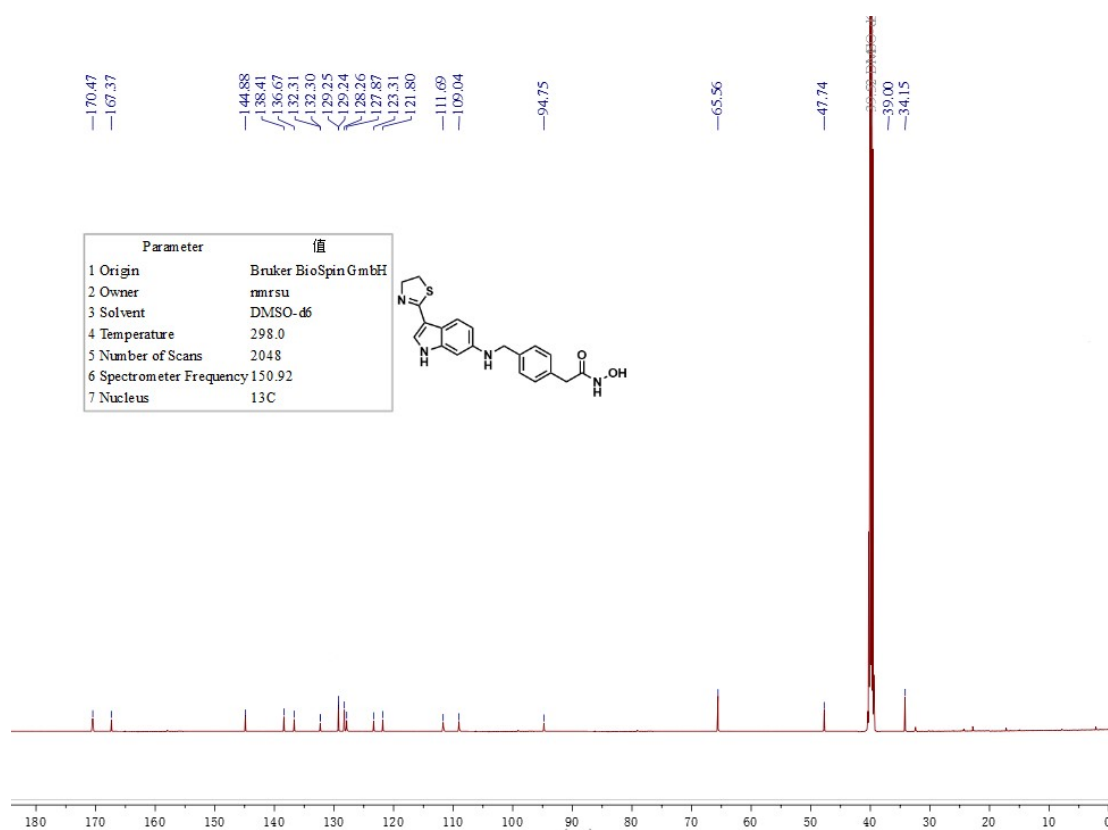
**<sup>13</sup>C-NMR spectrum of compound B6**



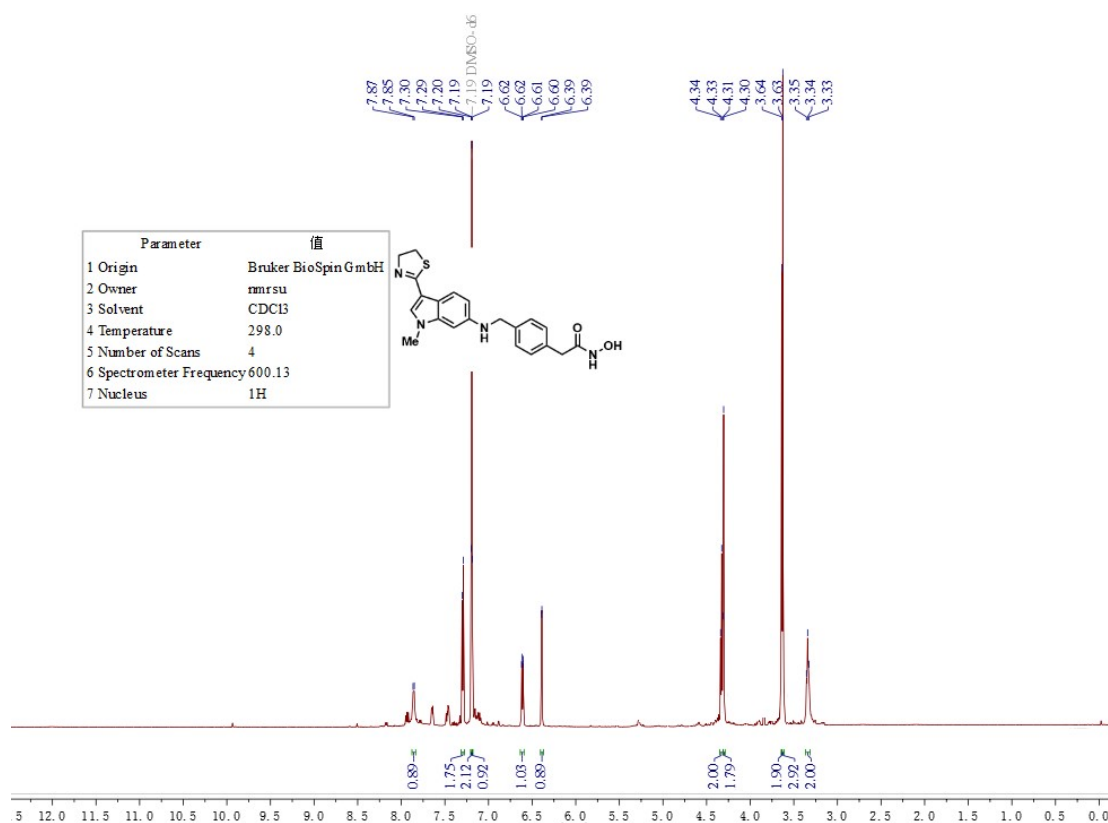
**<sup>1</sup>H-NMR spectrum of compound B7**



**<sup>13</sup>C-NMR spectrum of compound B7**

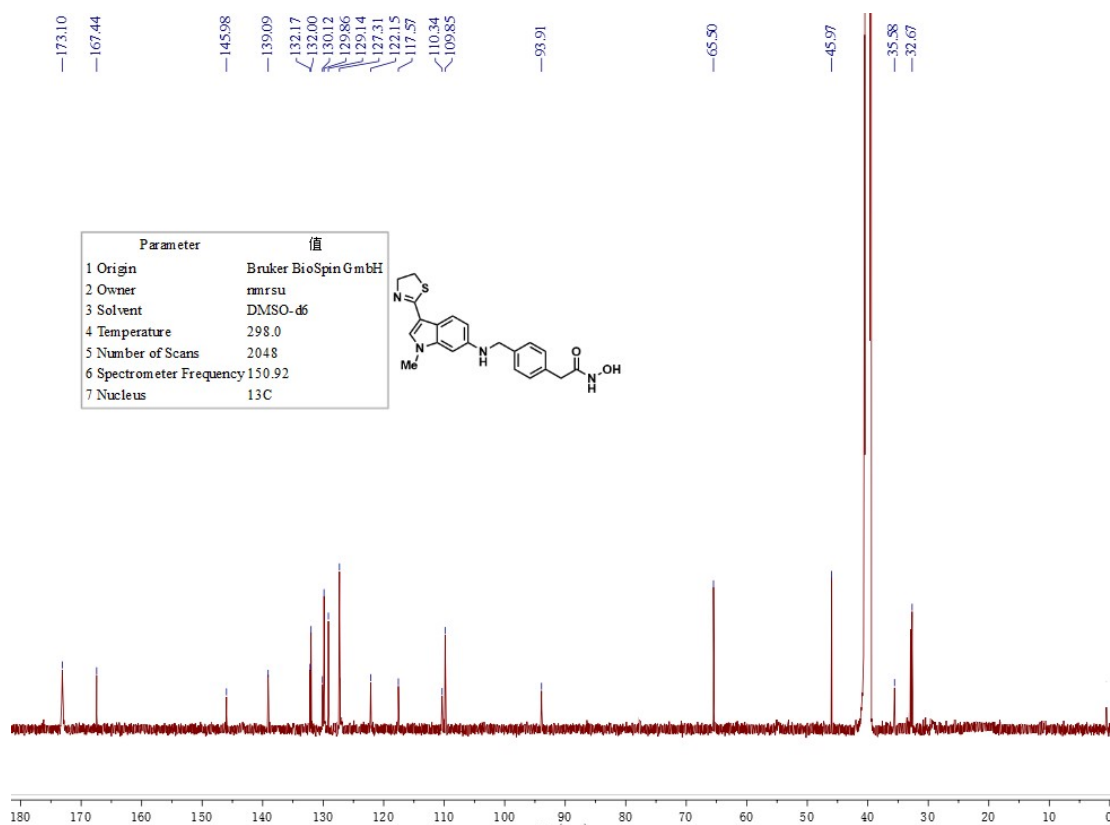


**<sup>1</sup>H-NMR spectrum of compound B8**

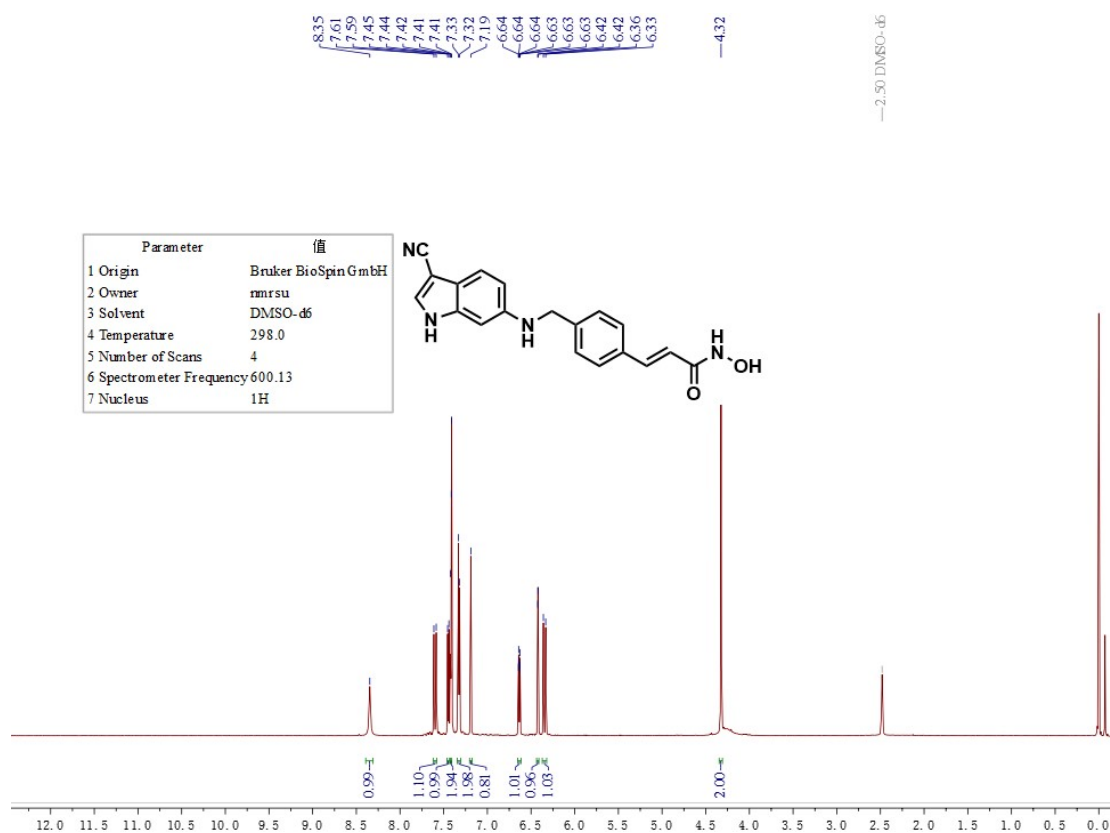


**<sup>13</sup>C-NMR spectrum of compound B8**

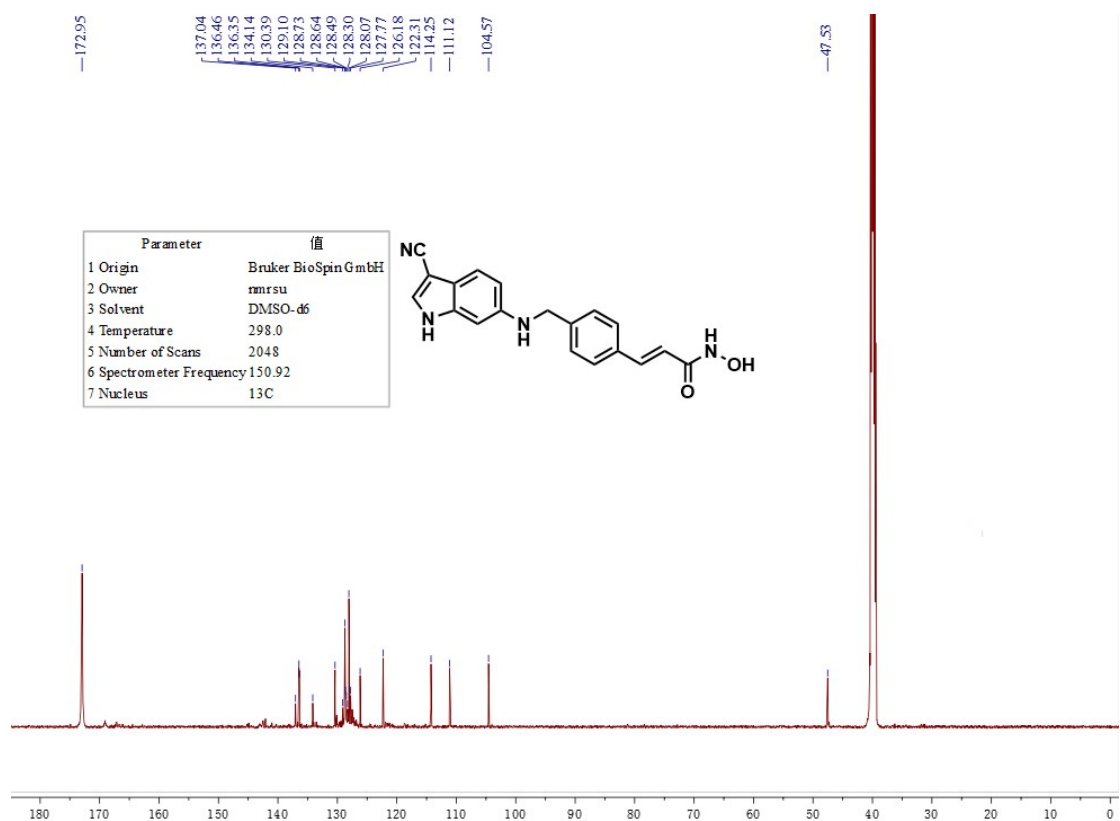




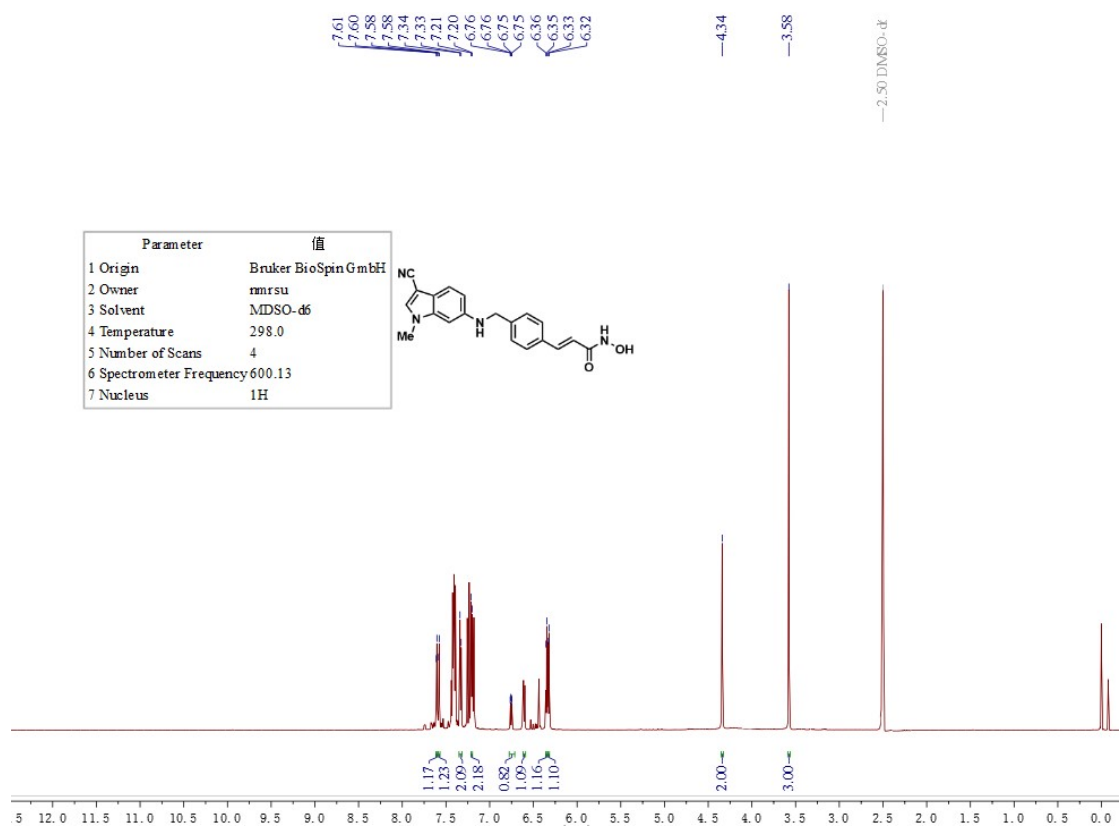
**<sup>1</sup>H-NMR spectrum of compound B9**



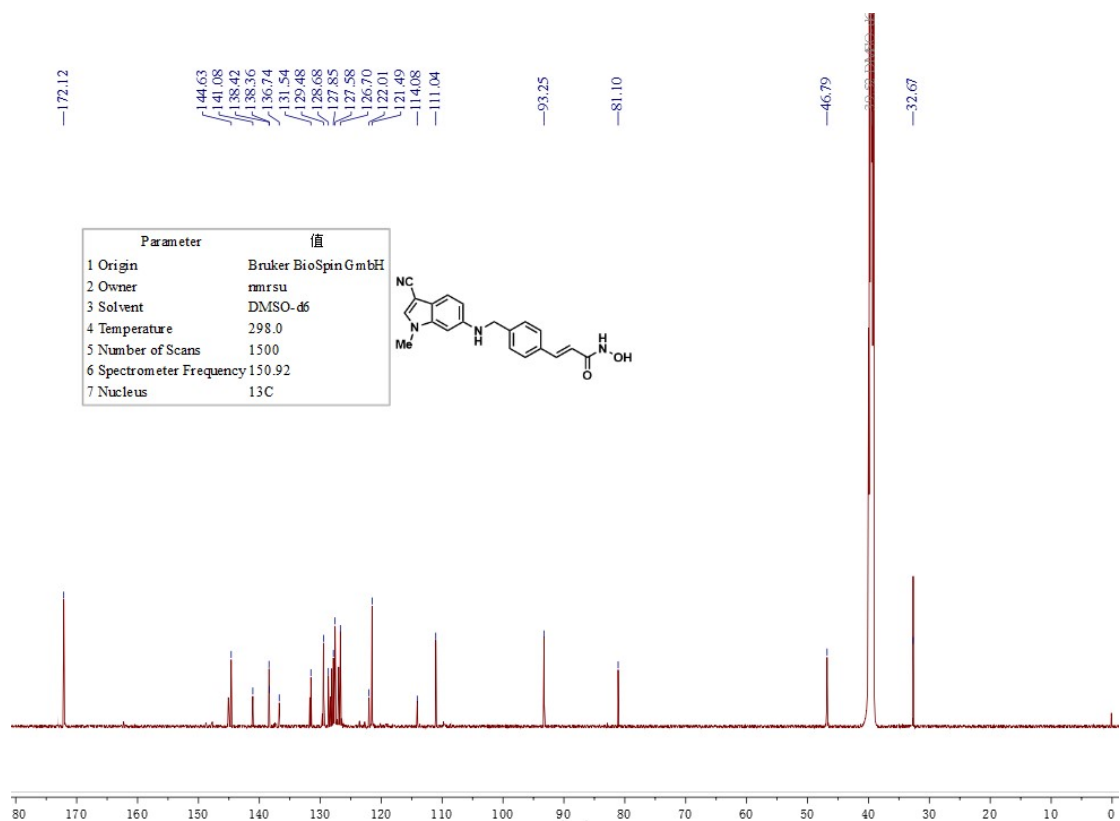
**<sup>13</sup>C-NMR spectrum of compound B9**



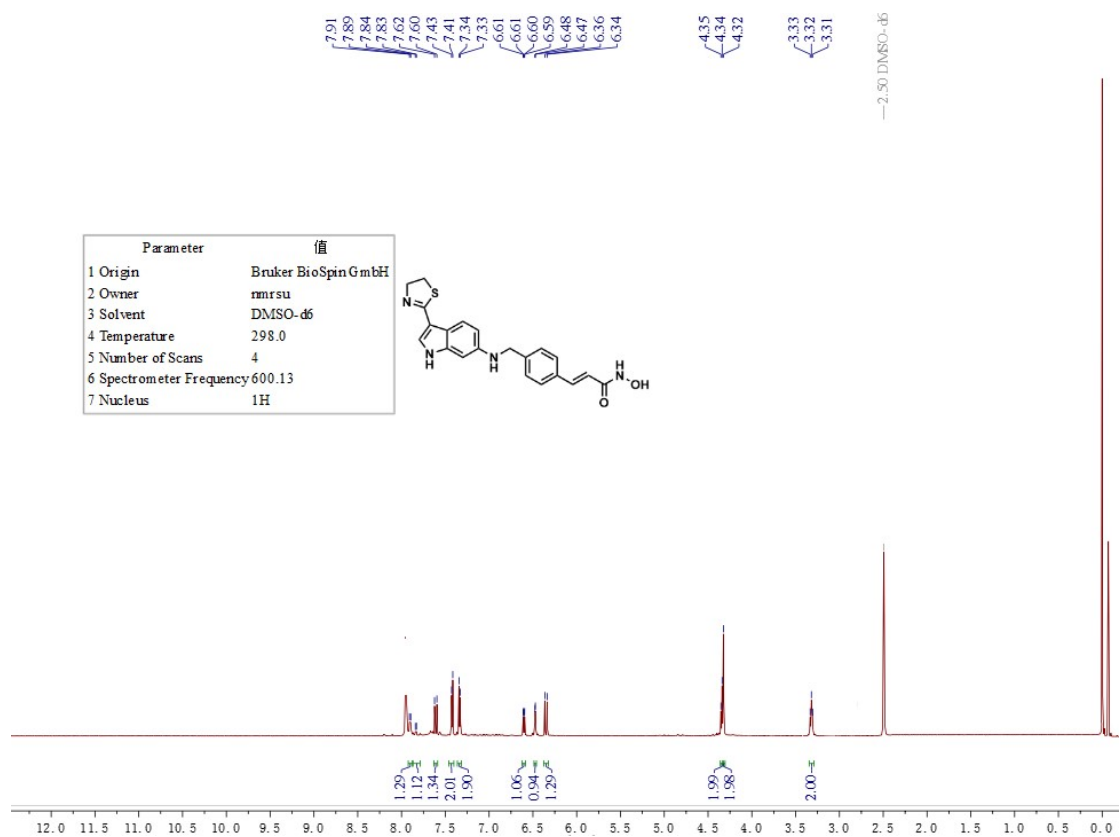
**<sup>1</sup>H-NMR spectrum of compound B10**



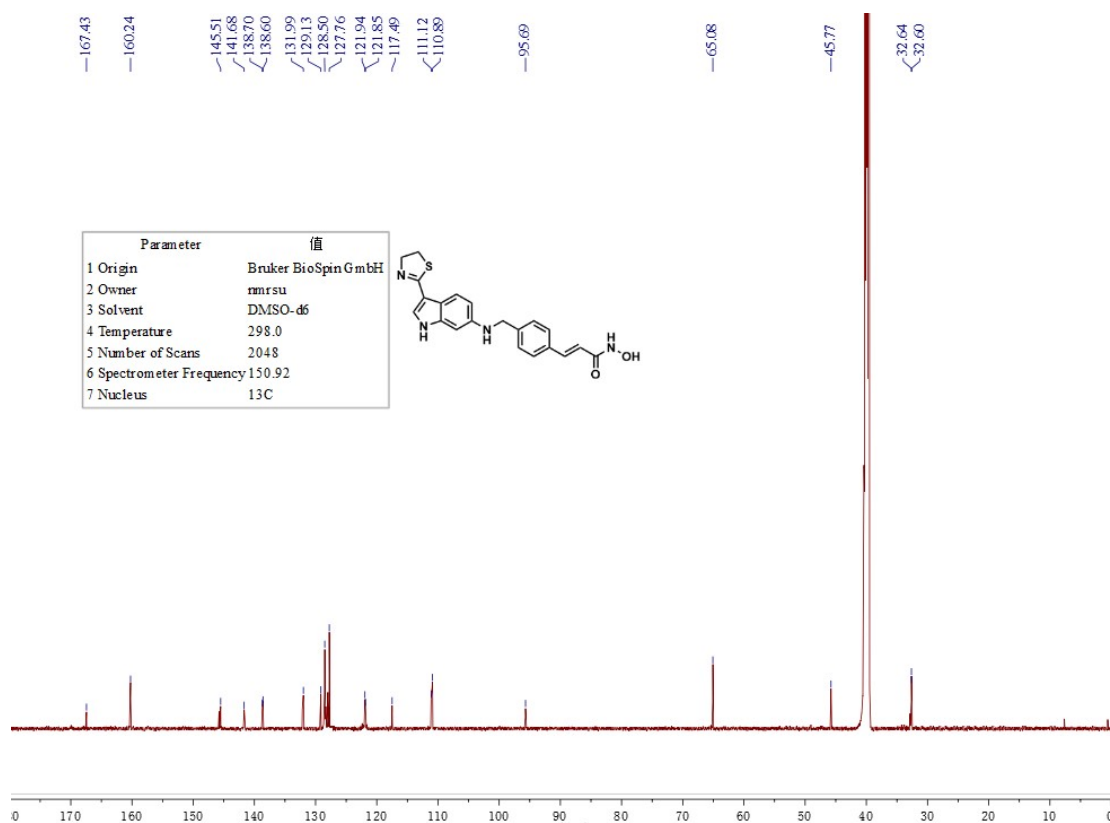
**<sup>13</sup>C-NMR spectrum of compound B10**



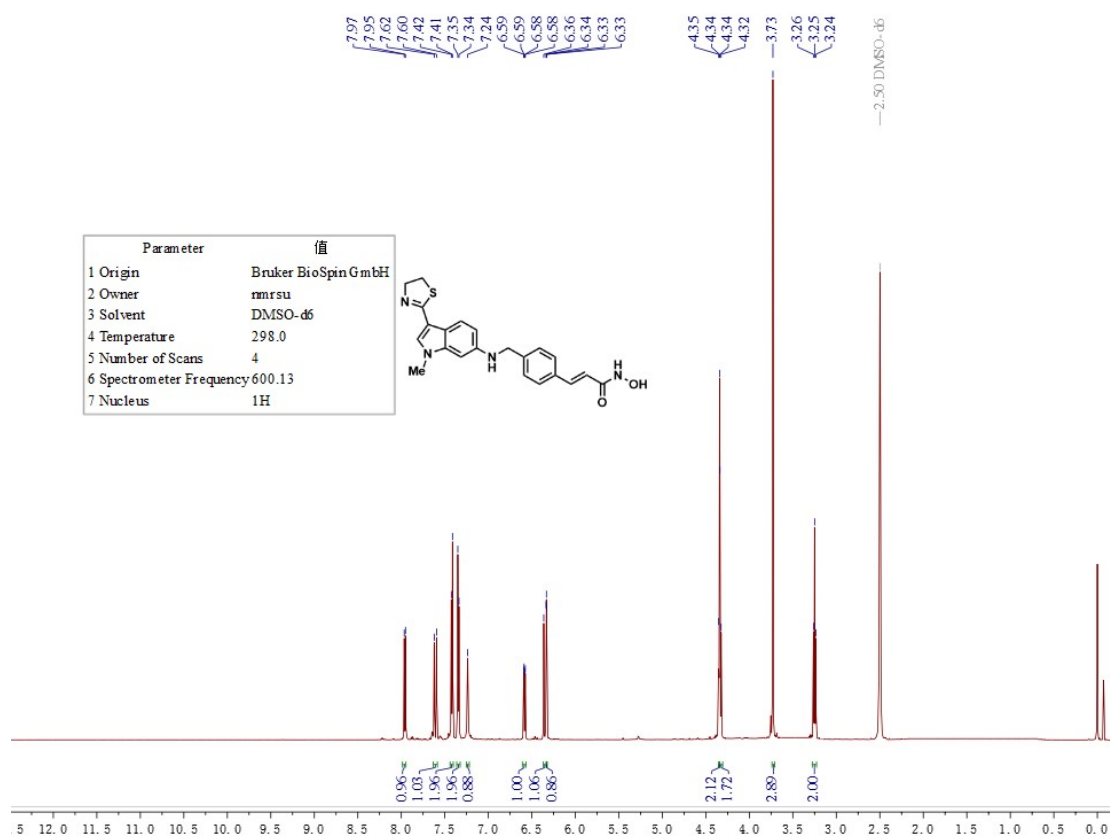
## <sup>1</sup>H-NMR spectrum of compound B11



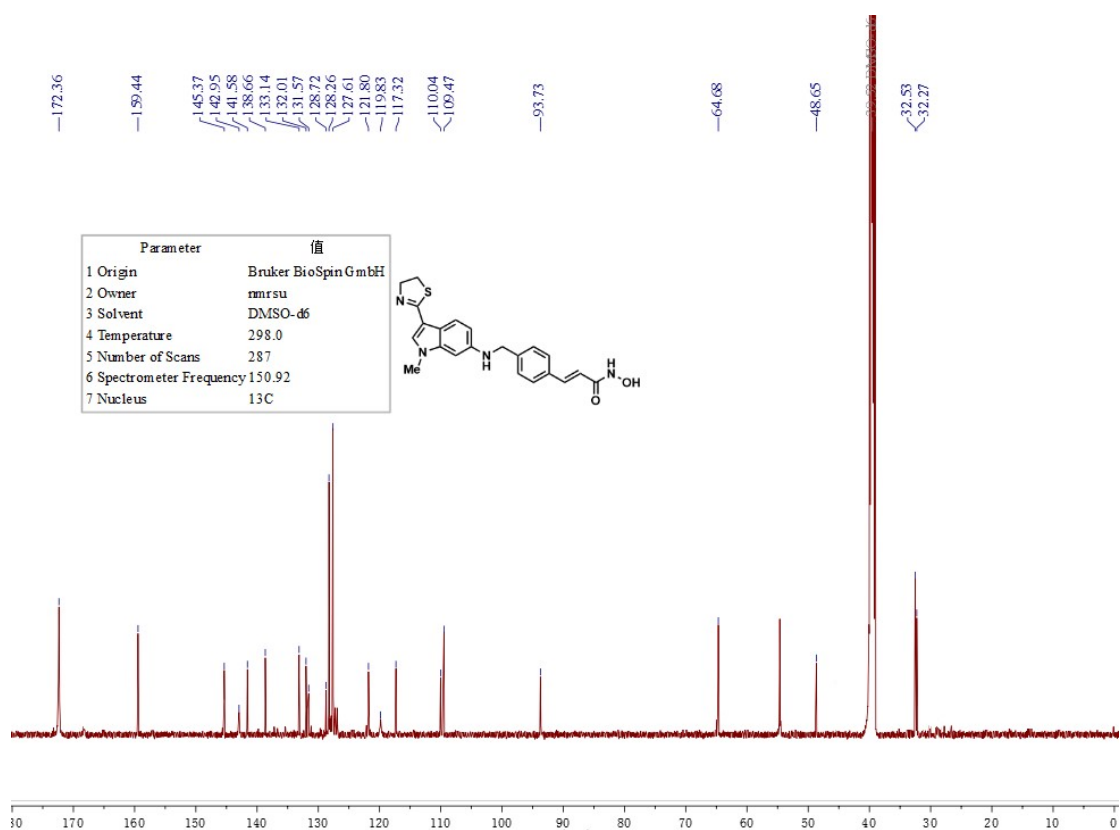
## <sup>13</sup>C-NMR spectrum of compound B11



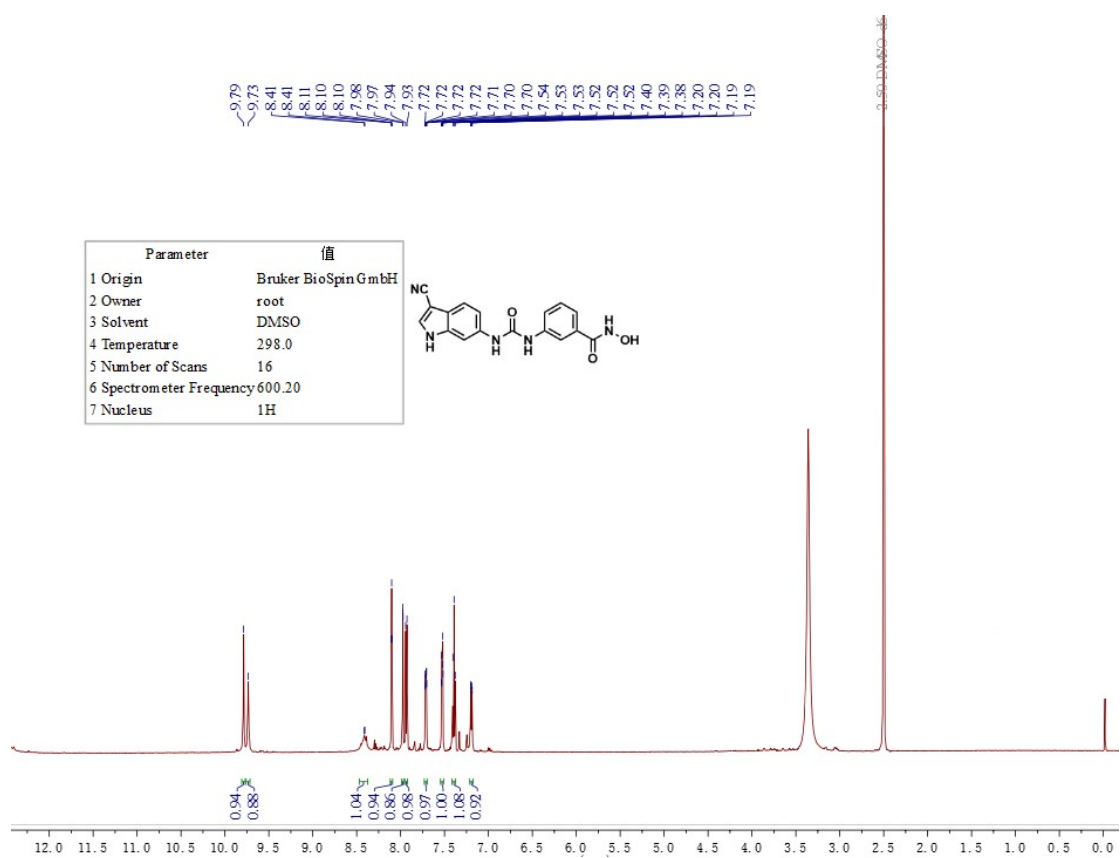
<sup>1</sup>H-NMR spectrum of compound B12



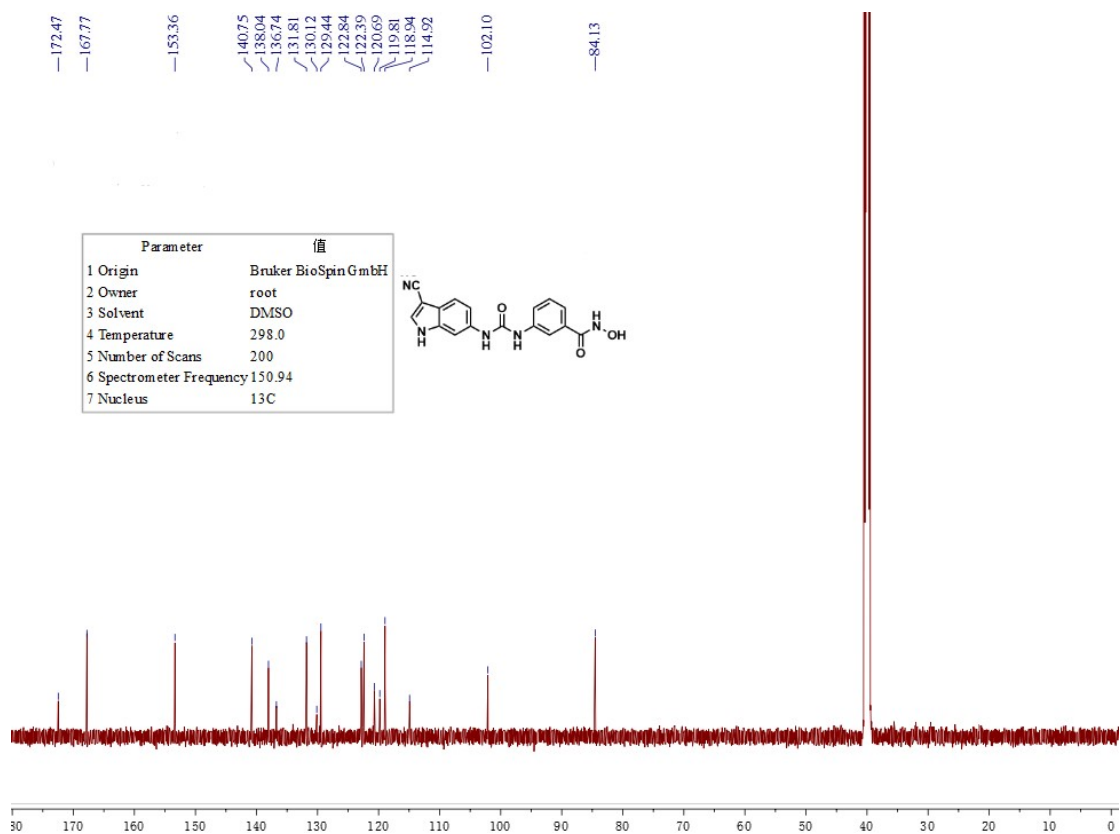
<sup>13</sup>C-NMR spectrum of compound B12



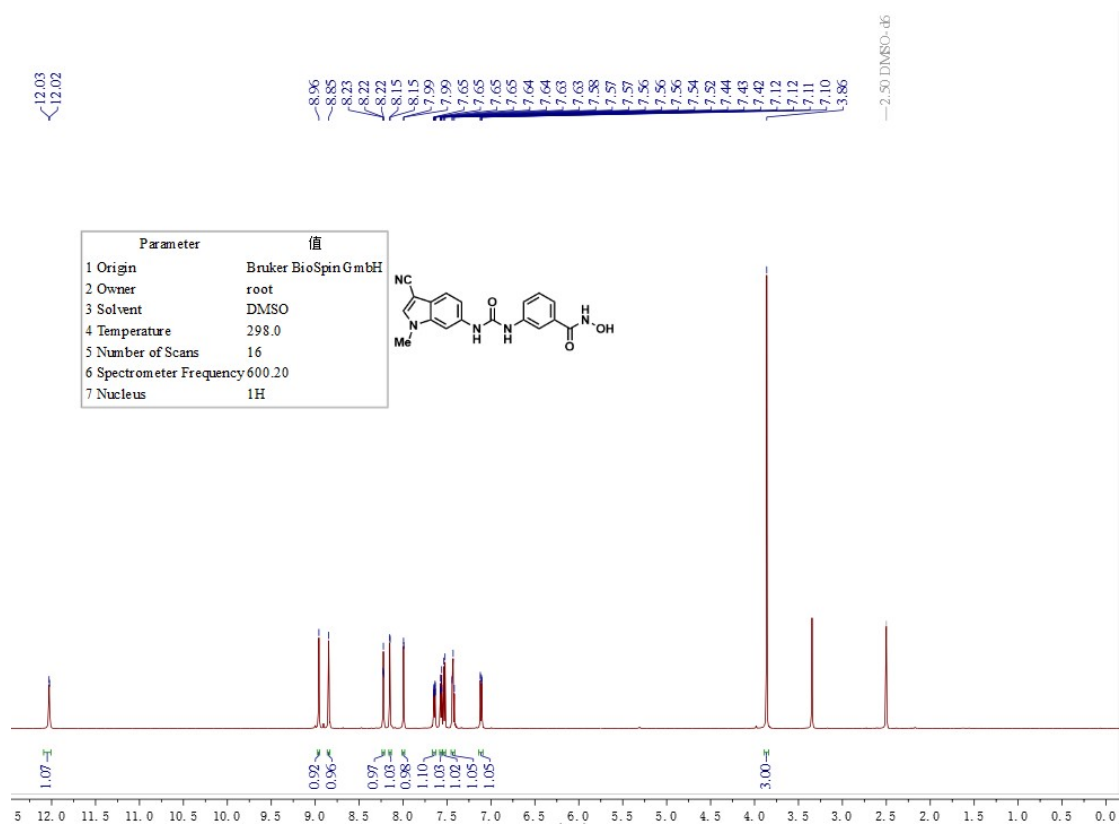
**<sup>1</sup>H-NMR spectrum of compound C1**



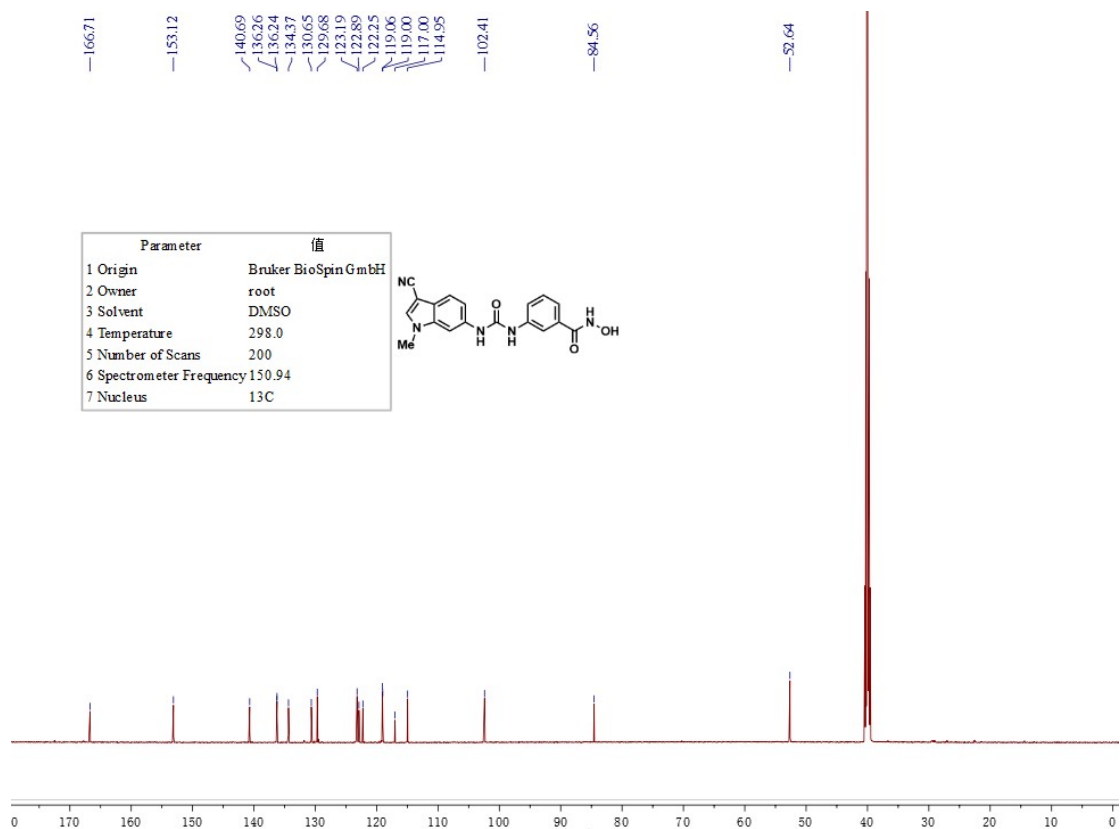
**<sup>13</sup>C-NMR spectrum of compound C1**



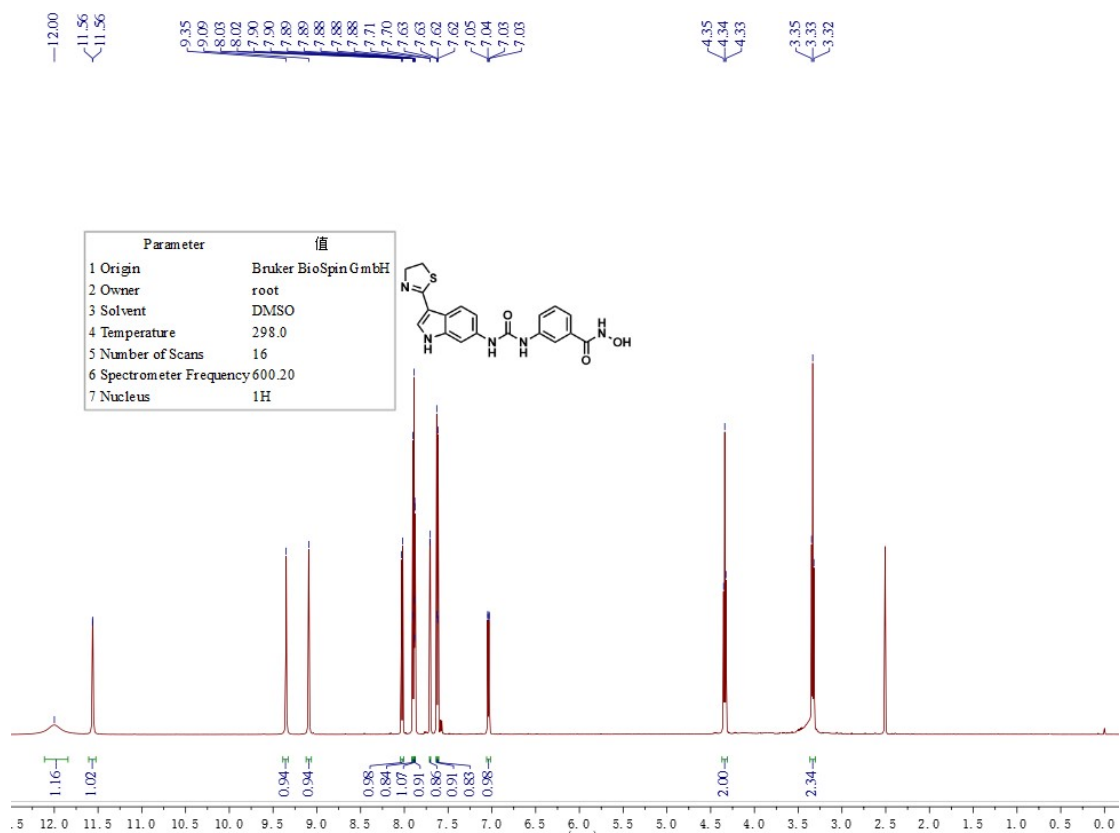
<sup>1</sup>H-NMR spectrum of compound C2



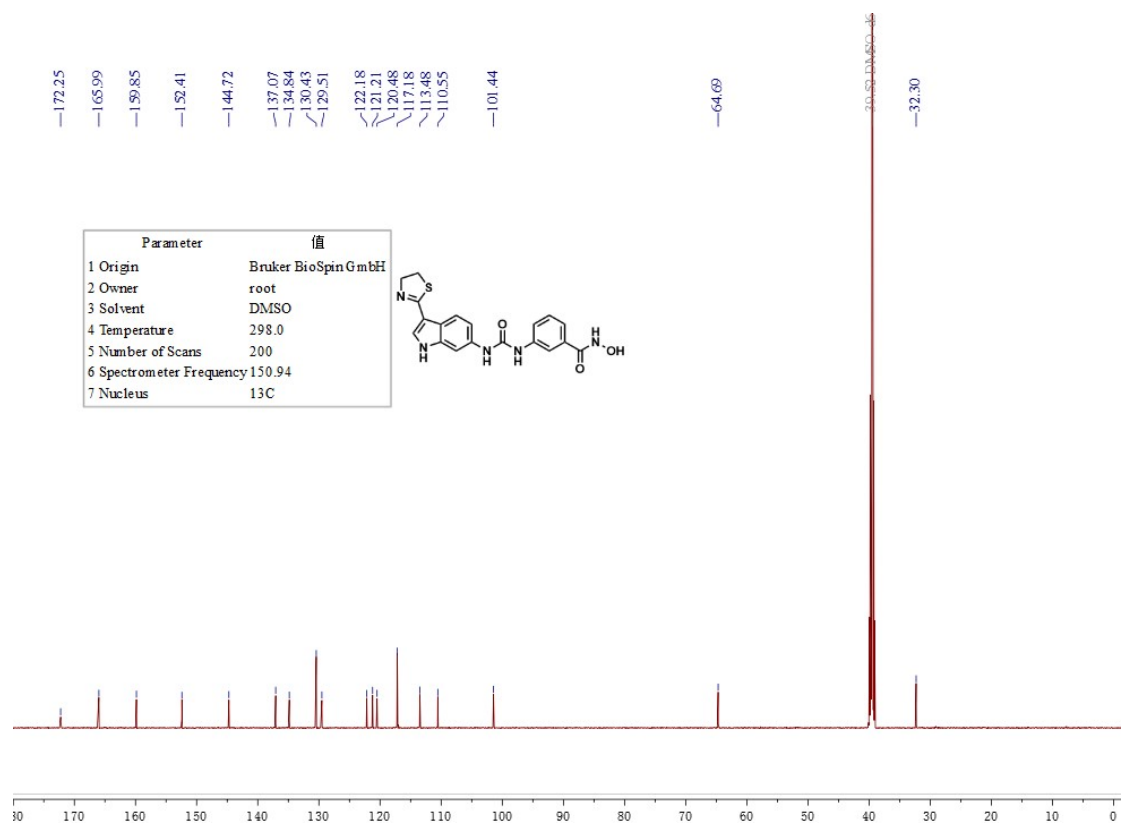
<sup>13</sup>C-NMR spectrum of compound C2



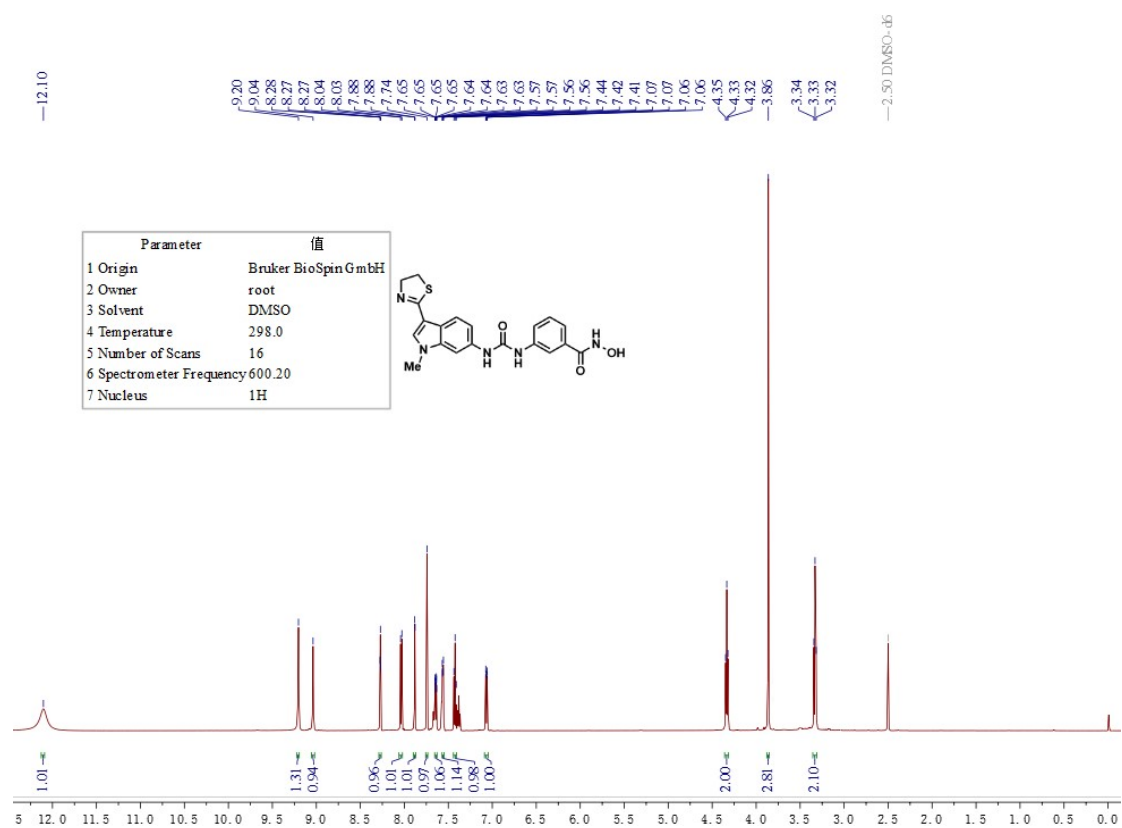
**<sup>1</sup>H-NMR spectrum of compound C3**



**<sup>13</sup>C-NMR spectrum of compound C3**

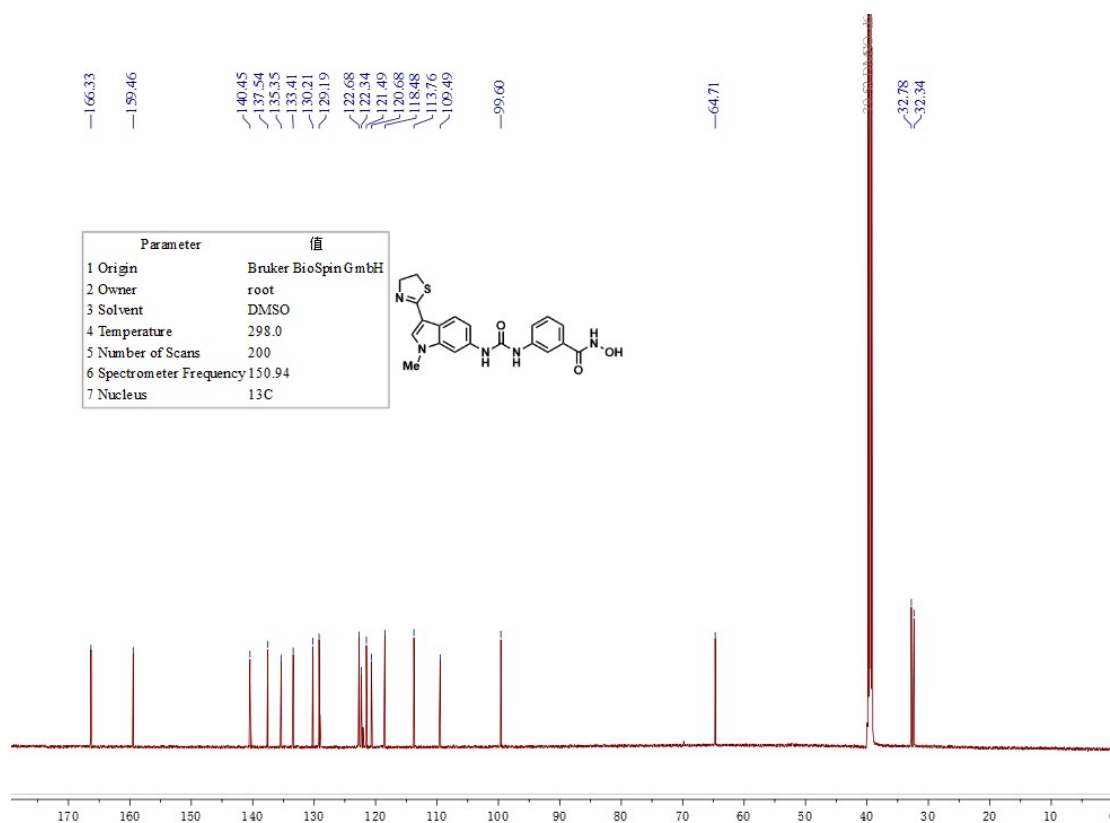


**<sup>1</sup>H-NMR spectrum of compound C4**

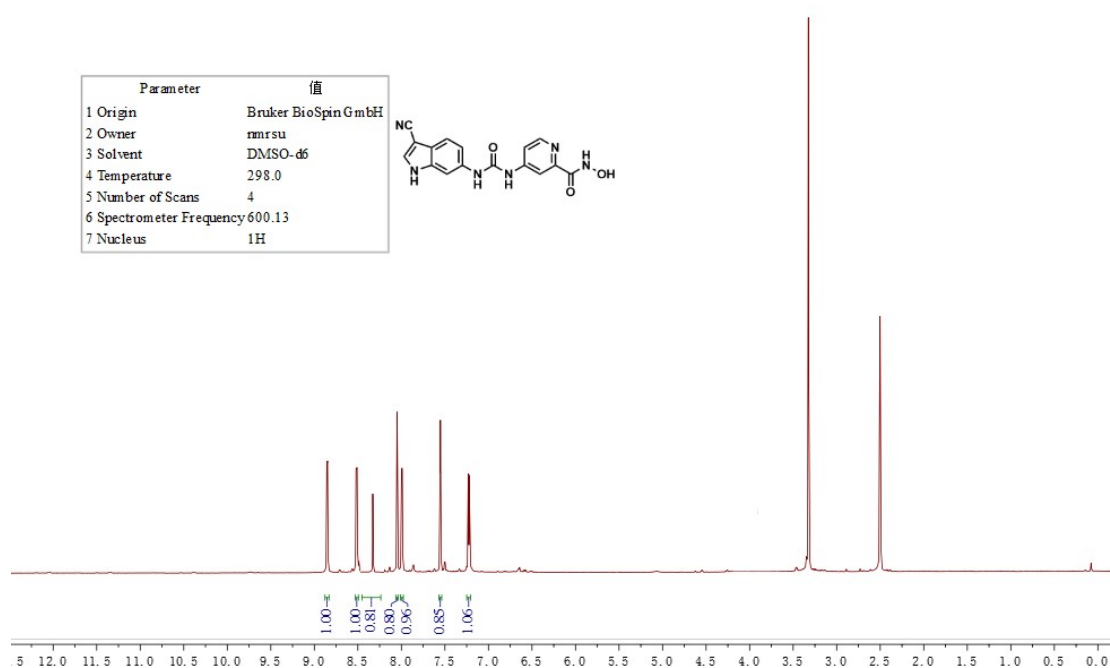


**<sup>13</sup>C-NMR spectrum of compound C4**

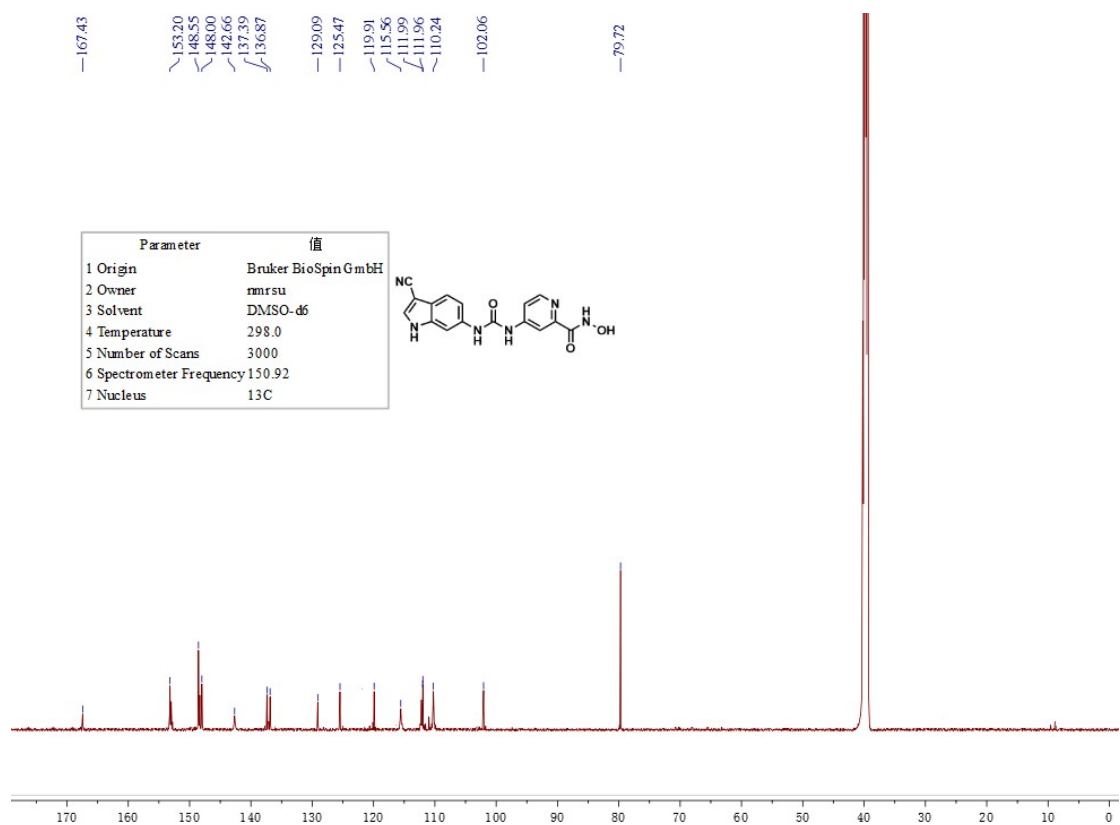




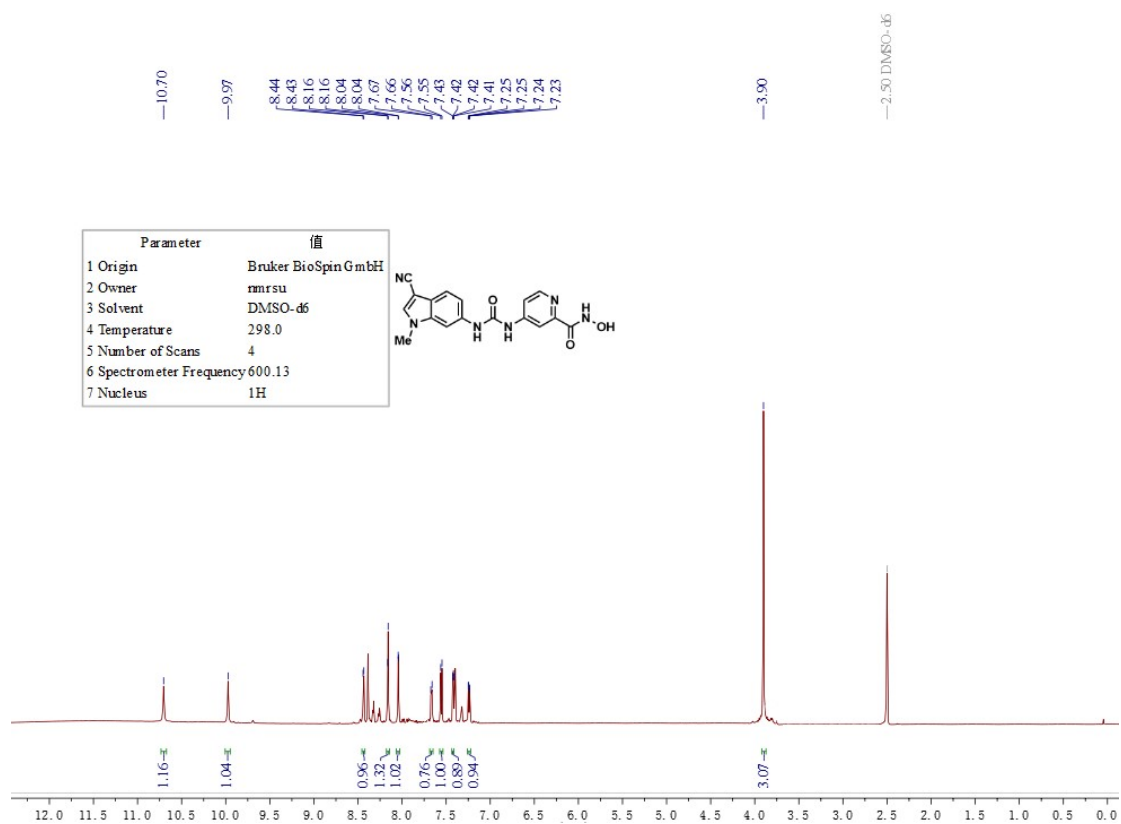
**<sup>1</sup>H-NMR spectrum of compound C5**



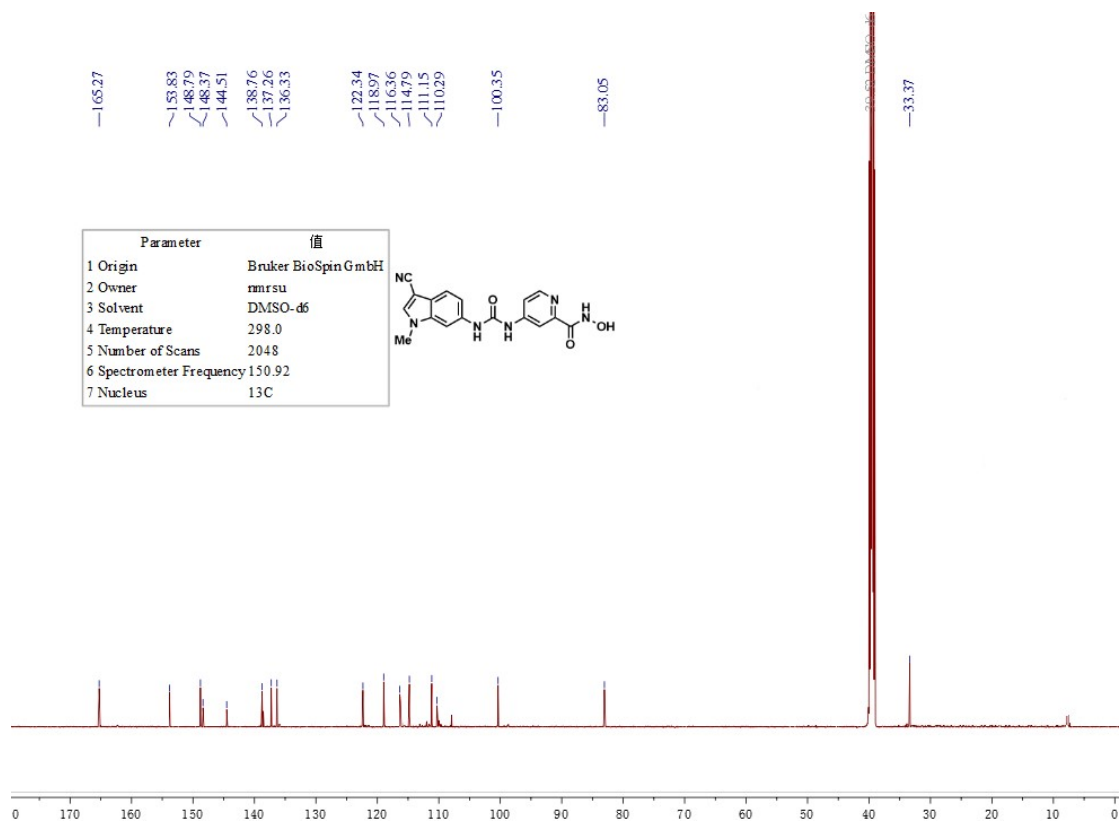
**<sup>13</sup>C-NMR spectrum of compound C5**



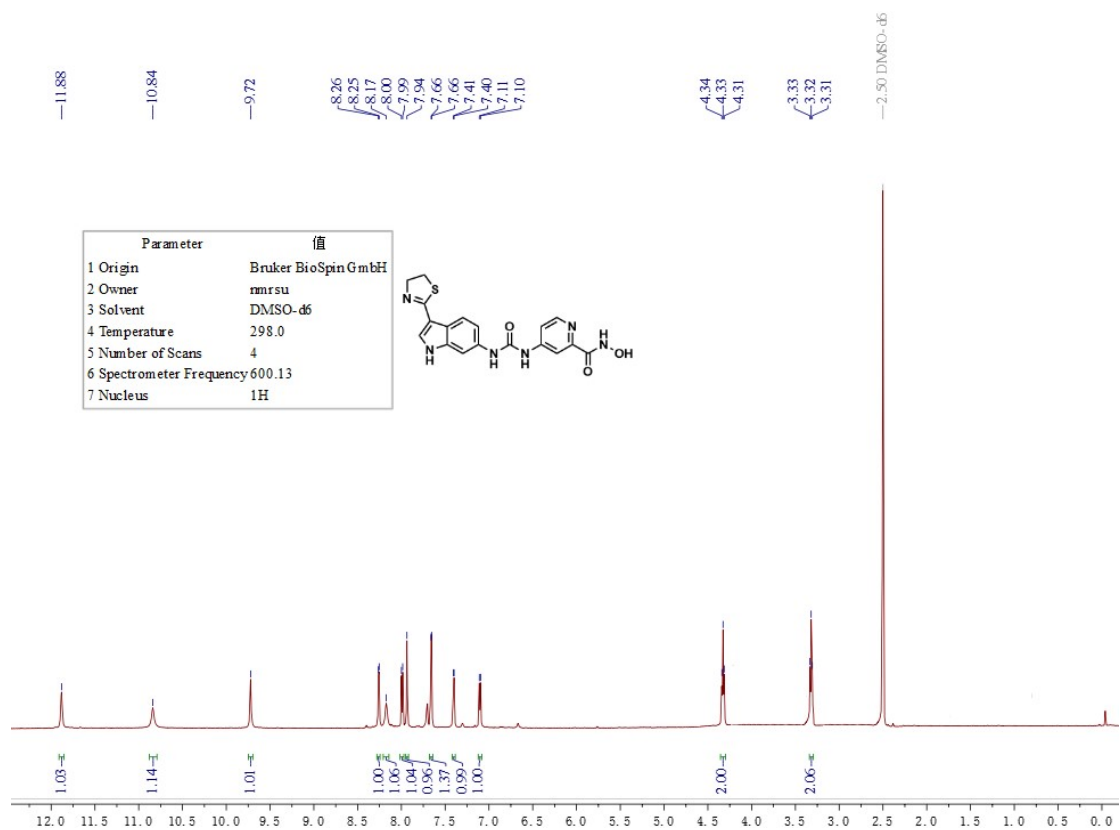
<sup>1</sup>H-NMR spectrum of compound C6



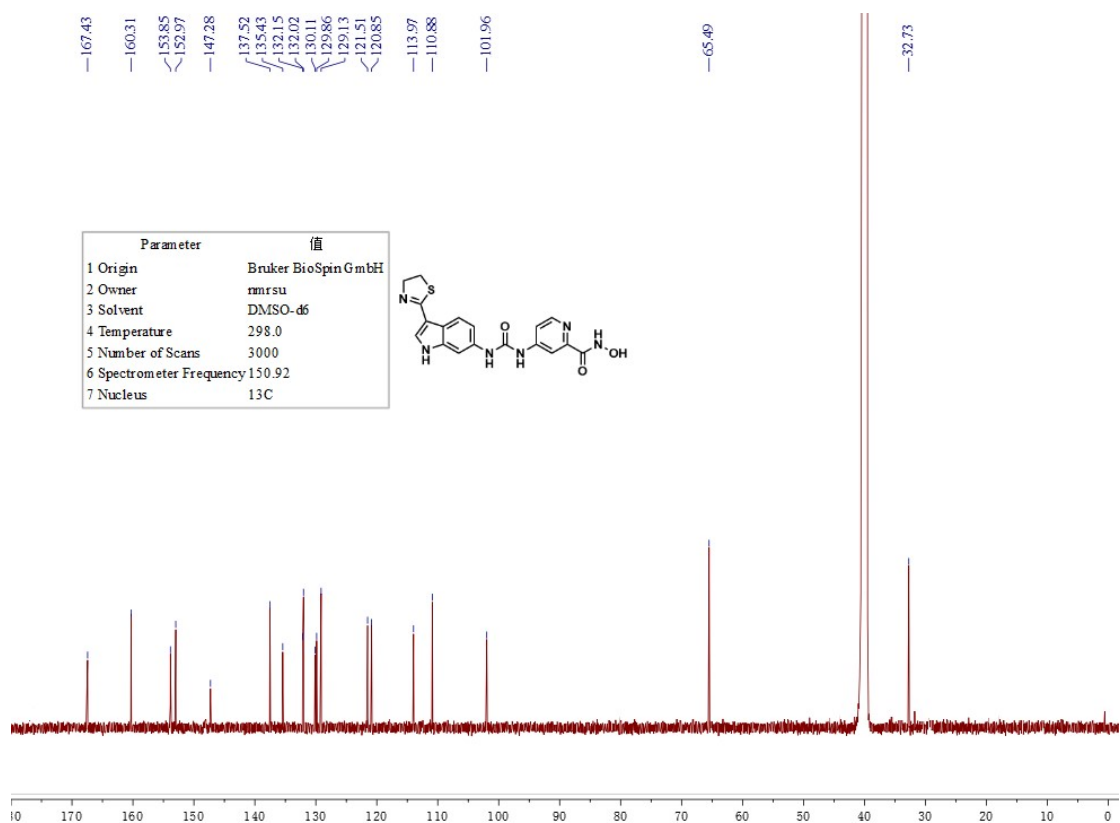
<sup>13</sup>C-NMR spectrum of compound C6



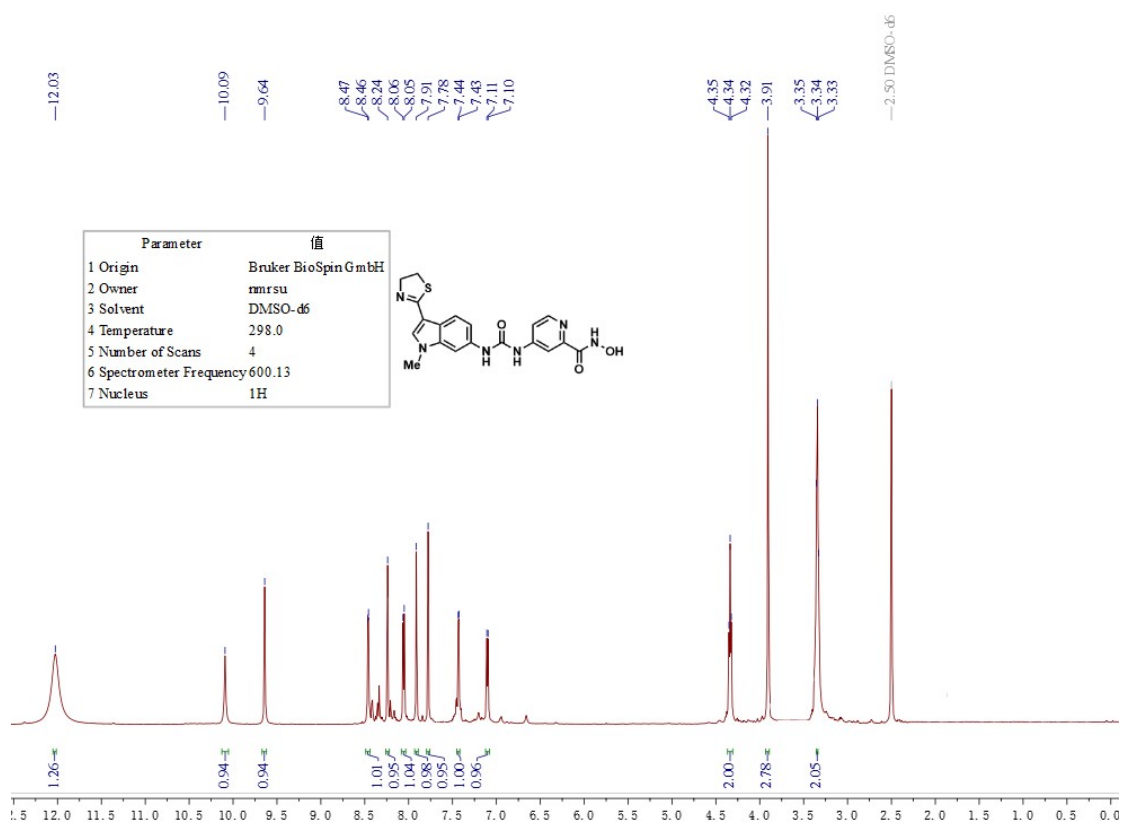
**<sup>1</sup>H-NMR spectrum of compound C7**



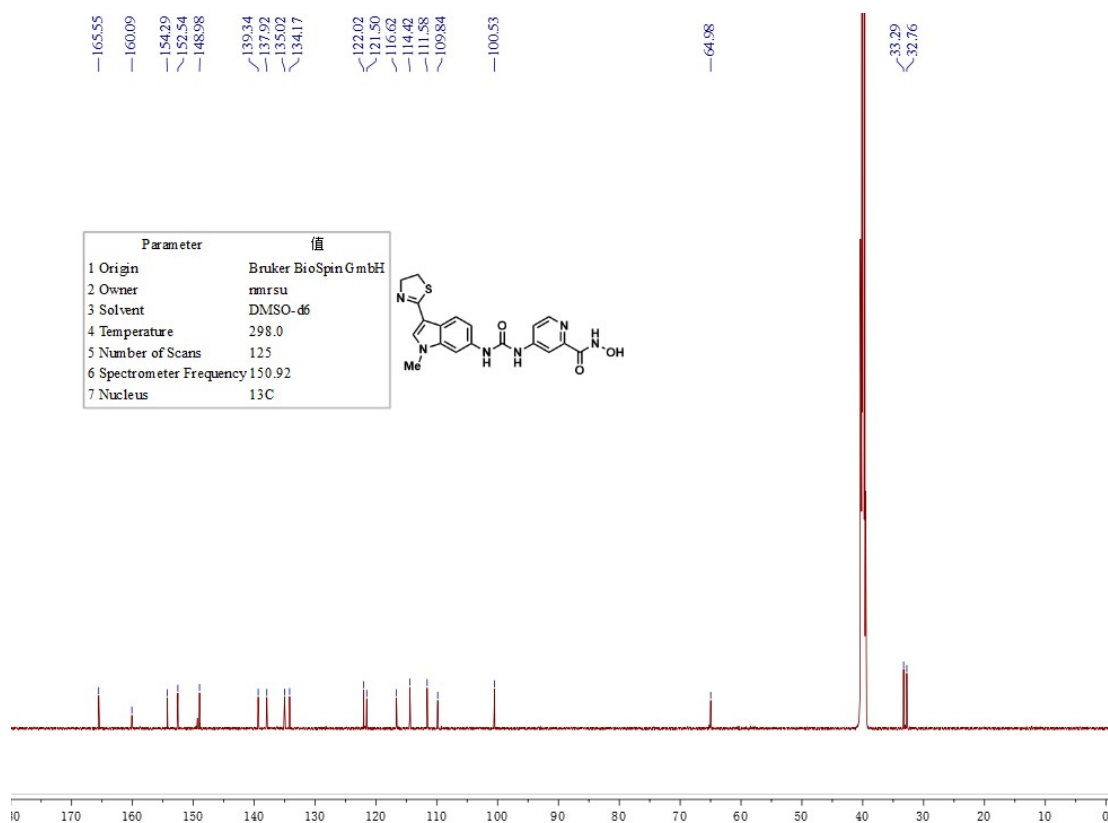
**<sup>13</sup>C-NMR spectrum of compound C7**



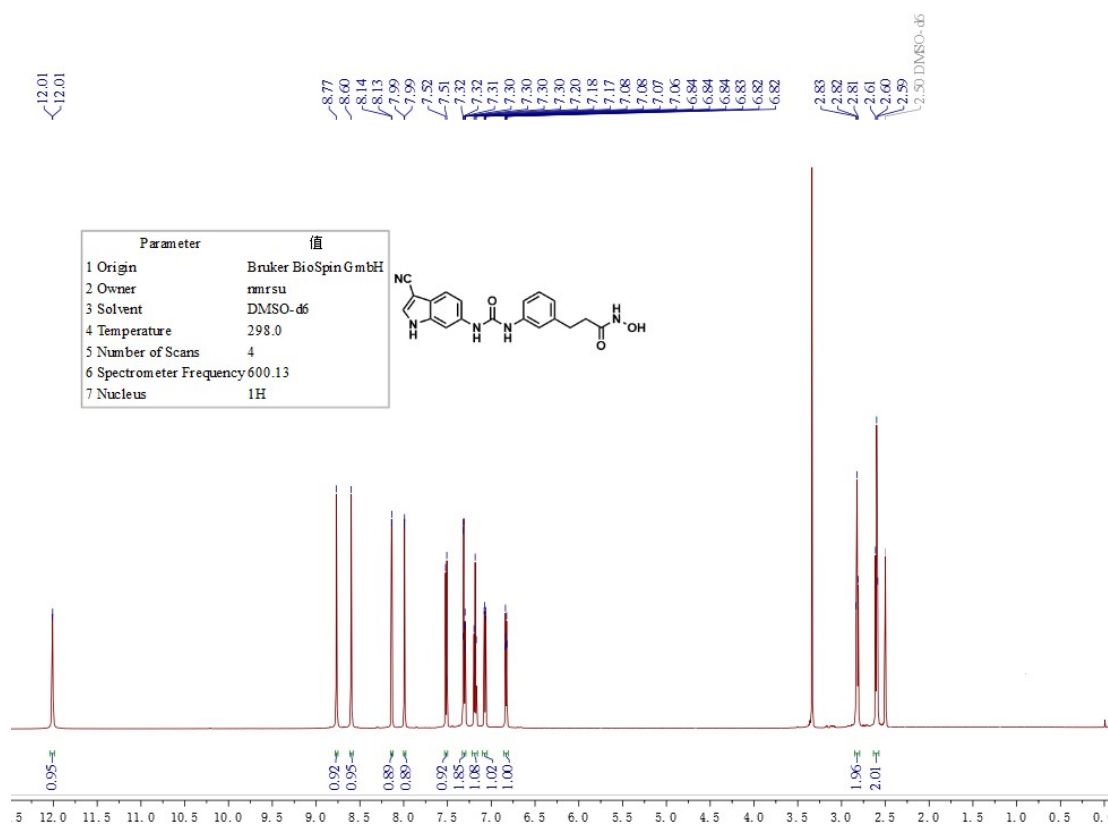
<sup>1</sup>H-NMR spectrum of compound C8



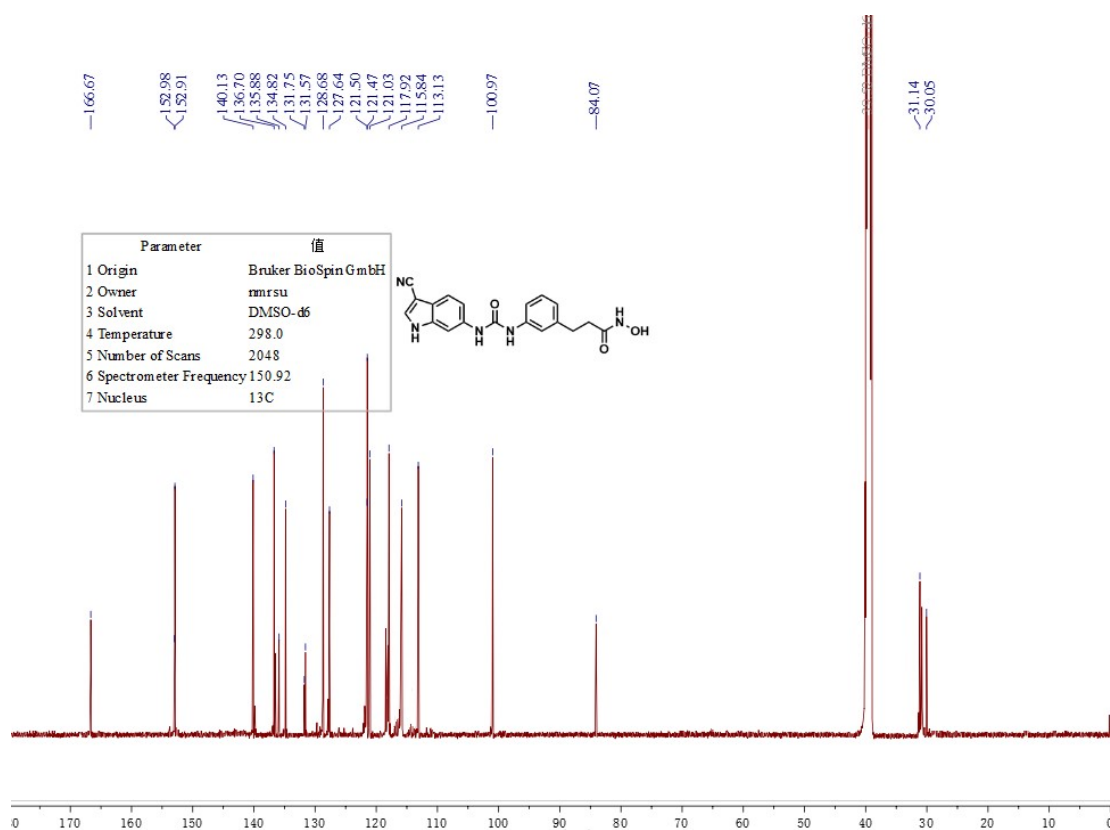
<sup>13</sup>C-NMR spectrum of compound C8



**<sup>1</sup>H-NMR spectrum of compound C9**



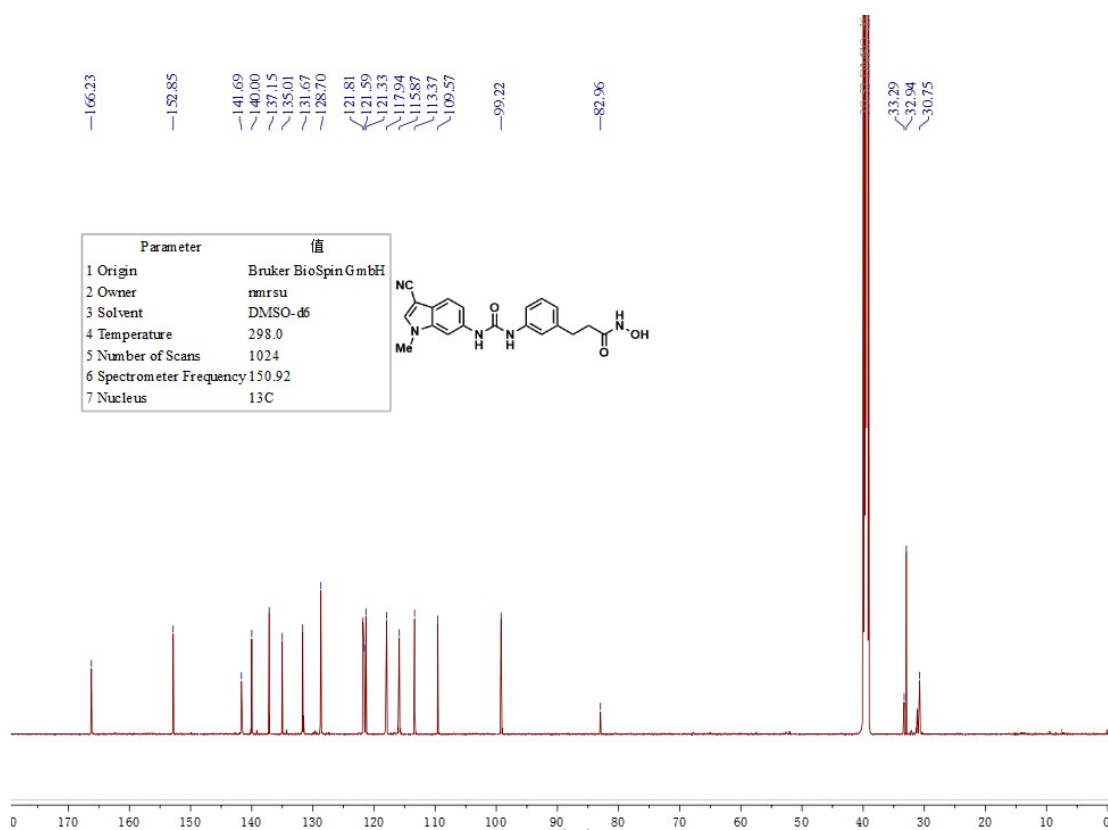
**<sup>13</sup>C-NMR spectrum of compound C9**



**<sup>1</sup>H-NMR spectrum of compound C10**



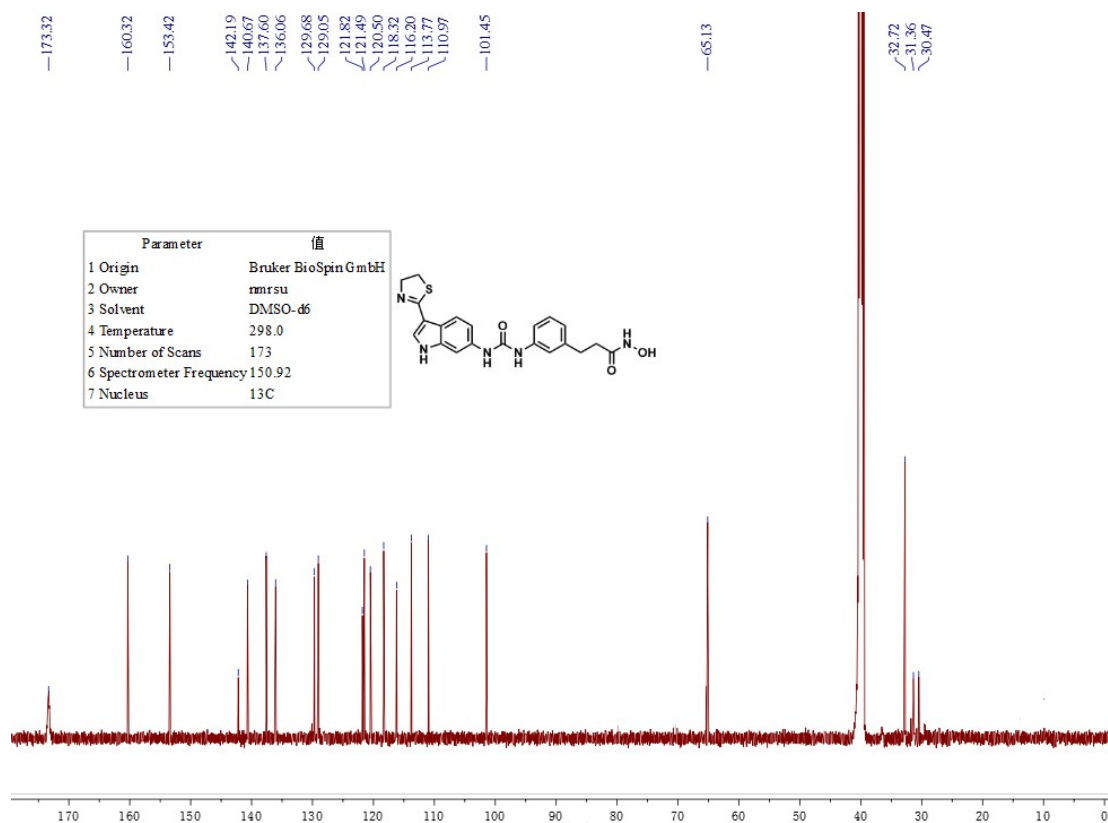
**<sup>13</sup>C-NMR spectrum of compound C10**



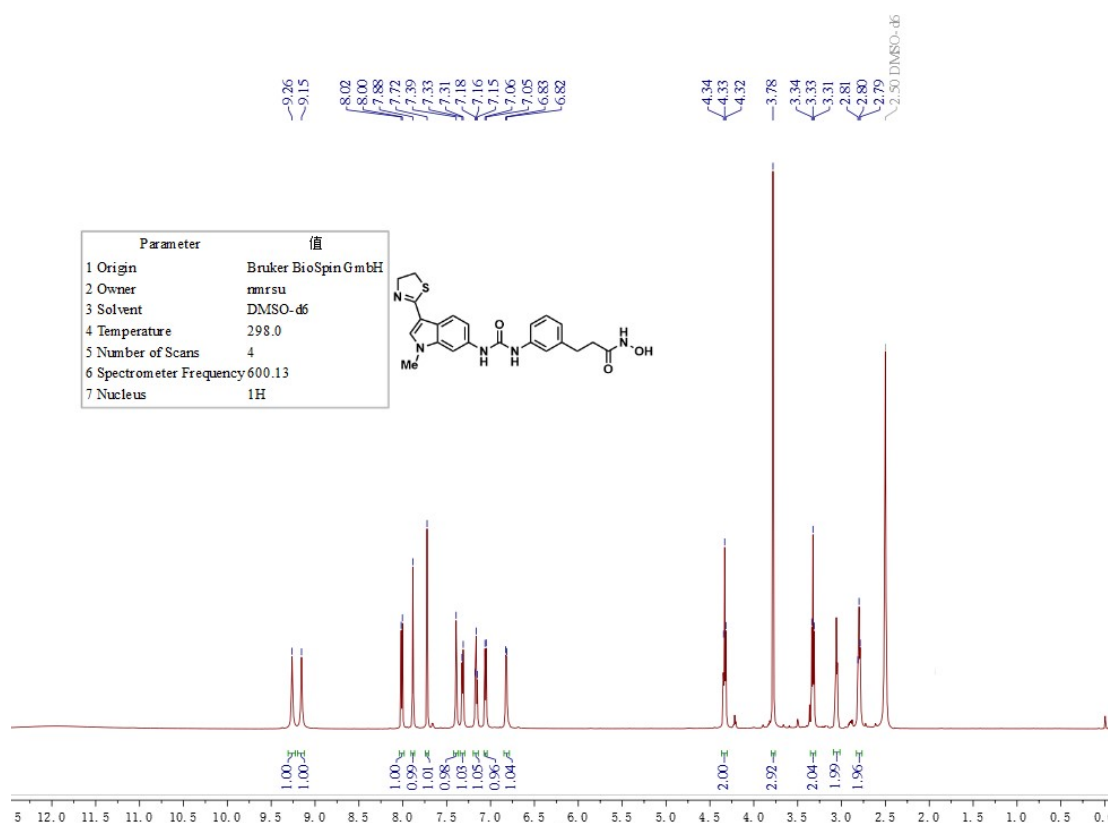
**<sup>1</sup>H-NMR spectrum of compound C11**



**<sup>13</sup>C-NMR spectrum of compound C11**

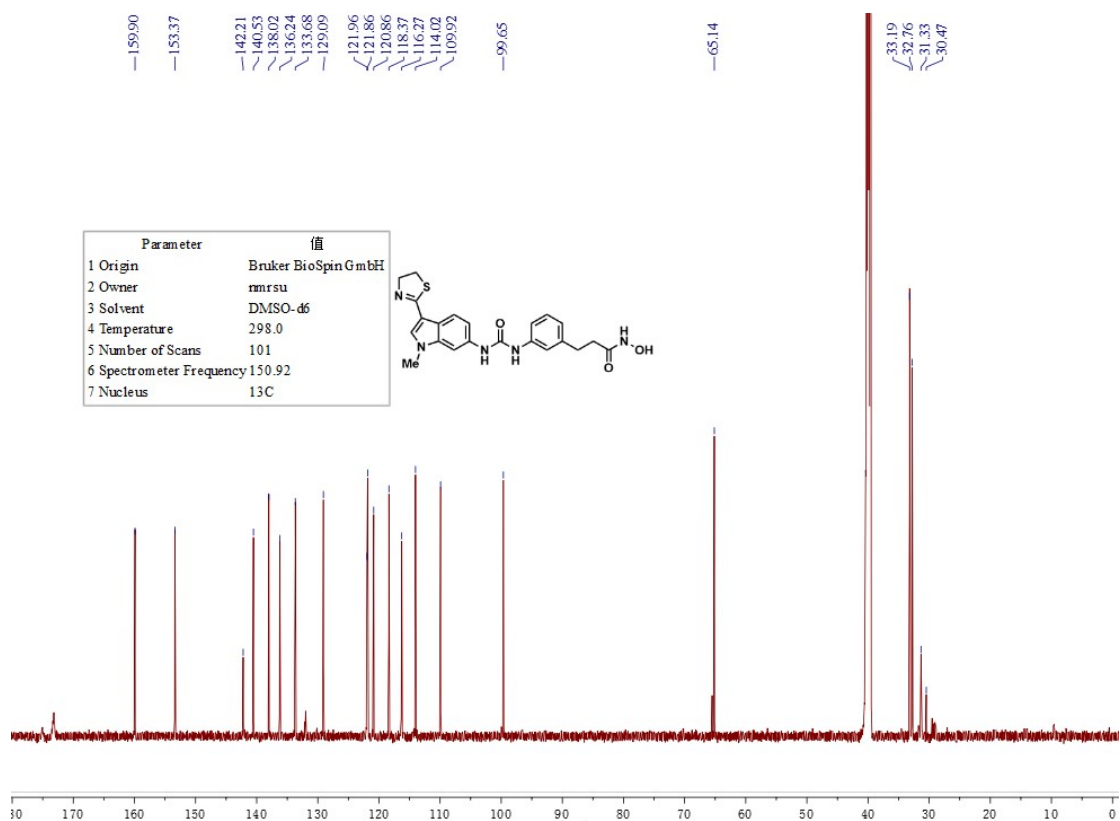


<sup>1</sup>H-NMR spectrum of compound C12

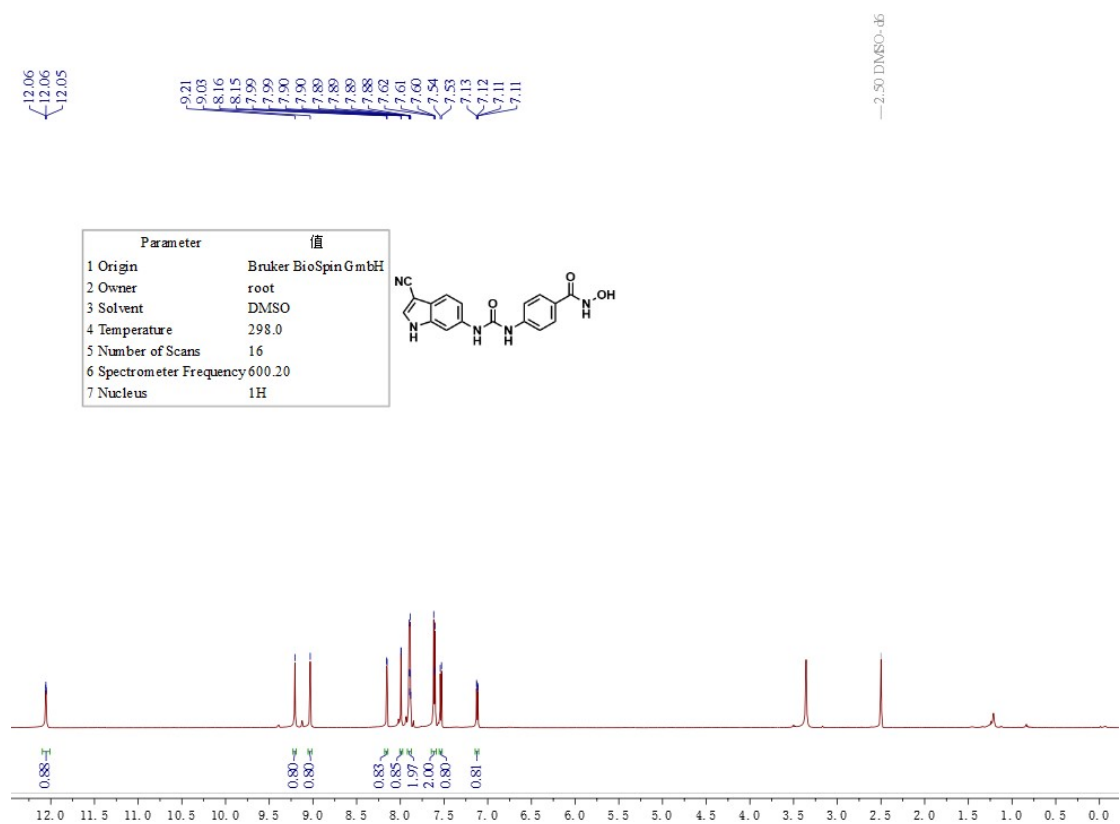


<sup>13</sup>C-NMR spectrum of compound C12

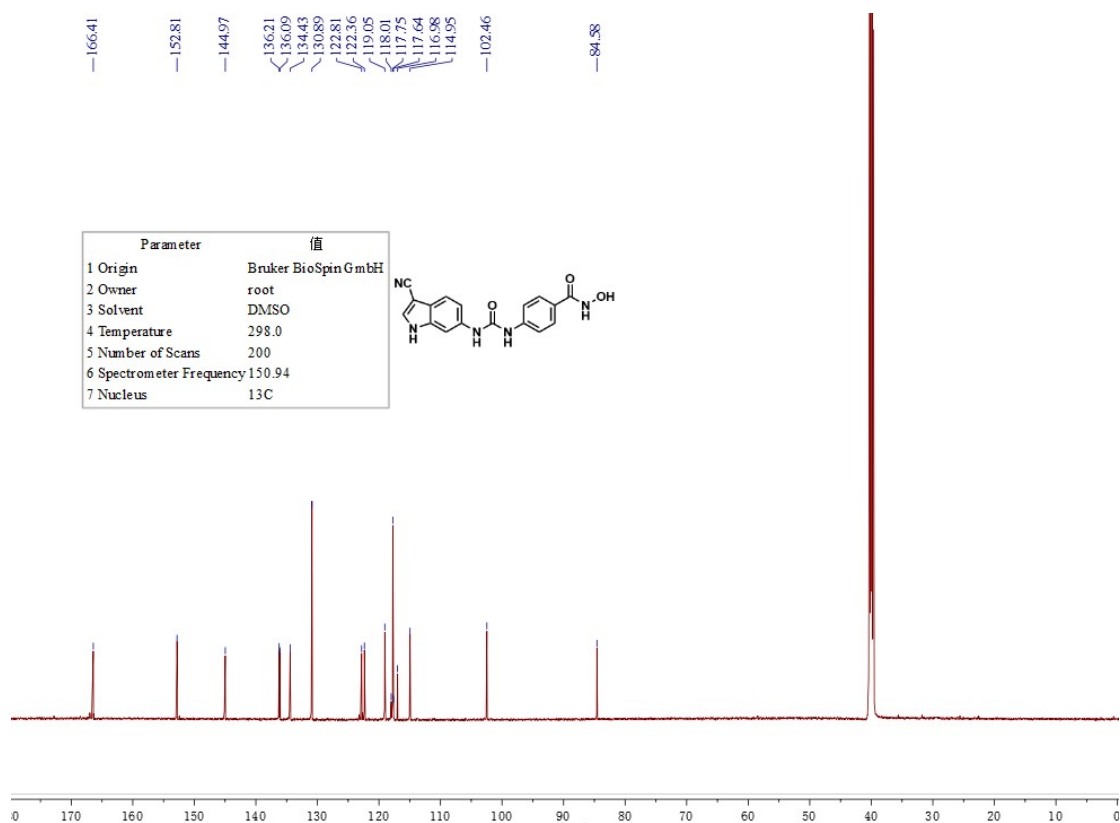




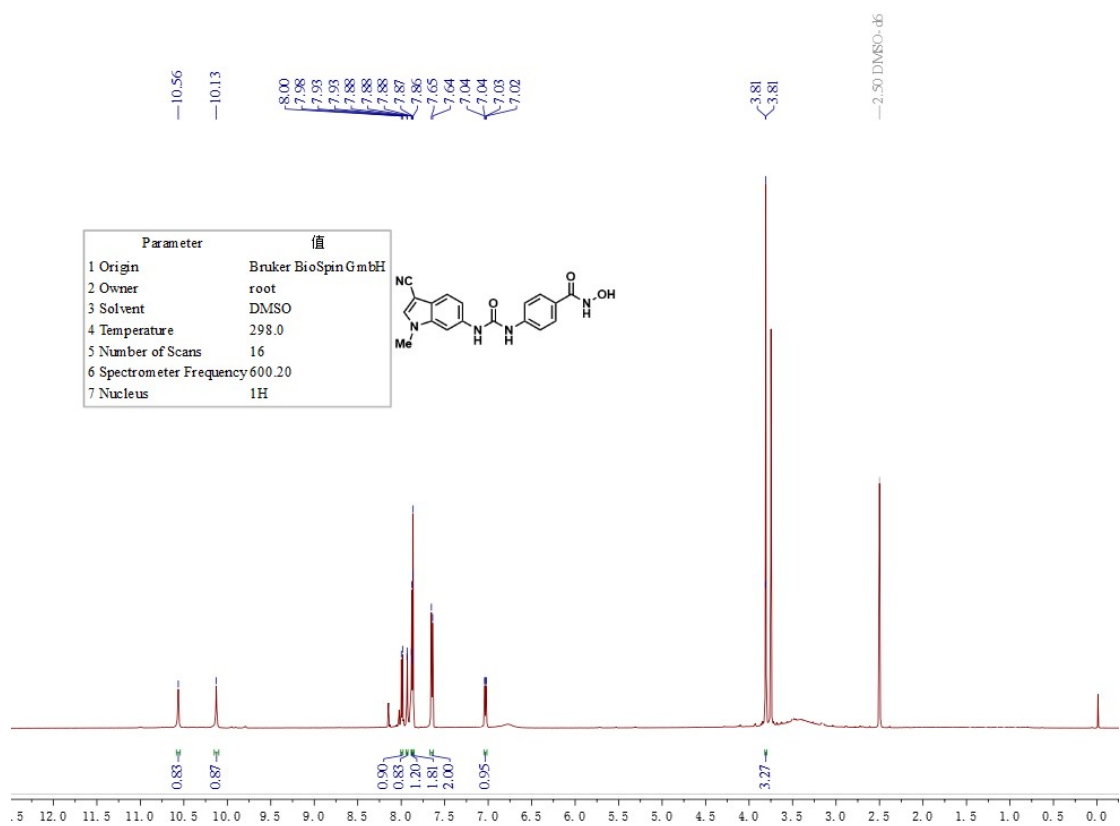
**<sup>1</sup>H-NMR spectrum of compound C13**



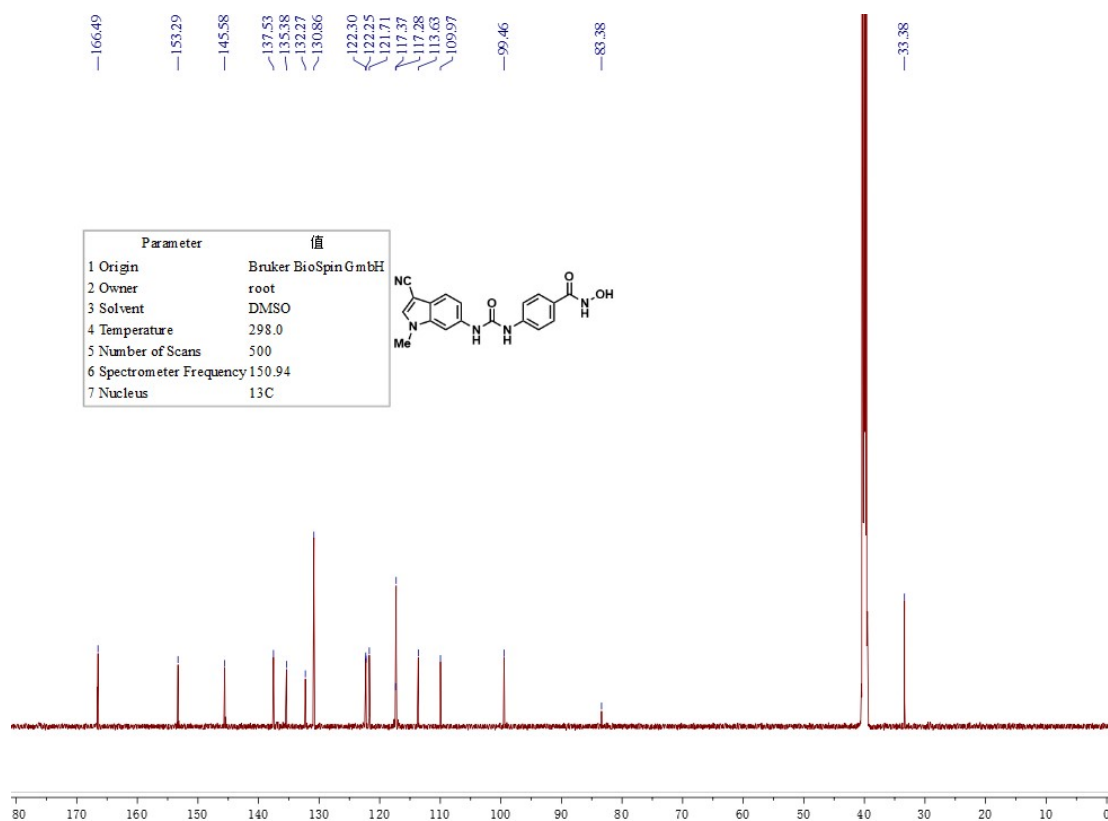
**<sup>13</sup>C-NMR spectrum of compound C13**



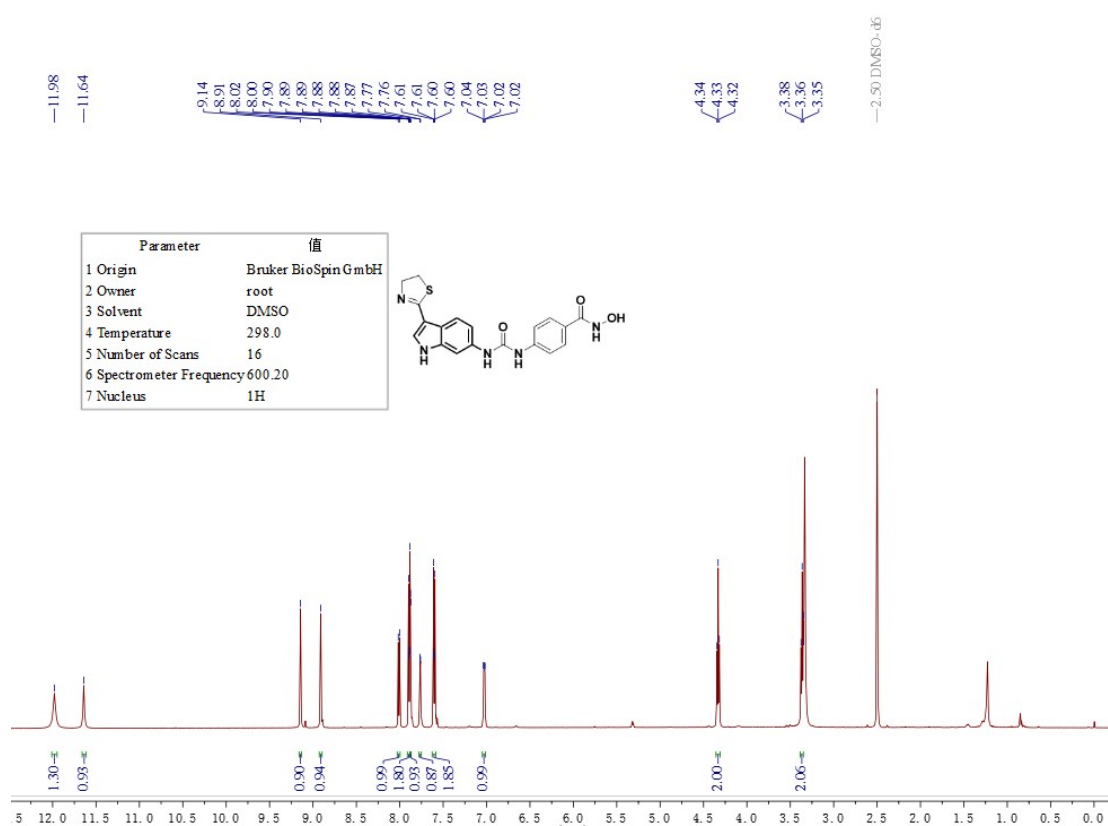
**<sup>1</sup>H-NMR spectrum of compound C14**



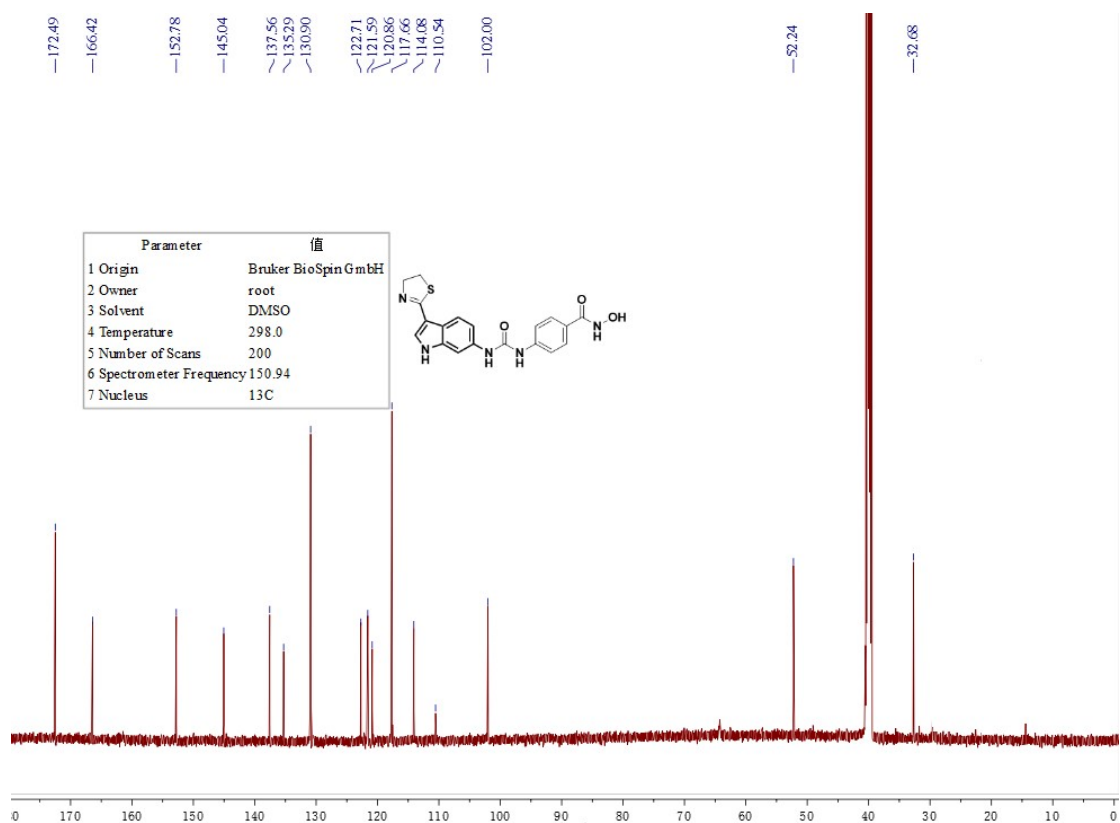
**<sup>13</sup>C-NMR spectrum of compound C14**



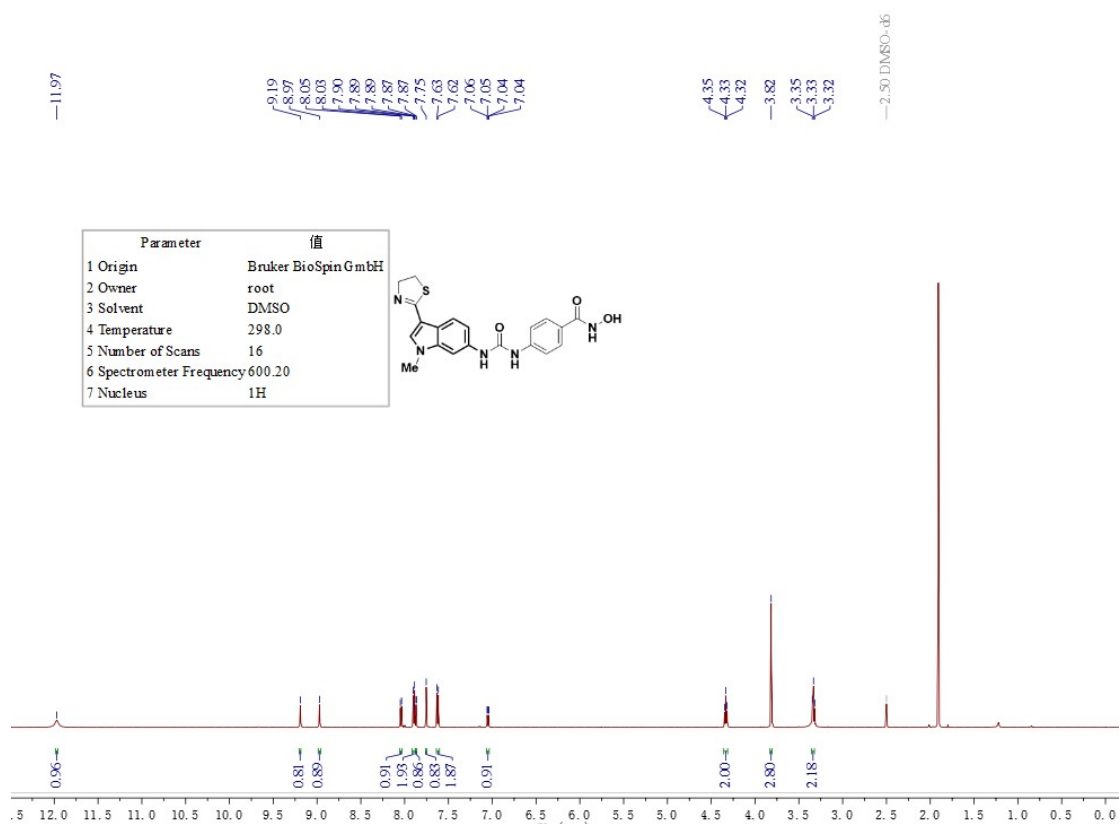
<sup>1</sup>H-NMR spectrum of compound C15



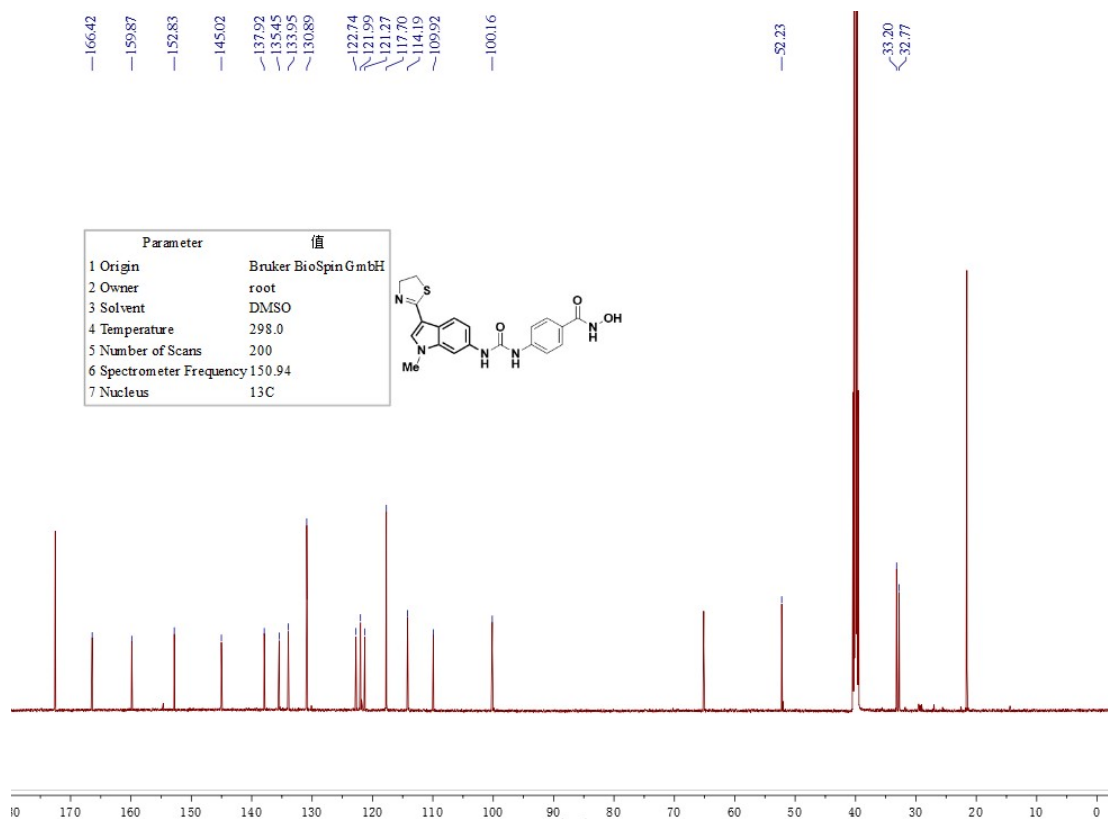
<sup>13</sup>C-NMR spectrum of compound C15



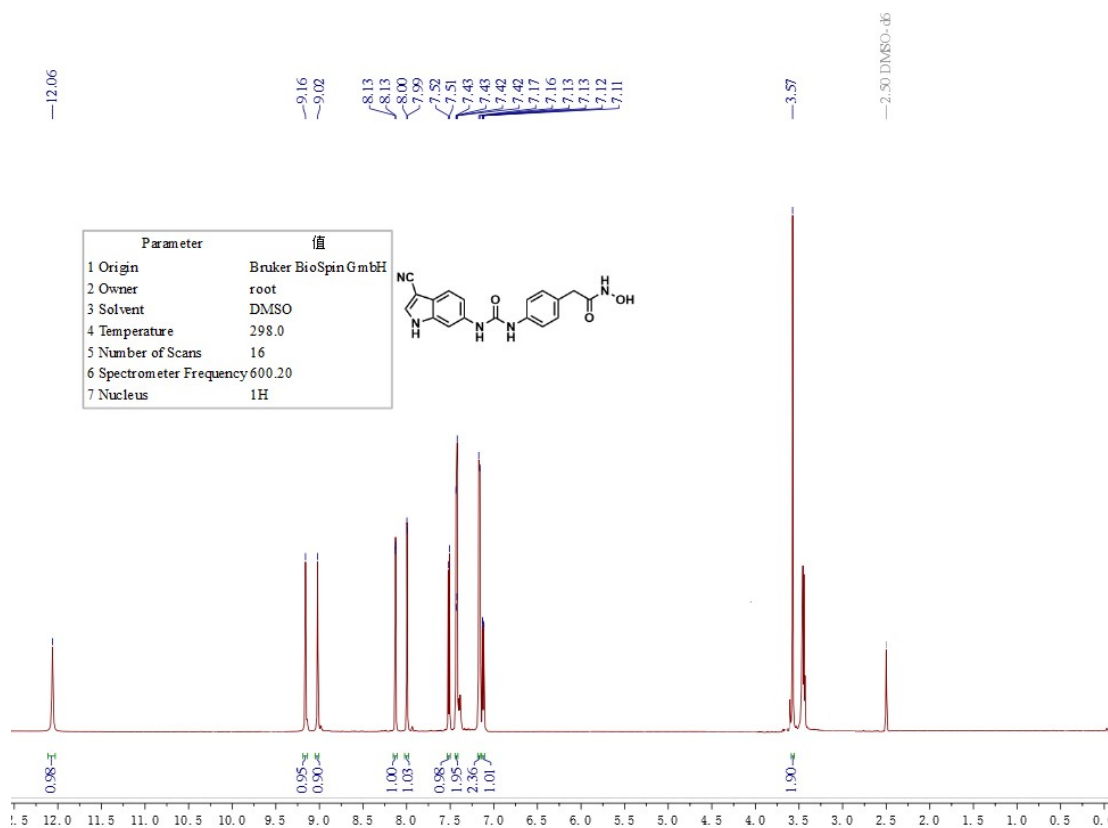
**<sup>1</sup>H-NMR spectrum of compound C16**



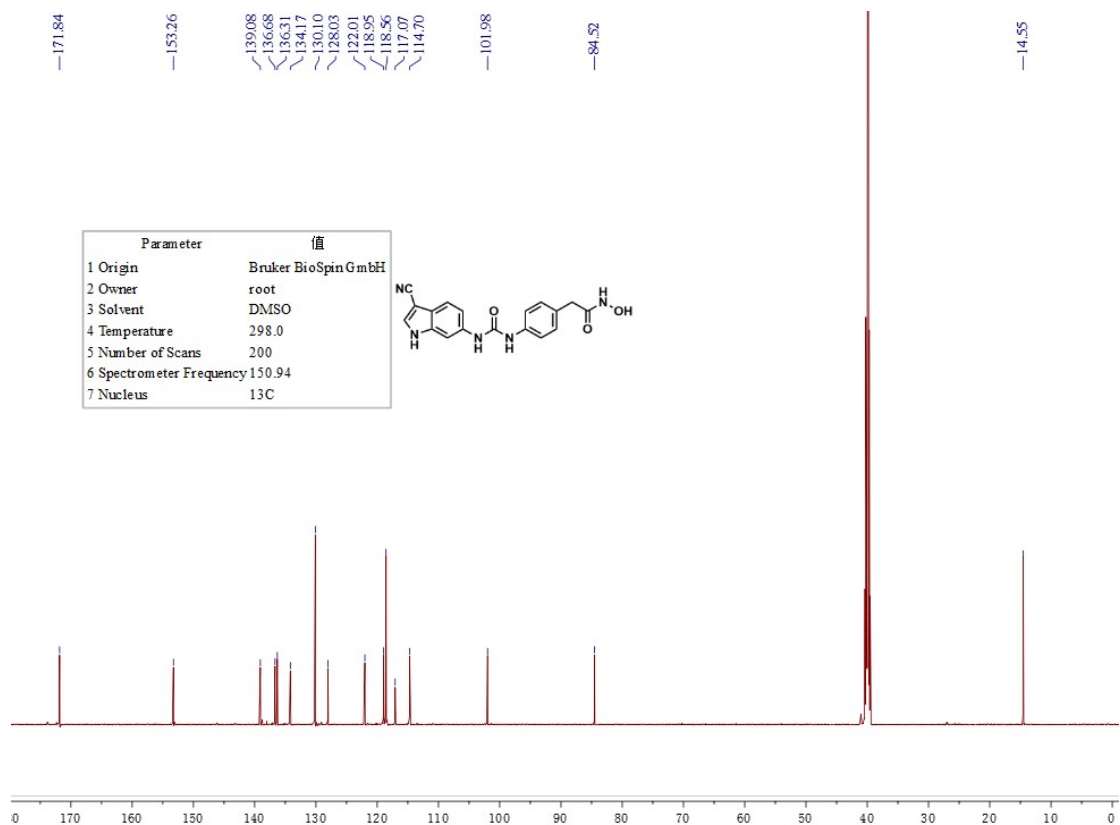
**<sup>13</sup>C-NMR spectrum of compound C16**



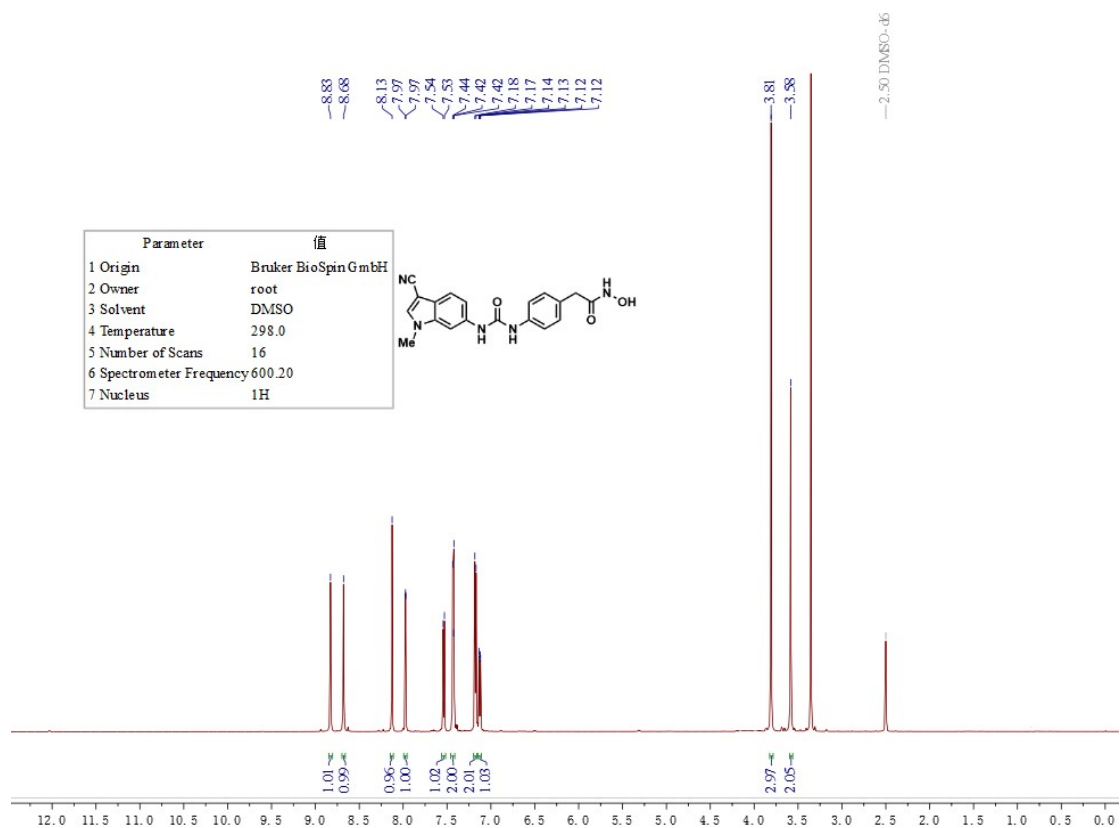
<sup>1</sup>H-NMR spectrum of compound C17



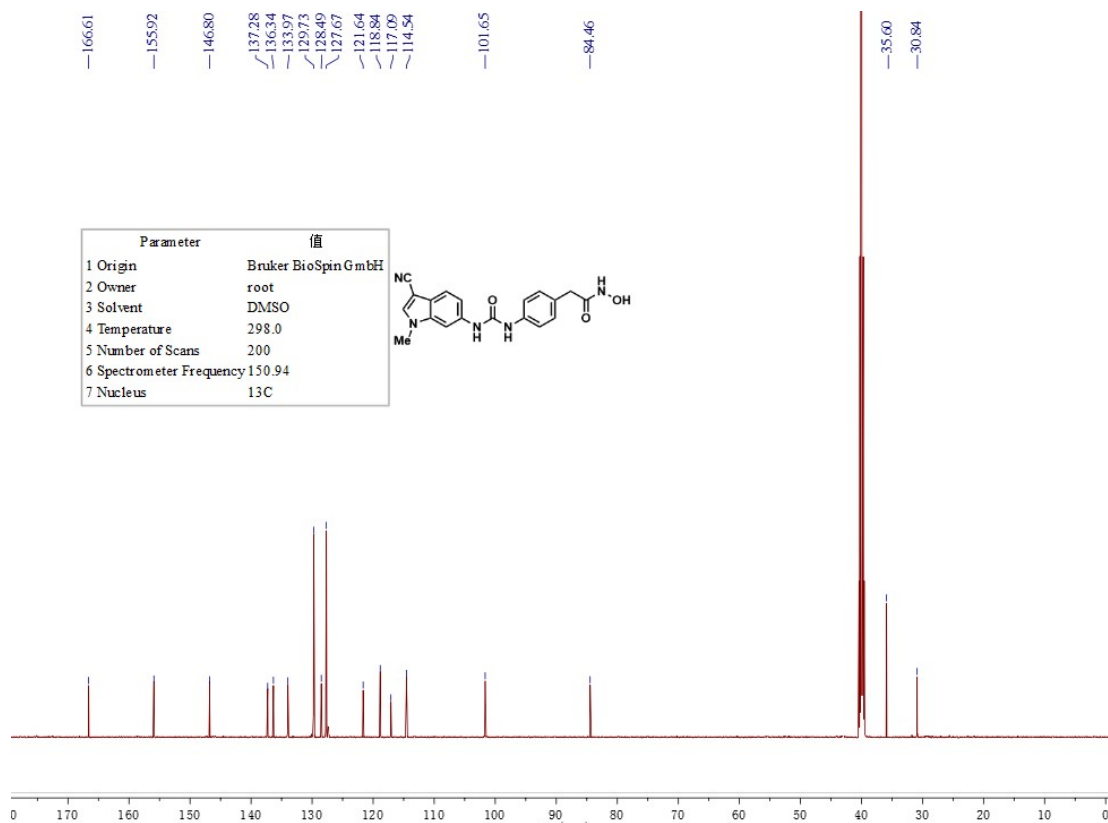
<sup>13</sup>C-NMR spectrum of compound C17



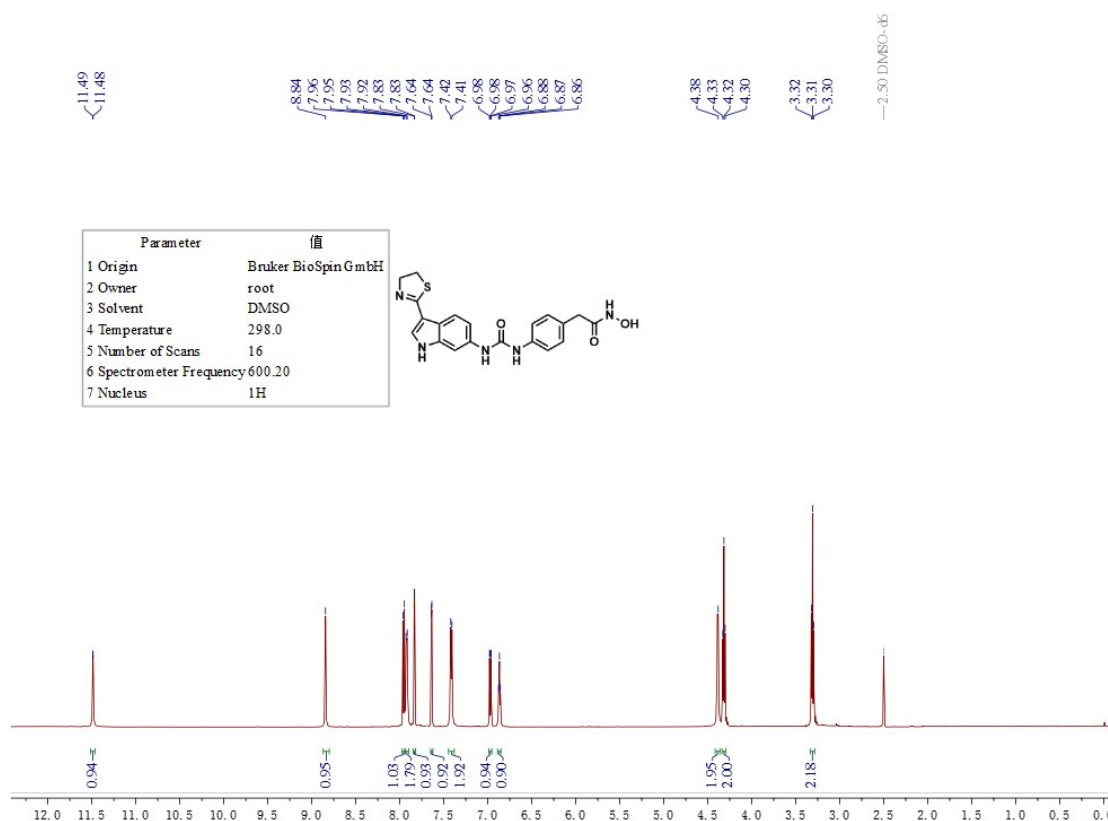
<sup>1</sup>H-NMR spectrum of compound C18



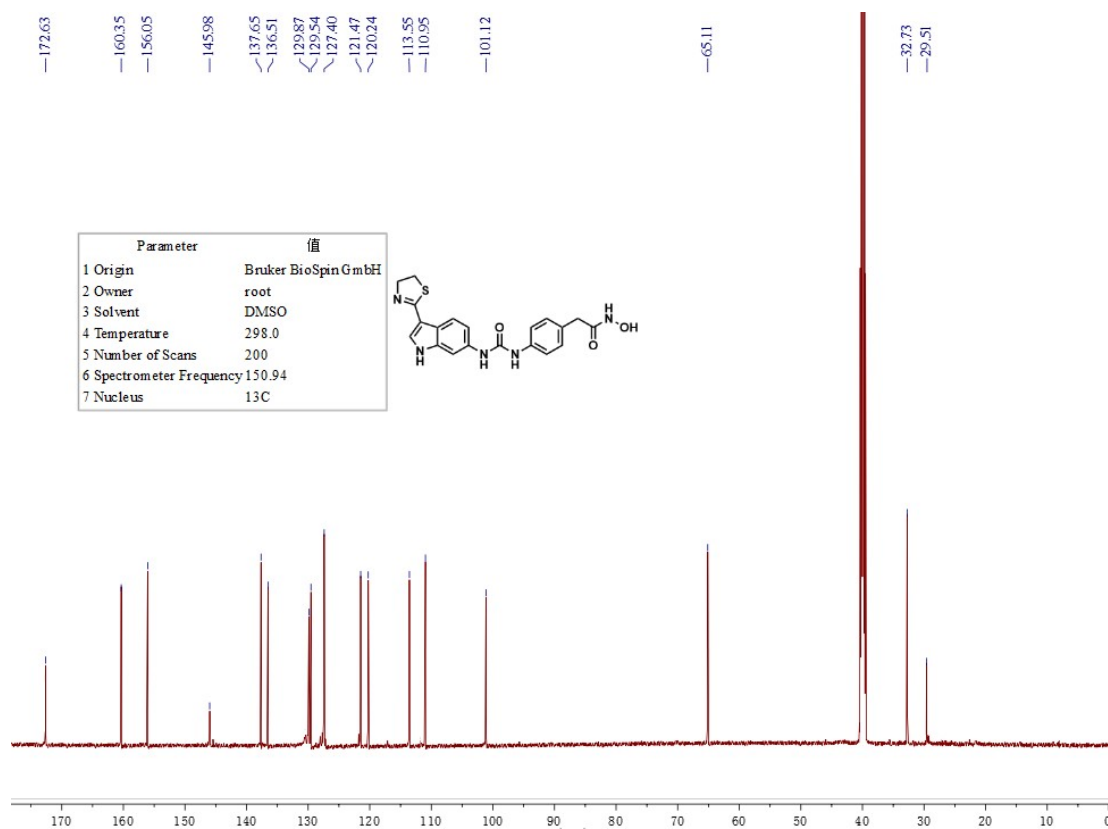
<sup>13</sup>C-NMR spectrum of compound C18



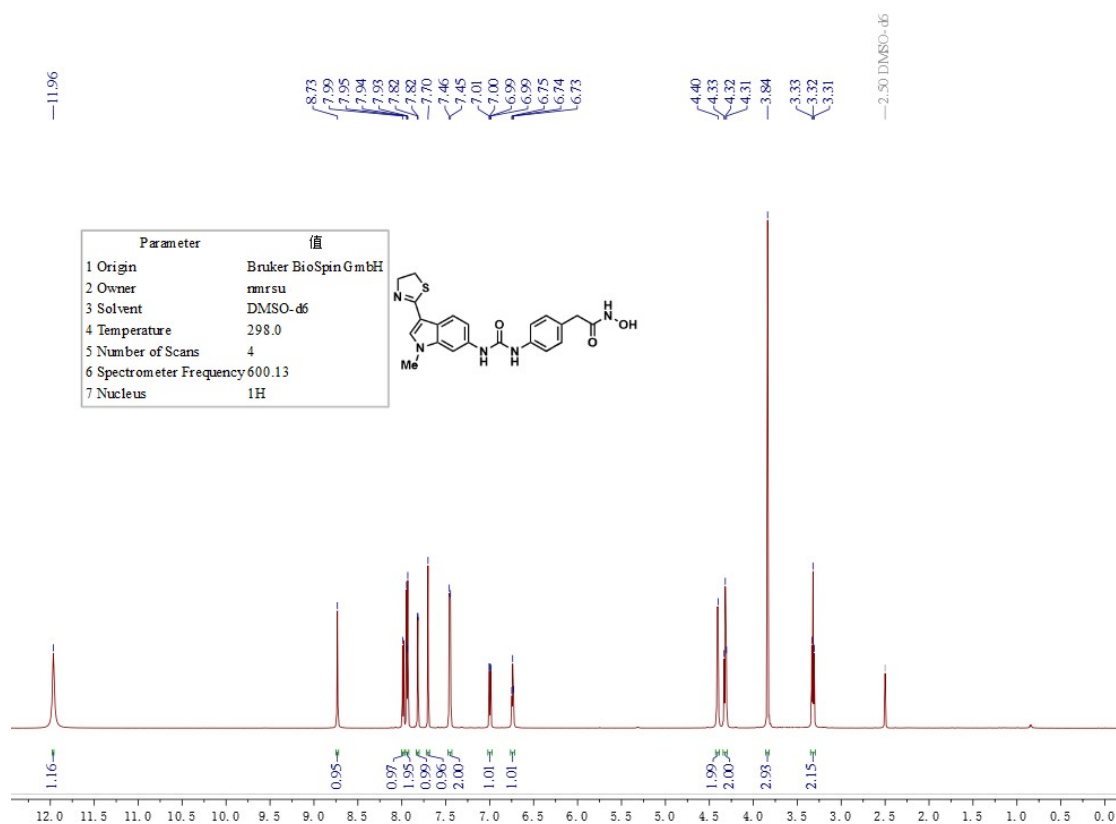
**<sup>1</sup>H-NMR spectrum of compound C19**



**<sup>13</sup>C-NMR spectrum of compound C19**

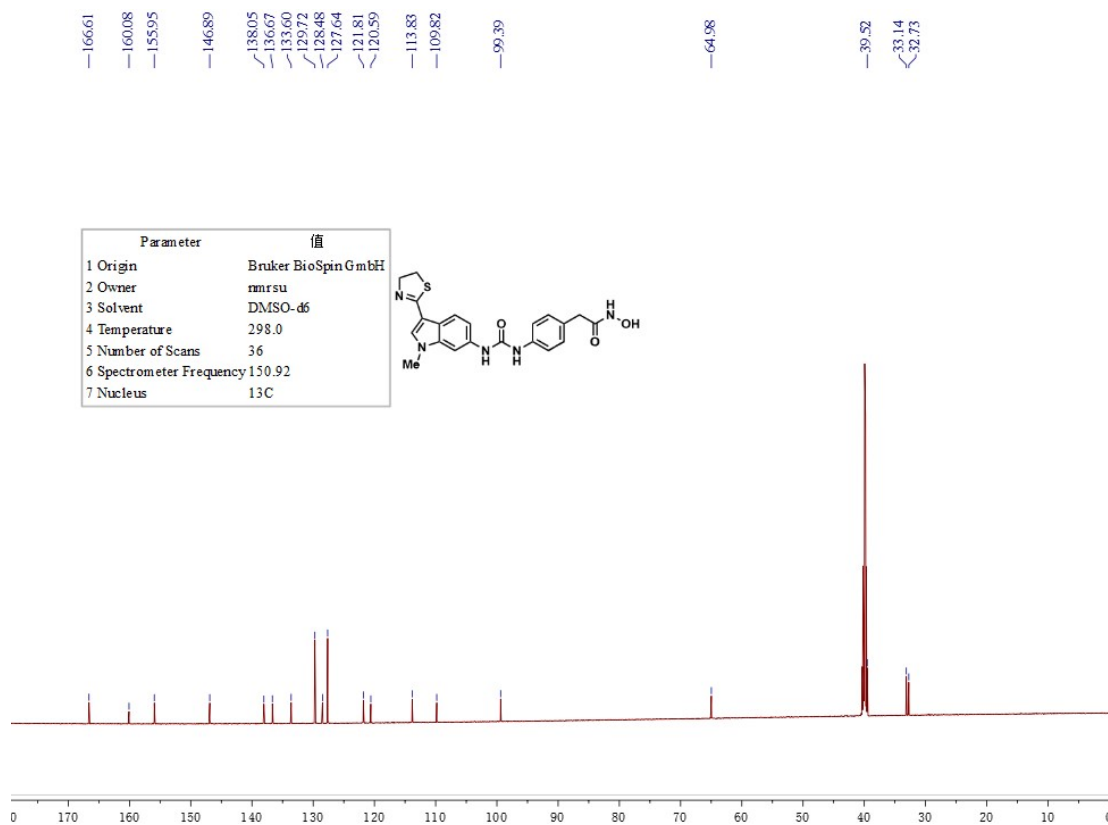


**<sup>1</sup>H-NMR spectrum of compound C20**

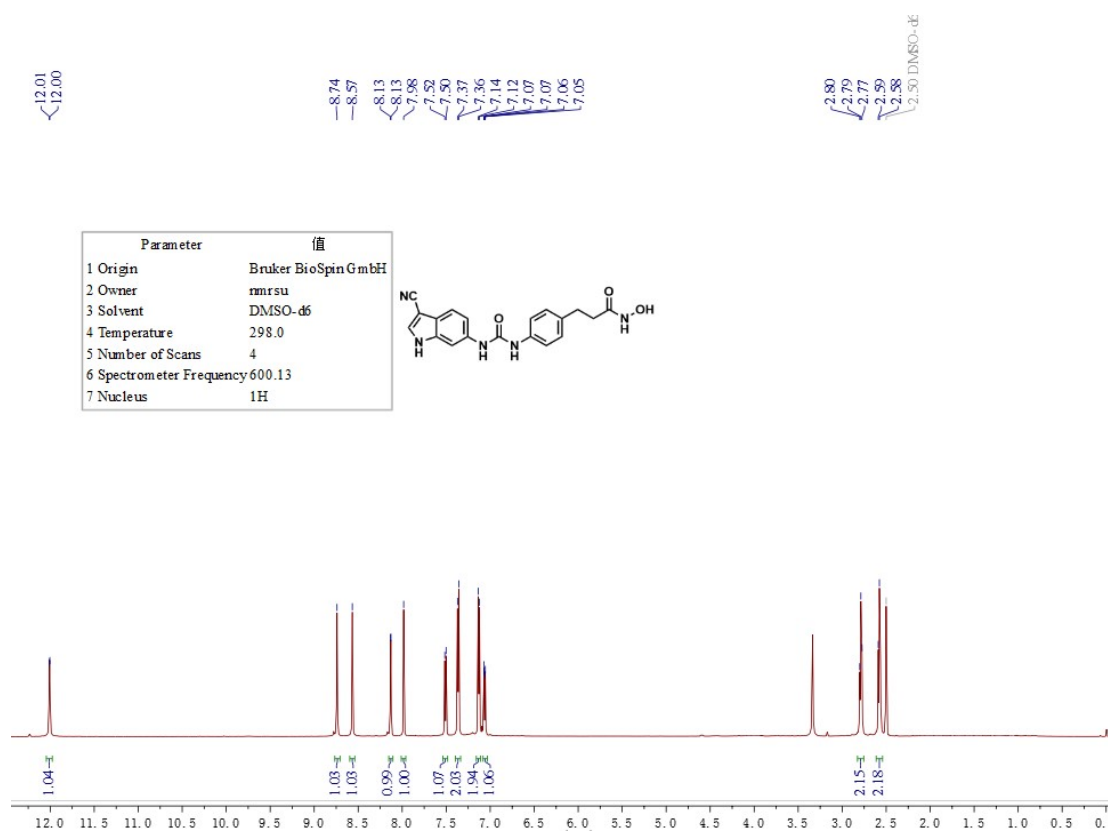


**<sup>13</sup>C-NMR spectrum of compound C20**

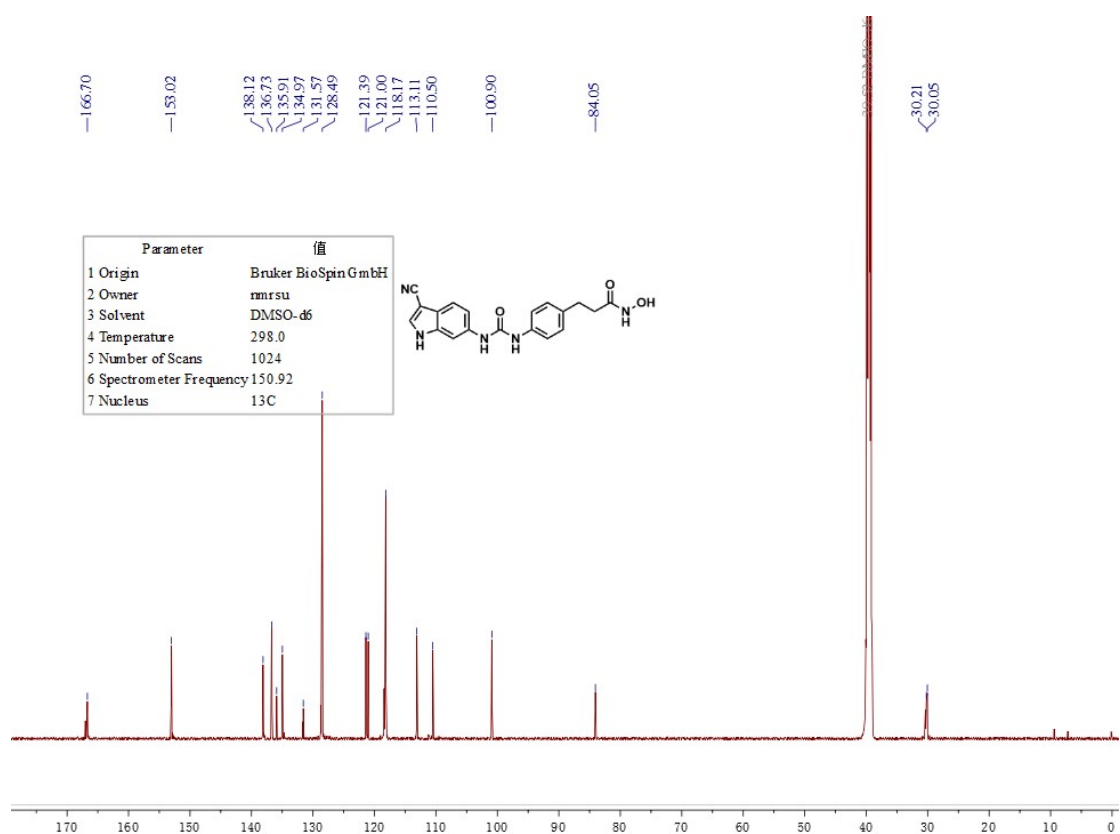




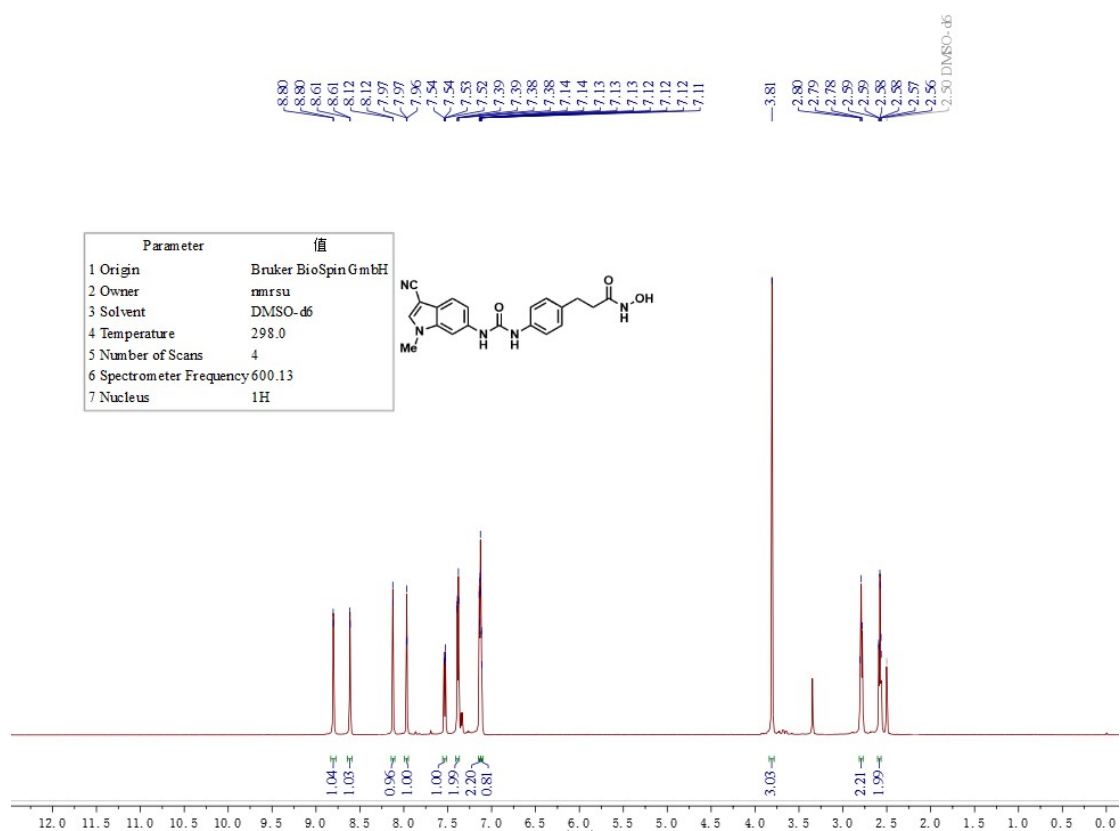
<sup>1</sup>H-NMR spectrum of compound C21



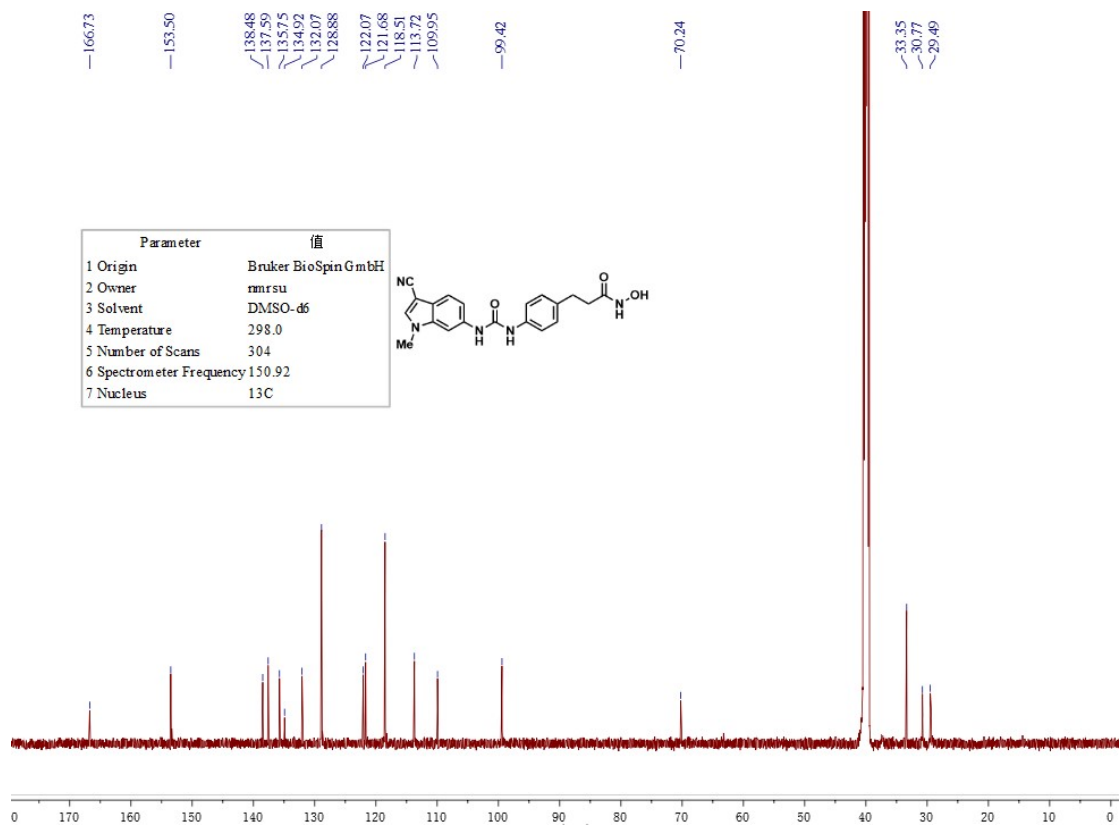
<sup>13</sup>C-NMR spectrum of compound C21



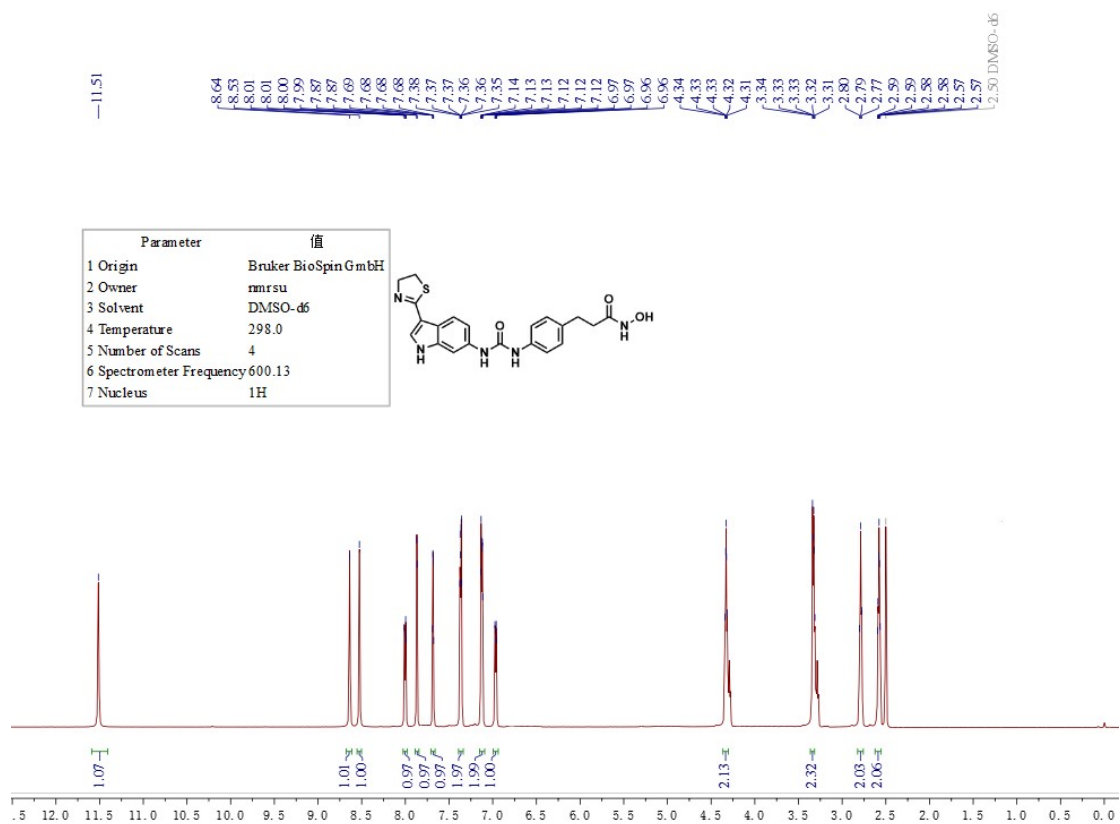
**<sup>1</sup>H-NMR spectrum of compound C22**



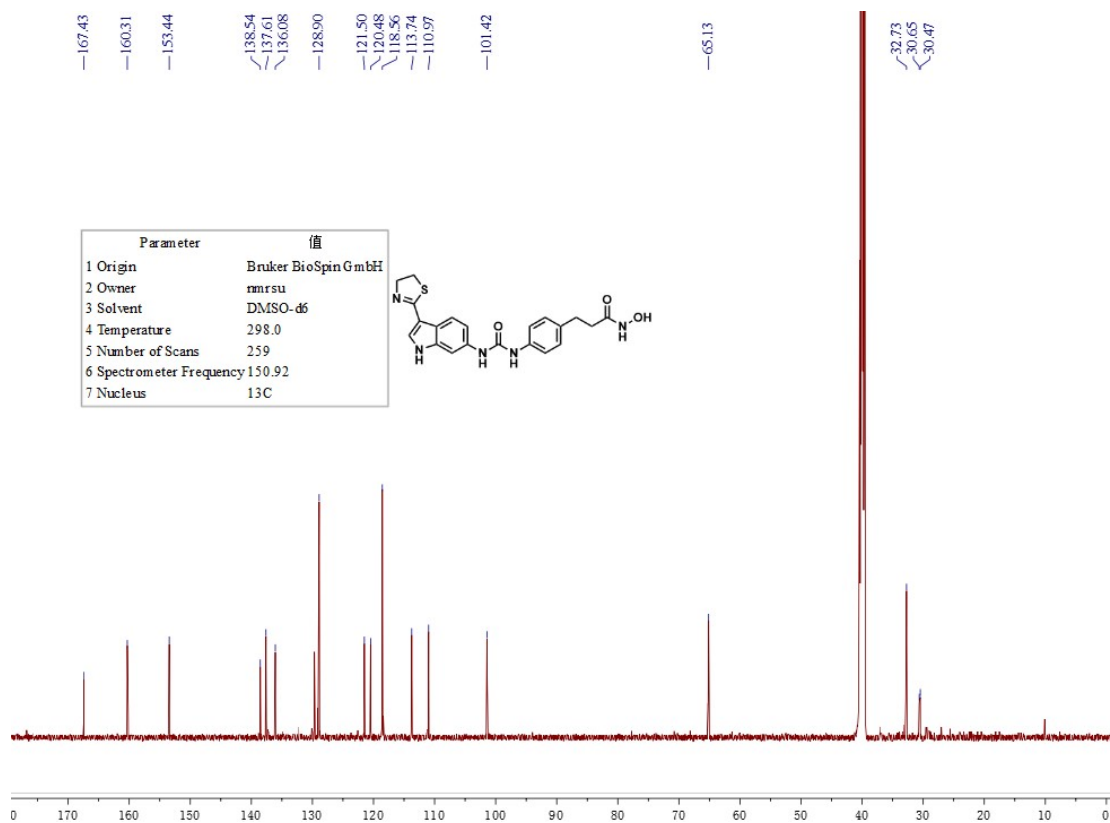
**<sup>13</sup>C-NMR spectrum of compound C22**



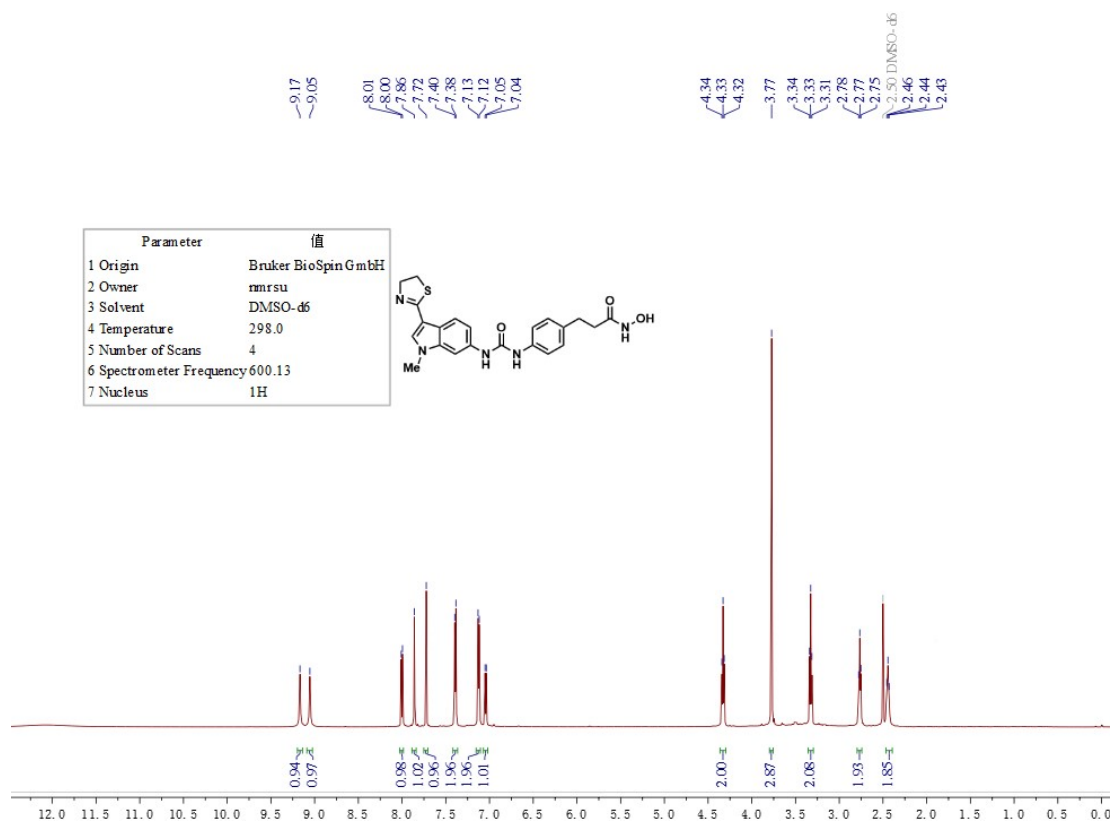
<sup>1</sup>H-NMR spectrum of compound C23



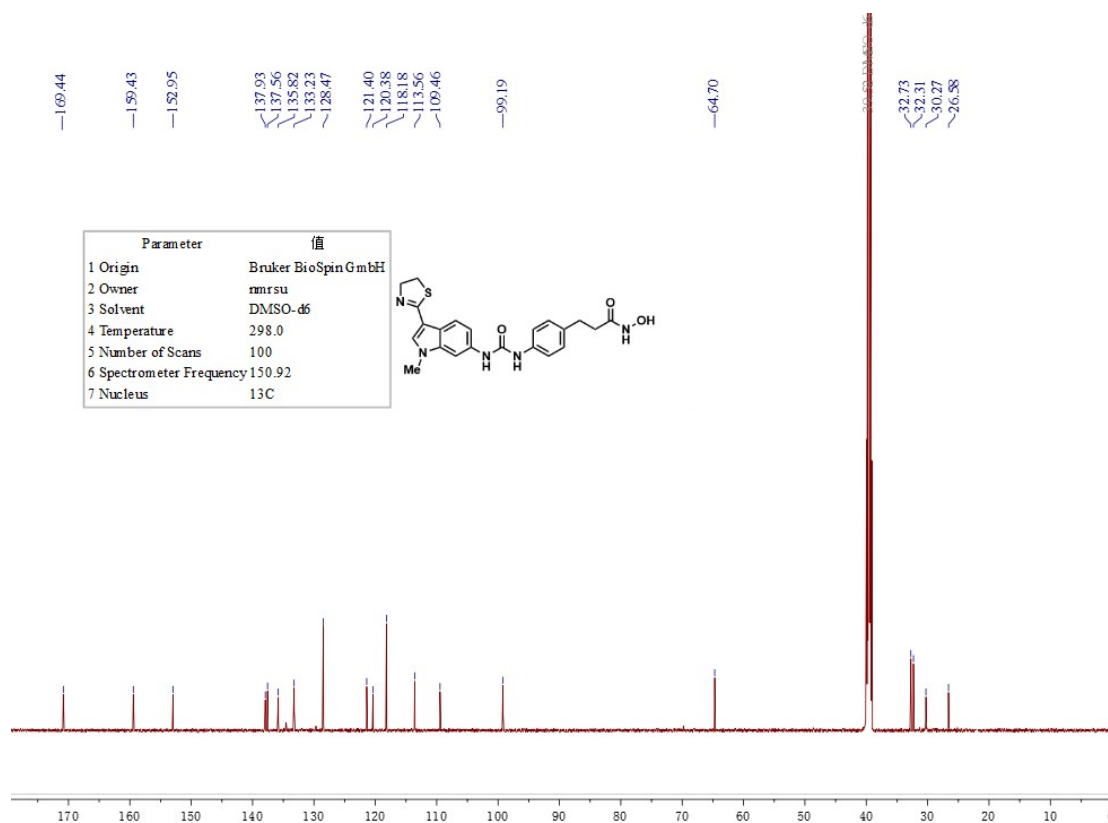
<sup>13</sup>C-NMR spectrum of compound C23



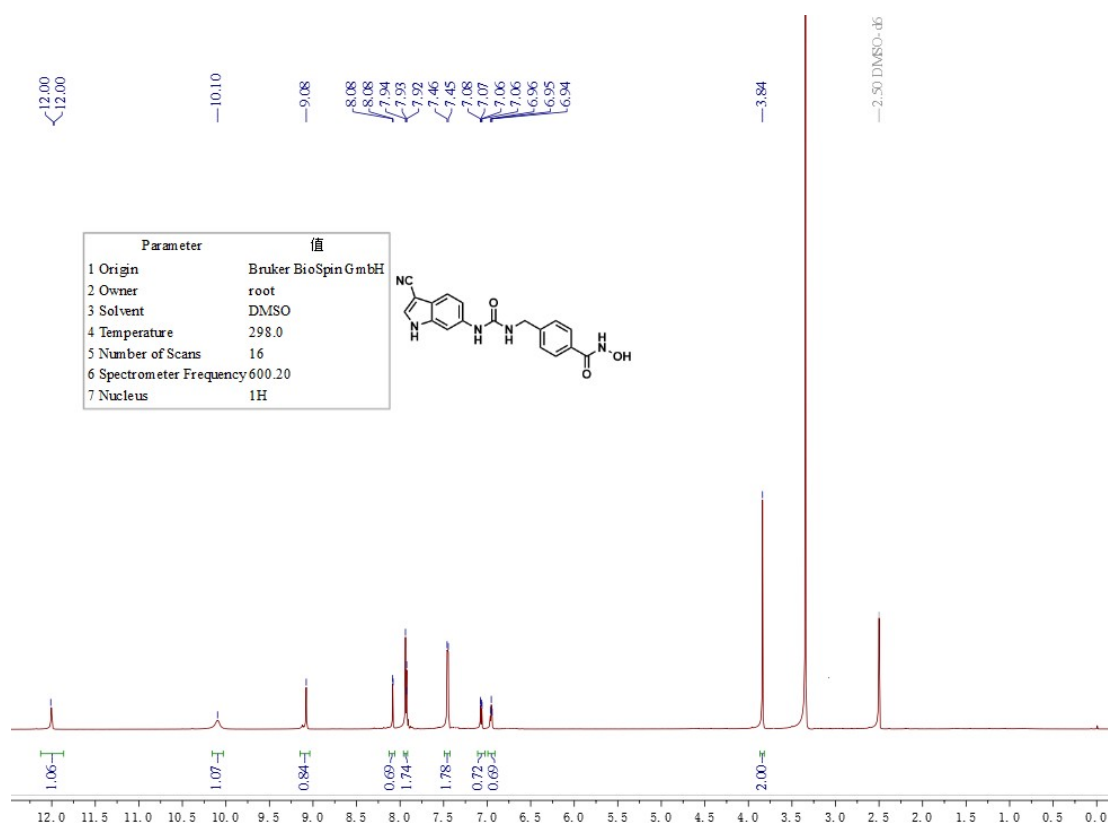
<sup>1</sup>H-NMR spectrum of compound C24



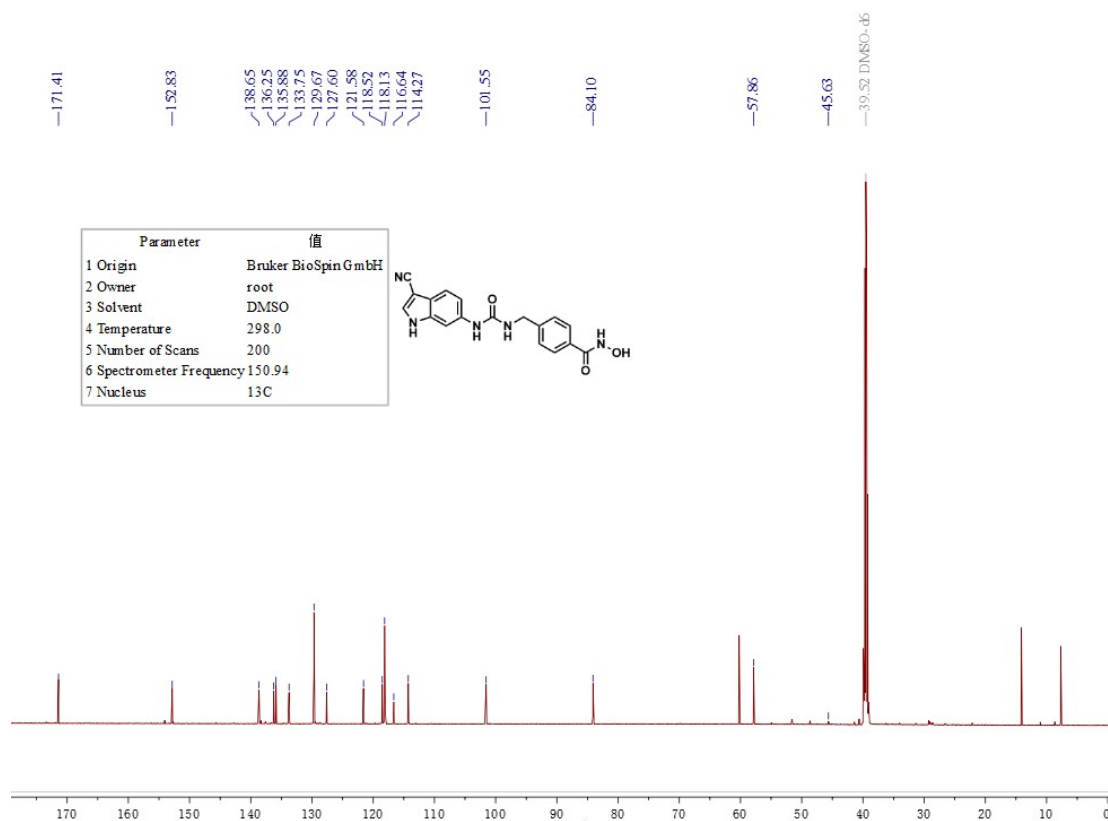
<sup>13</sup>C-NMR spectrum of compound C24



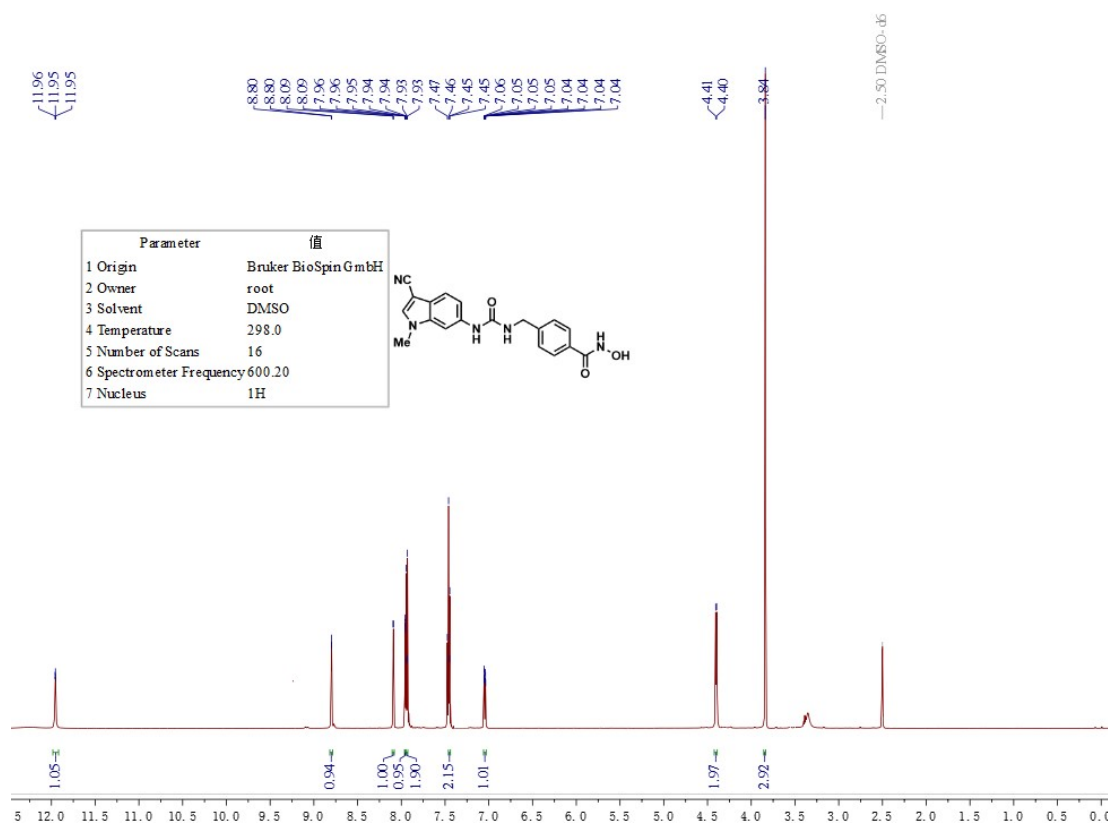
**<sup>1</sup>H-NMR spectrum of compound C25**



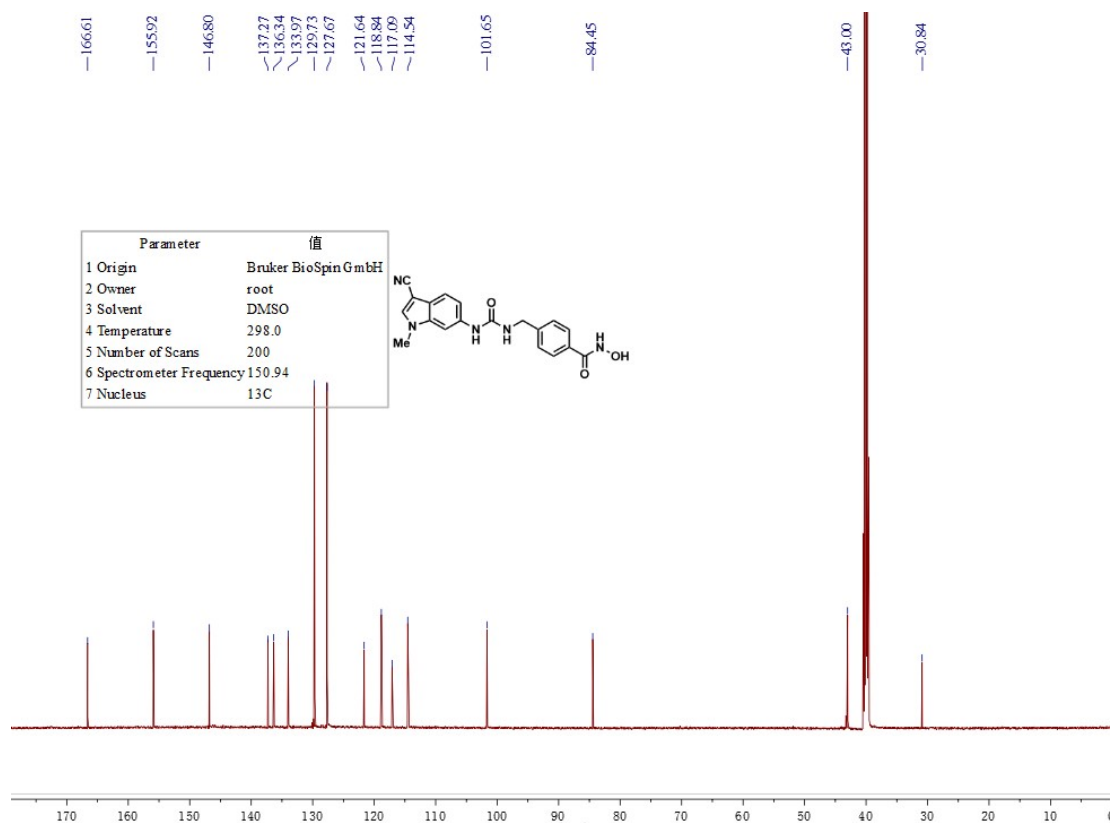
**<sup>13</sup>C-NMR spectrum of compound C25**



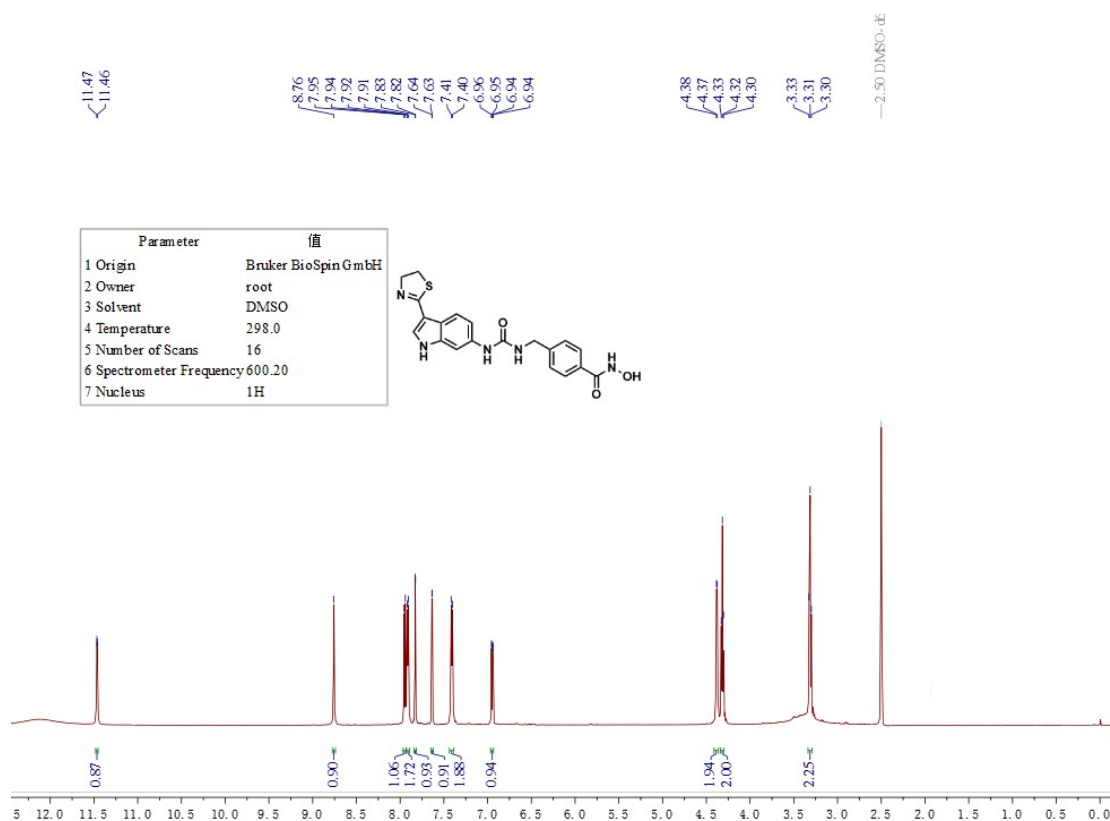
<sup>1</sup>H-NMR spectrum of compound C26



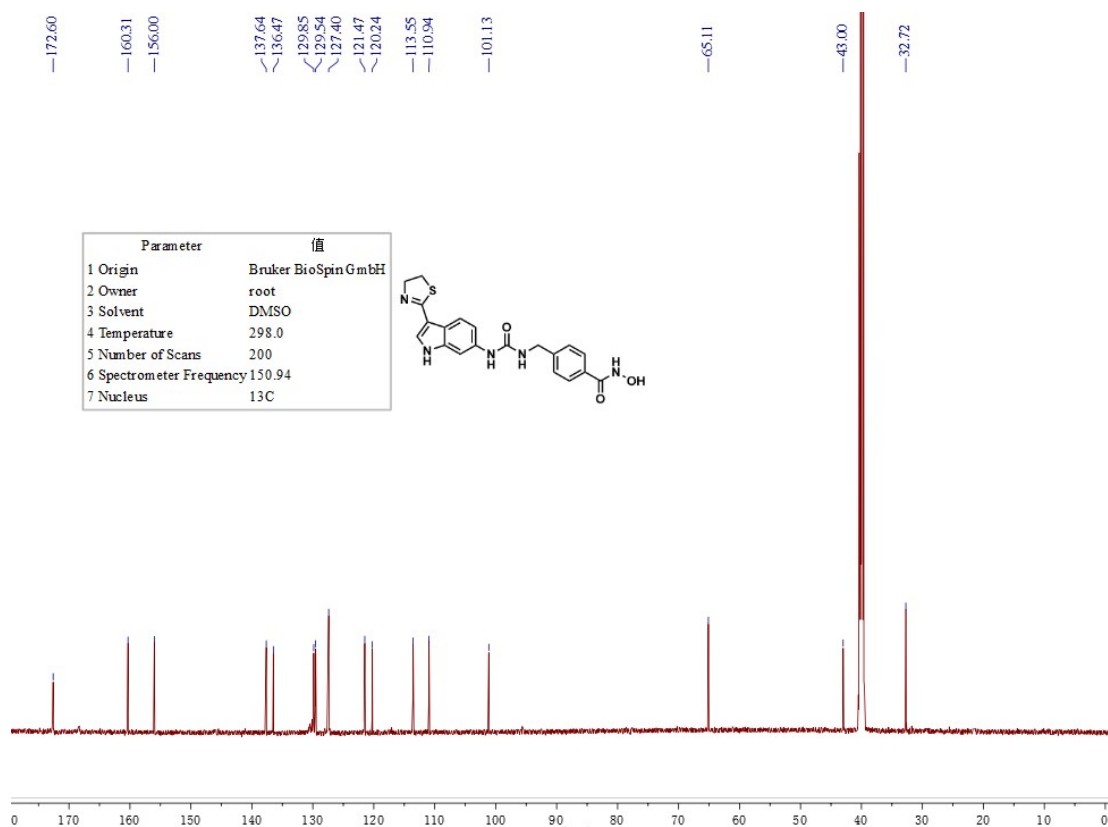
<sup>13</sup>C-NMR spectrum of compound C26



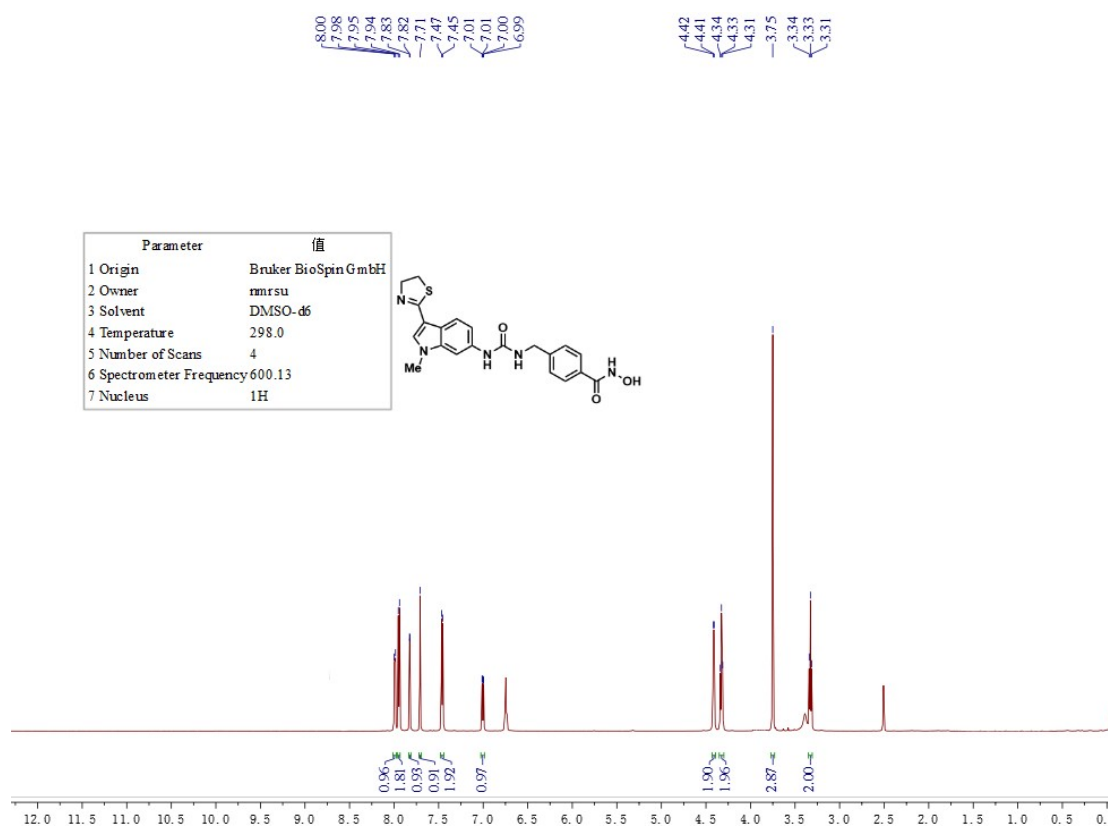
**<sup>1</sup>H-NMR spectrum of compound C27**



**<sup>13</sup>C-NMR spectrum of compound C27**

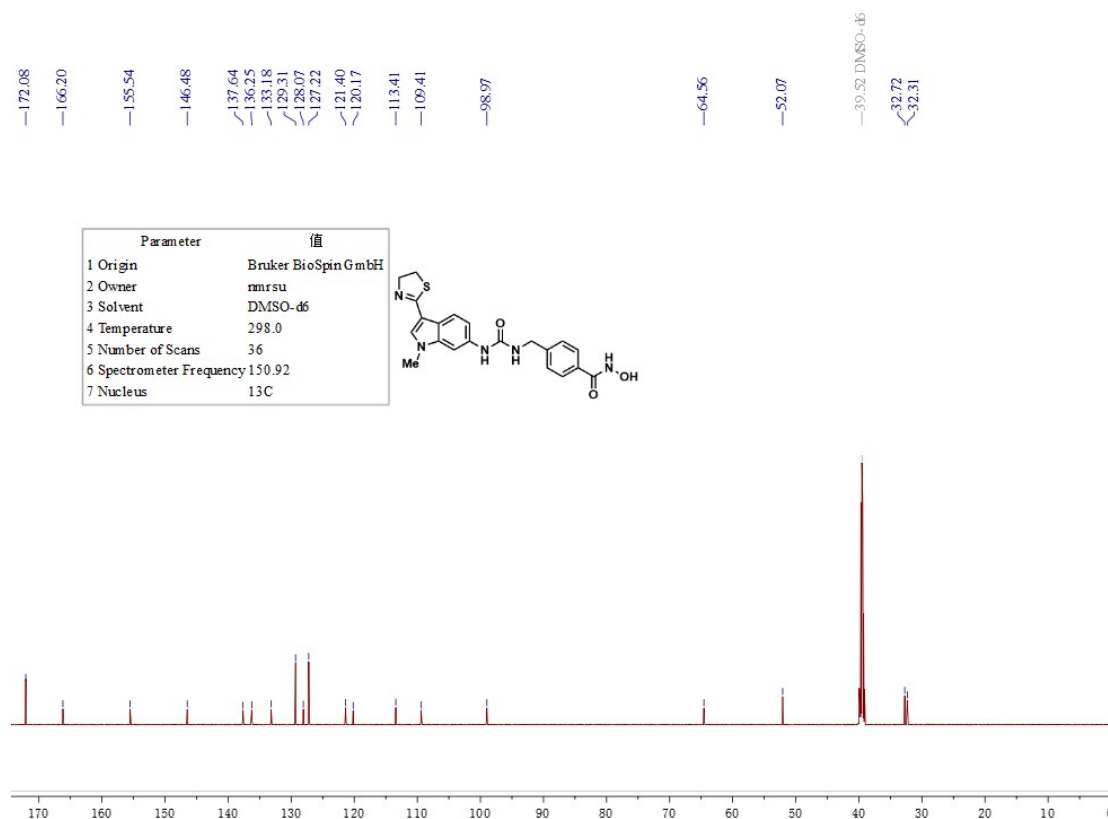


**<sup>1</sup>H-NMR spectrum of compound C28**

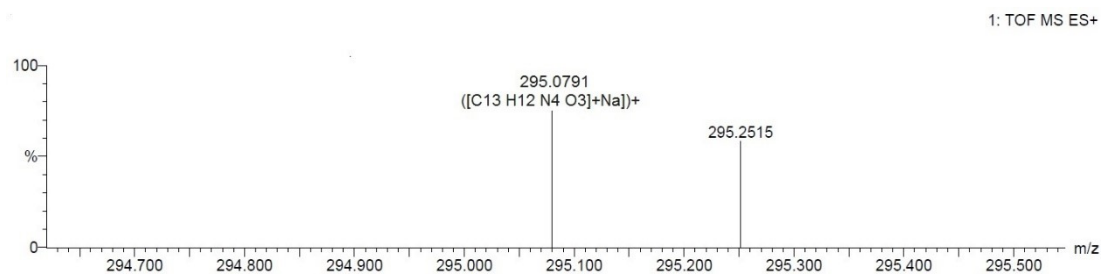


**<sup>13</sup>C-NMR spectrum of compound C28**

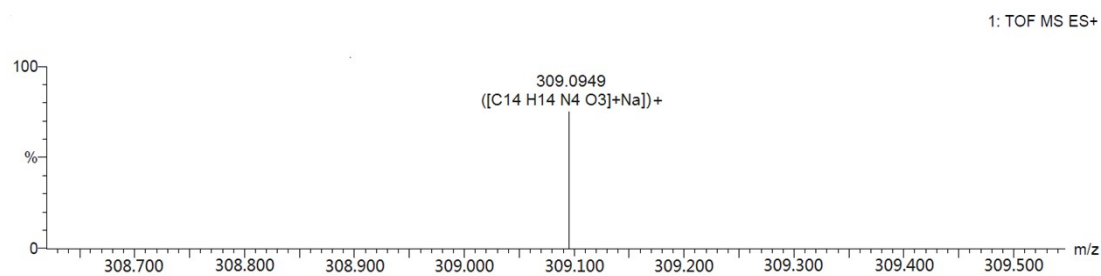




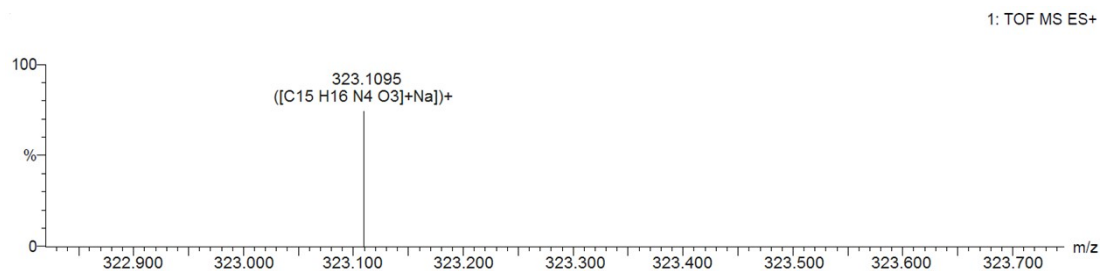
## HRMS (ESI) spectrum of A1-A40,B1-B12 and C1-C28



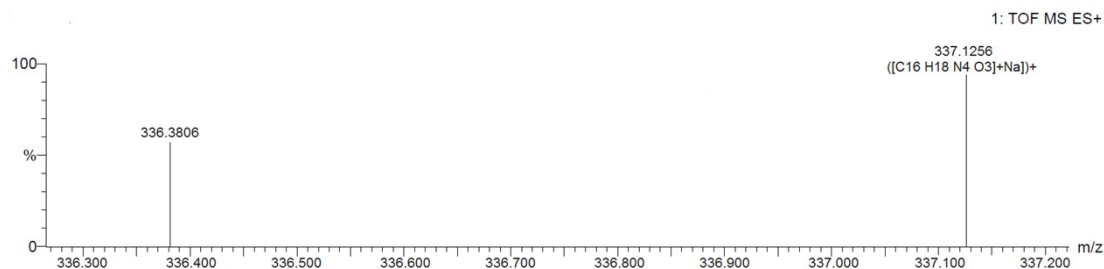
The HRMS spectrum of compound **A1**



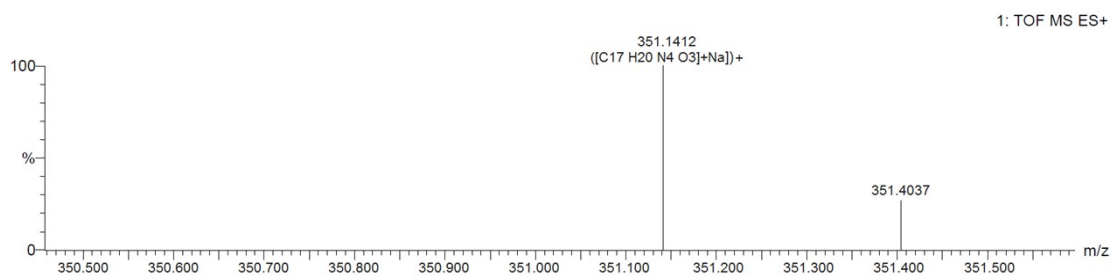
The HRMS spectrum of compound **A2**



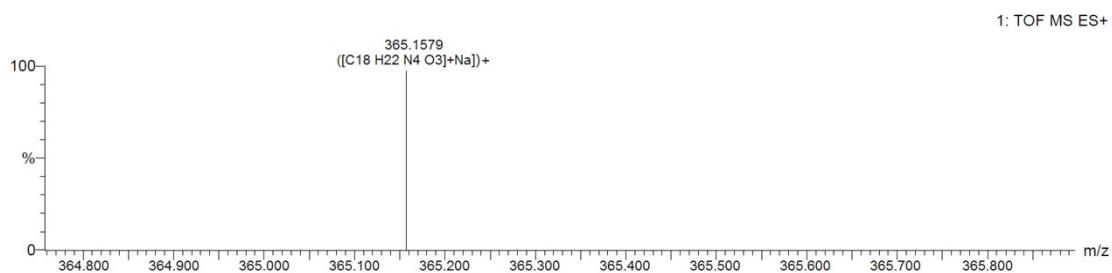
The HRMS spectrum of compound A3



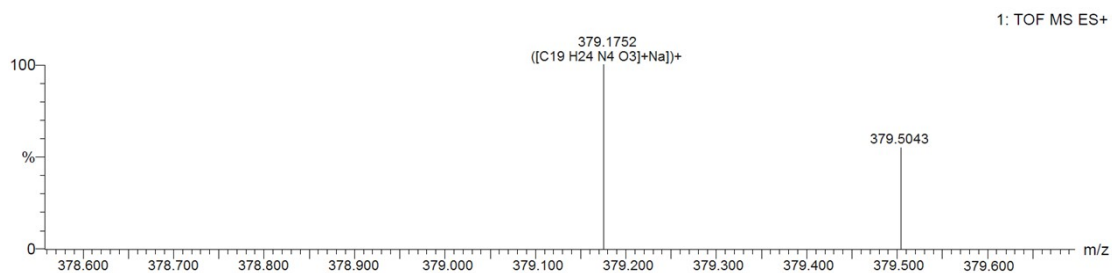
The HRMS spectrum of compound A4



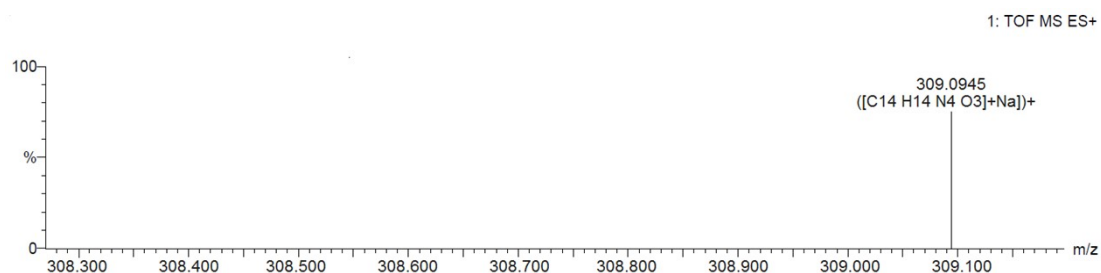
The HRMS spectrum of compound A5



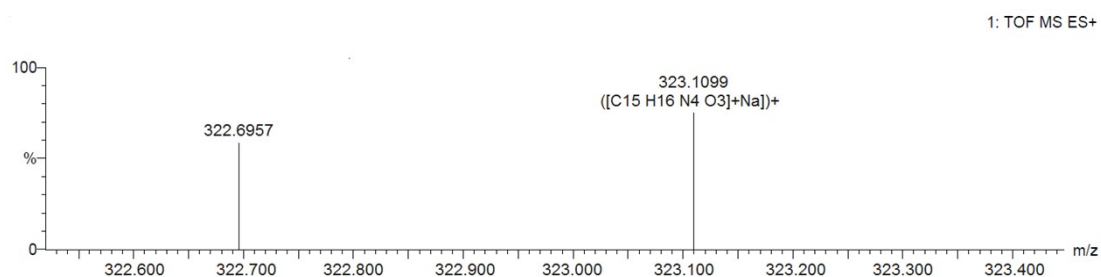
The HRMS spectrum of compound A6



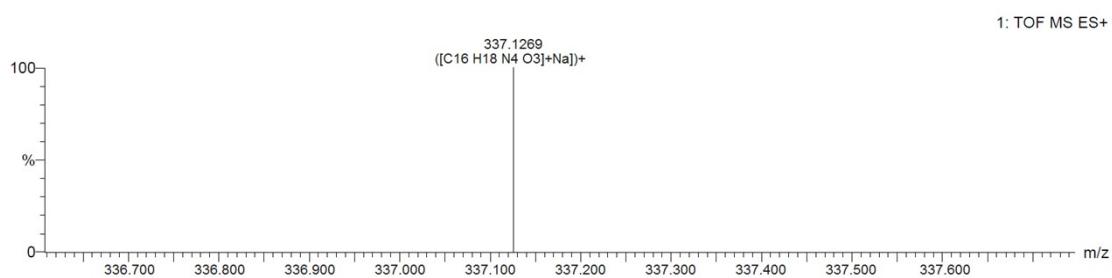
The HRMS spectrum of compound A7



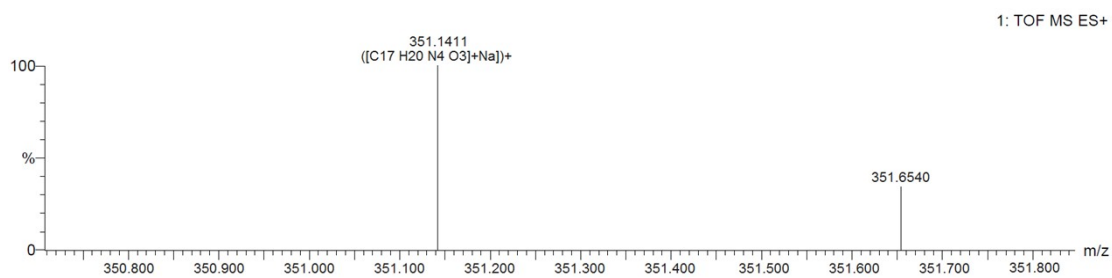
The HRMS spectrum of compound **A8**



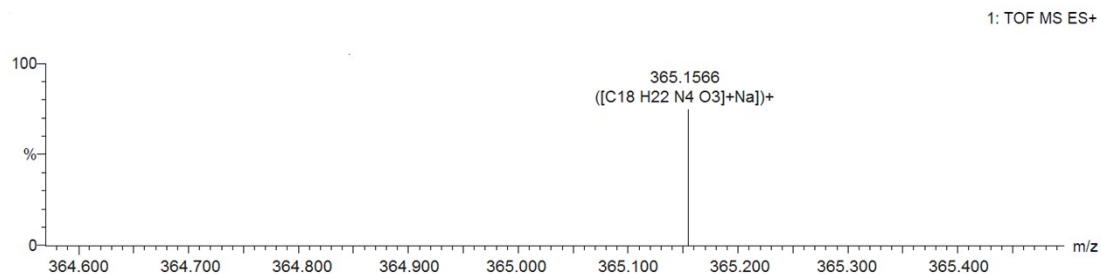
The HRMS spectrum of compound **A9**



The HRMS spectrum of compound **A10**

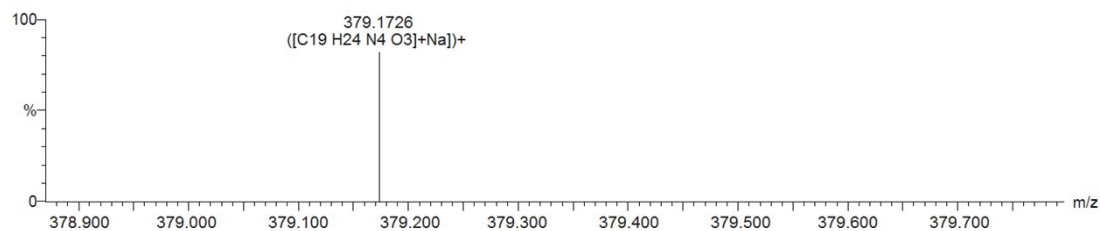


The HRMS spectrum of compound **A11**



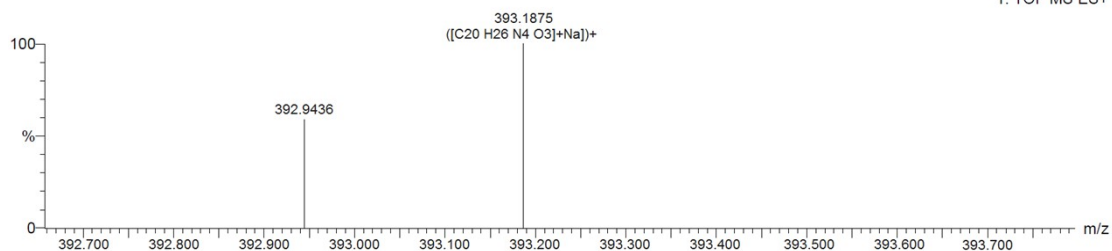
The HRMS spectrum of compound **A12**

1: TOF MS ES+



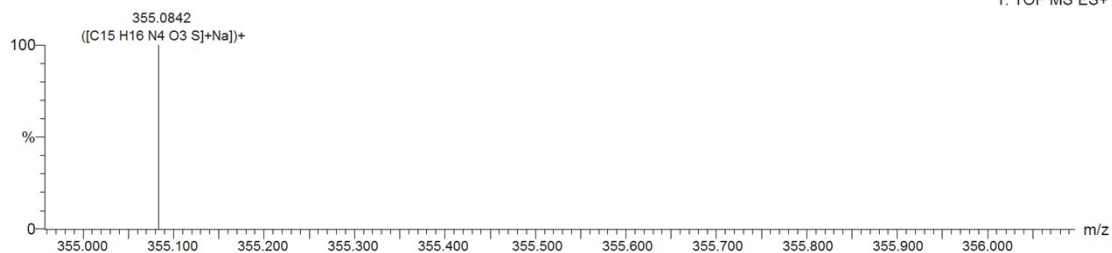
The HRMS spectrum of compound A13

1: TOF MS ES+



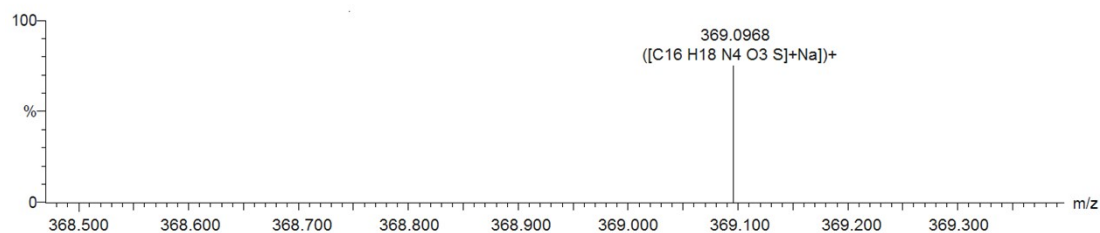
The HRMS spectrum of compound A14

1: TOF MS ES+



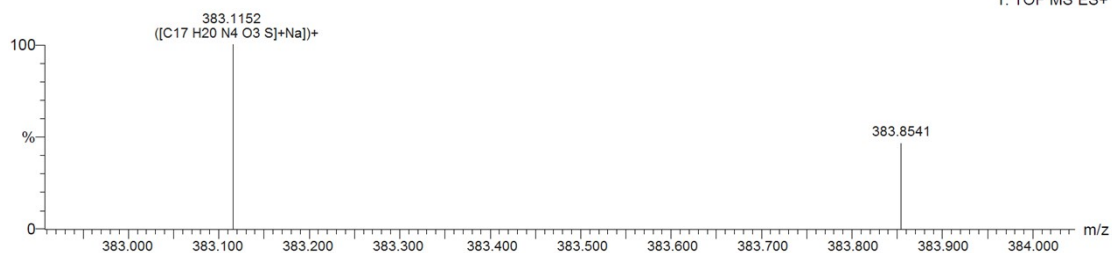
The HRMS spectrum of compound A15

1: TOF MS ES+

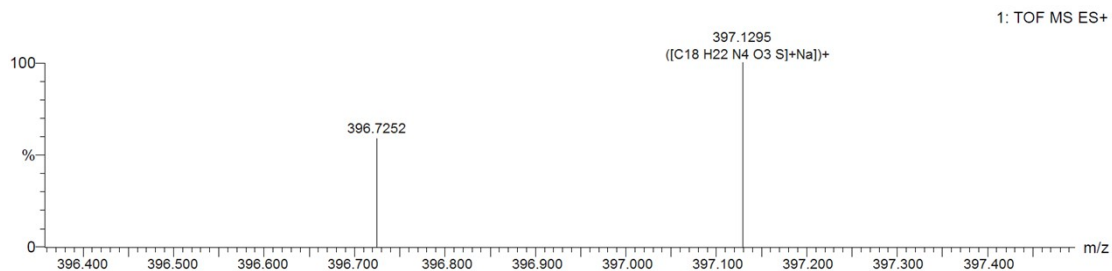


The HRMS spectrum of compound A16

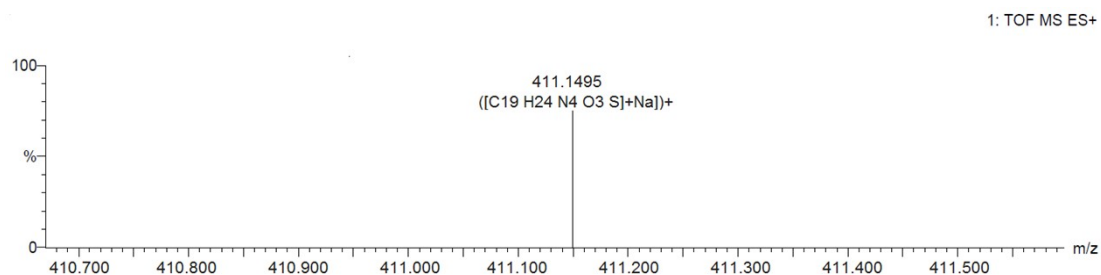
1: TOF MS ES+



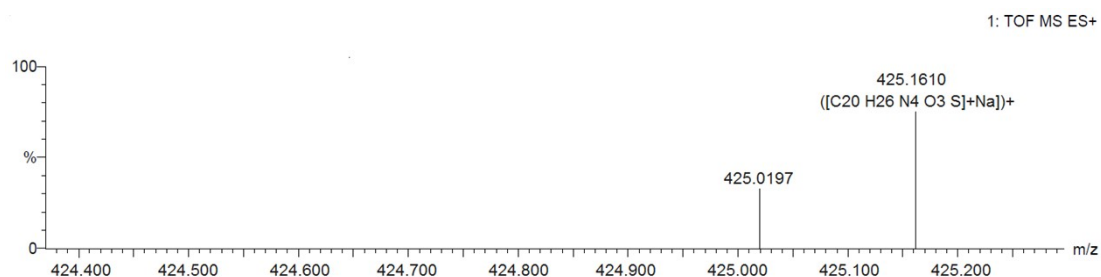
The HRMS spectrum of compound A17



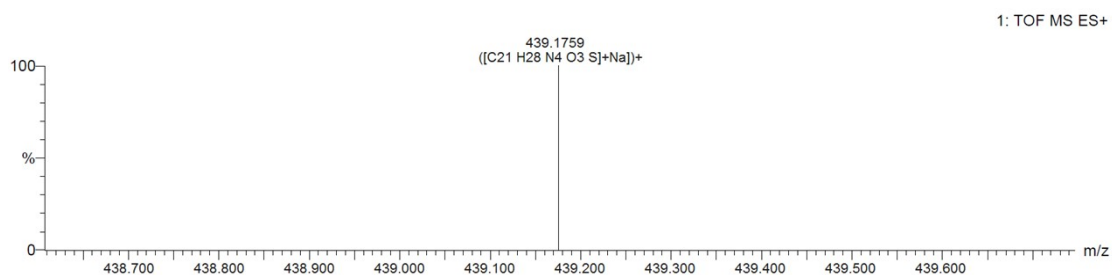
The HRMS spectrum of compound A18



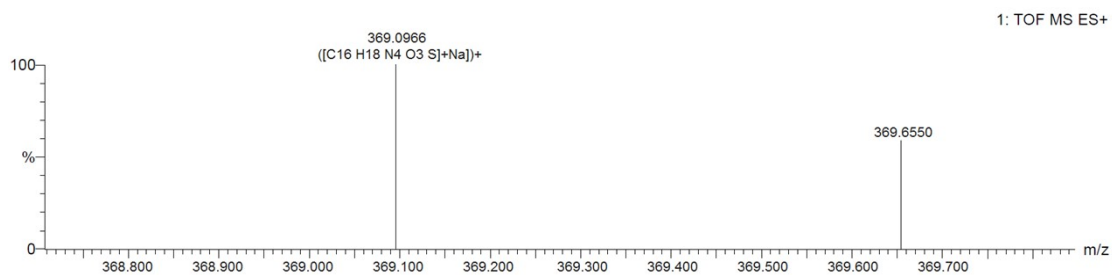
The HRMS spectrum of compound A19



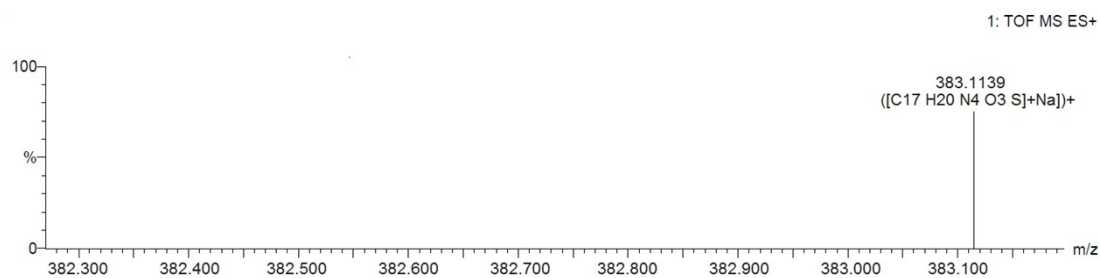
The HRMS spectrum of compound A20



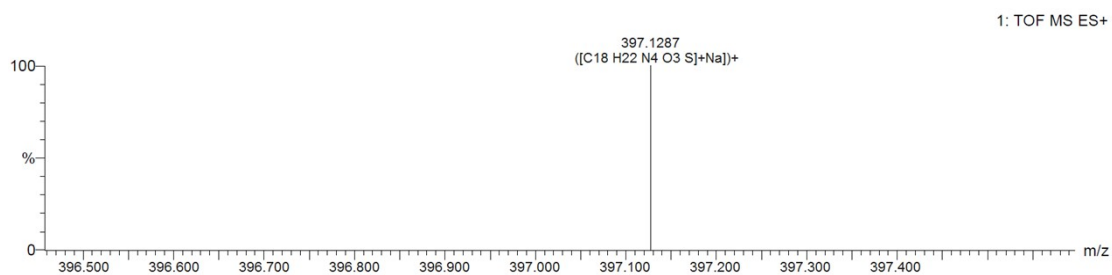
The HRMS spectrum of compound A21



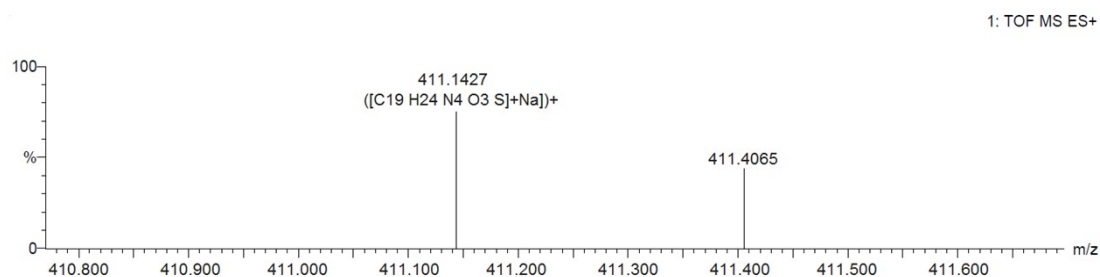
The HRMS spectrum of compound A22



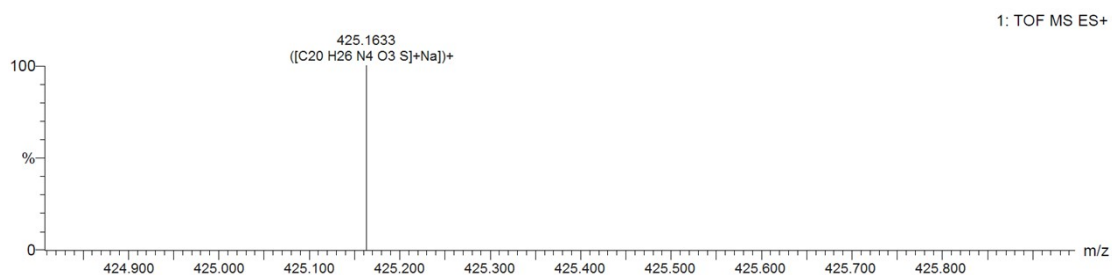
The HRMS spectrum of compound **A23**



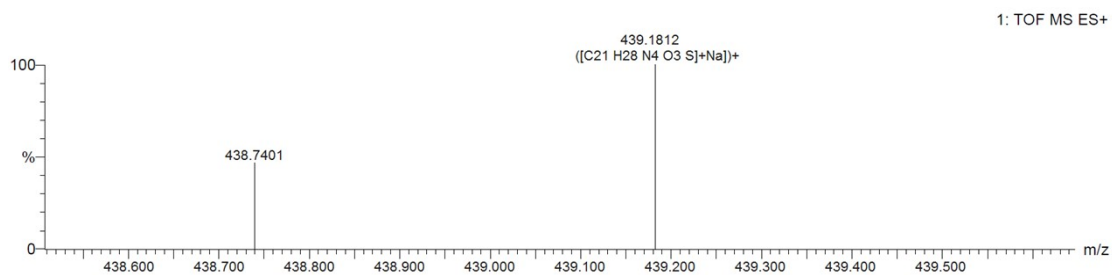
The HRMS spectrum of compound **A24**



The HRMS spectrum of compound **A25**

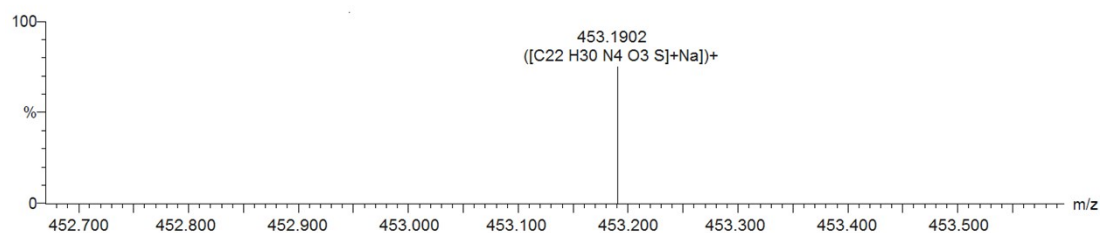


The HRMS spectrum of compound **A26**



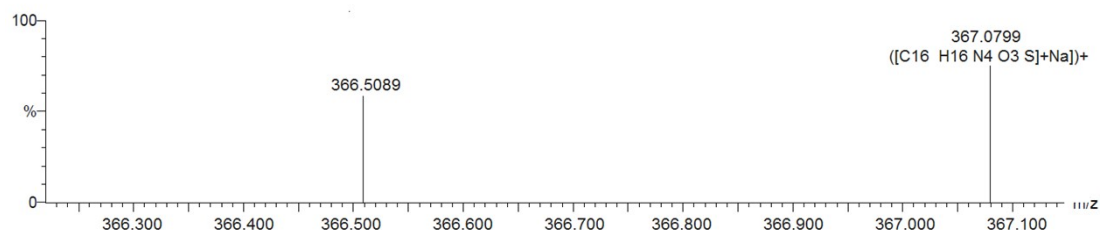
The HRMS spectrum of compound **A27**

1: TOF MS ES+



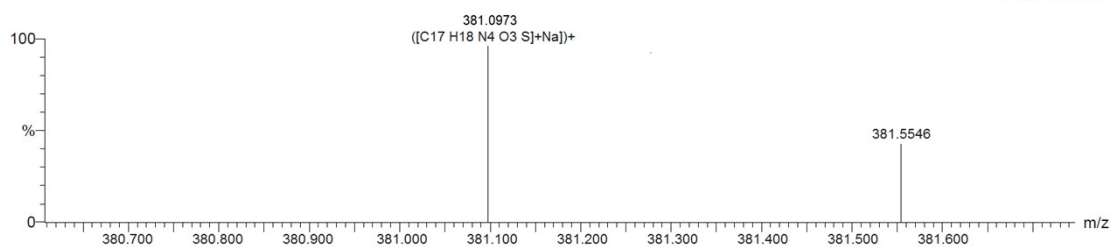
The HRMS spectrum of compound A28

1: TOF MS ES+



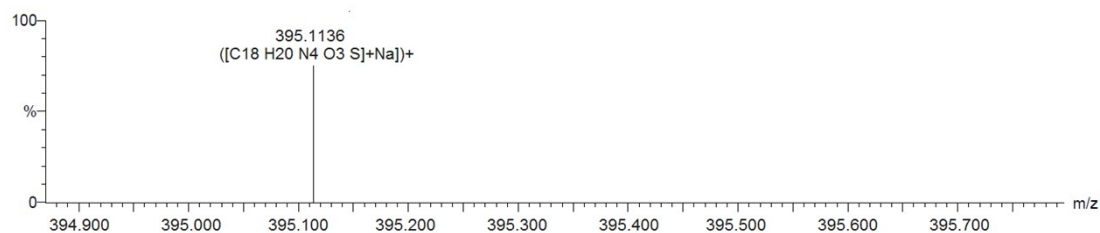
The HRMS spectrum of compound A29

1: TOF MS ES+



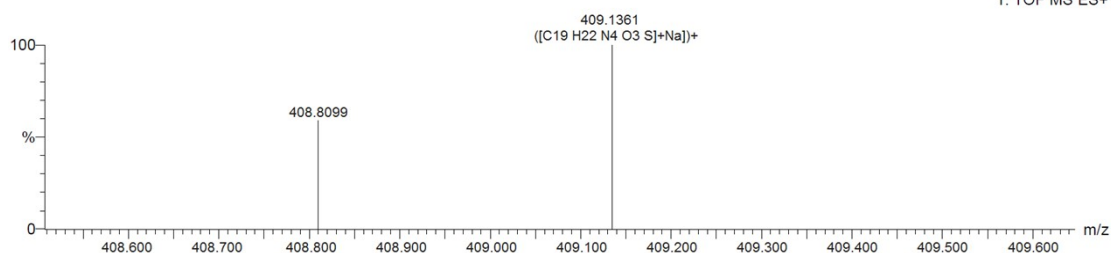
The HRMS spectrum of compound A30

1: TOF MS ES+



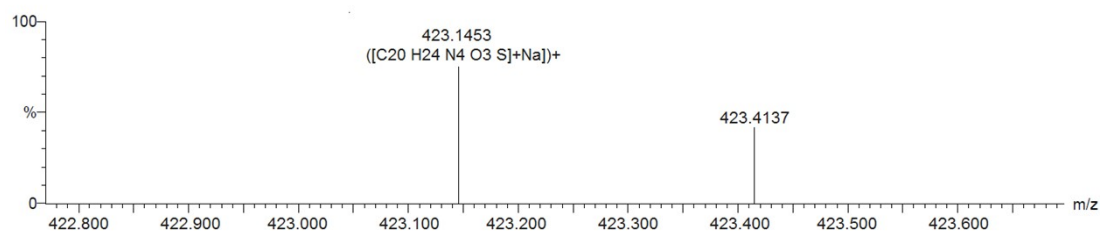
The HRMS spectrum of compound A31

1: TOF MS ES+



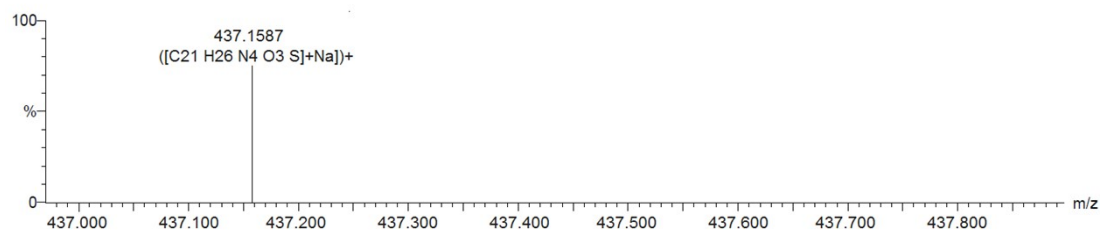
The HRMS spectrum of compound A32

1: TOF MS ES+



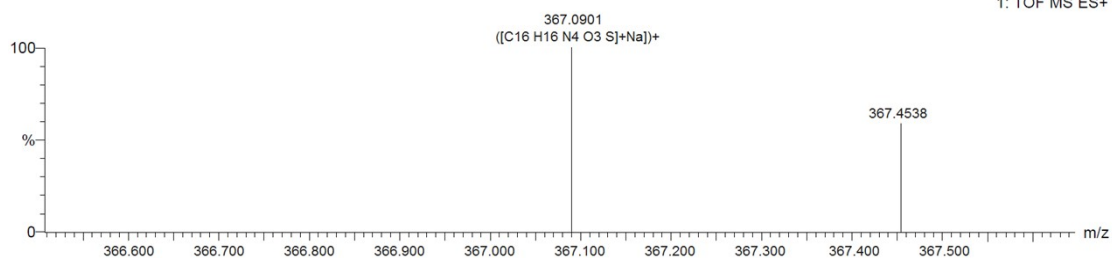
The HRMS spectrum of compound A33

1: TOF MS ES+



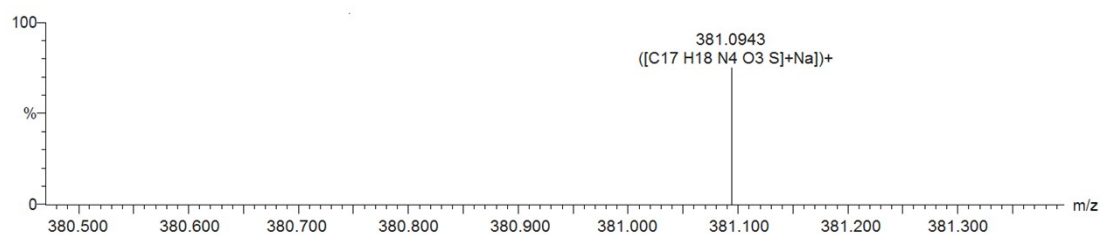
The HRMS spectrum of compound A34

1: TOF MS ES+



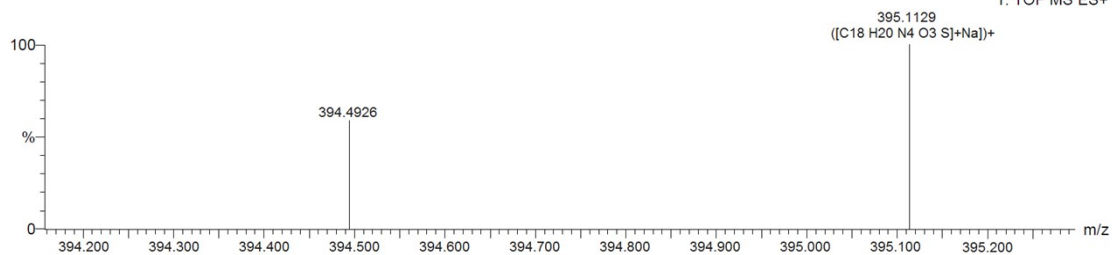
The HRMS spectrum of compound A35

1: TOF MS ES+



The HRMS spectrum of compound A36

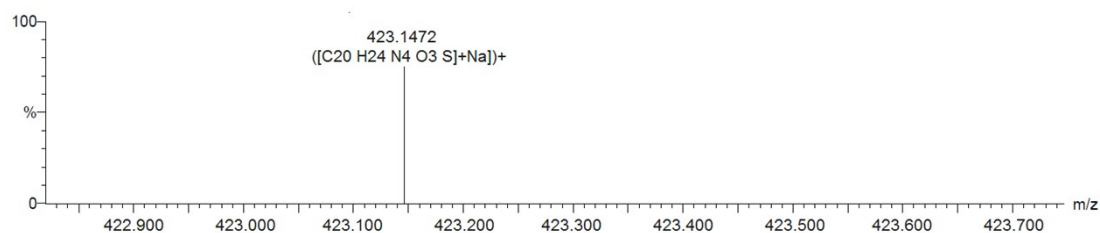
1: TOF MS ES+



The HRMS spectrum of compound A37

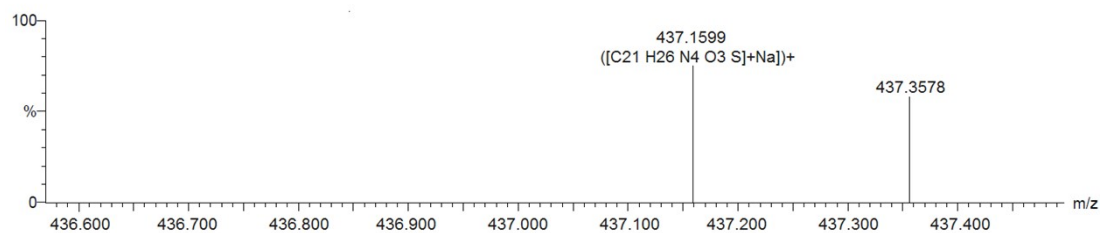


1: TOF MS ES+



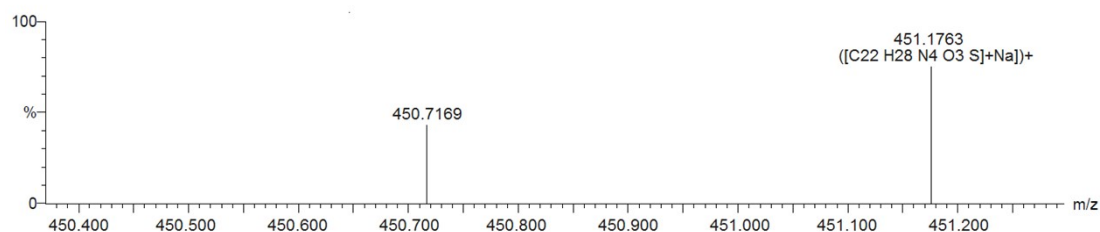
The HRMS spectrum of compound A38

1: TOF MS ES+



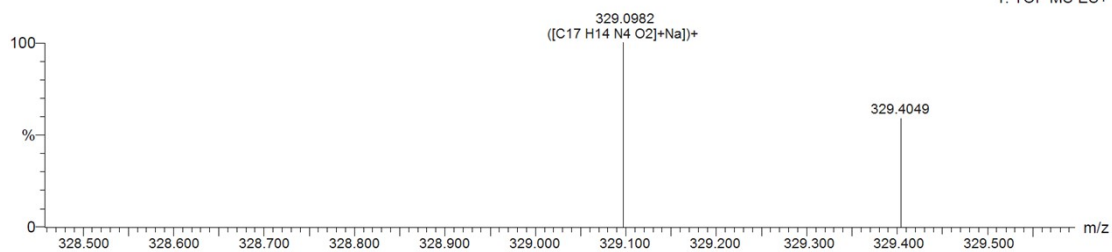
The HRMS spectrum of compound A39

1: TOF MS ES+



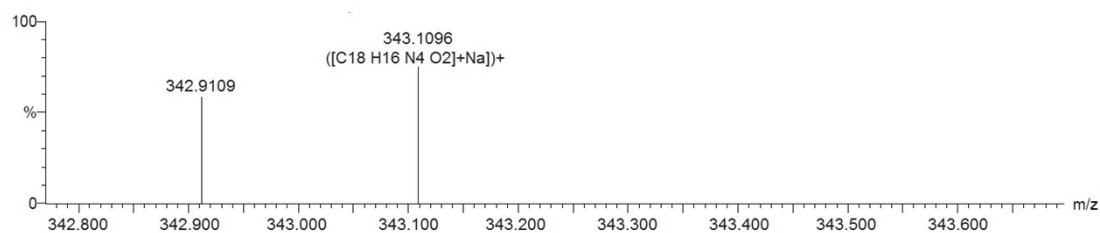
The HRMS spectrum of compound A40

1: TOF MS ES+



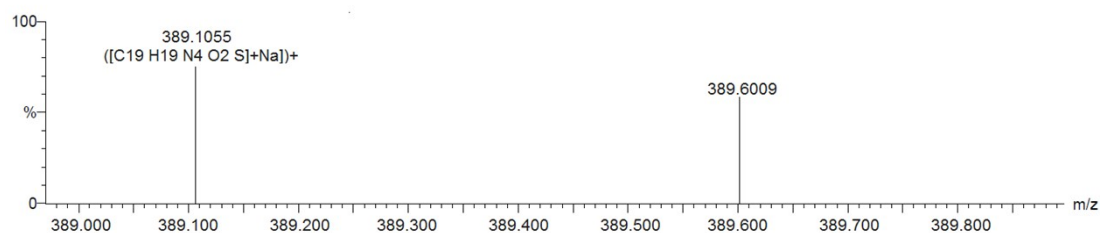
The HRMS spectrum of compound B1

1: TOF MS ES+



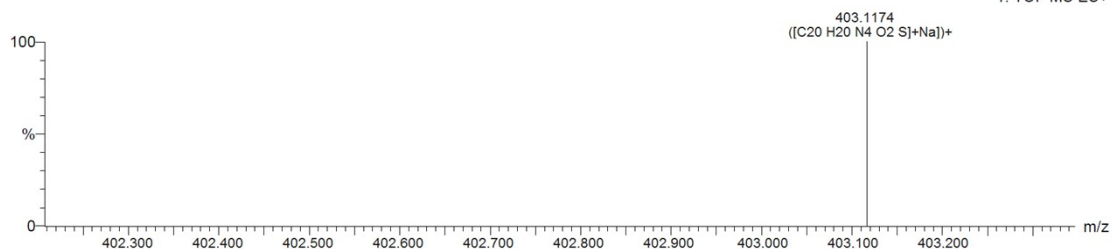
The HRMS spectrum of compound B2

1: TOF MS ES+



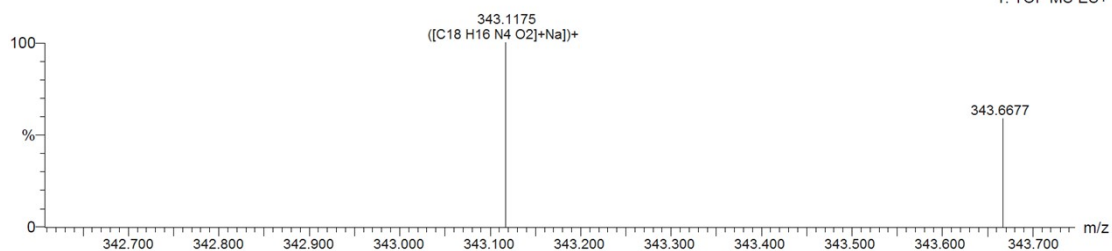
The HRMS spectrum of compound **B3**

1: TOF MS ES+



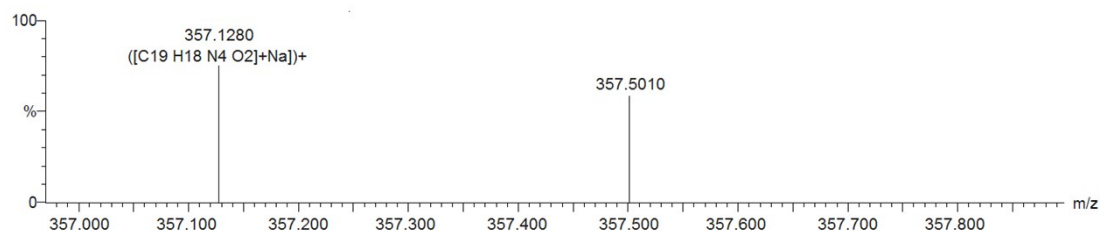
The HRMS spectrum of compound **B4**

1: TOF MS ES+



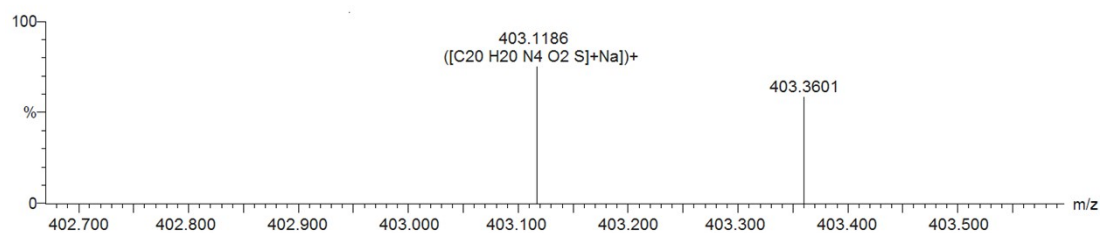
The HRMS spectrum of compound **B5**

1: TOF MS ES+

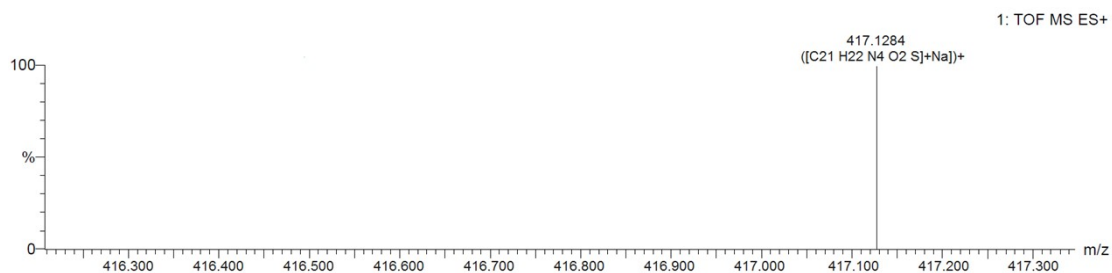


The HRMS spectrum of compound **B6**

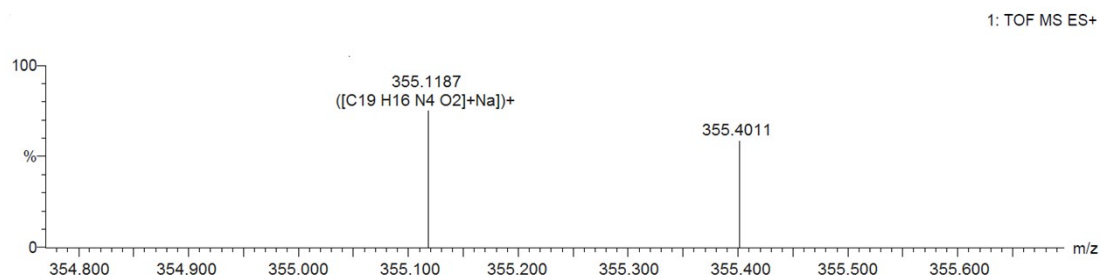
1: TOF MS ES+



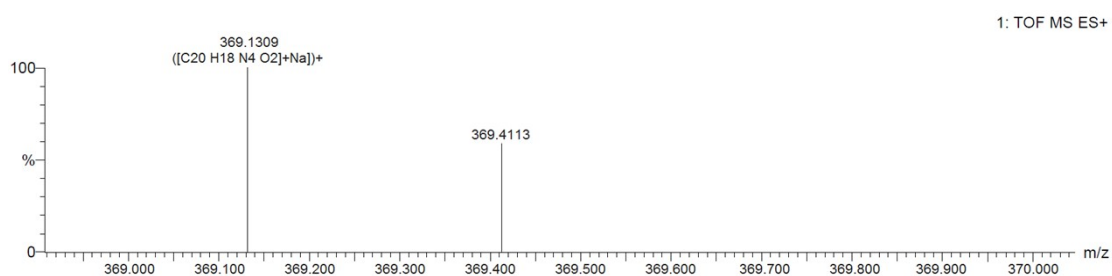
The HRMS spectrum of compound **B7**



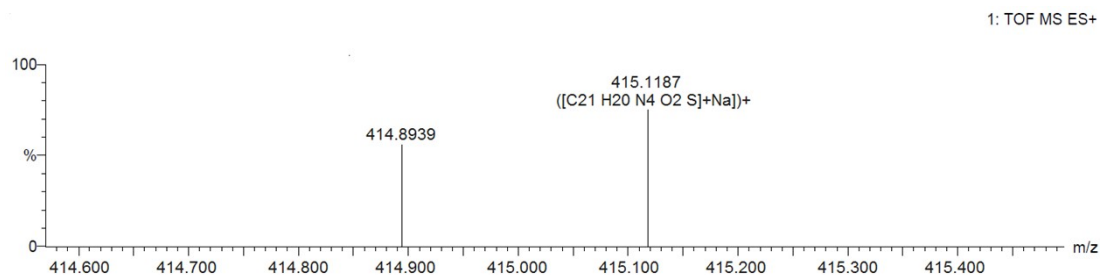
The HRMS spectrum of compound **B8**



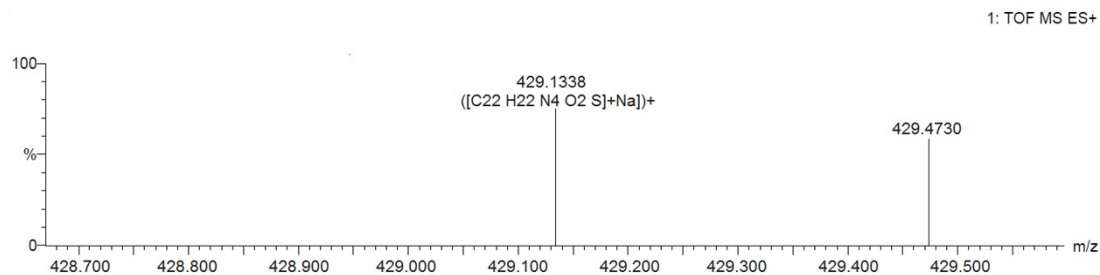
The HRMS spectrum of compound **B9**



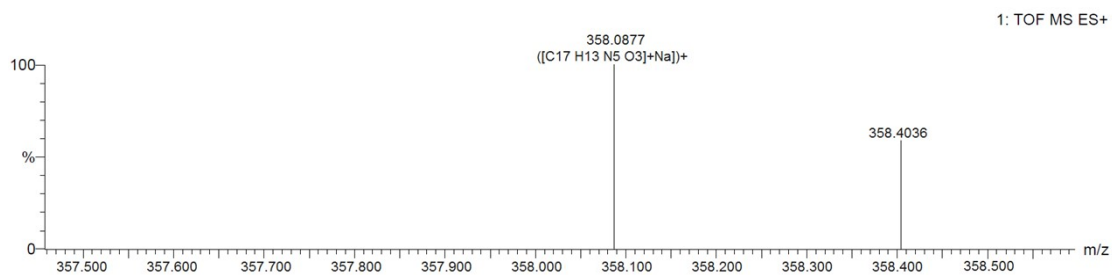
The HRMS spectrum of compound **B10**



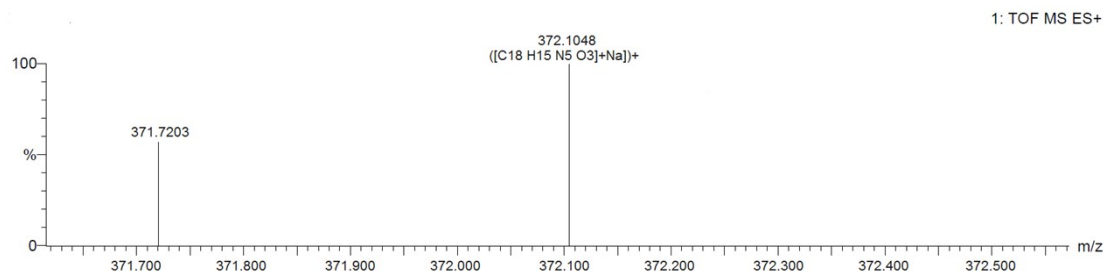
The HRMS spectrum of compound **B11**



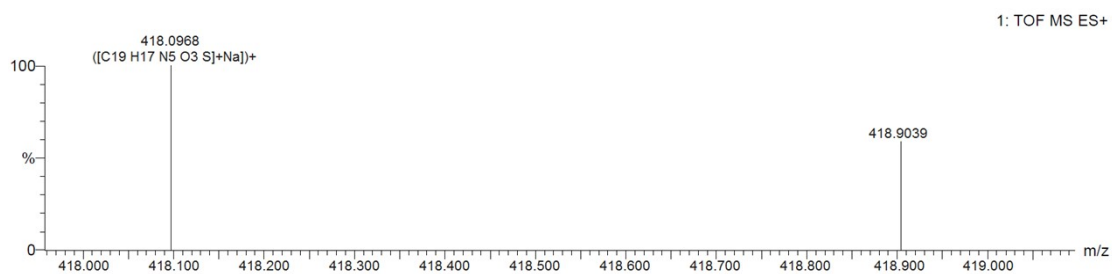
The HRMS spectrum of compound **B12**



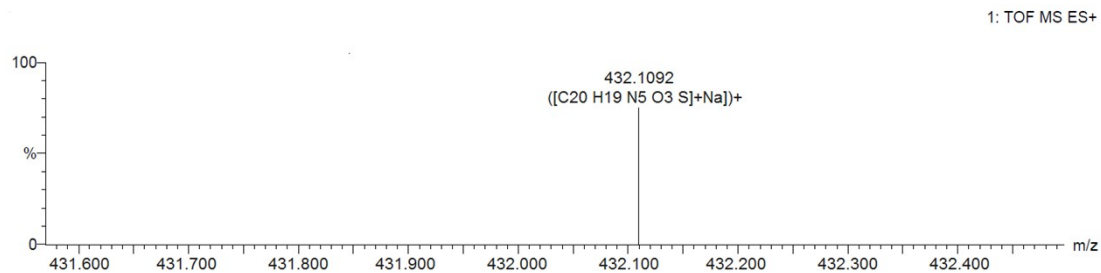
The HRMS spectrum of compound C1



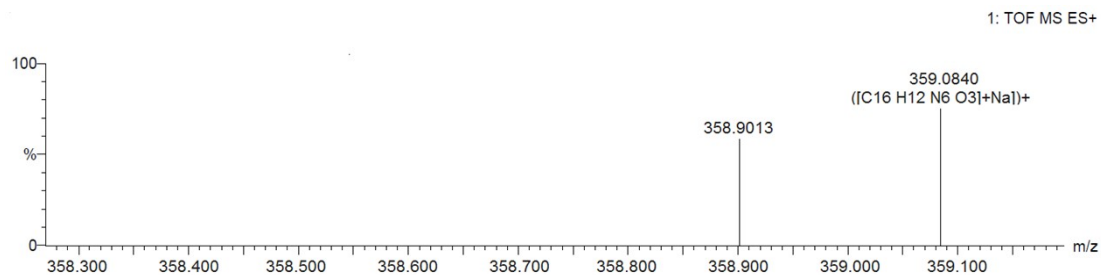
The HRMS spectrum of compound C2



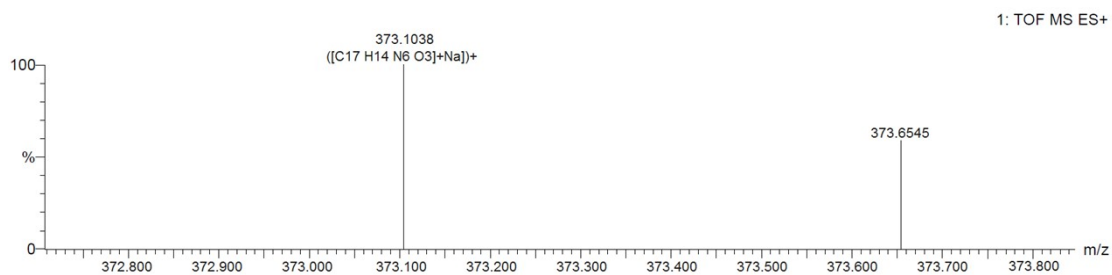
The HRMS spectrum of compound C3



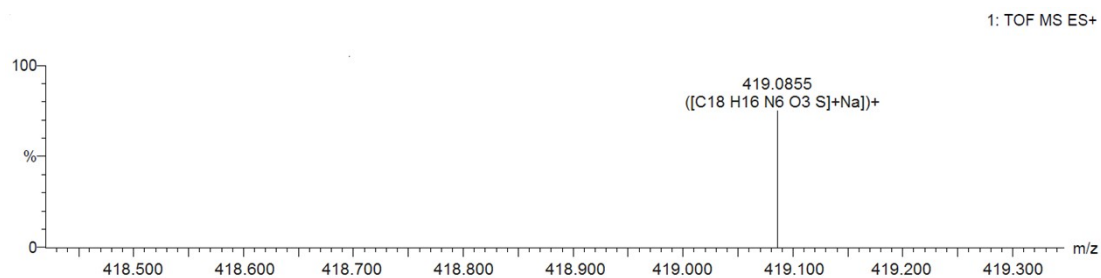
The HRMS spectrum of compound C4



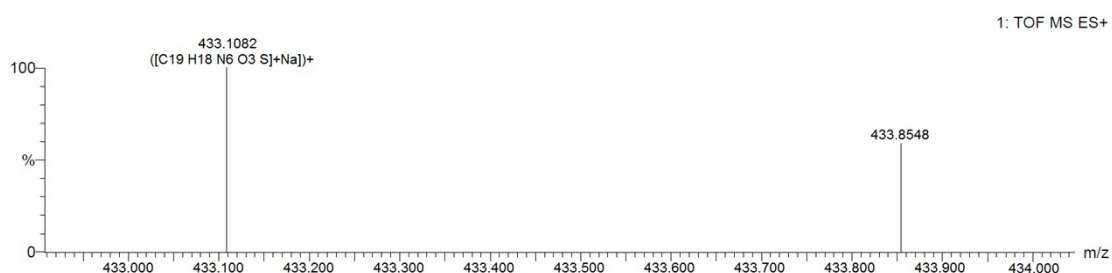
The HRMS spectrum of compound C5



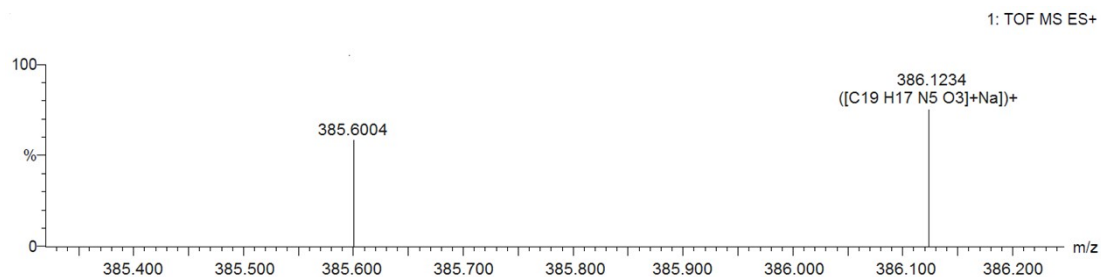
The HRMS spectrum of compound C6



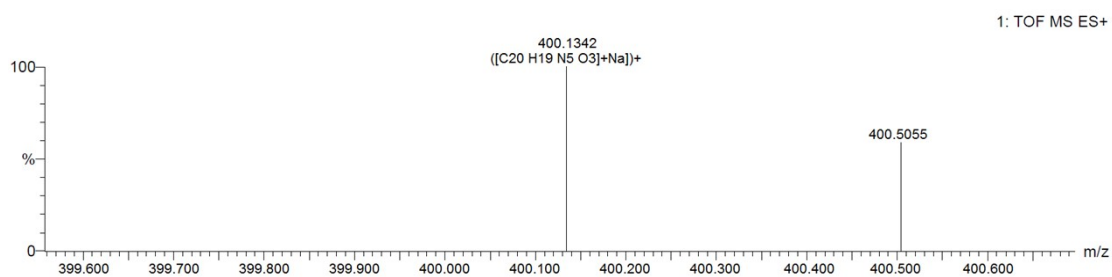
The HRMS spectrum of compound C7



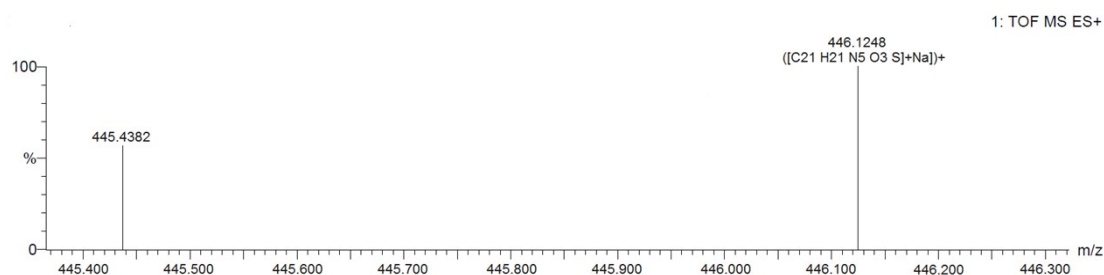
The HRMS spectrum of compound C8



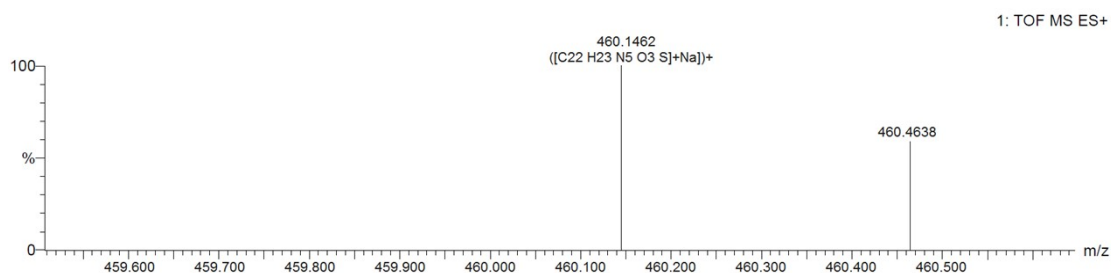
The HRMS spectrum of compound C9



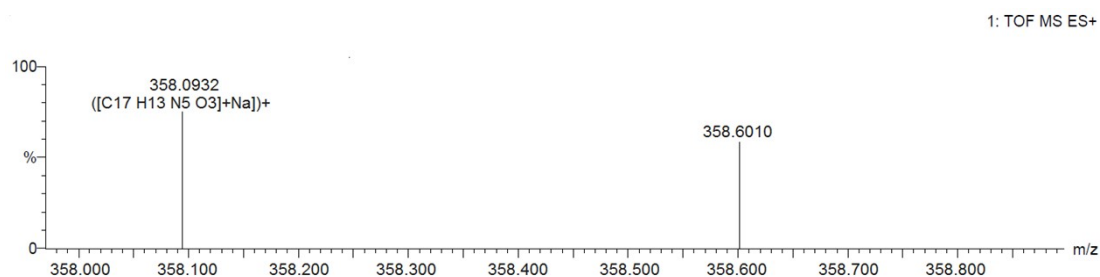
The HRMS spectrum of compound C10



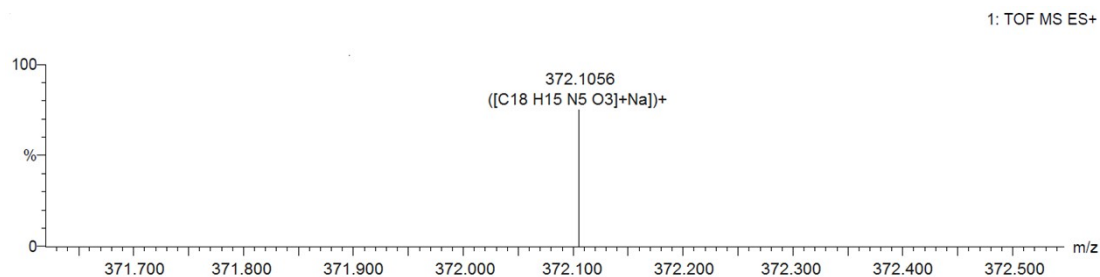
The HRMS spectrum of compound C11



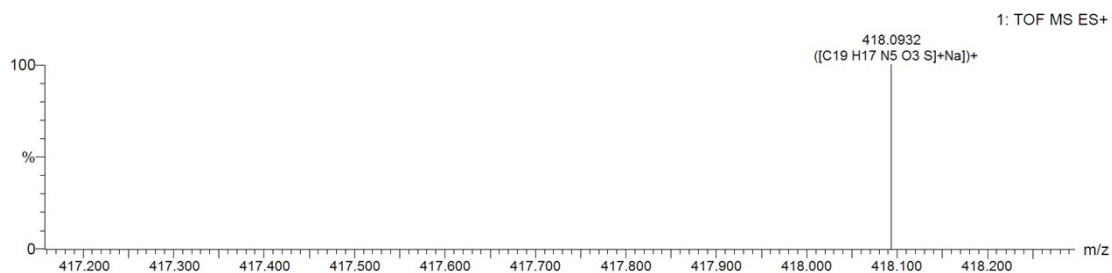
The HRMS spectrum of compound C12



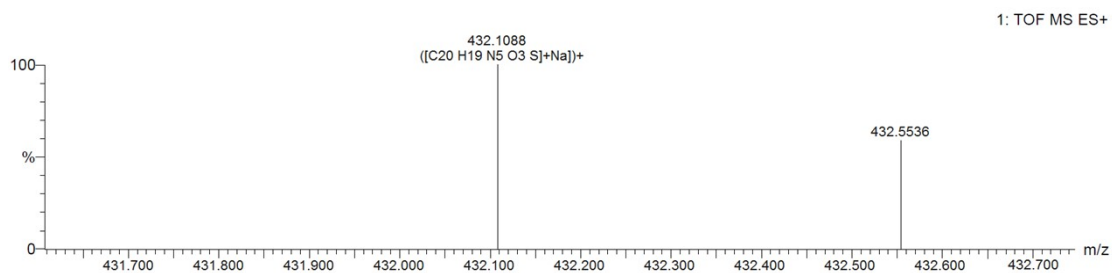
The HRMS spectrum of compound C13



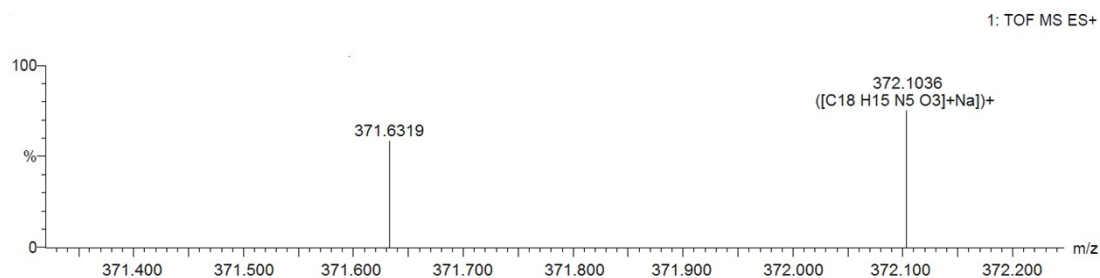
The HRMS spectrum of compound C14



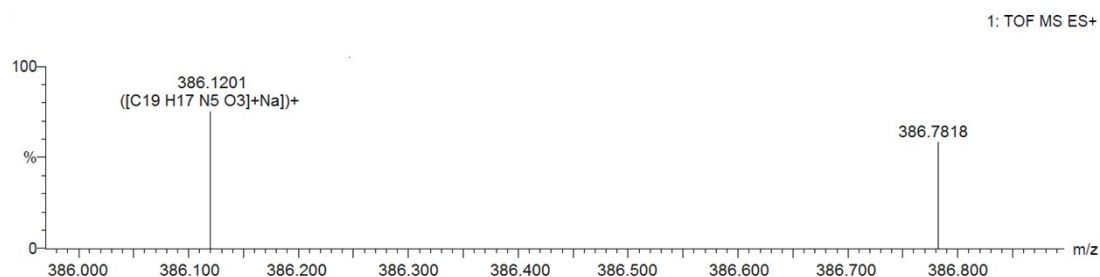
The HRMS spectrum of compound C15



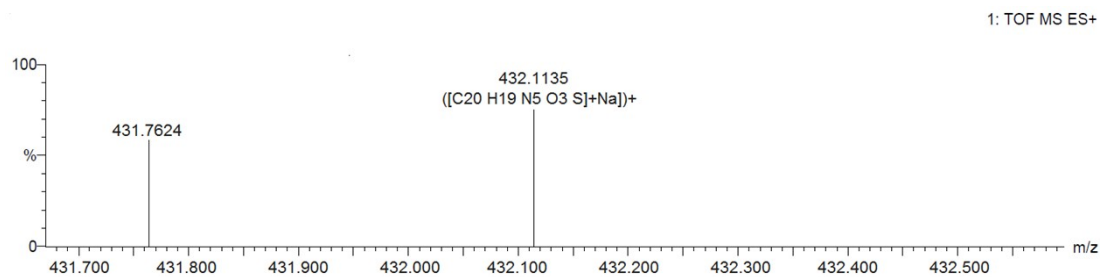
The HRMS spectrum of compound C16



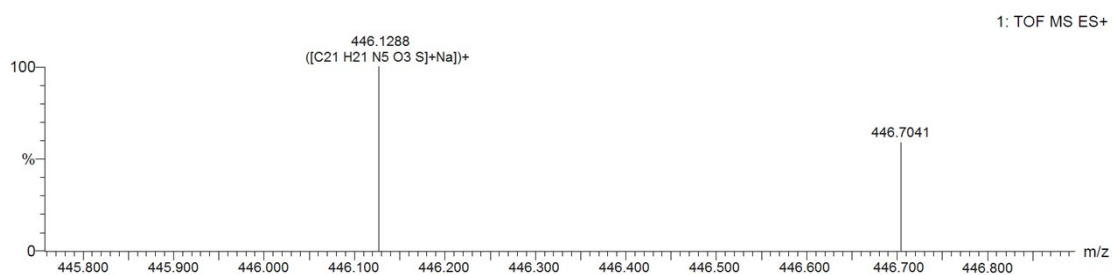
The HRMS spectrum of compound C17



The HRMS spectrum of compound C18

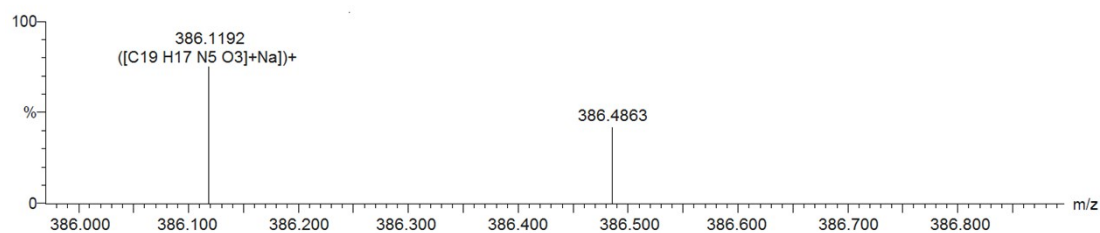


The HRMS spectrum of compound C19



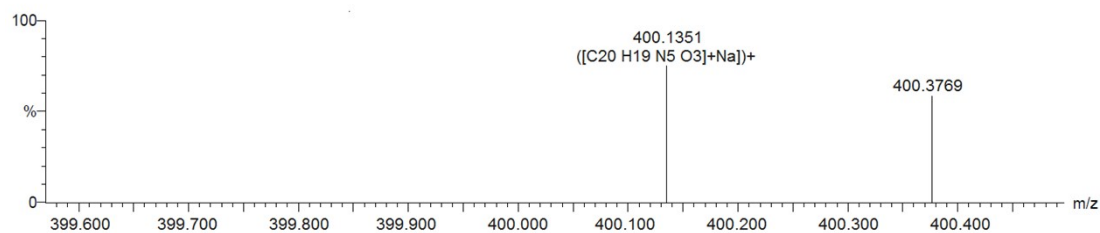
The HRMS spectrum of compound C20

1: TOF MS ES+



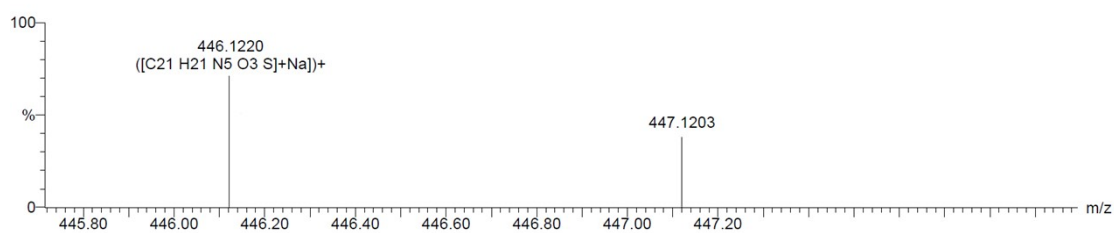
The HRMS spectrum of compound C21

1: TOF MS ES+



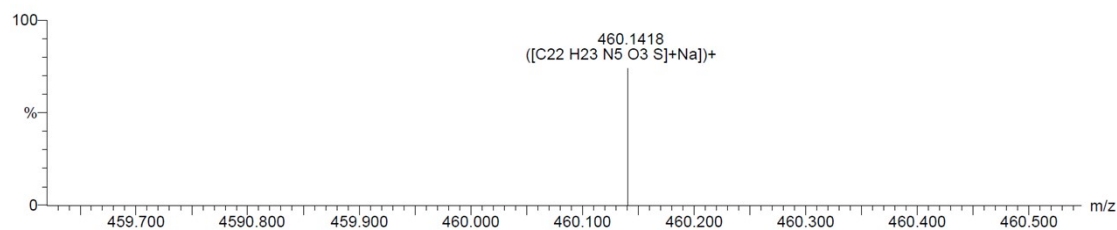
The HRMS spectrum of compound C22

1: TOF MS ES+



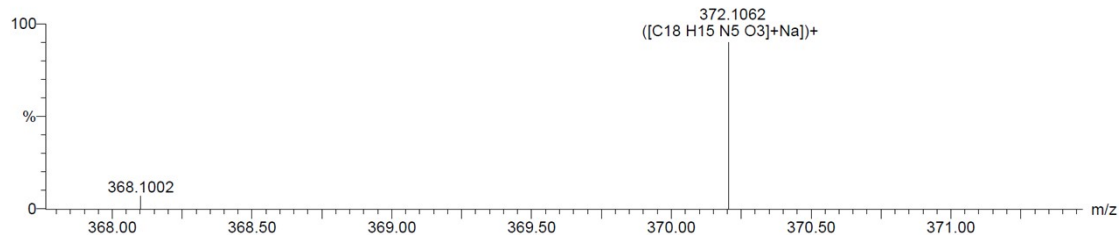
The HRMS spectrum of compound C23

1: TOF MS ES+



The HRMS spectrum of compound C24

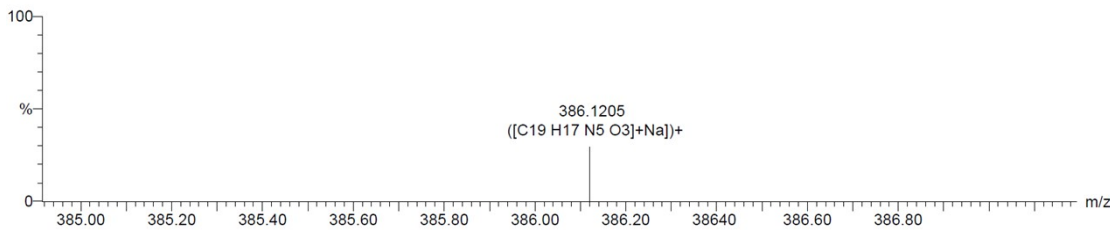
1: TOF MS ES+



The HRMS spectrum of compound C25

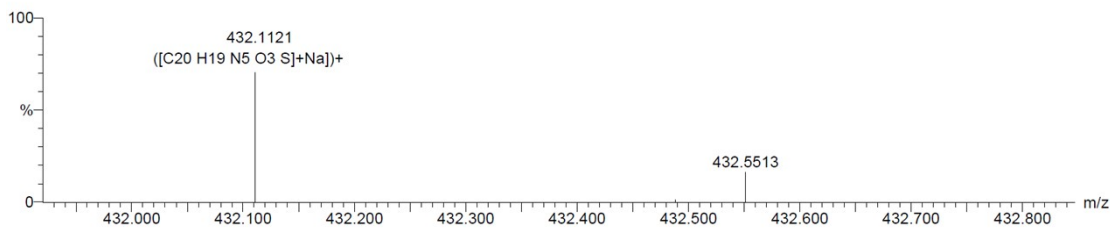


1: TOF MS ES+



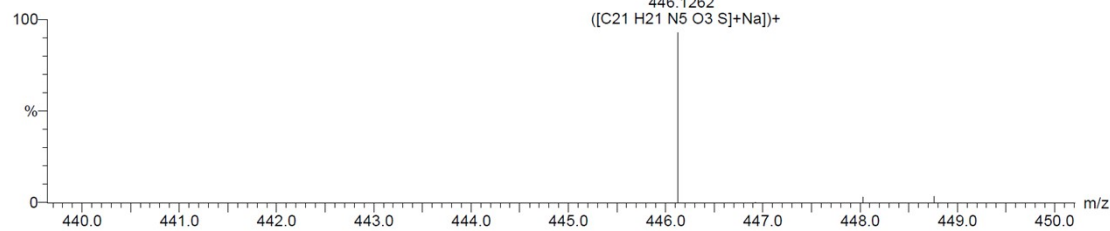
The HRMS spectrum of compound C26

1: TOF MS ES+

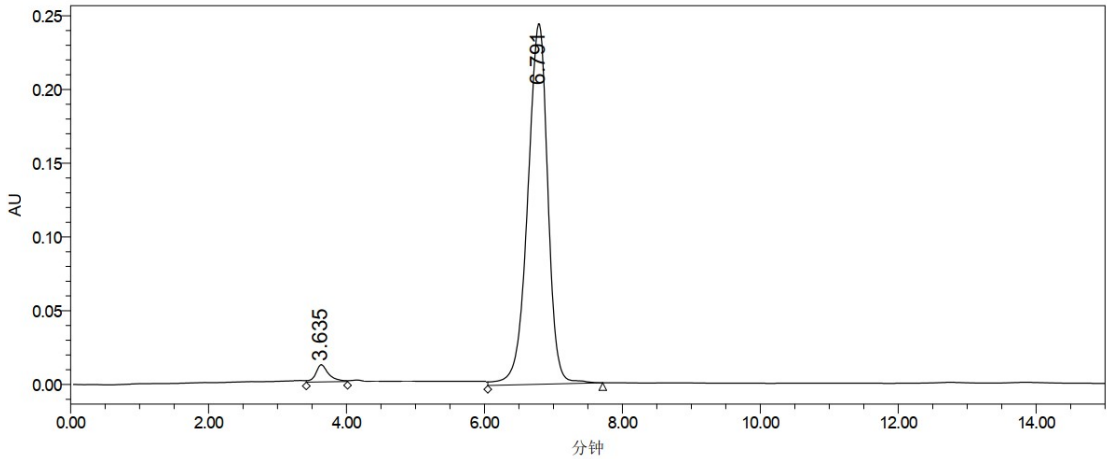


The HRMS spectrum of compound C27

1: TOF MS ES+



The HRMS spectrum of compound C28

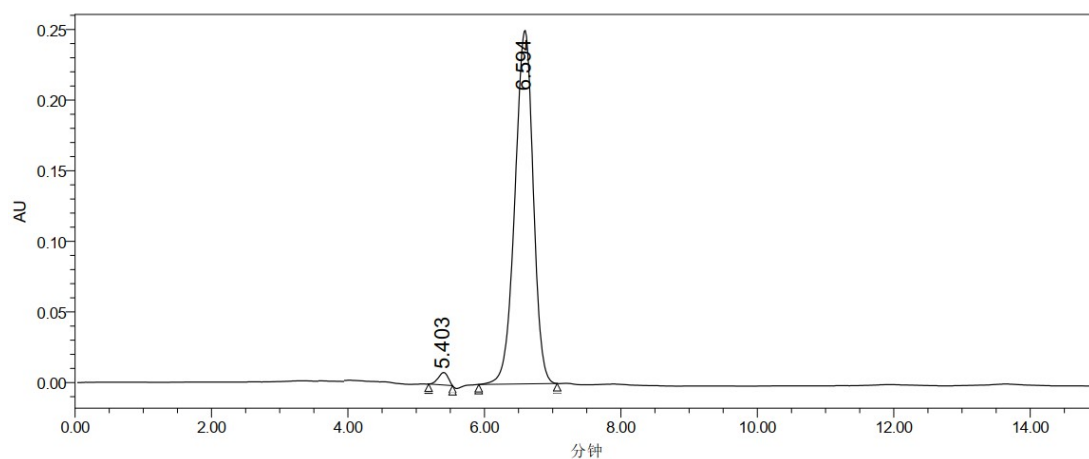


Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: JHW5

名称:

	通道说明	保留时间 (分钟)	面积 (微伏*秒)	% 面积	高度 (微伏)
1	W2489 ChA 254nm	3.635	152600	2.99	11688
2	W2489 ChA 254nm	6.791	4957449	97.01	244734

HPLC spectra of C12



Channel: W2489 ChA; Channel Desc.: W2489 ChA 254nm; Processing Method: JHW5

名称:

	通道说明	保留时间 (分钟)	面积 (微伏*秒)	% 面积	高度 (微伏)
1	W2489 ChA 254nm	5.403	89387	1.88	8939
2	W2489 ChA 254nm	6.594	4662063	98.12	250533

HPLC spectra of **C18**