

Research towards selective inhibition of the CLK3 kinase

Vinay Kumar Singh^{a,b}, Frédéric Justaud^a, Dabbugoddu Brahmaiah^c, Nangunoori Sampath Kumar^c, Blandine Baratte^{d,e}, Thomas Robert^{d,e}, Stéphane Bach^{d,e}, Chada Raji Reddy^f, Nicolas Levoin^{g*}, and René Grée^a

Keywords: Kinases • CLK3 • Quinazolines • Cancer • Triazoles • Molecular modelling •

^a Univ Rennes, CNRS, ISCR (Institut des Sciences Chimiques de Rennes), UMR 6226, F-35000 Rennes, France.

^b D.N.(P.G.) College, Khudwadhar, Gulaathi, Bulandshahr, Uttar Pradesh-203408, India

^c Chemveda Life Sciences India Pvt. Ltd., #B-11/1, IDA Uppal, Hyderabad-500039, Telangana, India

^d Sorbonne Université, CNRS, FR 2424, Plateforme de criblage KISSf (Kinase Inhibitor Specialized Screening facility), Station Biologique de Roscoff, CS 90074, 29688 Roscoff Cedex, France.

^e Sorbonne Université, CNRS, UMR 8227, Integrative Biology of Marine Models Laboratory (LBI2M), Station Biologique de Roscoff, CS 90074, 29688 Roscoff Cedex, France.

^f CSIR-Indian Institute of Chemical Technology, Uppal Road, Tarnaka, Hyderabad 500007, TS, India.

^g Bioprojet-Biotech, 4 rue du Chesnay Beauregard, BP 96205, 35762 Saint Grégoire, France.

Supplementary Information

Figure 1: Analysis of dose-dependent effect of VS-77 on the kinase activity of Mm_CLK1, Mm_CLK2, Mm_CLK3, Mm_CLK4.....	S 4
Figure 2: ^1H NMR spectrum of 3a.....	S 5
Figure 3: ^{13}C NMR spectra of 3a	S 6
Figure 5: ^1H NMR spectrum of 5a	S 8
Figure 6: ^{13}C NMR spectrum of 5a	S 9
Figure 7: ^1H NMR spectrum of 7a	S10
Figure 8: ^{13}C NMR spectra of 7a	S11
Figure 9: ^1H NMR spectrum of 3b	S12
Figure 10: ^{13}C NMR spectrum of 3b.....	S13
Figure 11: ^1H NMR spectrum of 4b	S14
Figure 12: ^{13}C NMR spectra of 4b	S15
Figure 14: 13C NMR spectra of 5b	S17
Figure 15: ^1H NMR spectrum of 7b	S18
Figure 16: ^{13}C NMR spectrum of 7b.....	S19
Figure 17: Extension of ^{13}C NMR spectrum of 7b.....	S 20
Figure 18: ^1H NMR spectrum of 9a	S 21
Figure 19: ^{13}C NMR spectrum of 9a	S 22
Figure 20: ^1H NMR spectrum of 10a	S 23
Figure 21: 13C NMR spectrum of 10a.....	S 24
Figure 22: ^1H NMR spectrum of 12a	S 25
Figure 23: ^{13}C NMR spectrum of 12a	S 26
Figure 24: ^1H NMR spectrum of 13a	S 27

Figure 25: ^{13}C NMR spectrum of 13a	S 28
Figure 26: ^1H NMR spectrum of 9b	S 29
Figure 27: ^{13}C NMR spectrum of 9b	S 30
Figure 28: ^1H NMR spectrum of 10b	S 31
Figure 29: ^{13}C NMR spectrum of 10b	S 32
Figure 30: ^1H NMR spectrum of 12b	S 33
Figure 31: ^{13}C spectrum of 12b	S 34
Figure 32: ^1H spectrum of 13b	S 35
Figure 33: ^{13}C NMR spectrum of 13b	S 36

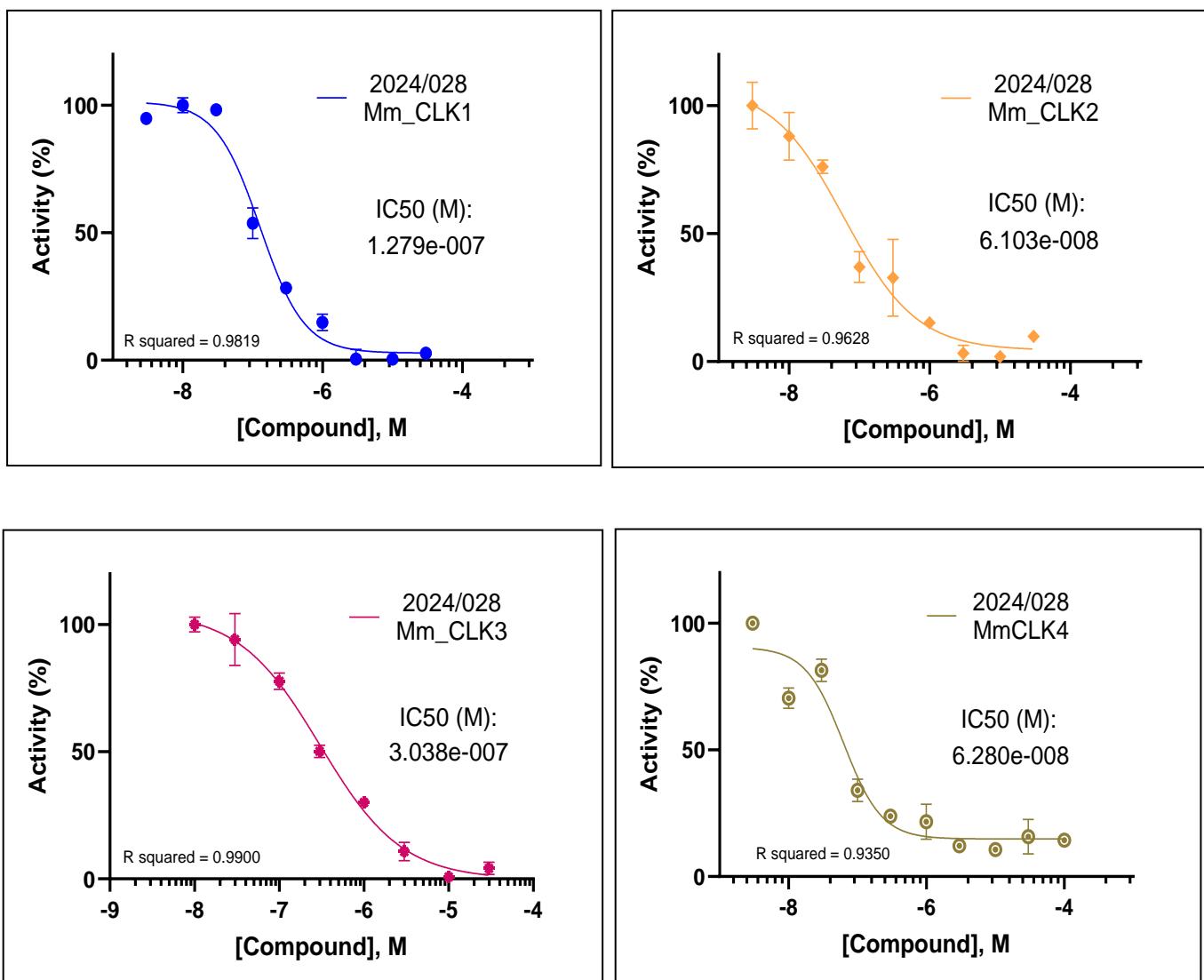


Figure 1: Analysis of dose-dependent effect of VS-77 on the kinase activity of Mm_CLK1, Mm_CLK2, Mm_CLK3, Mm_CLK4.

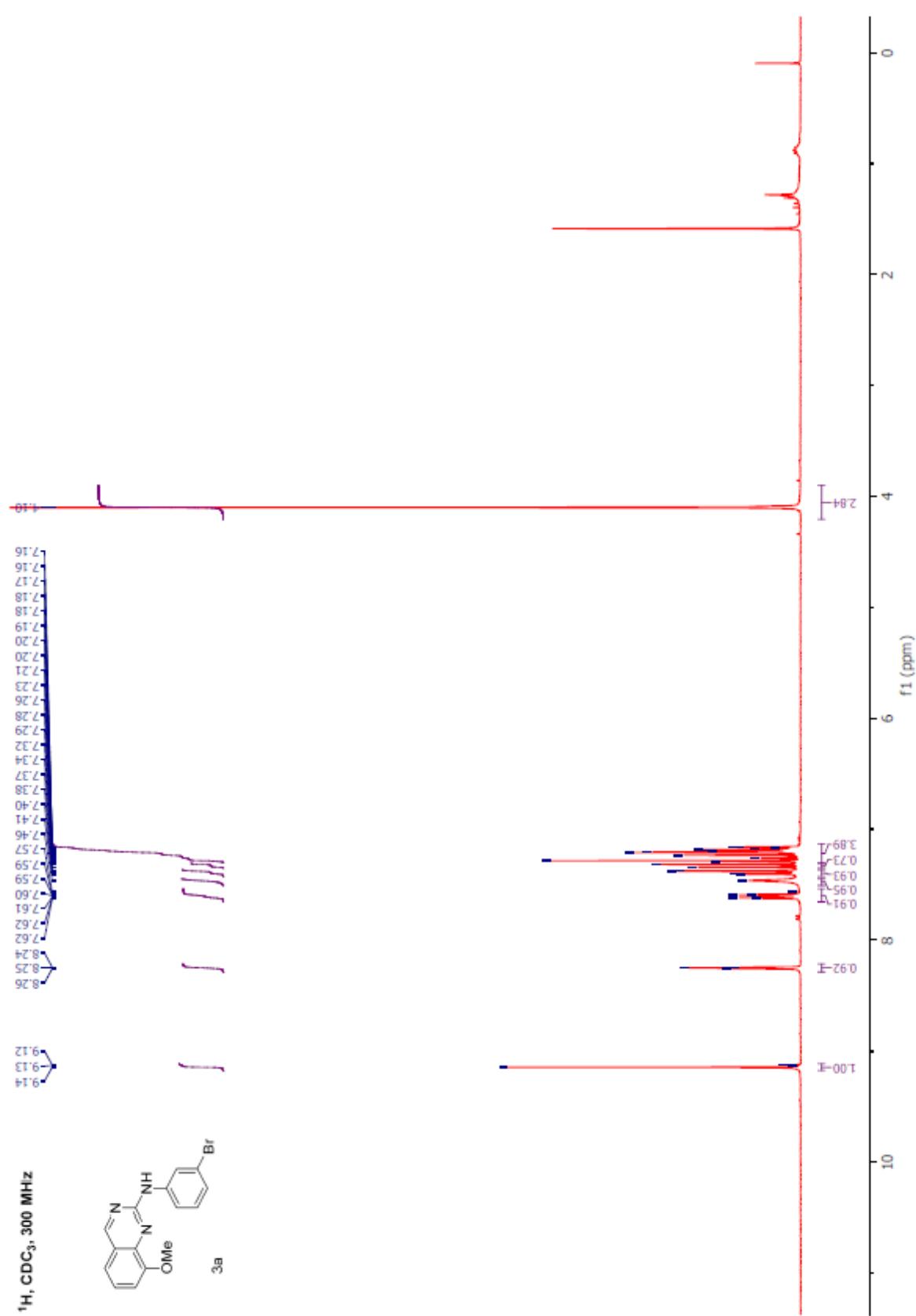


Figure 2: ¹H NMR spectrum of 3a

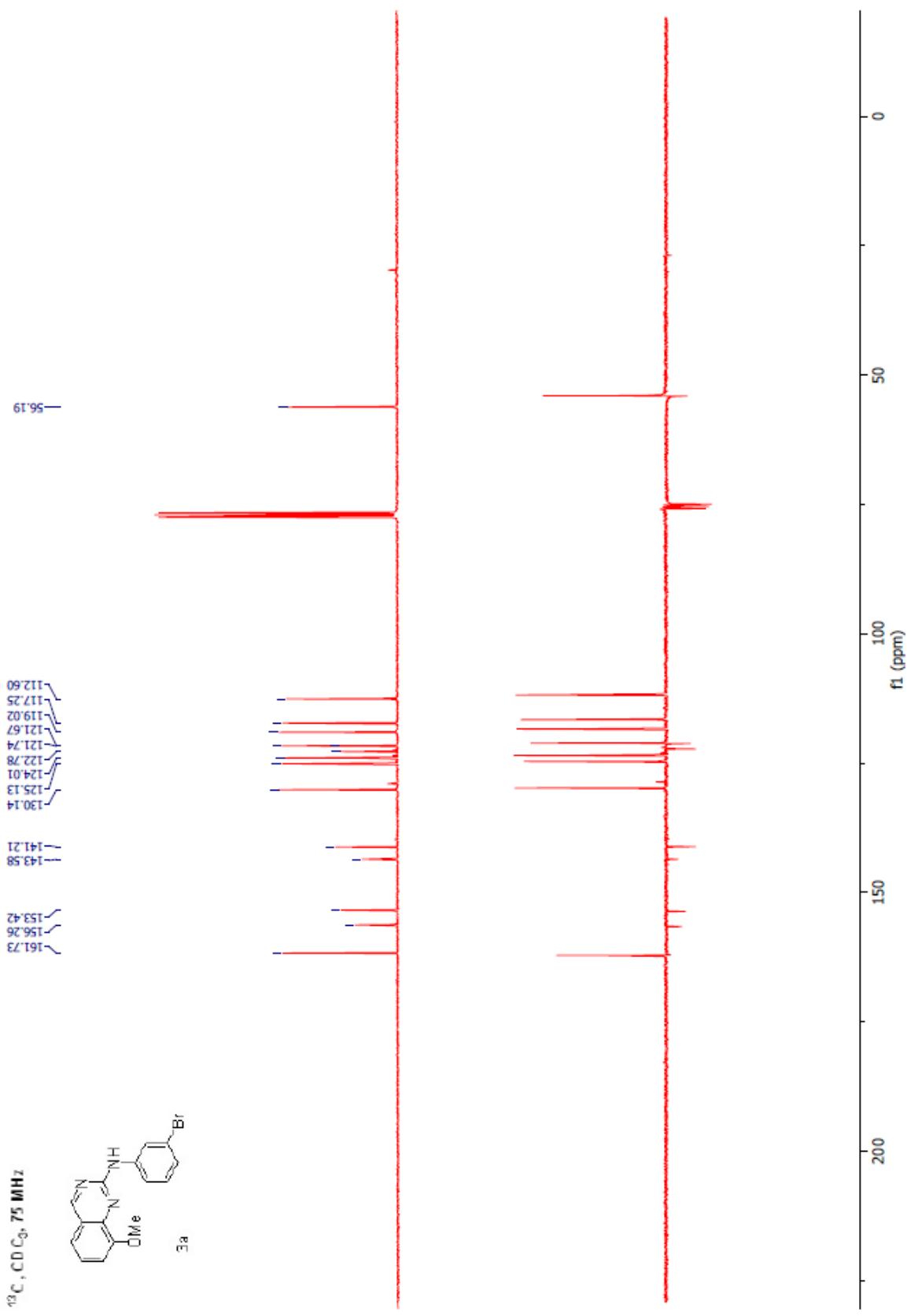


Figure 3: ¹³C NMR spectra of 3a

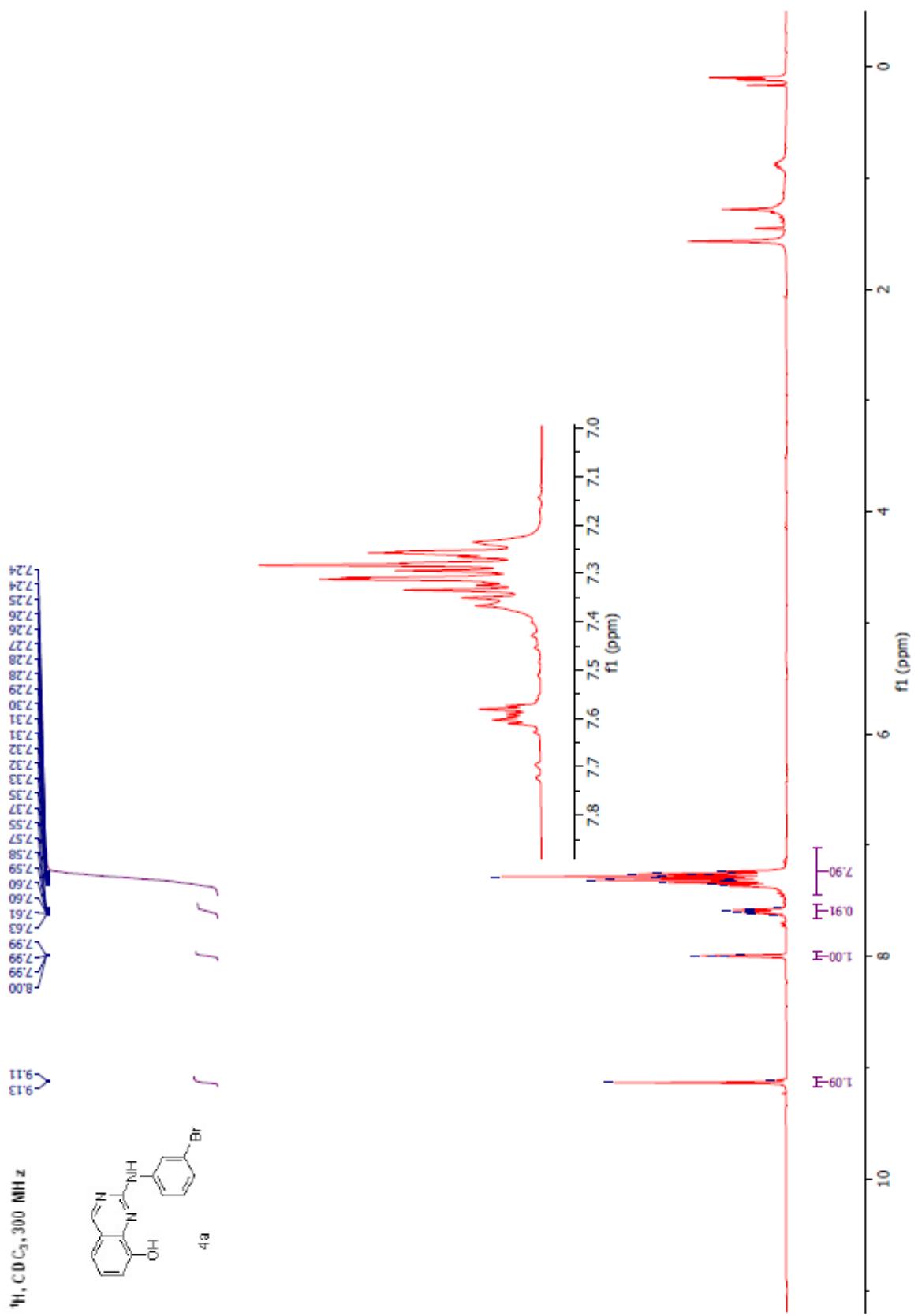


Figure 4: ^1H NMR spectrum of 4a

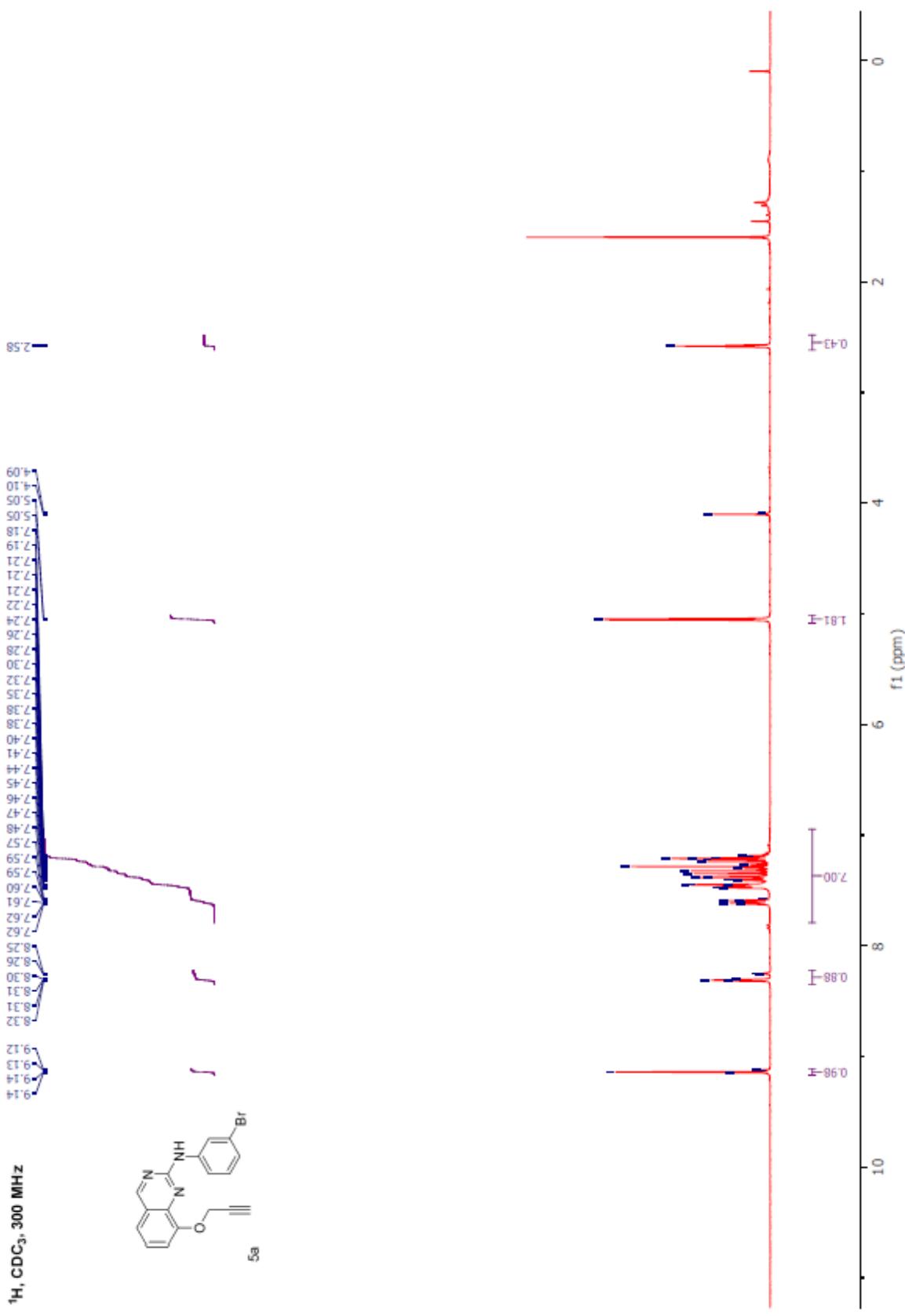


Figure 5: ¹H spectrum of 5a

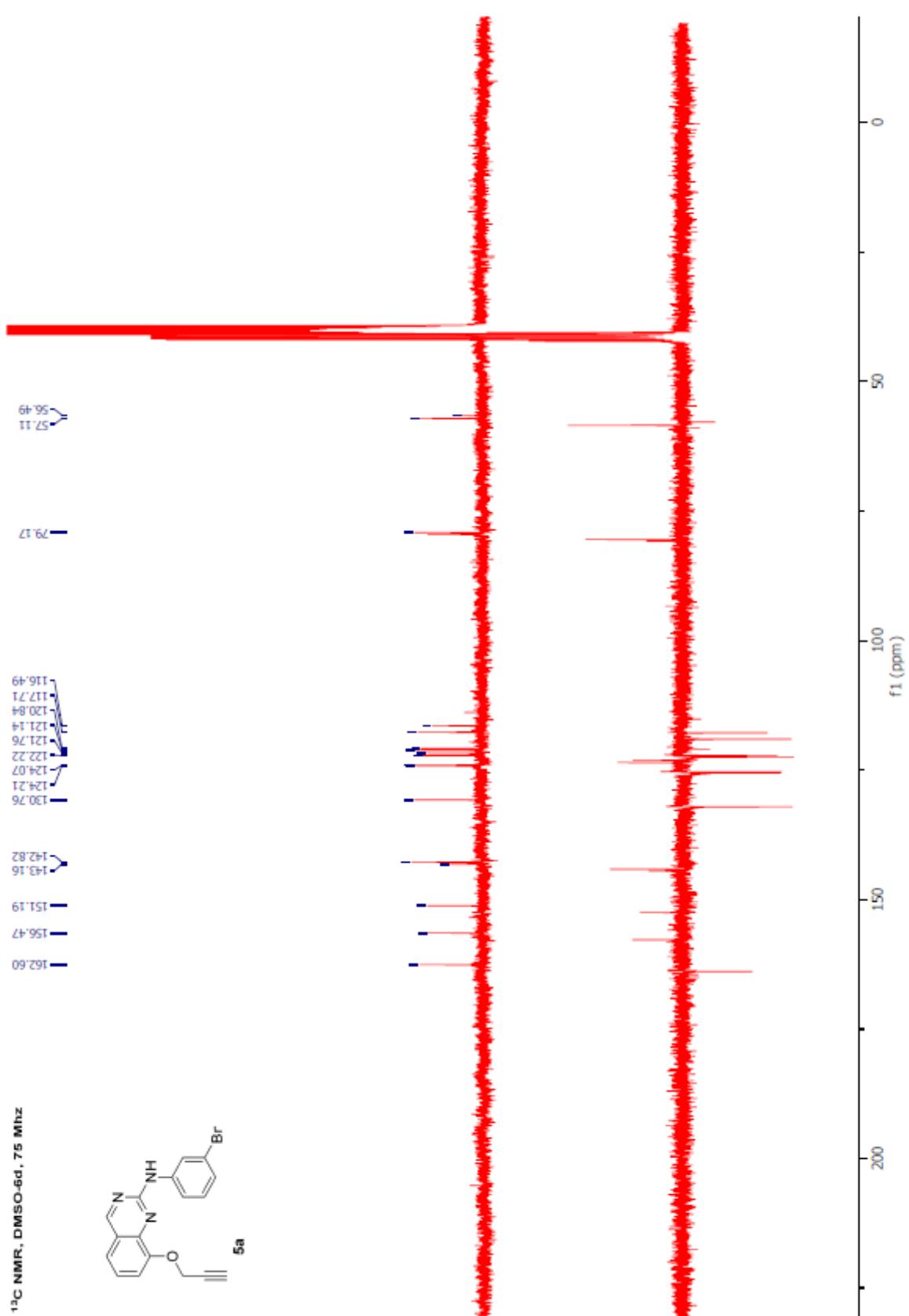


Figure 6: ¹³C NMR spectrum of 5a

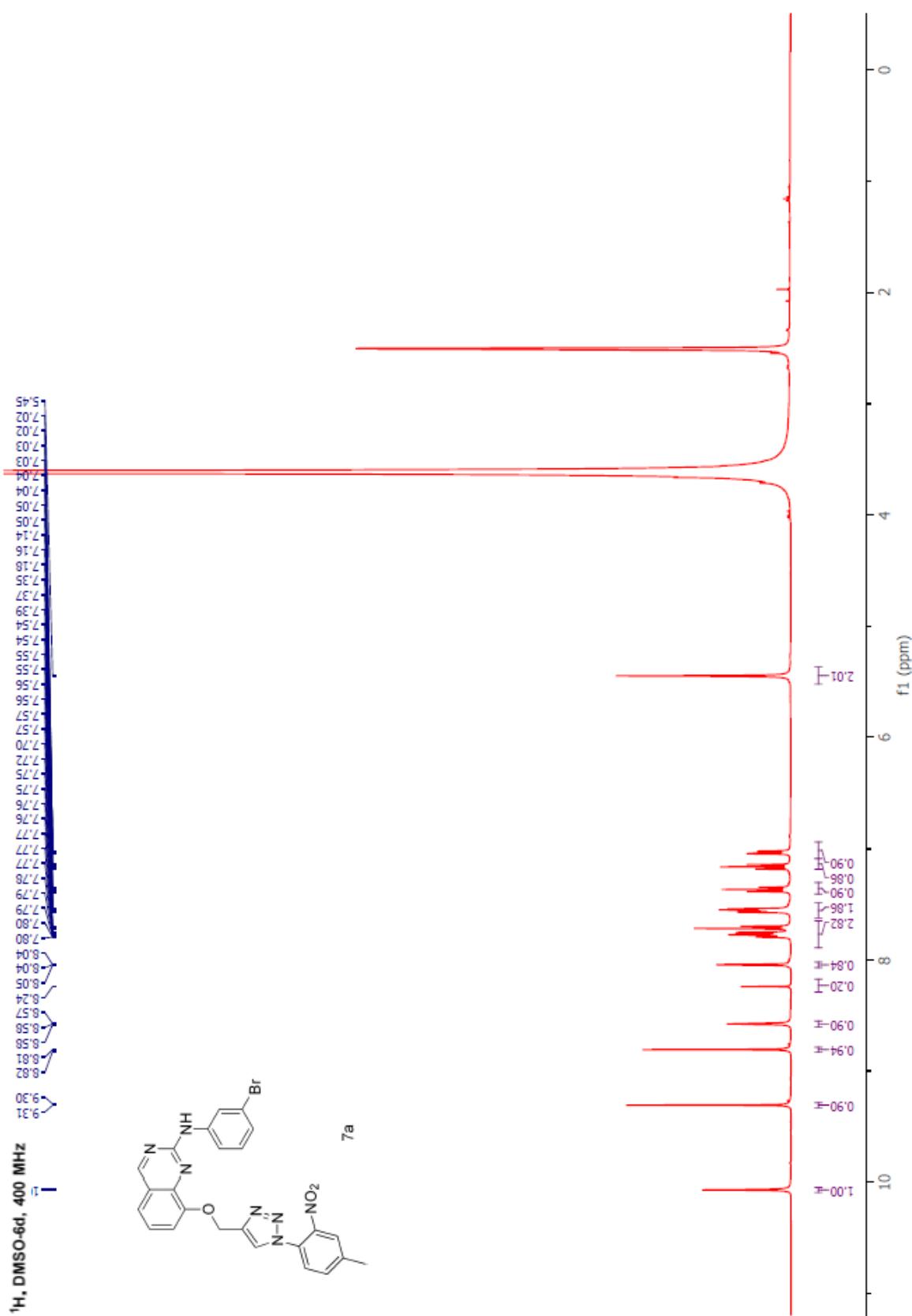


Figure 7: ¹H NMR spectrum of 7a

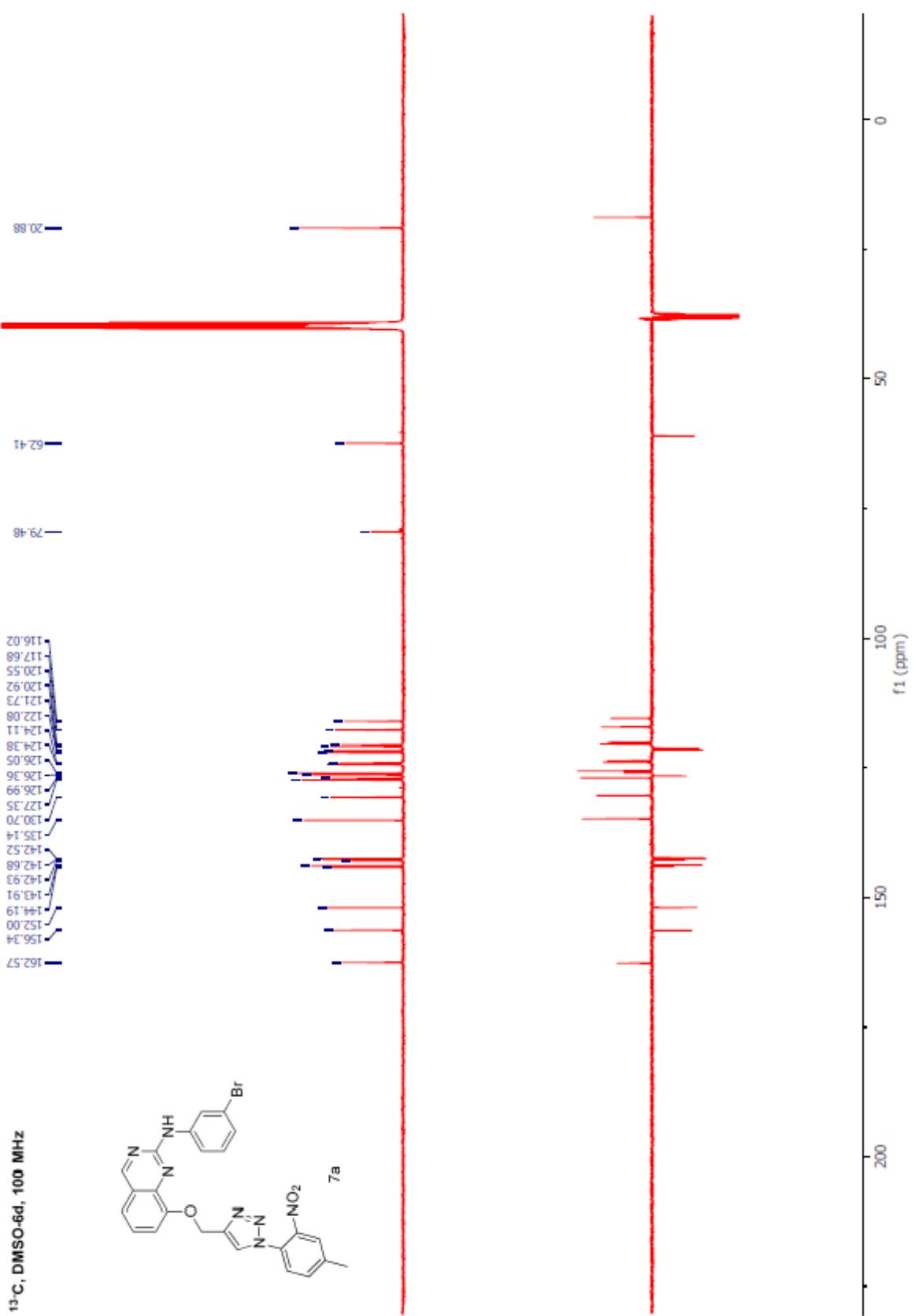


Figure 8: ¹³C NMR spectra of 7a

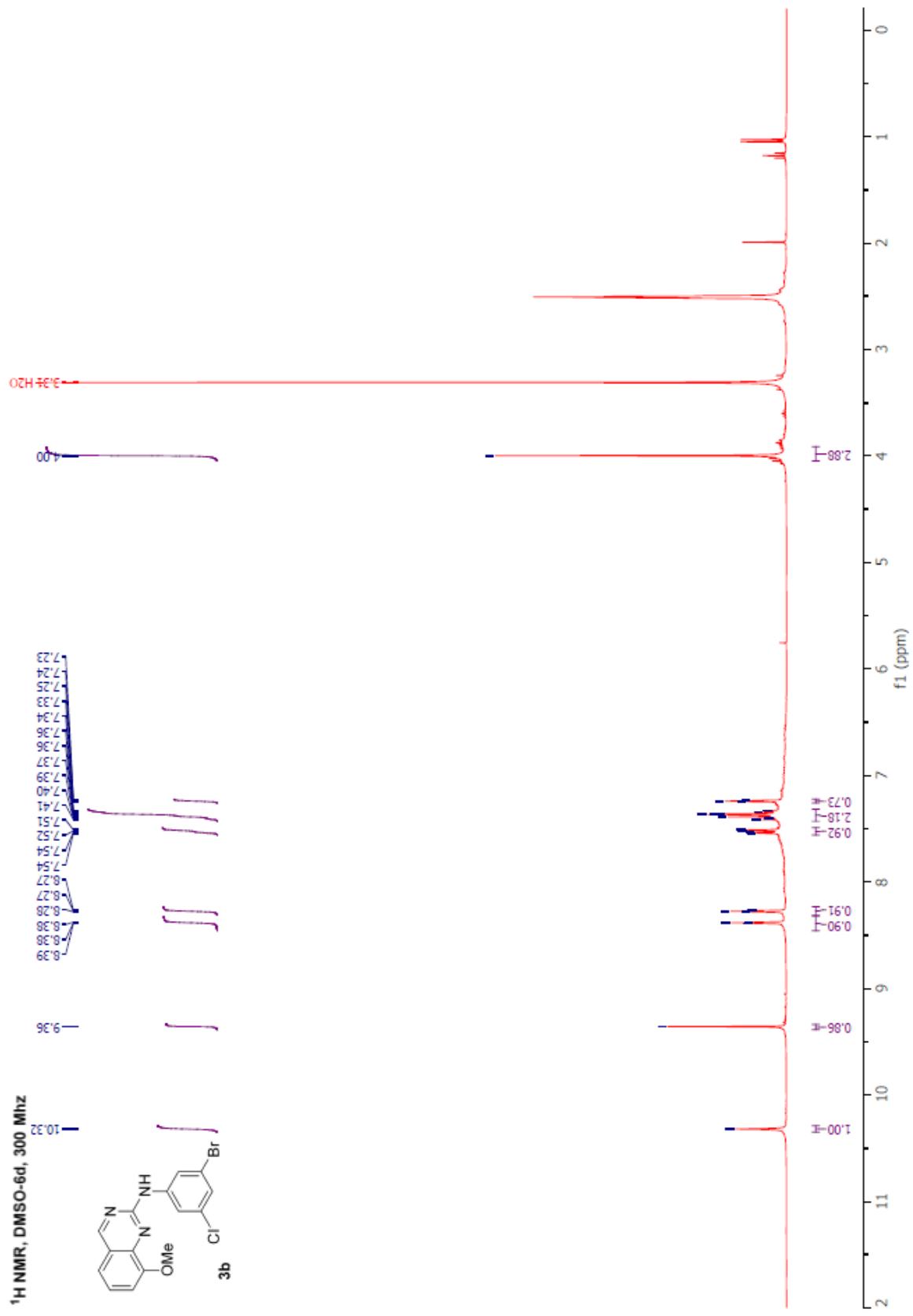


Figure 9: ^1H NMR spectra of 3b

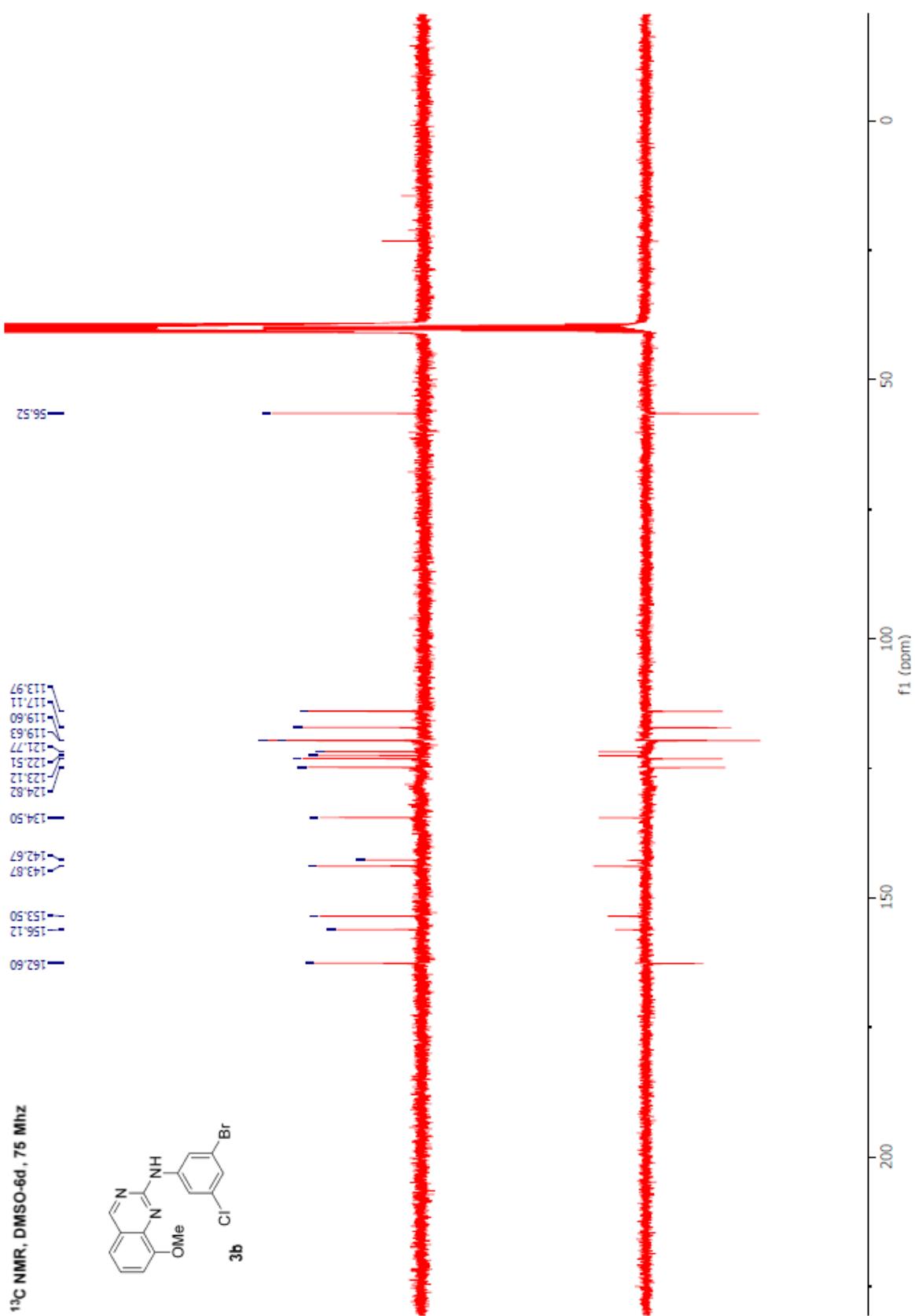


Figure 10: ¹³C NMR spectra of 3b

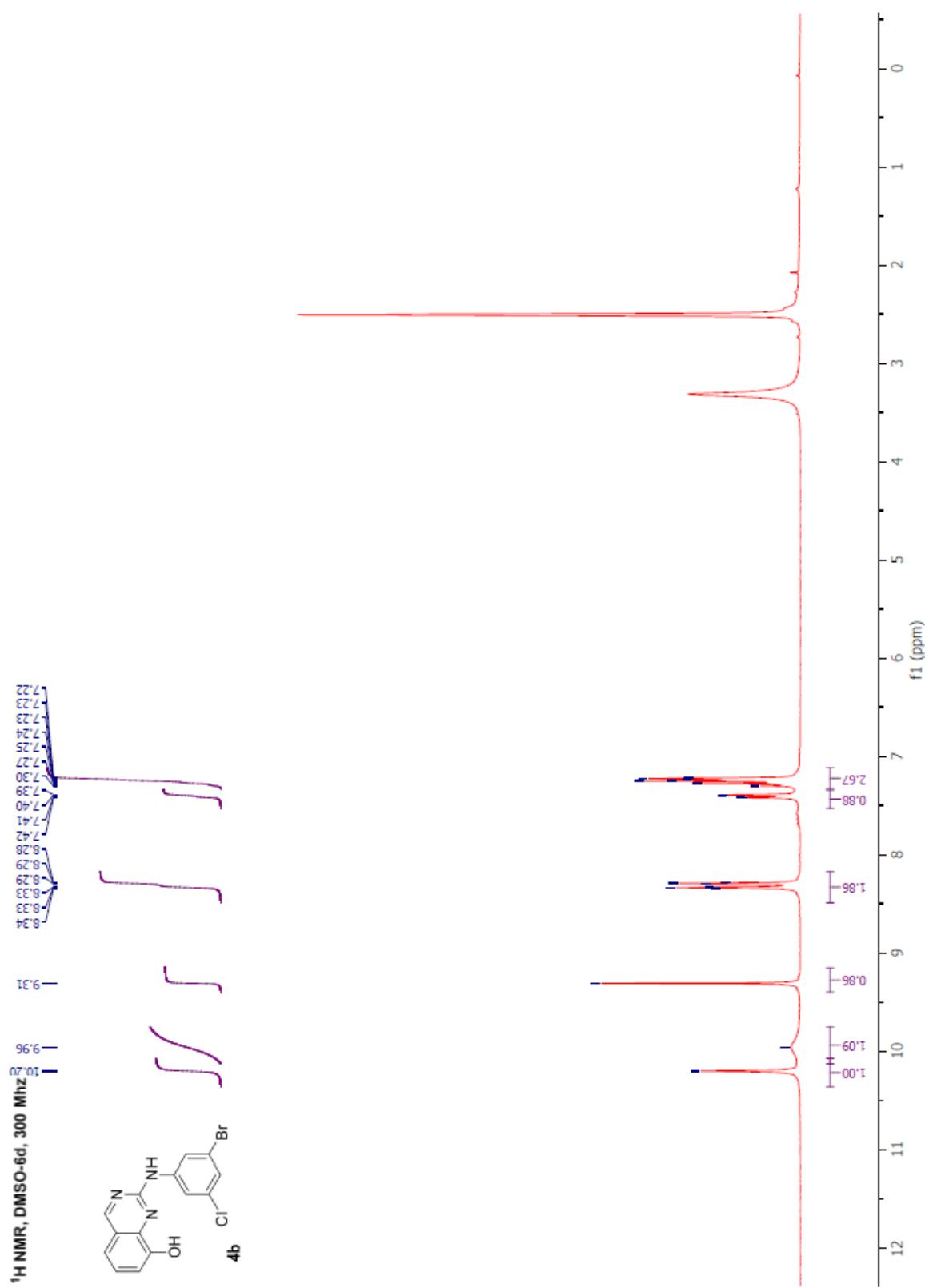


Figure 11: ^1H NMR spectrum of 4b

¹³C NMR, DMSO-*d*₆, 75 MHz

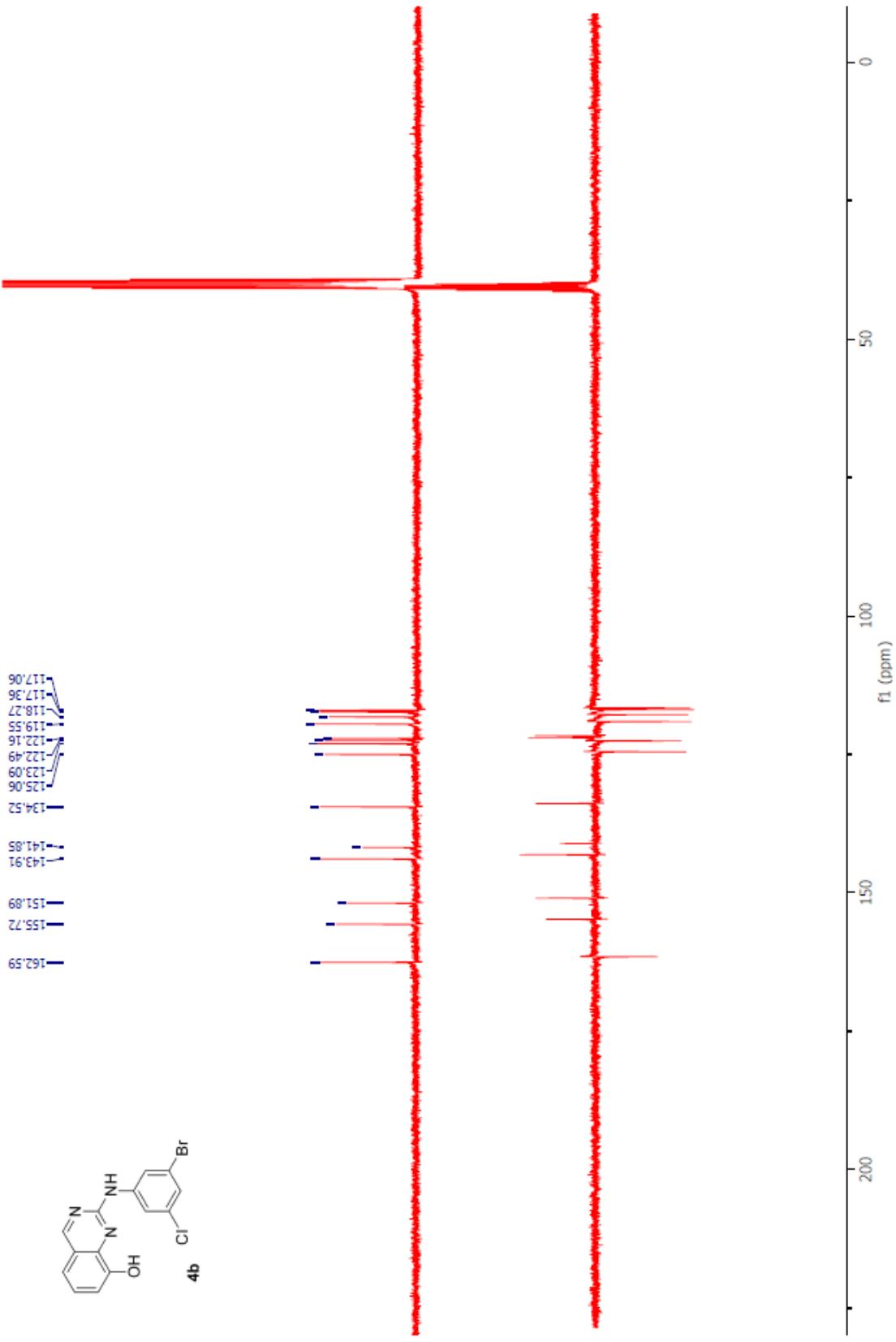
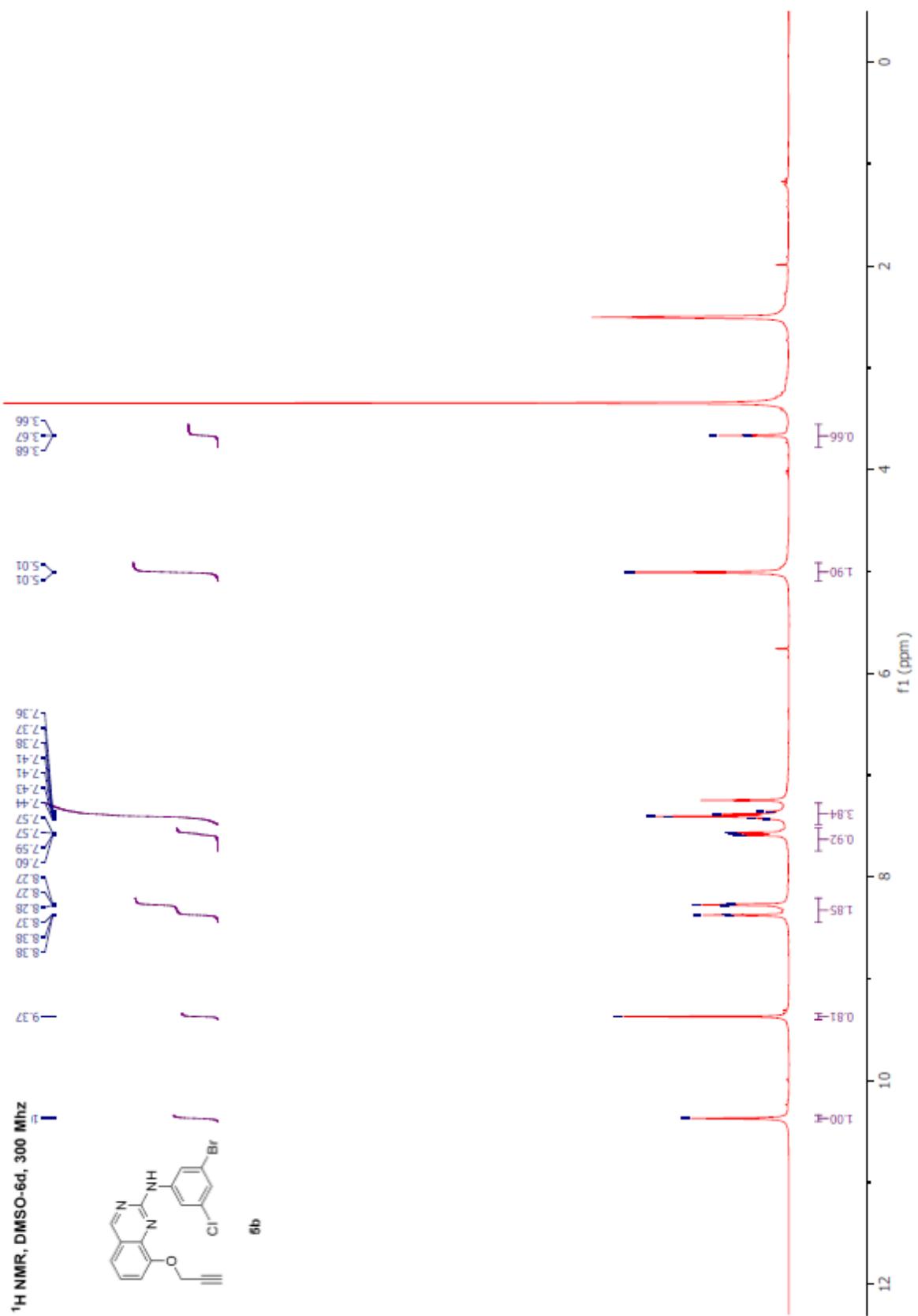


Figure 12: ¹³C NMR spectra of 4b



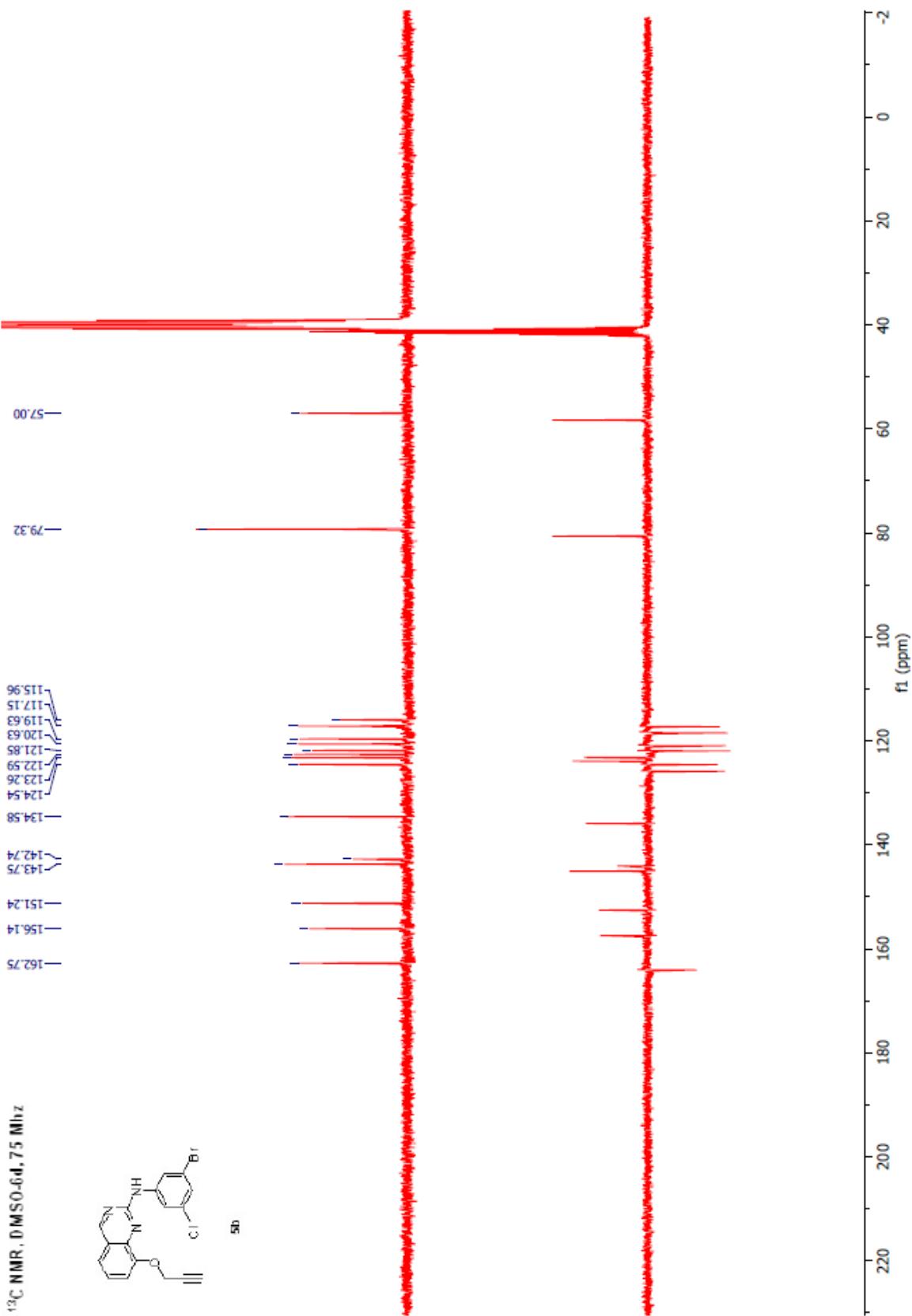


Figure 14: ¹³C NMR spectra of 5b

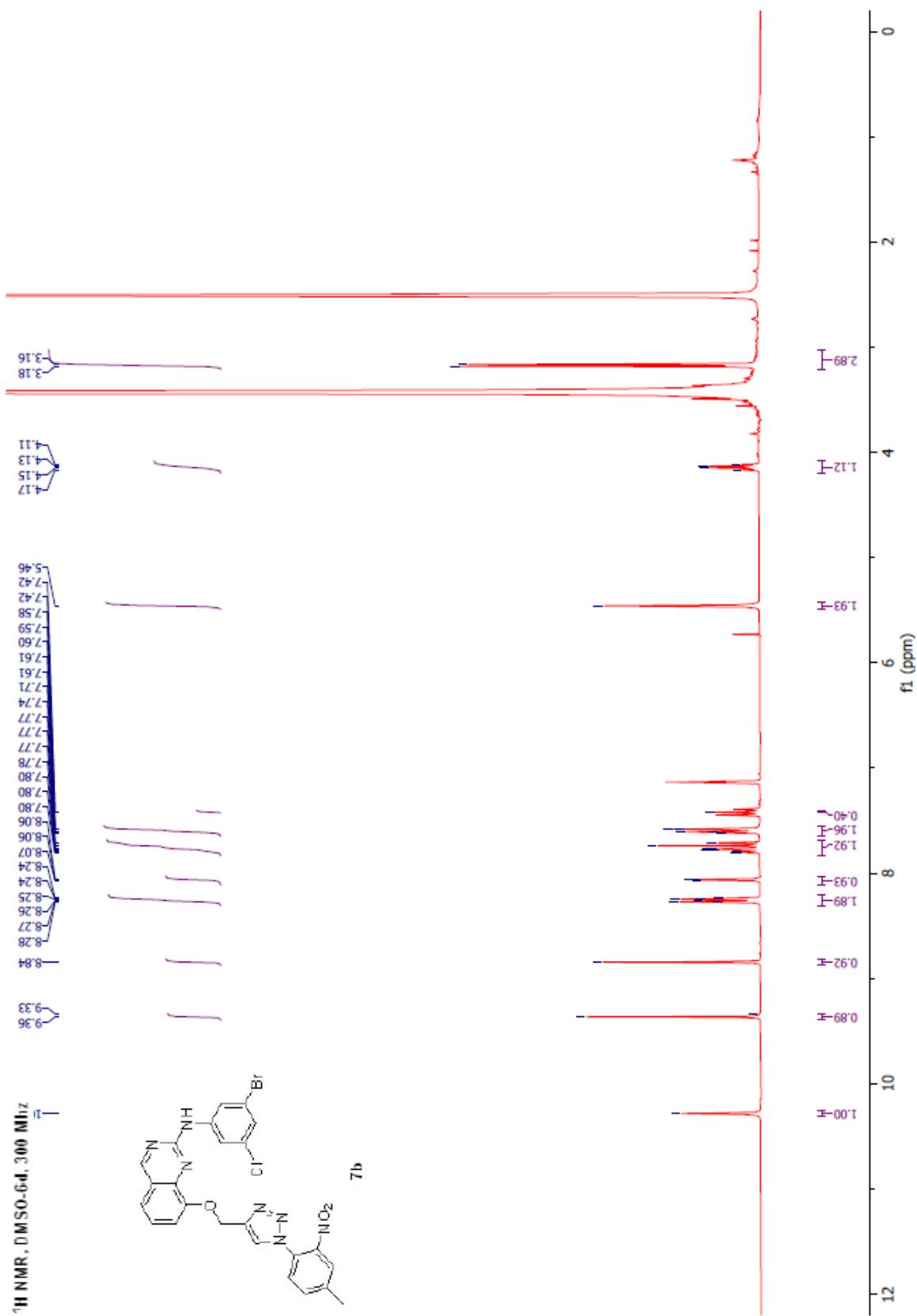


Figure 15: ¹H NMR spectrum of 7b

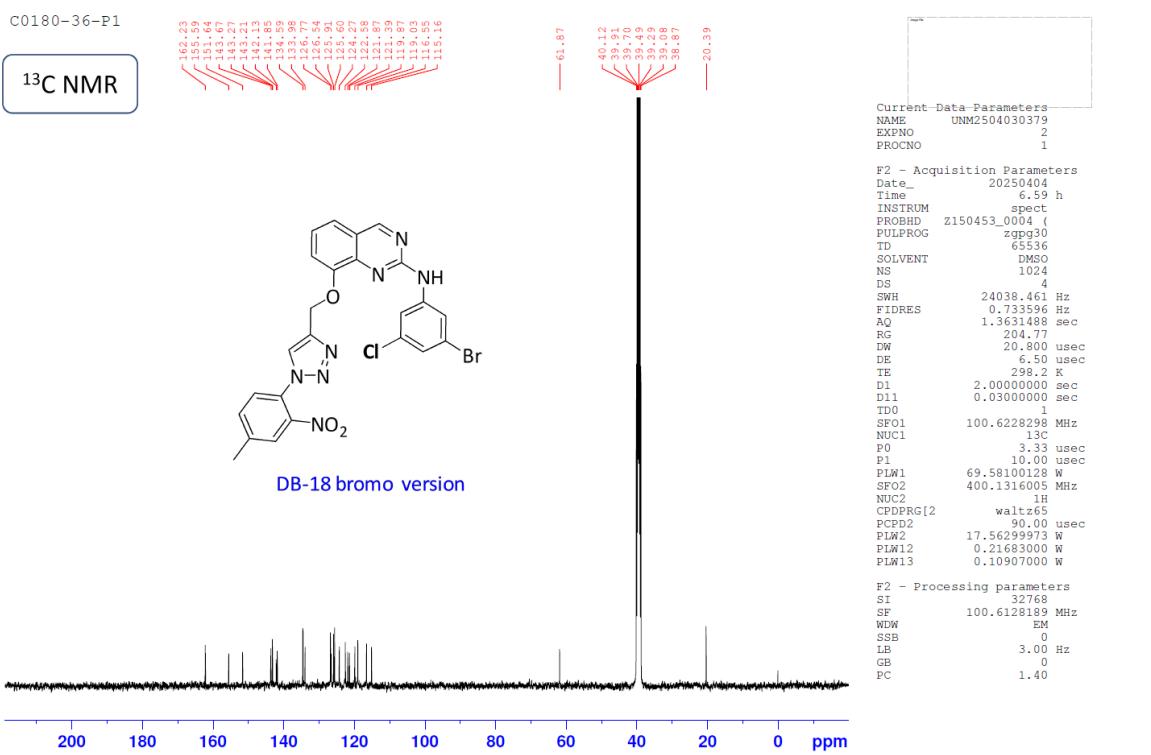
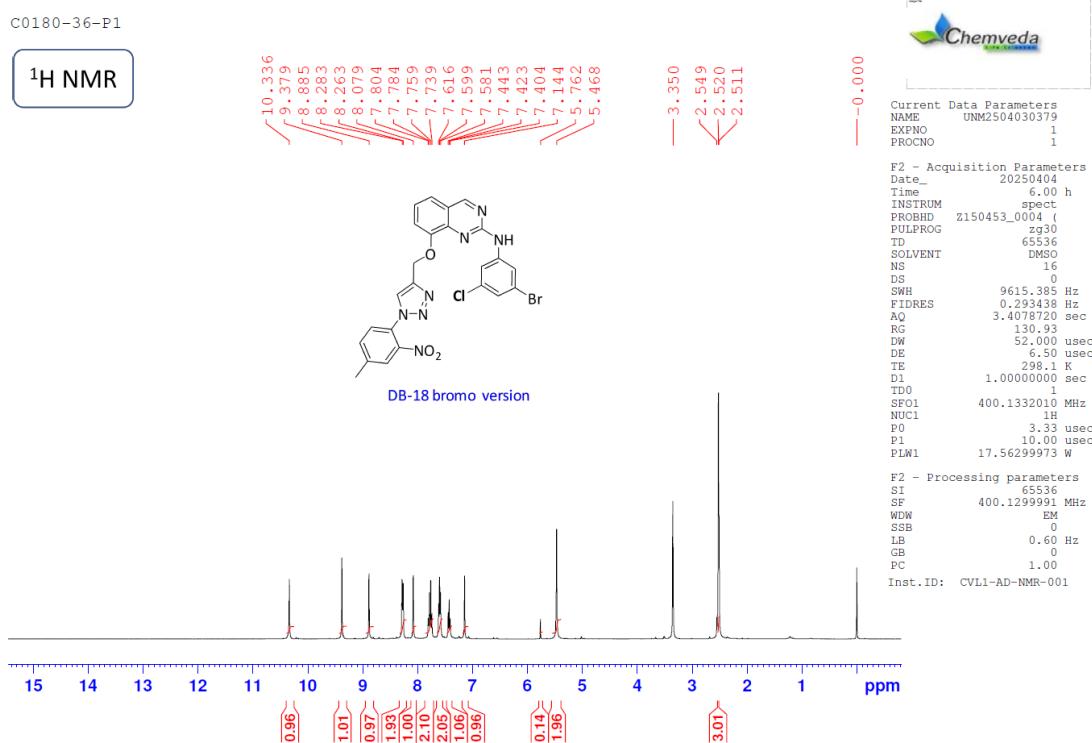


Figure 16: ^{13}C NMR spectrum of 7b



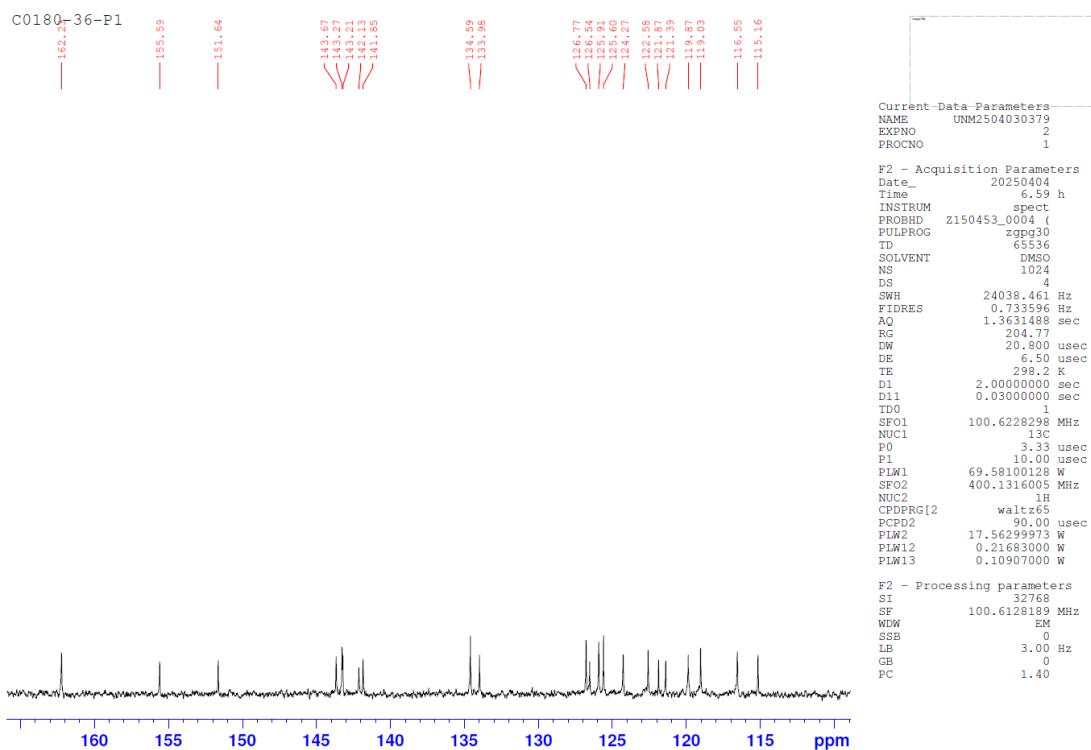


Figure 17: Extension of ¹³C NMR spectrum of 7b

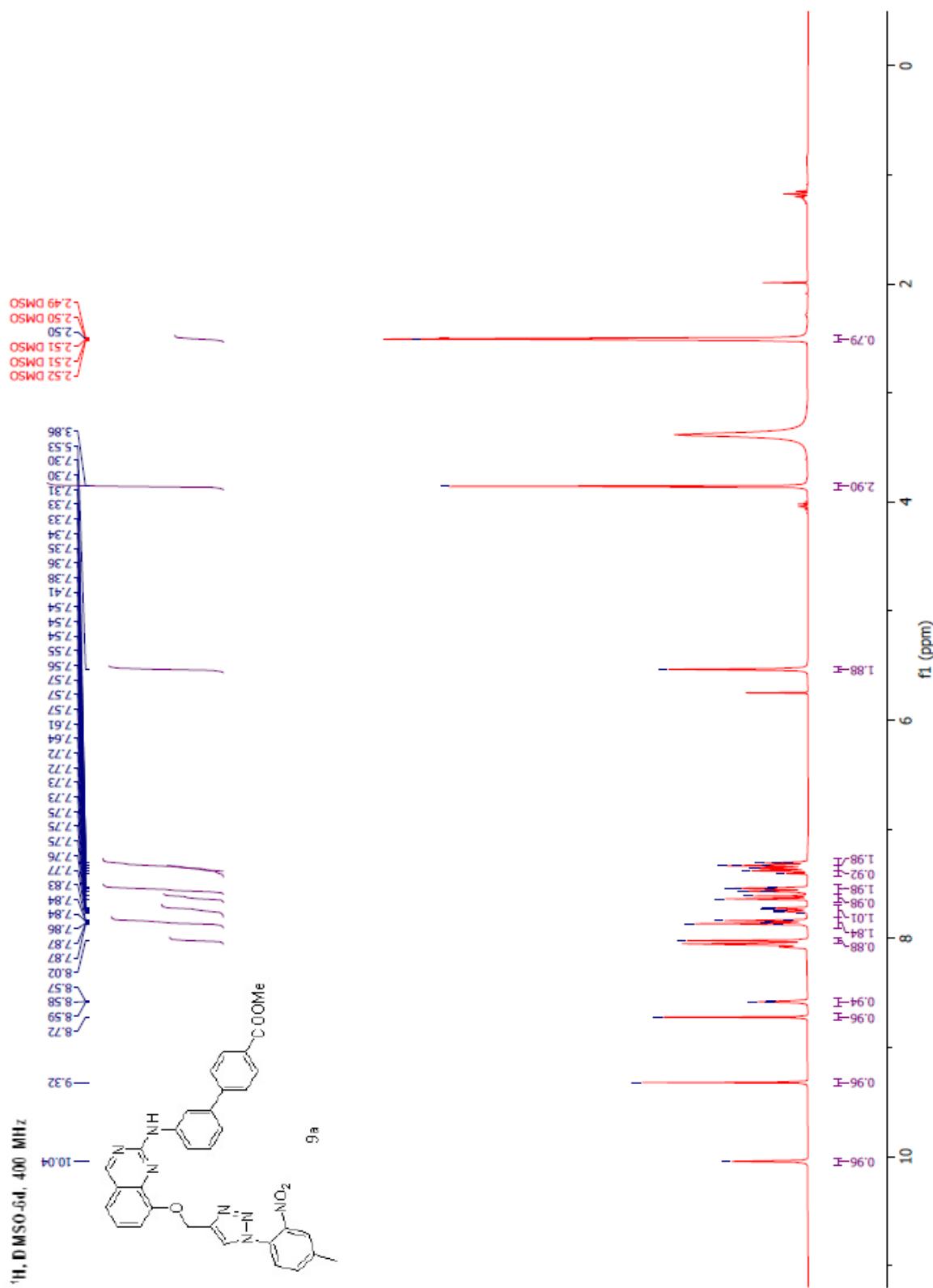


Figure 18: ^1H NMR spectra of 9a

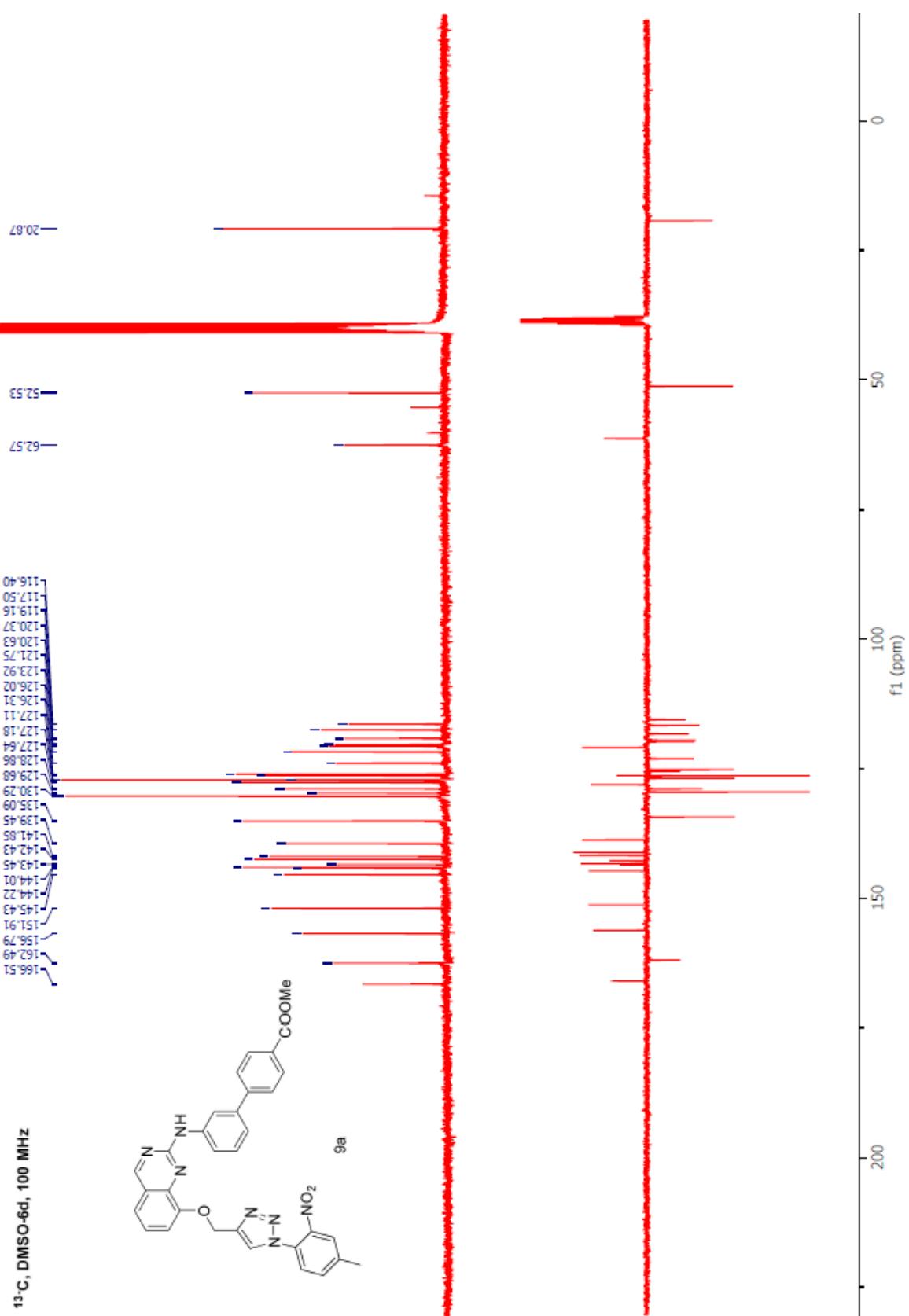


Figure 19: ^{13}C NMR spectra of 9a

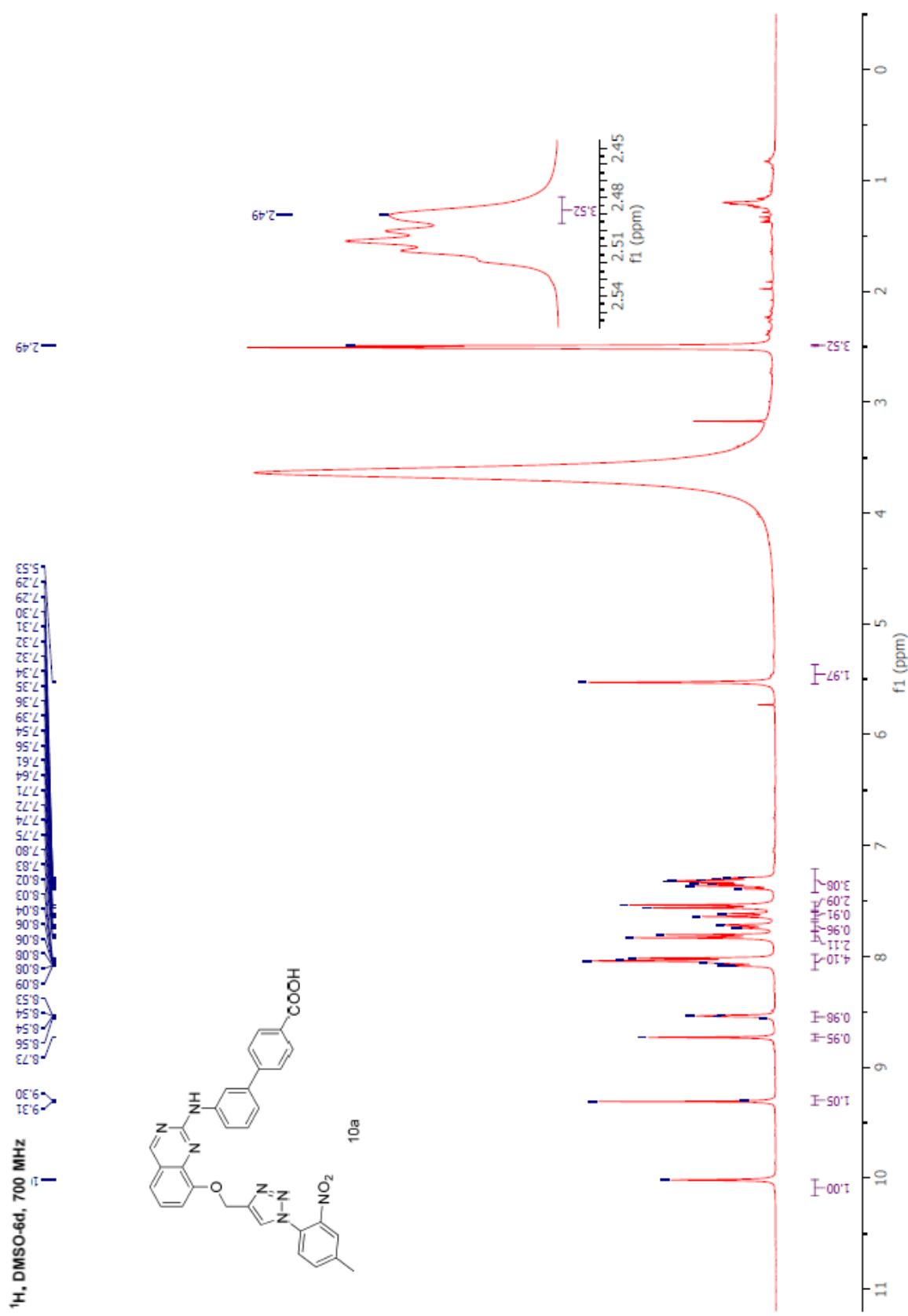


Figure 20: ^1H NMR spectra of 10a

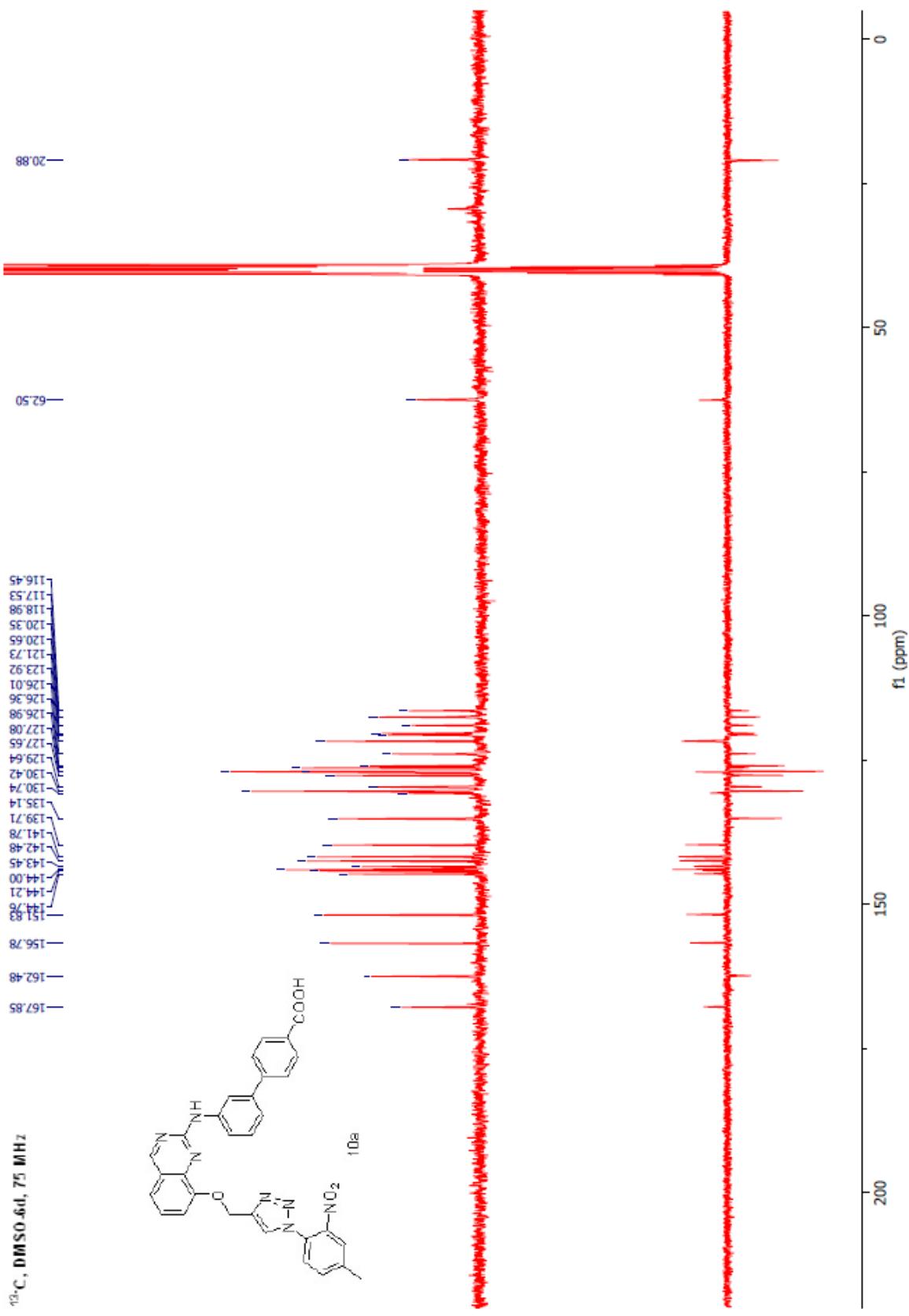


Figure 21: ^{13}C NMR spectra of 10a

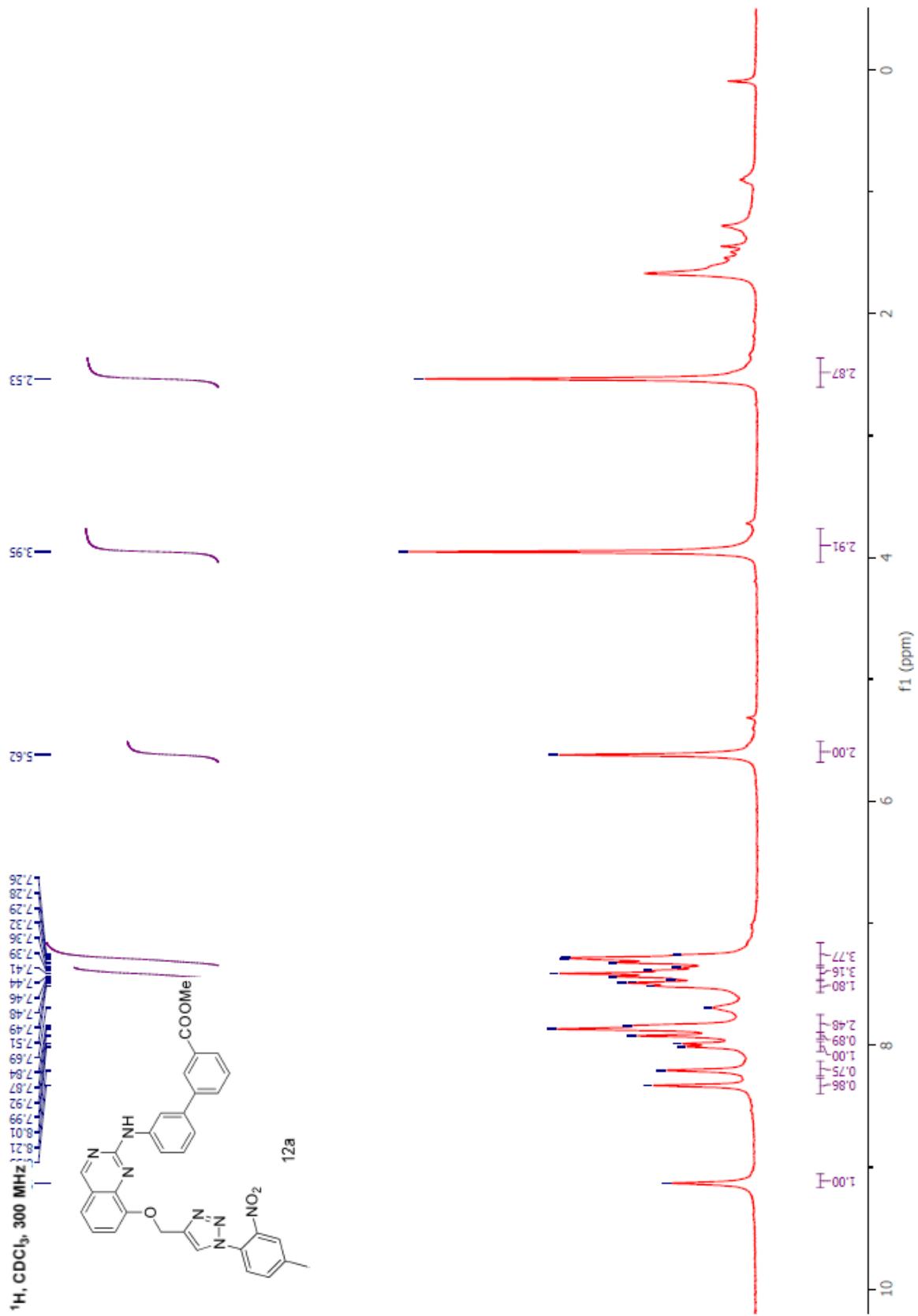


Figure 22: ^1H NMR spectra of 12a

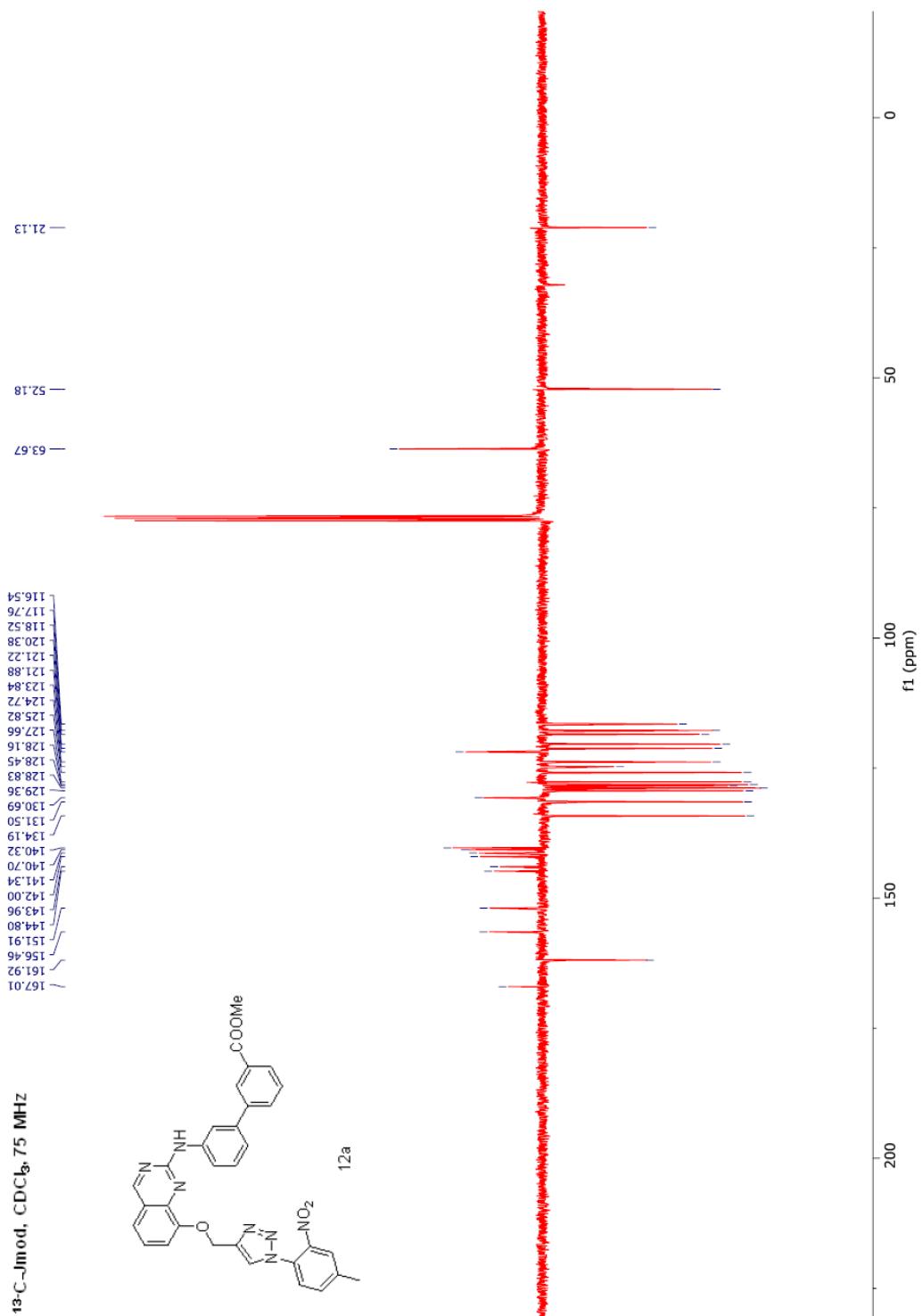


Figure 23: ^{13}C NMR spectrum of 12a

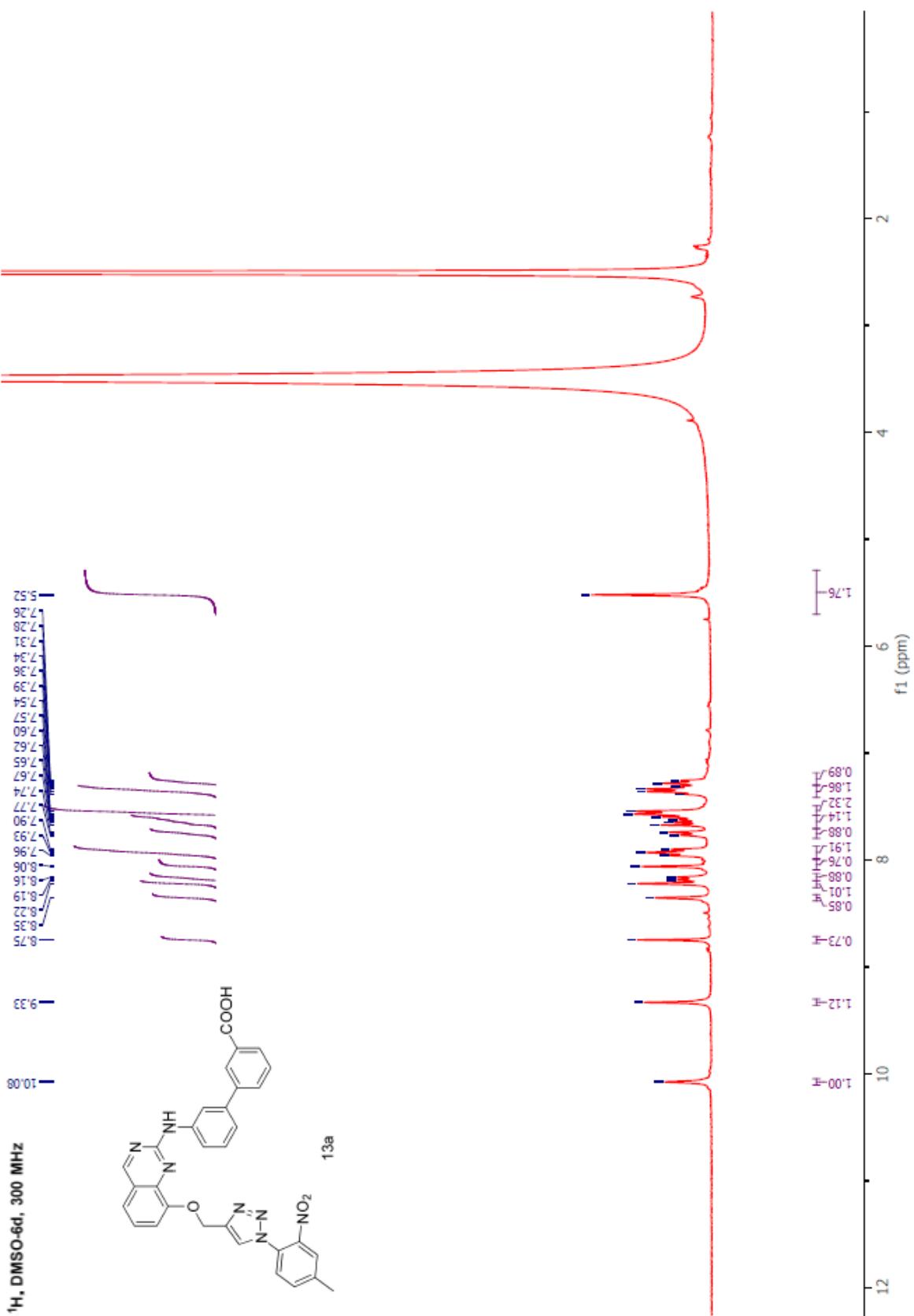


Figure 24: ¹H NMR spectrum of 13a

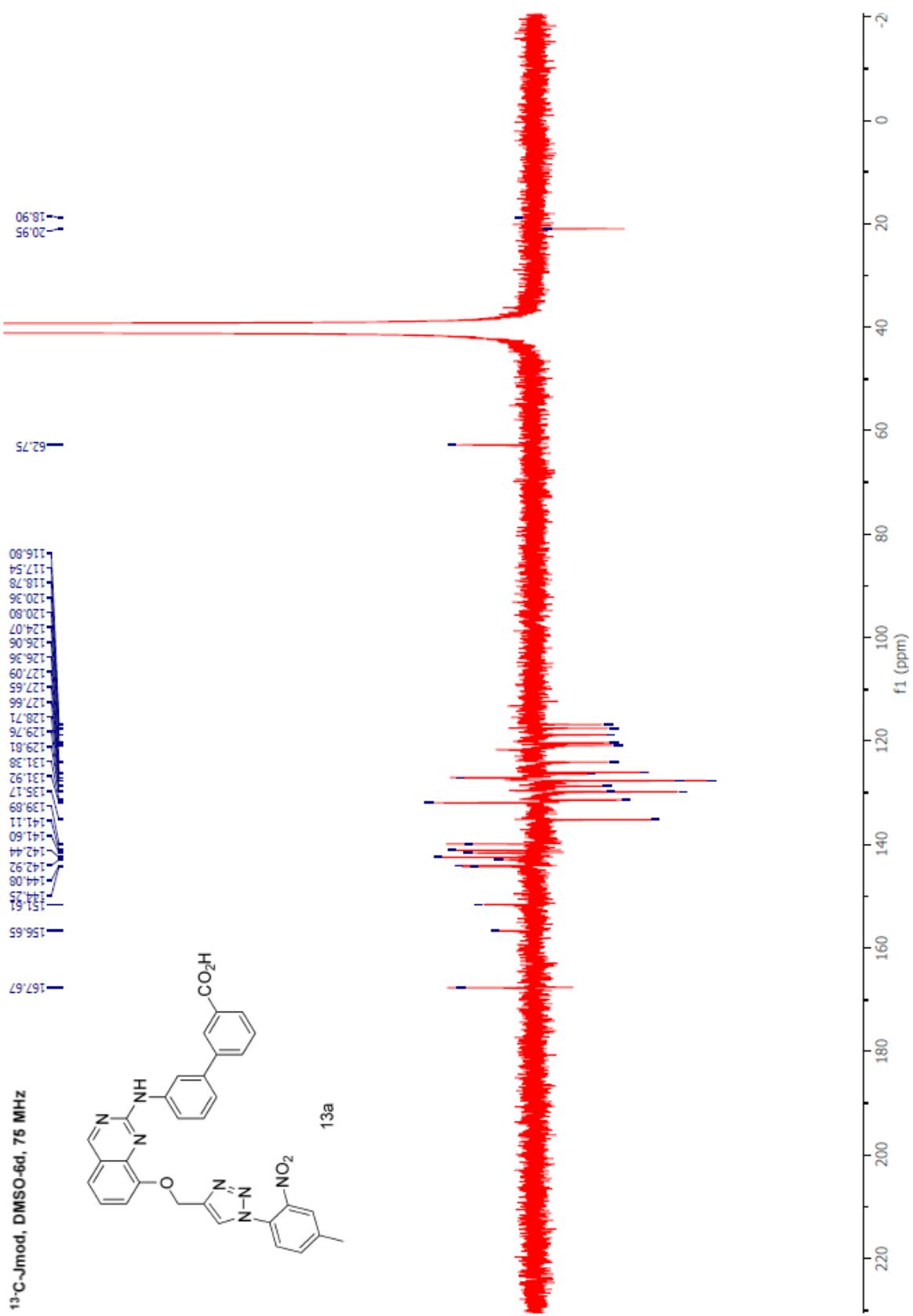


Figure 25: ¹³C NMR spectrum of 13a

Figure 2: ^{13}C NMR spectrum of 13a

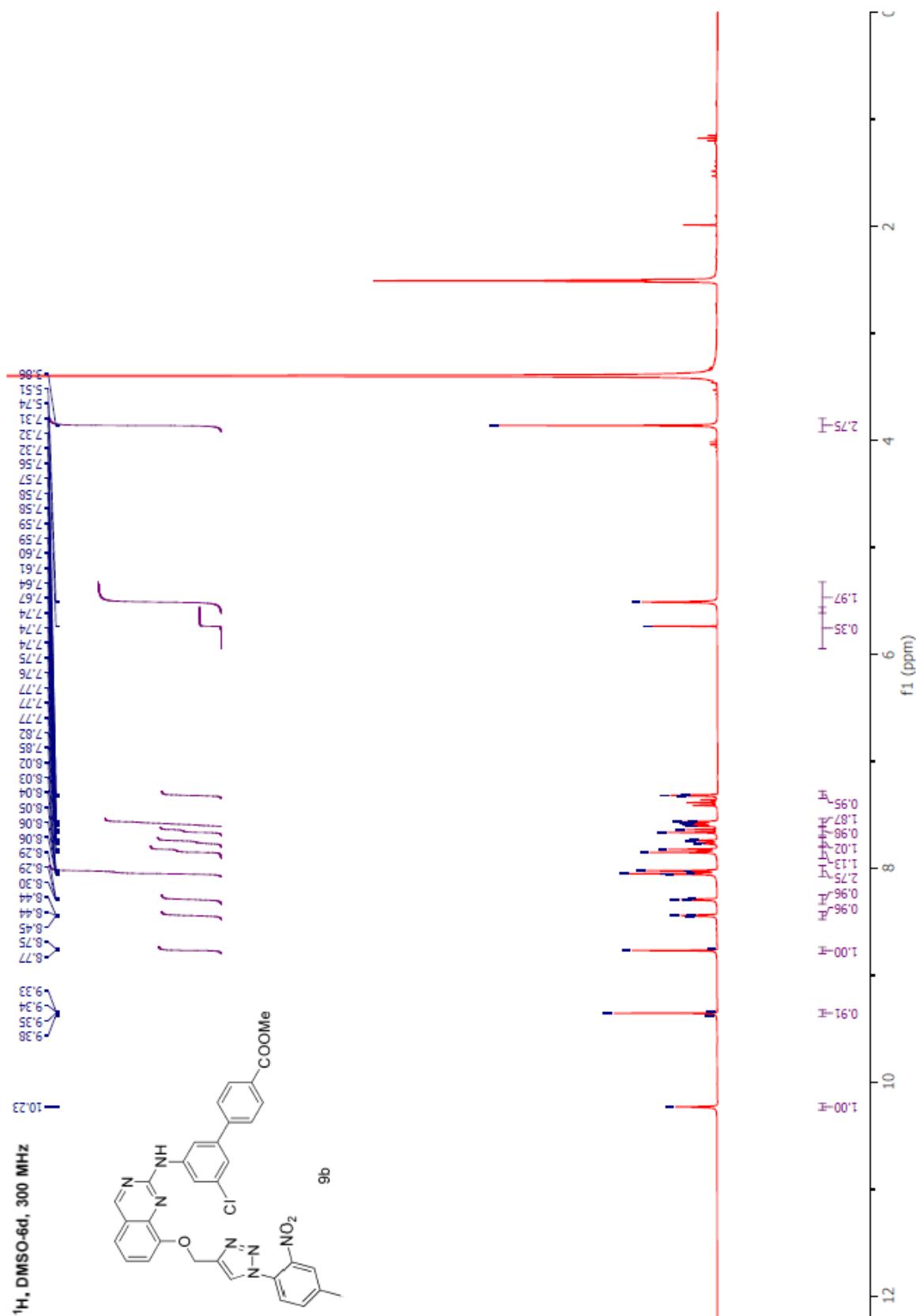


Figure 26: ^1H NMR spectrum of 9b

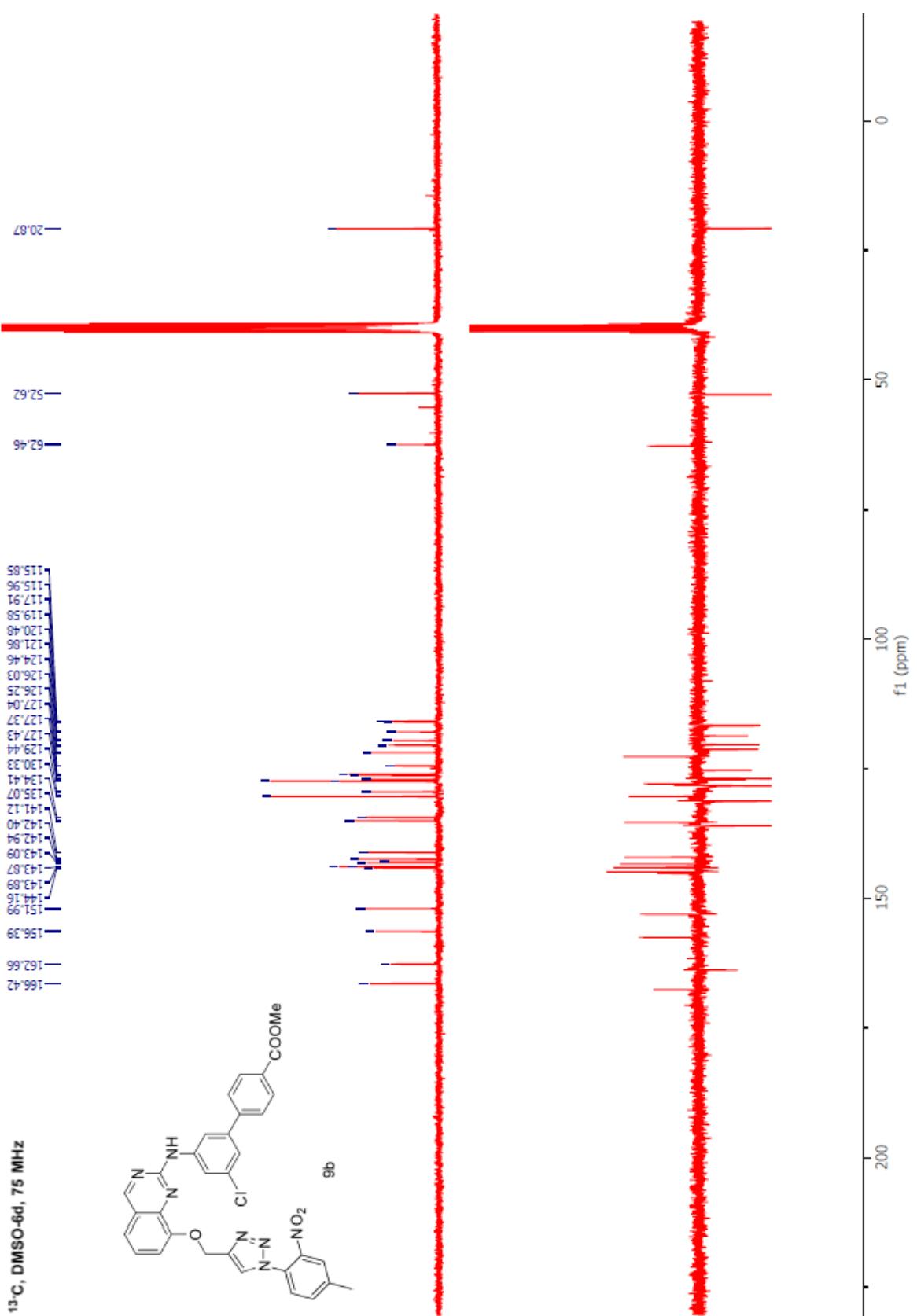


Figure 27: ¹³C NMR spectra of 9b

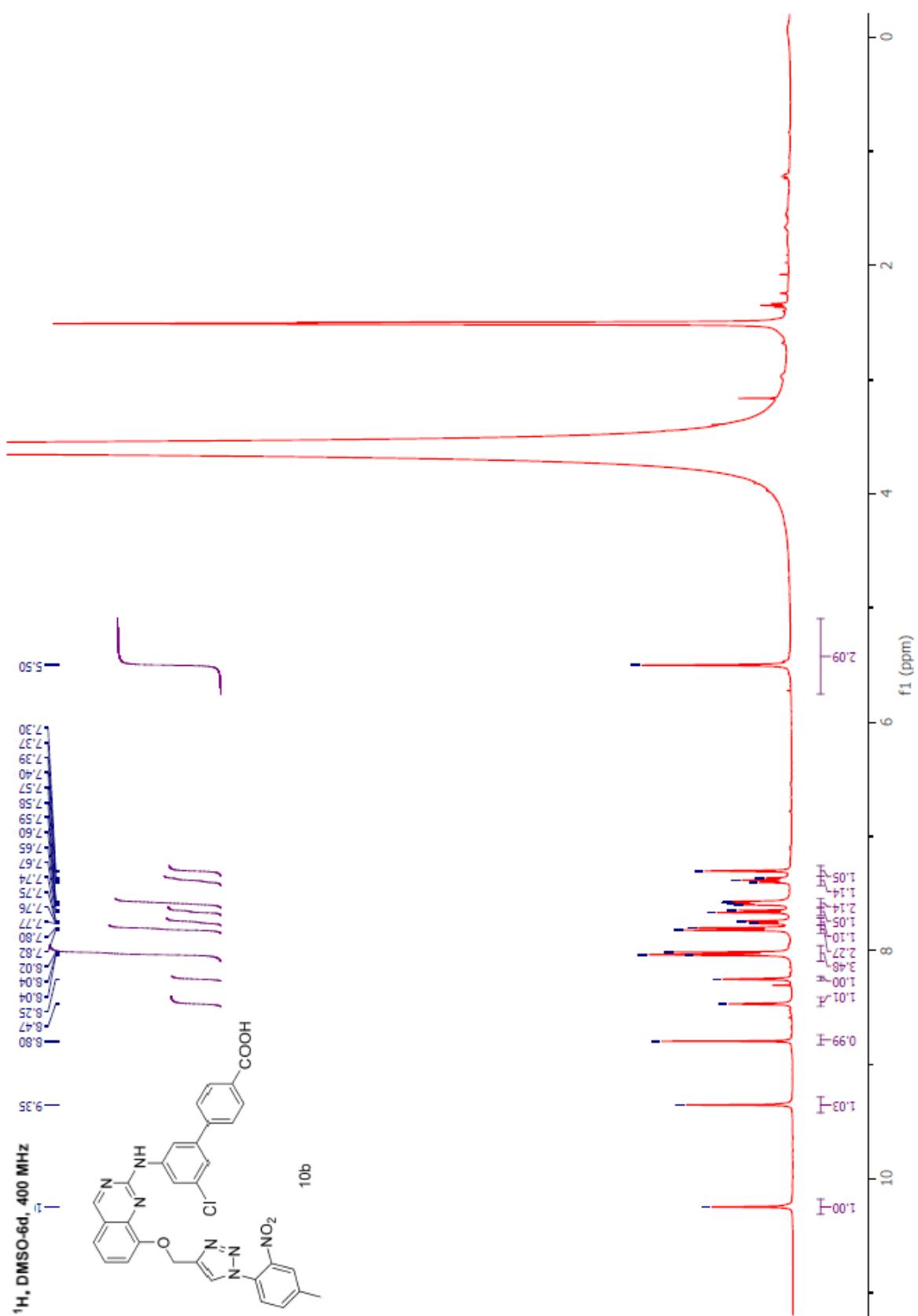


Figure 28: ¹H NMR spectrum of 10b

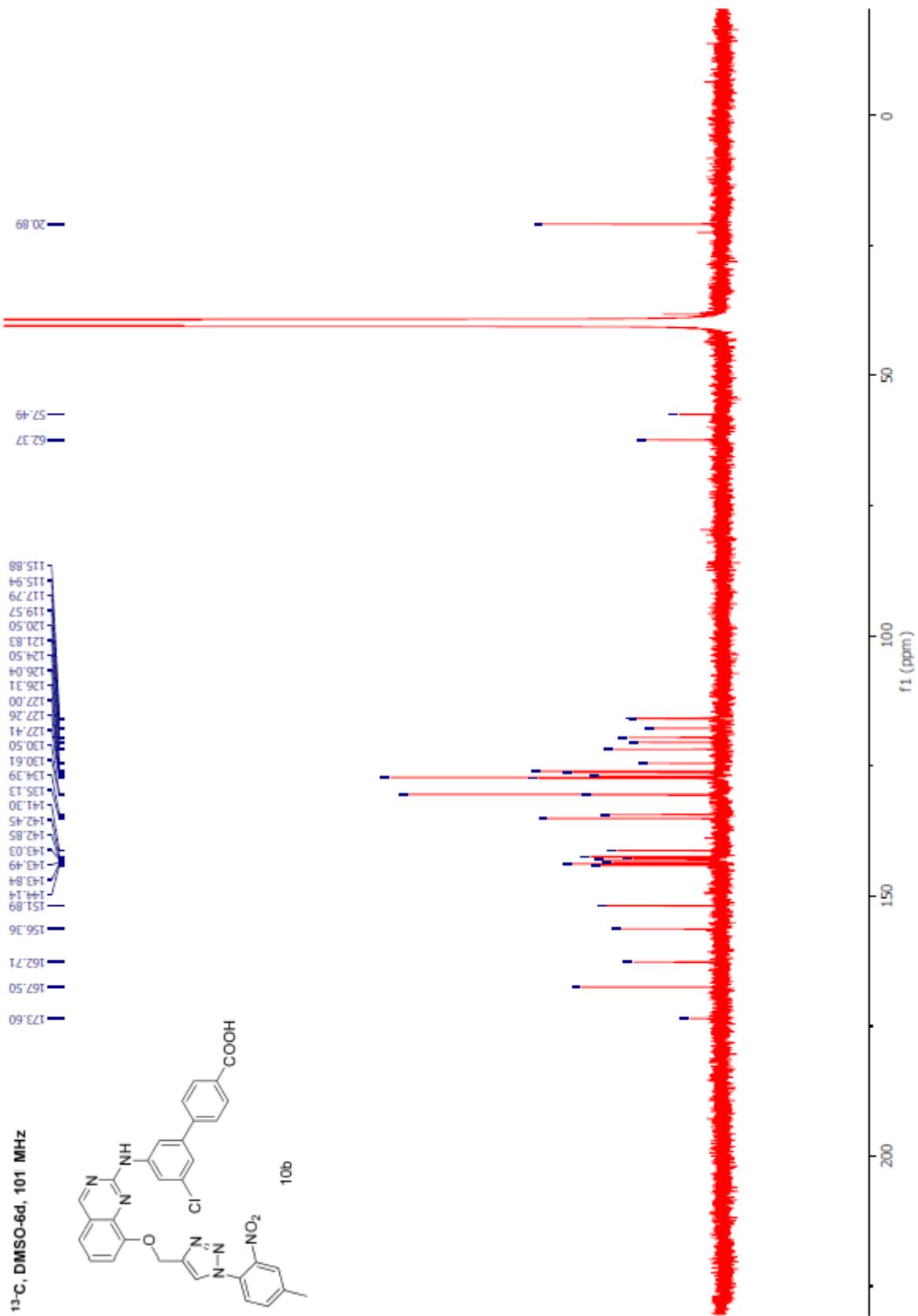


Figure 29: ^{13}C NMR spectrum of 10b

¹H, DMSO-6d, 400 MHz

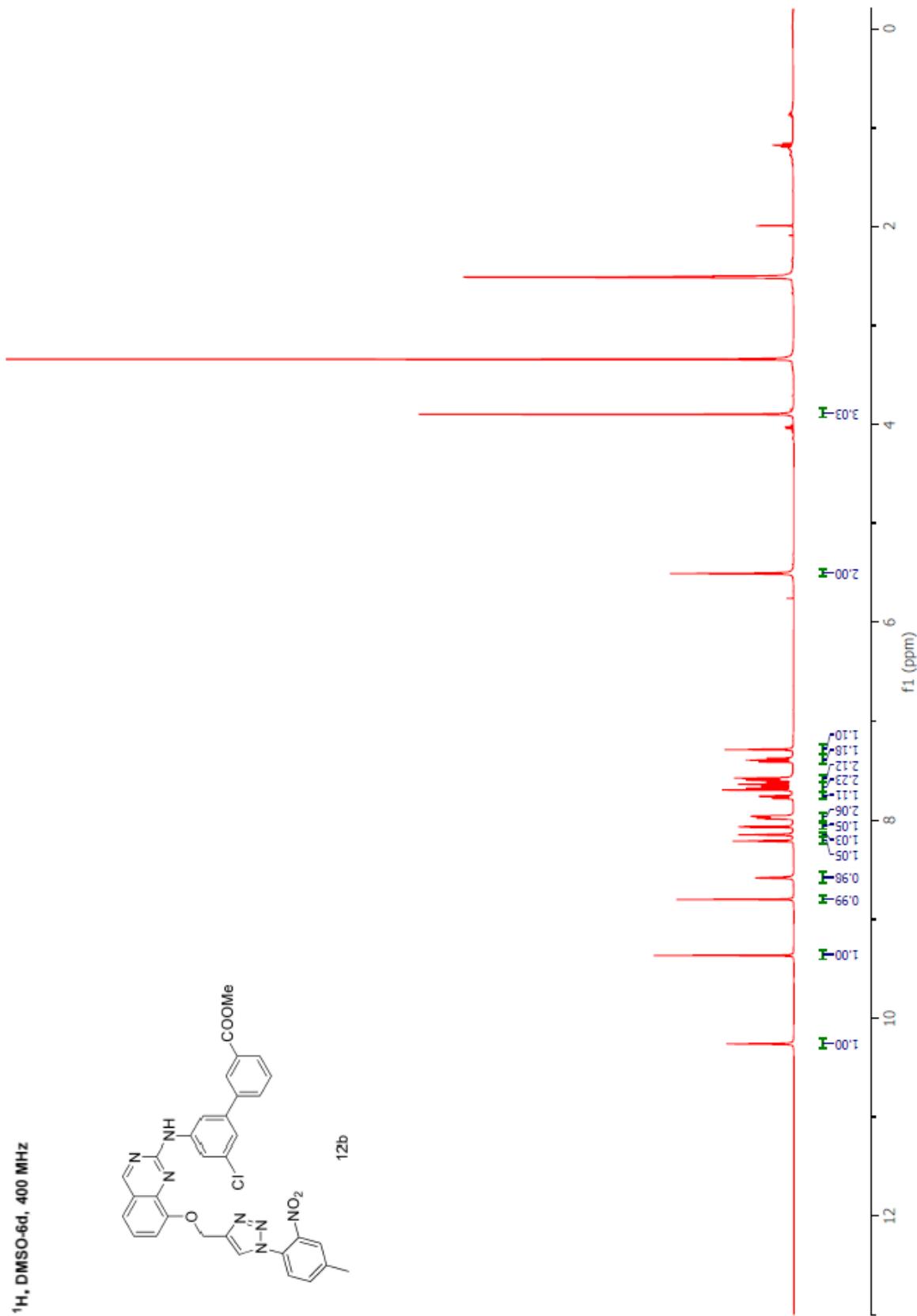
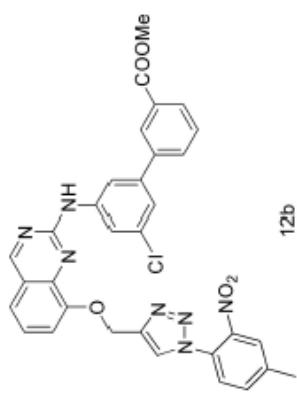


Figure 30: ¹H NMR spectrum of 12b

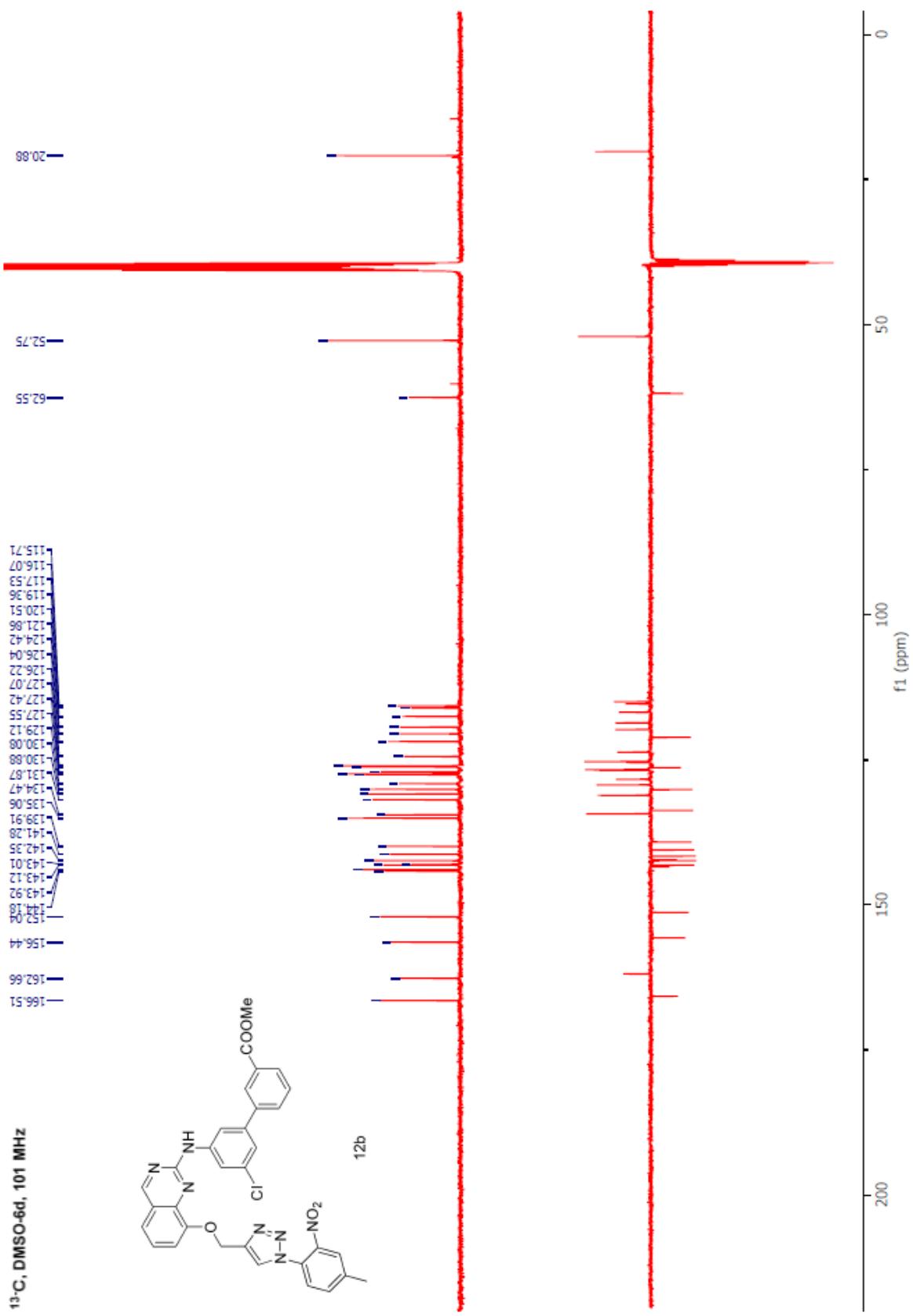


Figure 31: ¹³C spectra of 12b

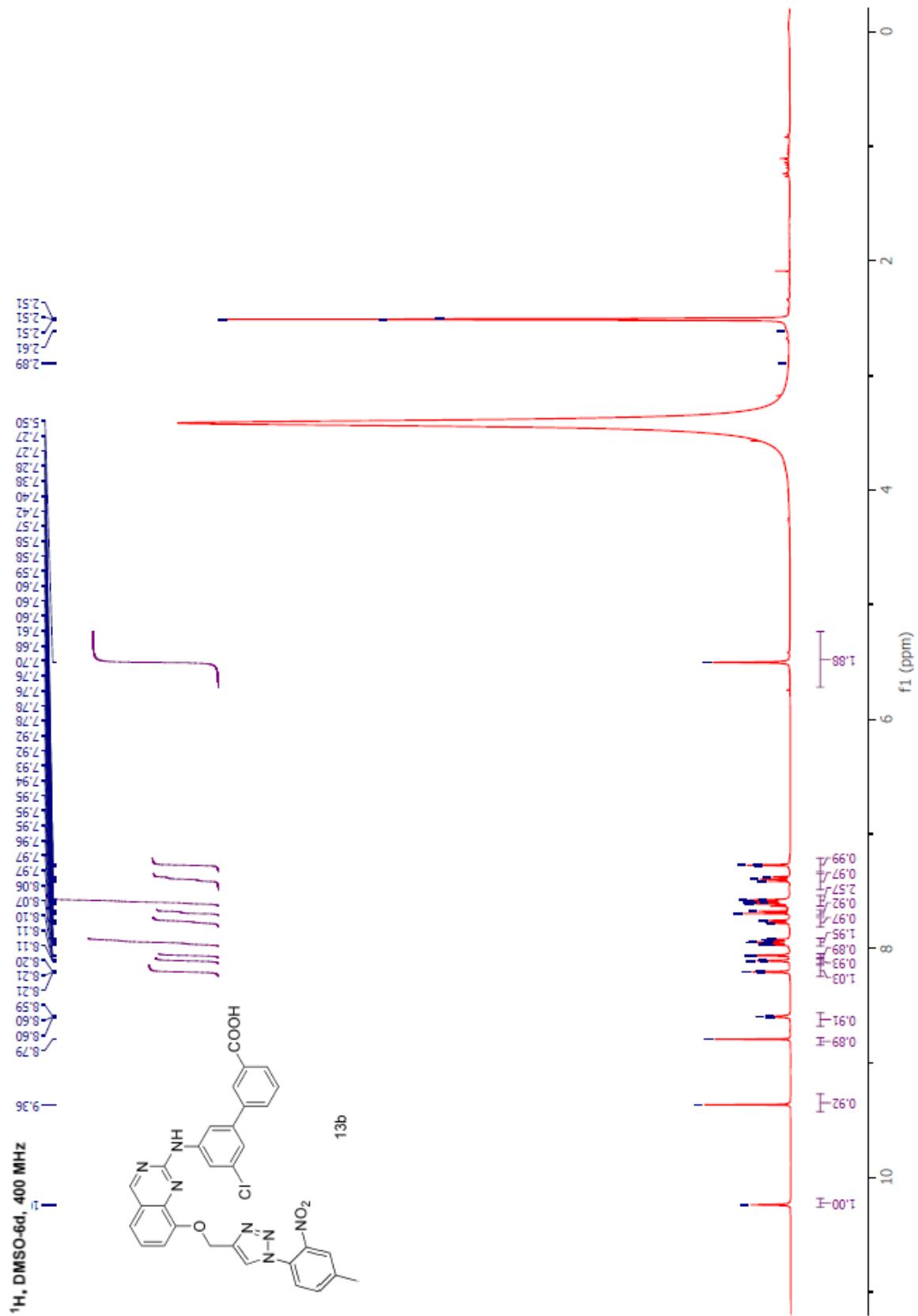


Figure 32: ^1H spectrum of 13b

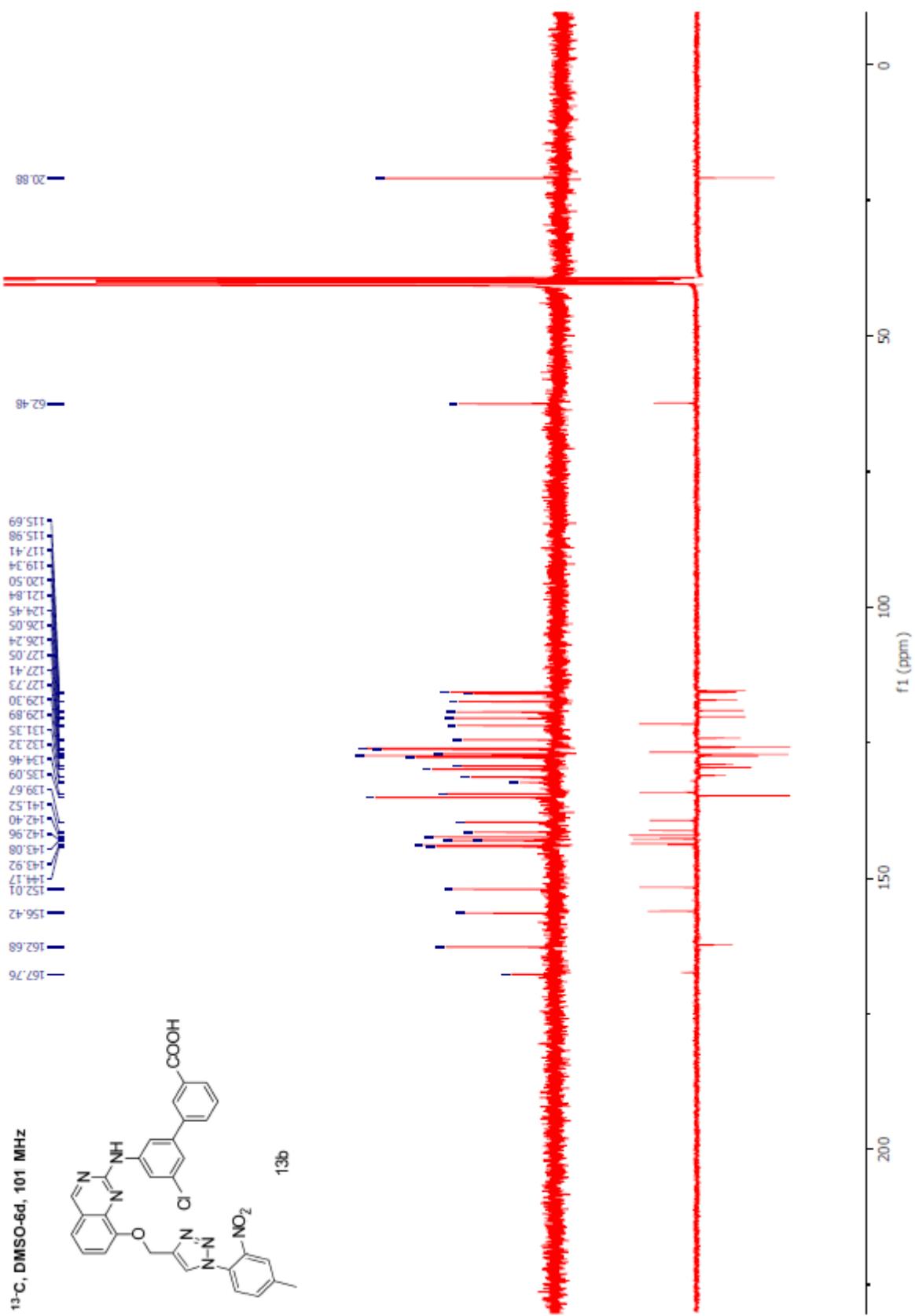


Figure 33: ¹³C NMR spectrum of 13b