Supporting information

Design, Synthesis and Biological Evaluation of Biphenylglyoxamide-based Small Molecular Antimicrobial Peptide Mimics as Antibacterial Agents

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Supplementary figures for the antibiofilm activity of compounds 15c-15d, 22a-22d

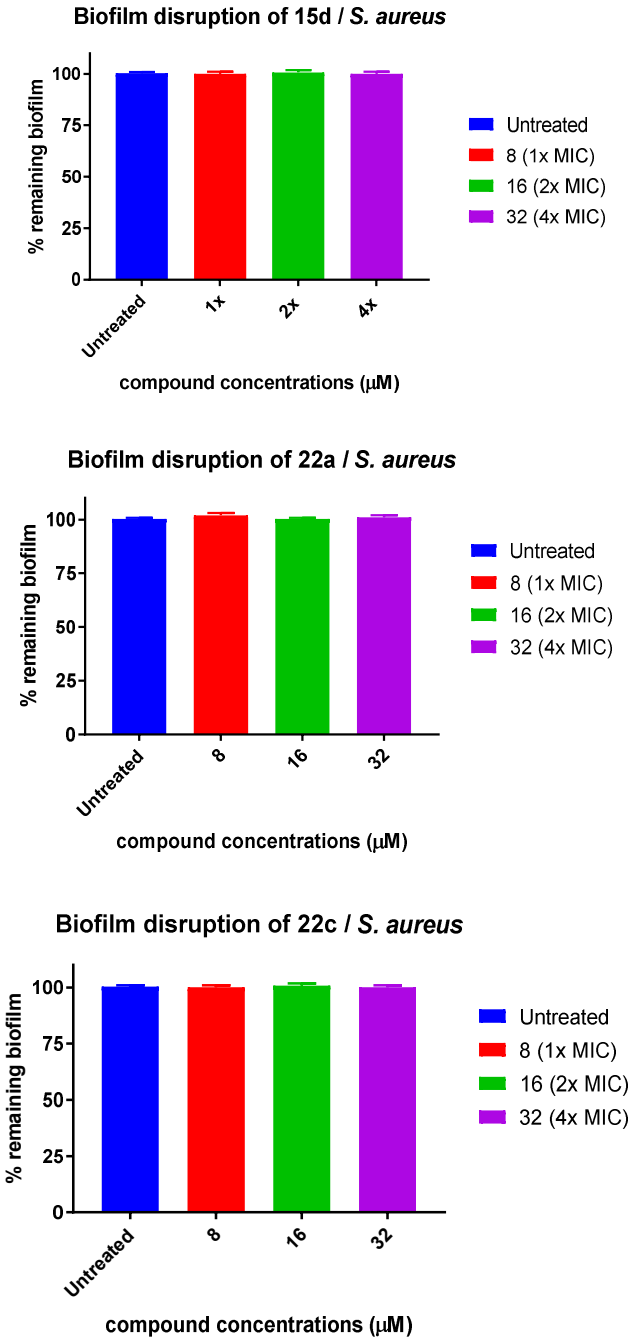


Figure S1. Percentage of remaining *S. aureus* biofilms after 24 h treatment with compounds **15d** (top), **22a** (middle) or **22c** (bottom) at 1×, 2× and 4× of their MIC. Error bars represent the standard error of triplicates (n = 3).

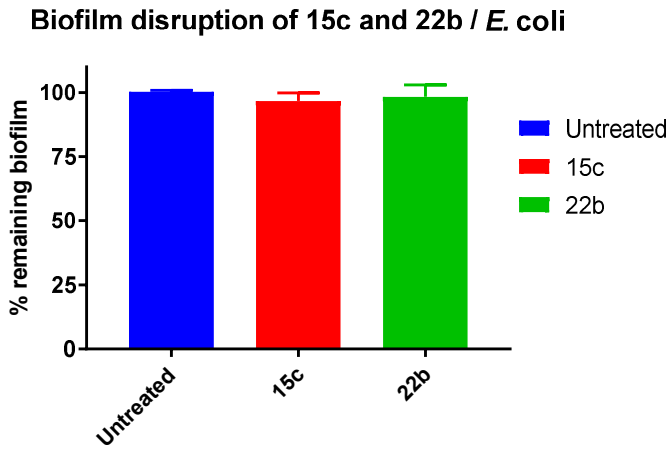
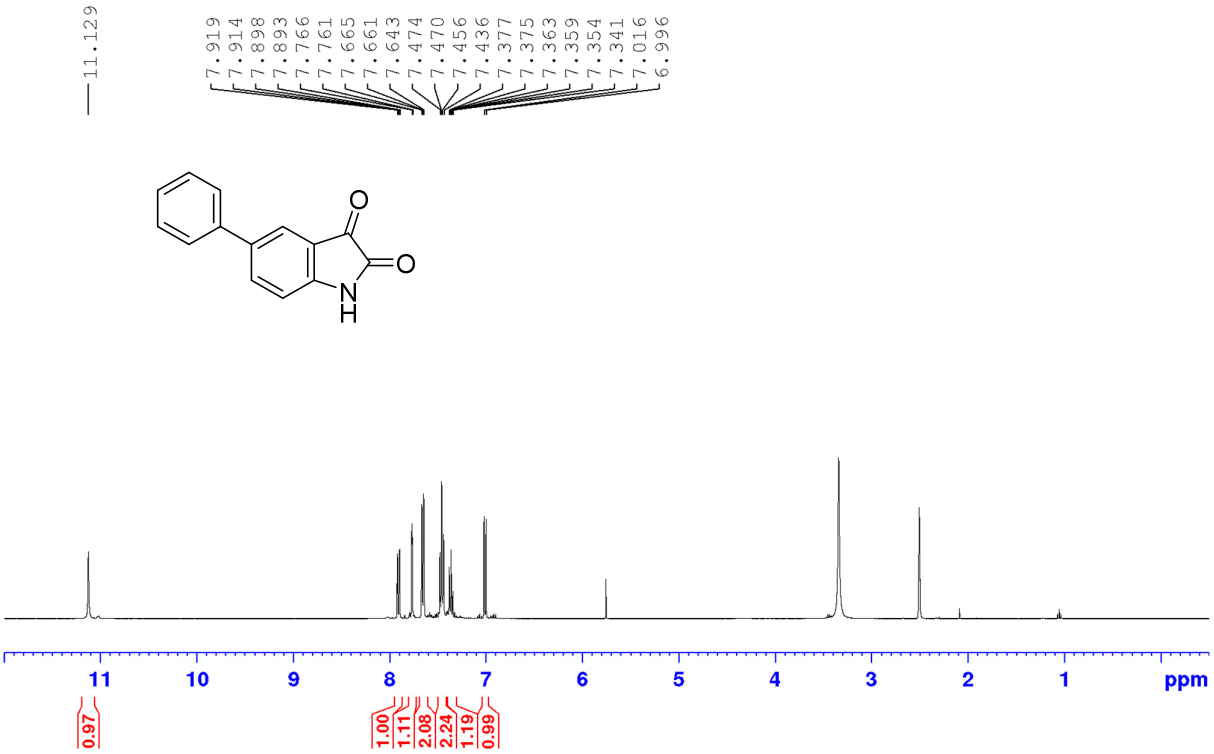


Figure S2. Percentage of remaining *E. coli* biofilms after 24 h treatment with compounds **15c** or **22c** at 4× of their MIC (64 μM). Error bars represent the standard error of triplicates (n = 3).

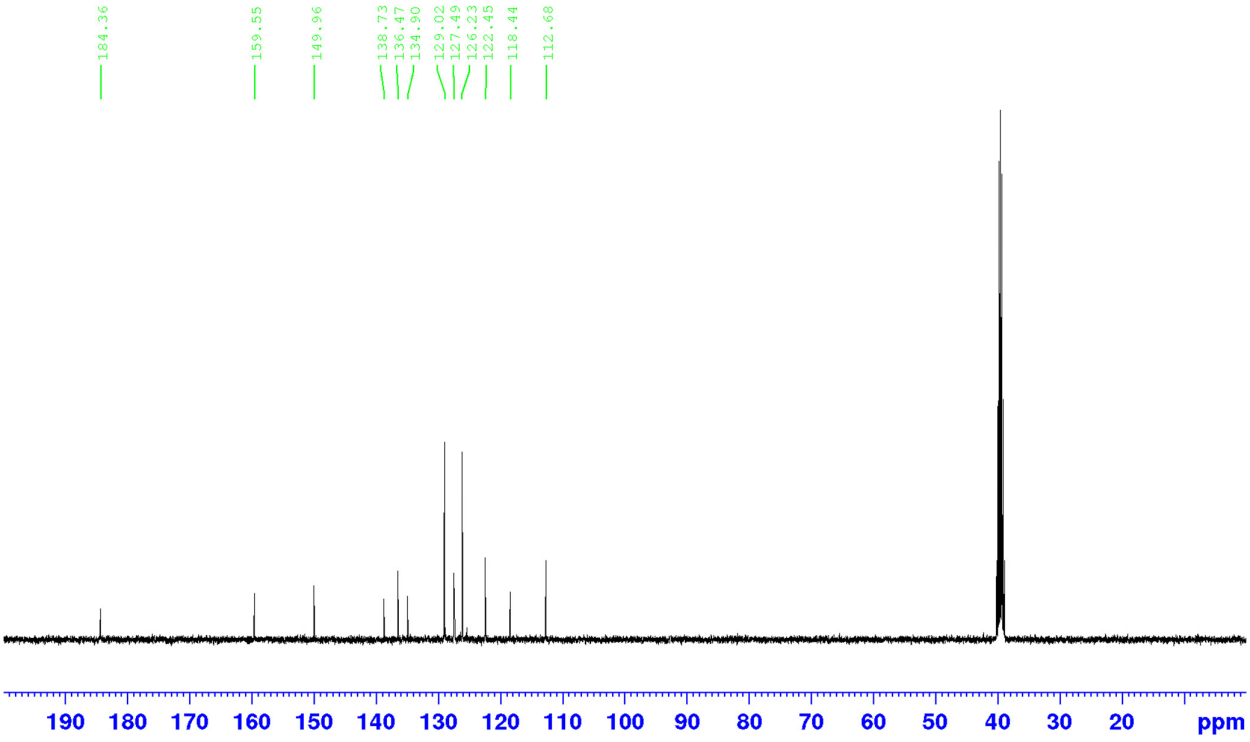
^{1}H NMR and ^{13}C NMR spectra of synthesized compounds

5-Phenylindoline-2,3-dione (**7a**)

^{1}H NMR (400 MHz, DMSO-d_6):

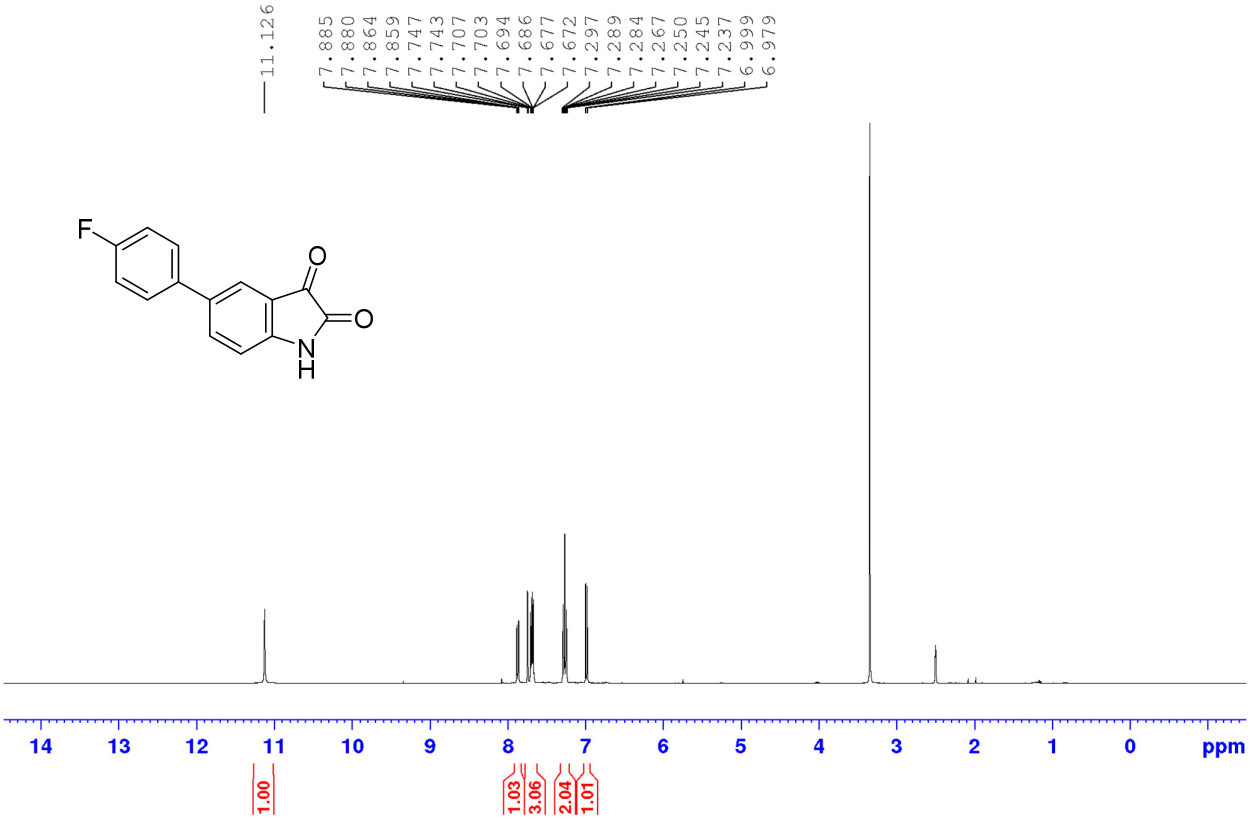


^{13}C NMR (100 MHz, DMSO-d_6):

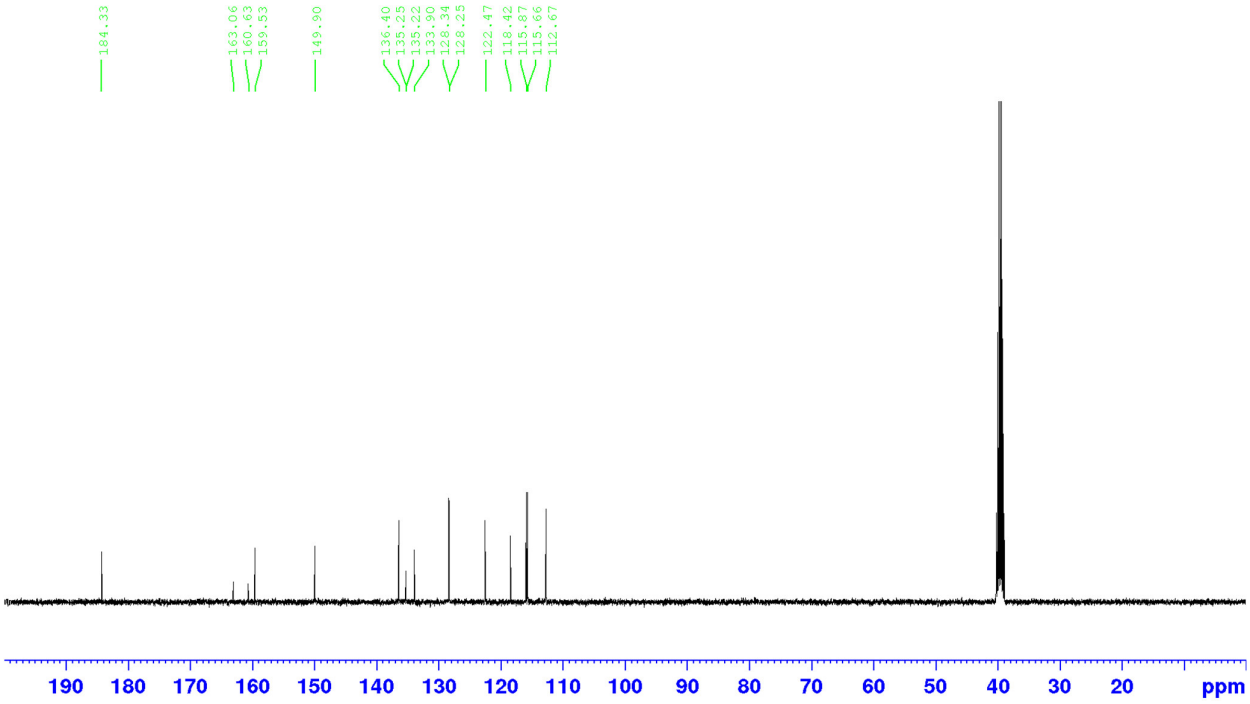


5-(4-Fluorophenyl)indoline-2,3-dione (**7b**)

^{1}H NMR (400 MHz, DMSO-d_6):

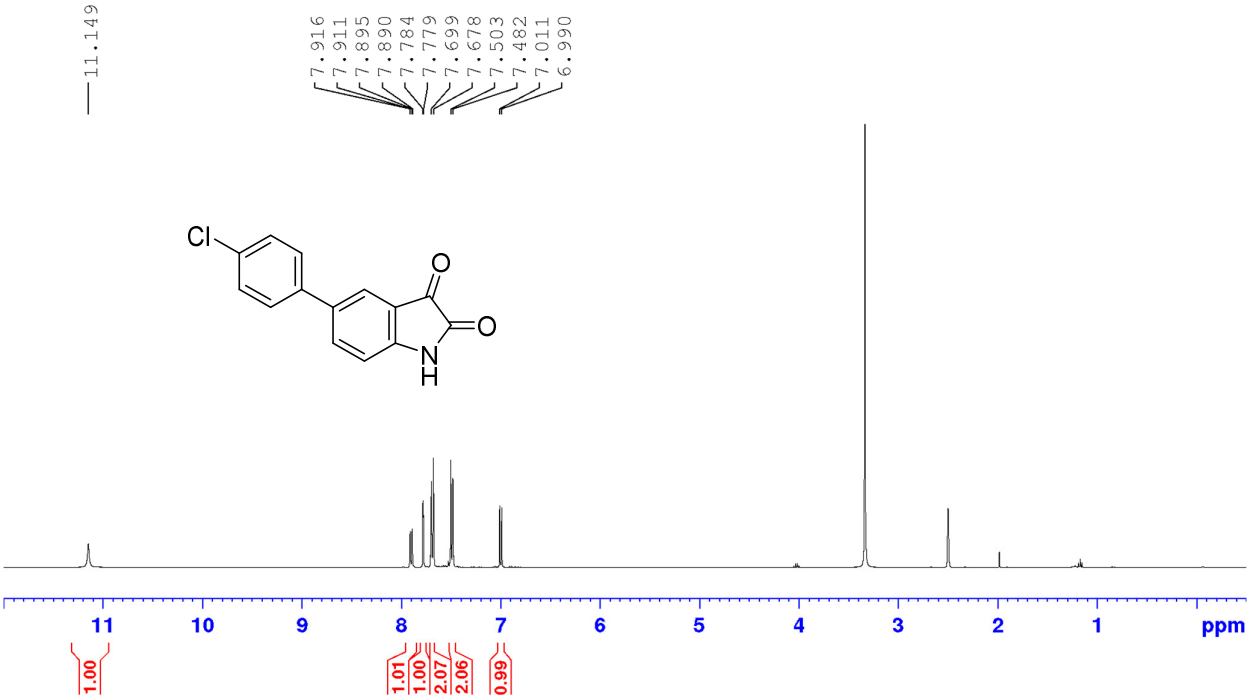


^{13}C NMR (100 MHz, DMSO-d_6):

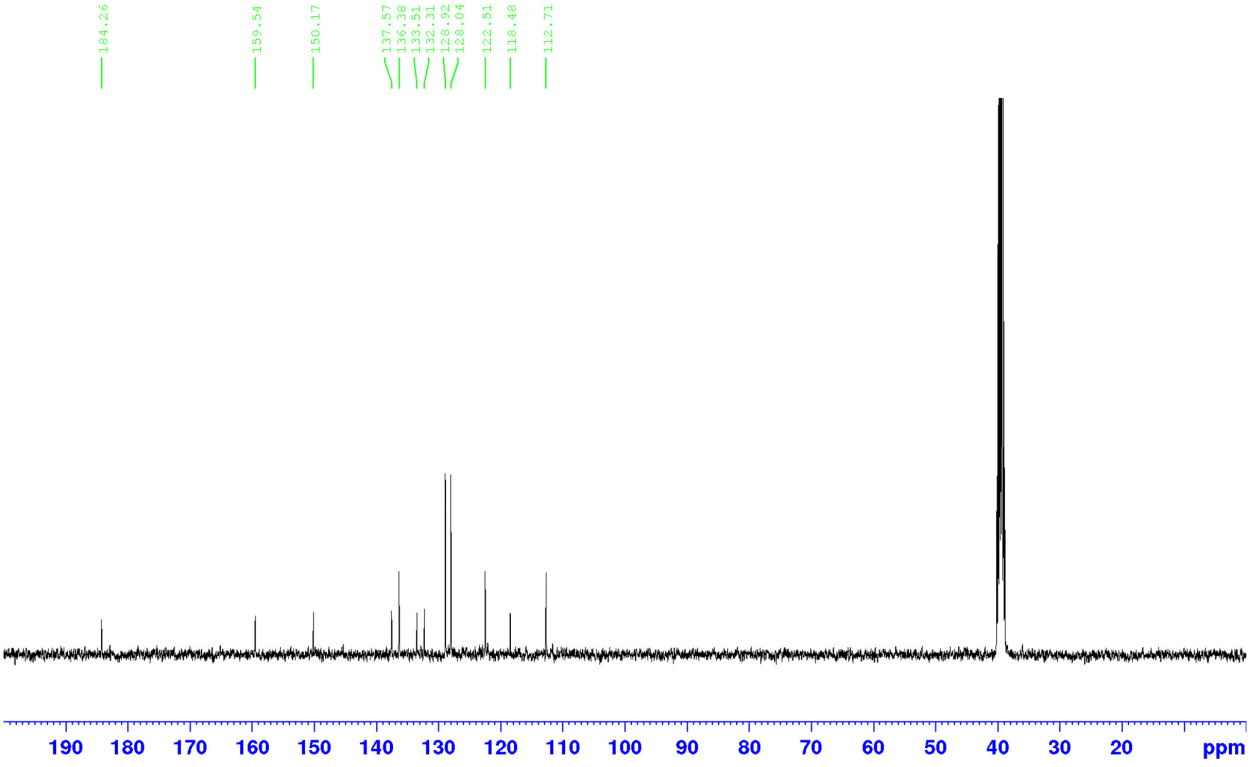


5-(4-Chlorophenyl)indoline-2,3-dione (**7c**)

^{1}H NMR (400 MHz, DMSO-d_6):

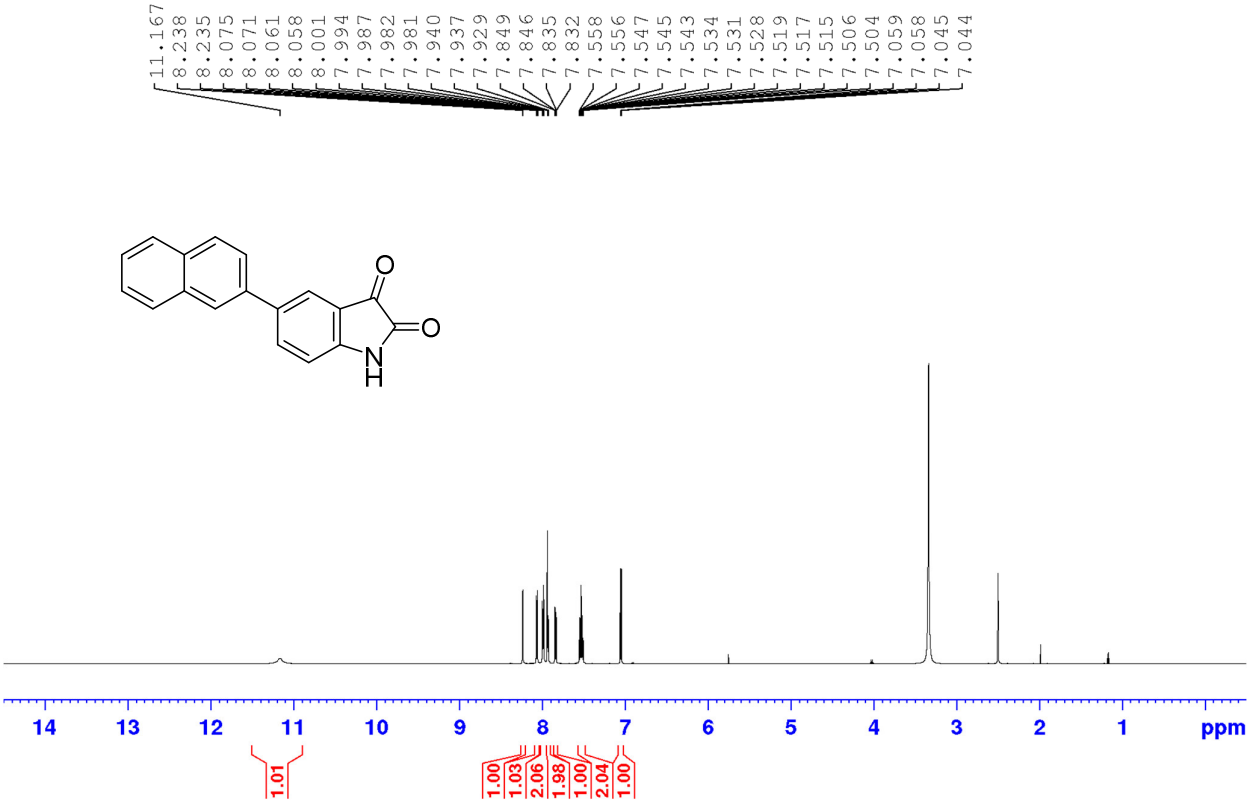


^{13}C NMR (100 MHz, DMSO-d_6):

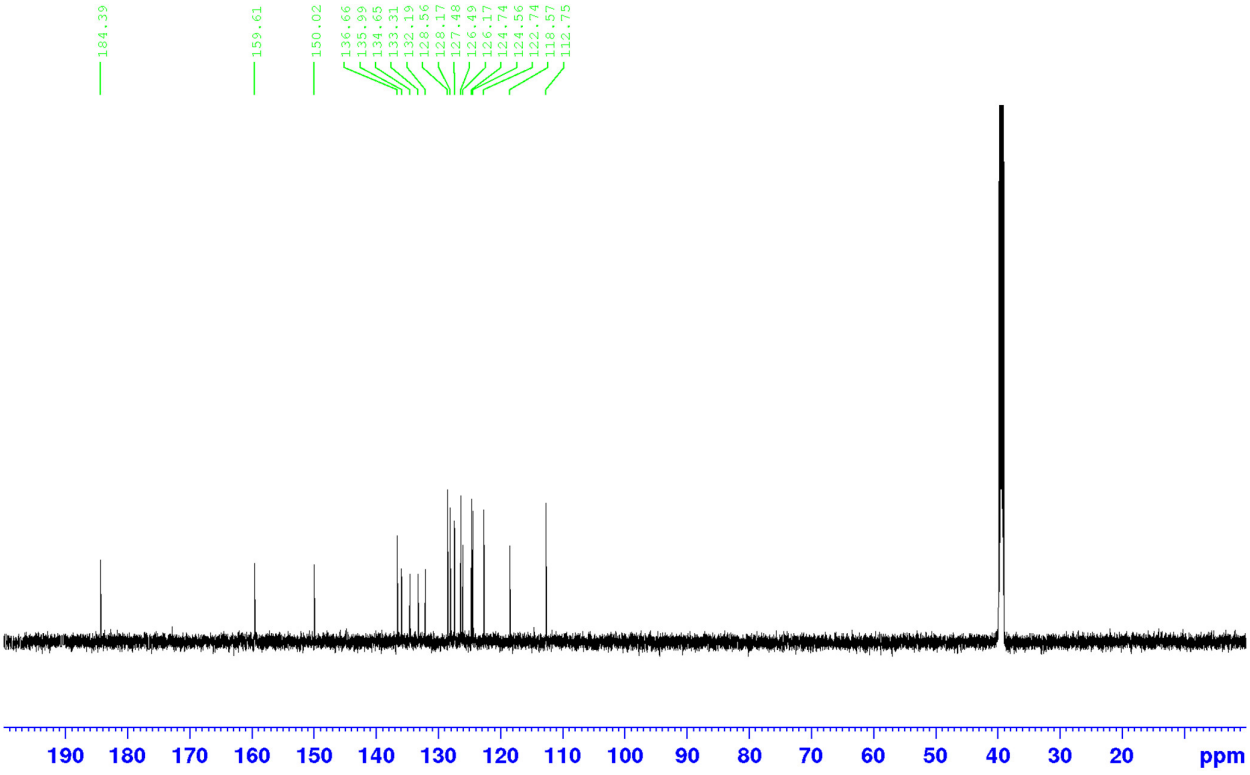


5-(Naphthalen-2-yl)indoline-2,3-dione (**7d**)

^{1}H NMR (600 MHz, DMSO-d_6):

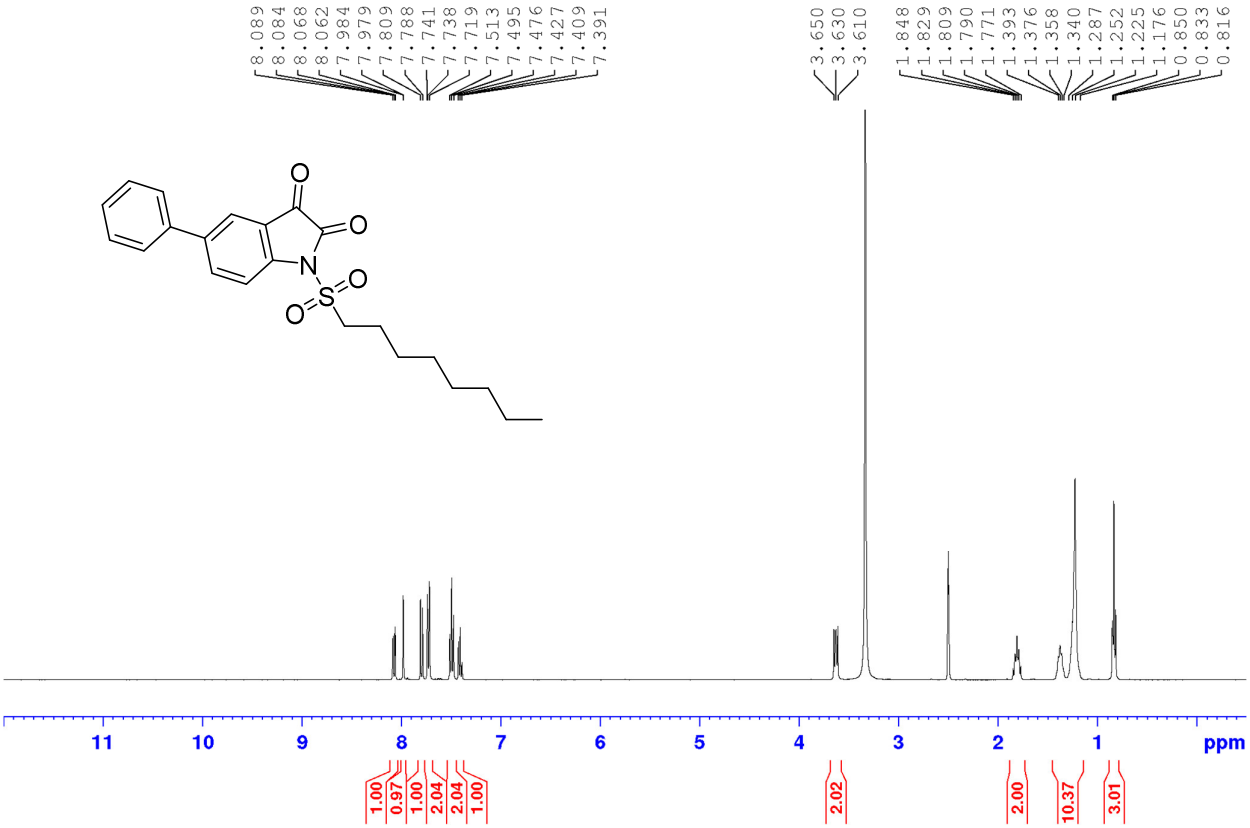


^{13}C NMR (150 MHz, DMSO-d_6):

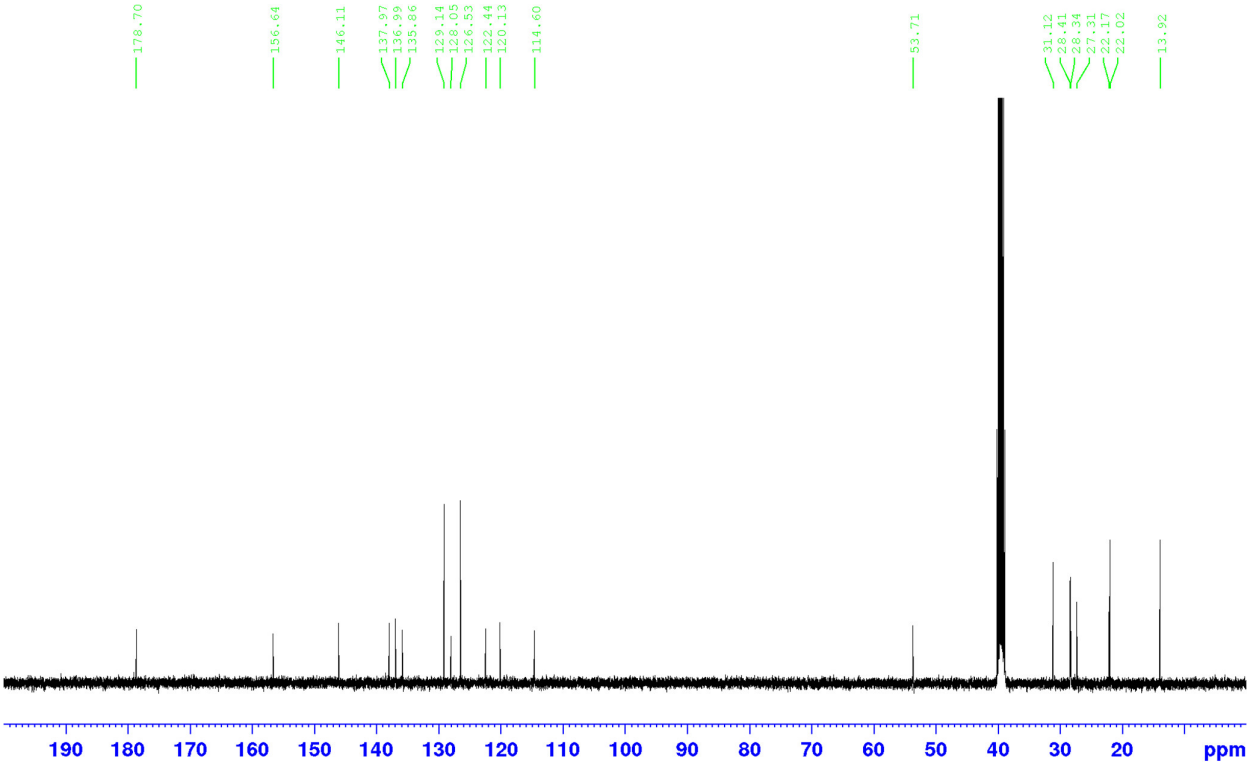


1-(Octylsulfonyl)-5-phenylindoline-2,3-dione (**8a**)

^{1}H NMR (400 MHz, DMSO-d_6):

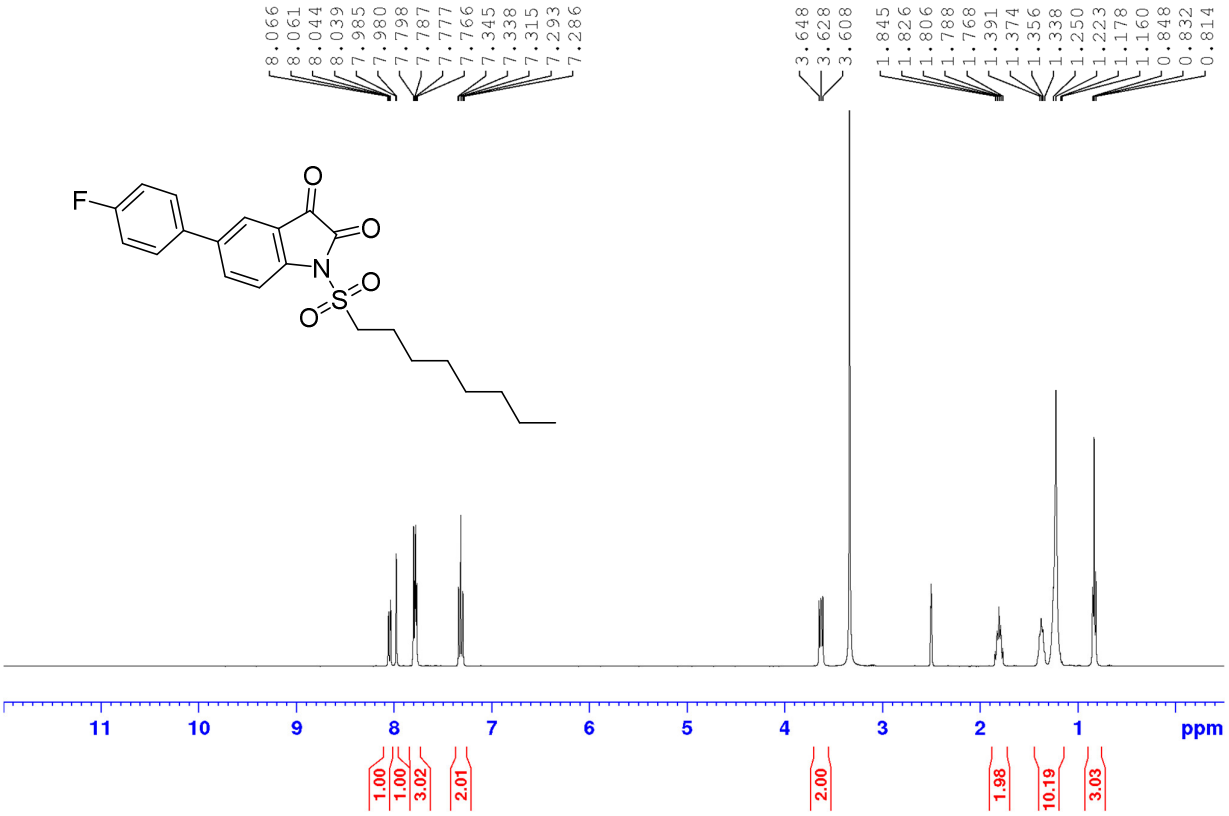


^{13}C NMR (100 MHz, DMSO-d_6):

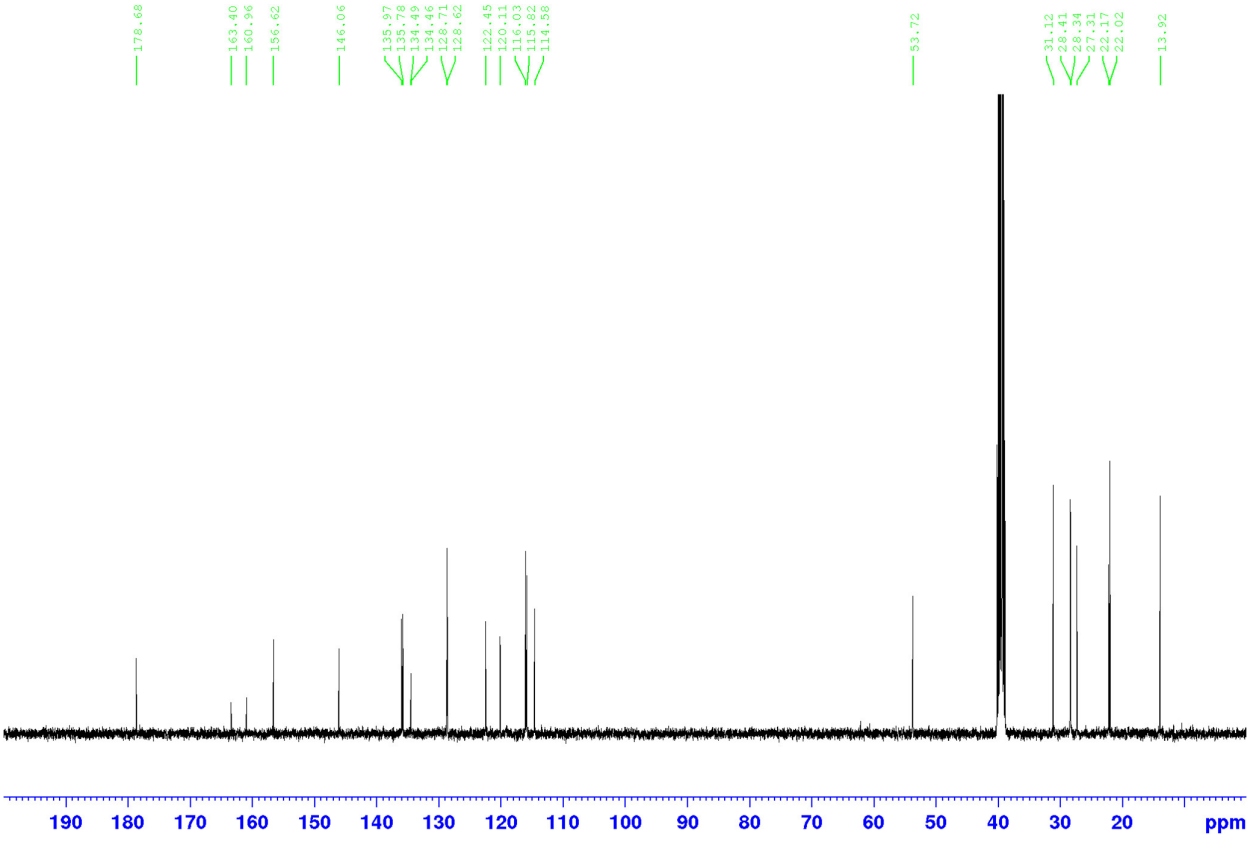


5-(4-Fluorophenyl)-1-(octylsulfonyl)indoline-2,3-dione (**8b**)

^{1}H NMR (400 MHz, DMSO-d_6):

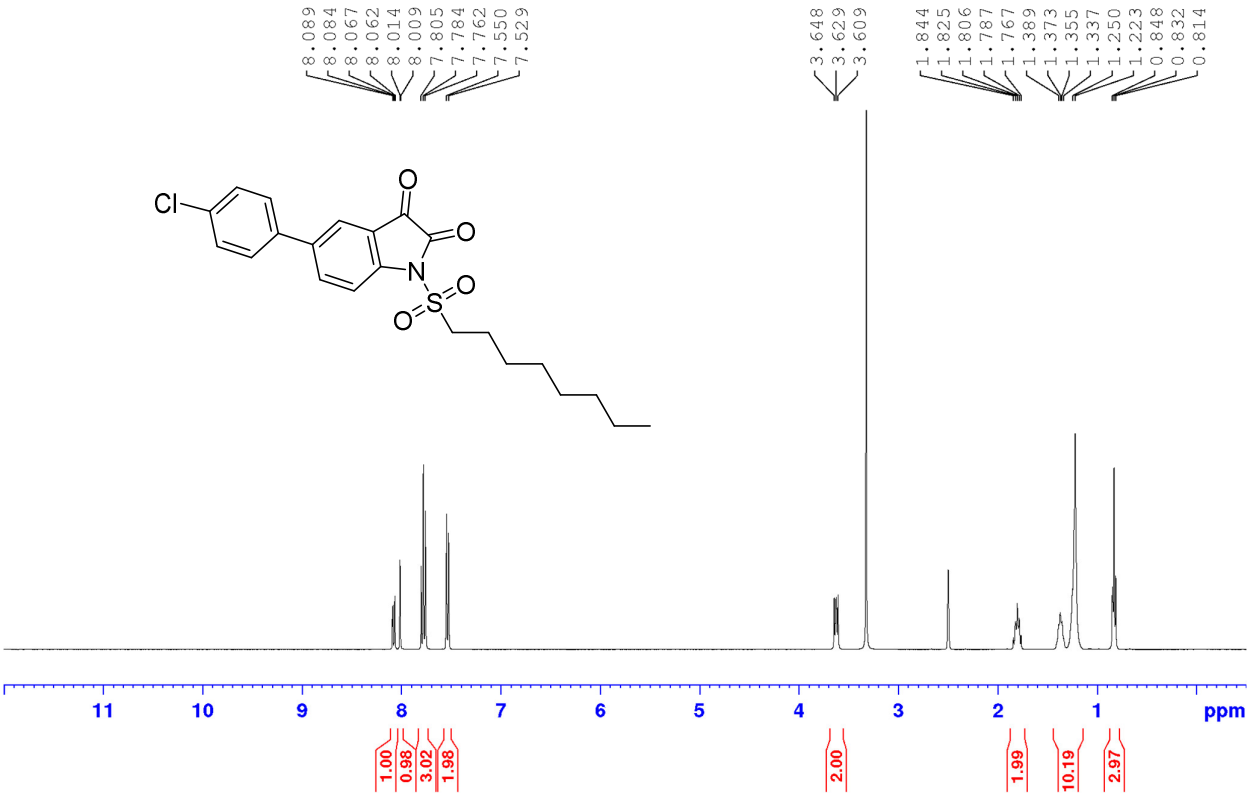


^{13}C NMR (100 MHz, DMSO-d_6):

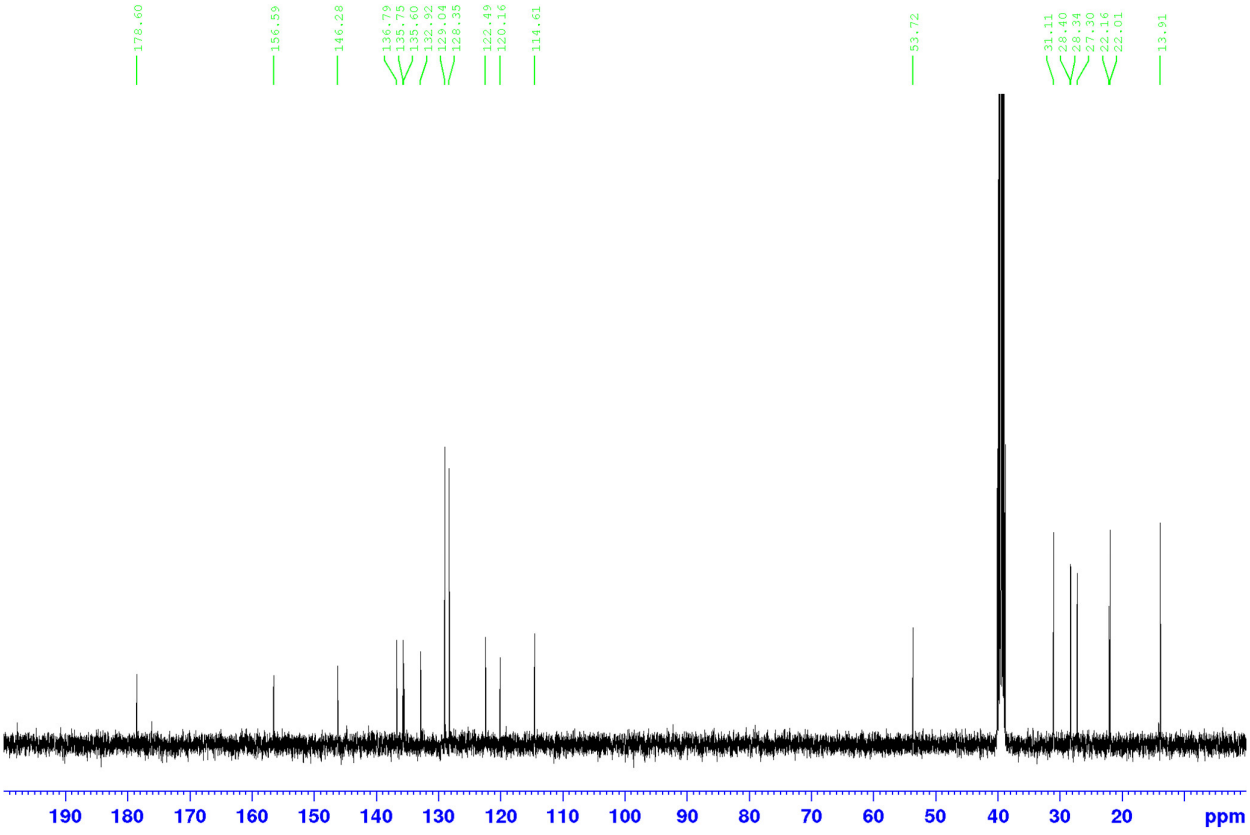


5-(4-Chlorophenyl)-1-(octylsulfonyl)indoline-2,3-dione (**8c**)

^{1}H NMR (400 MHz, DMSO-d_6):

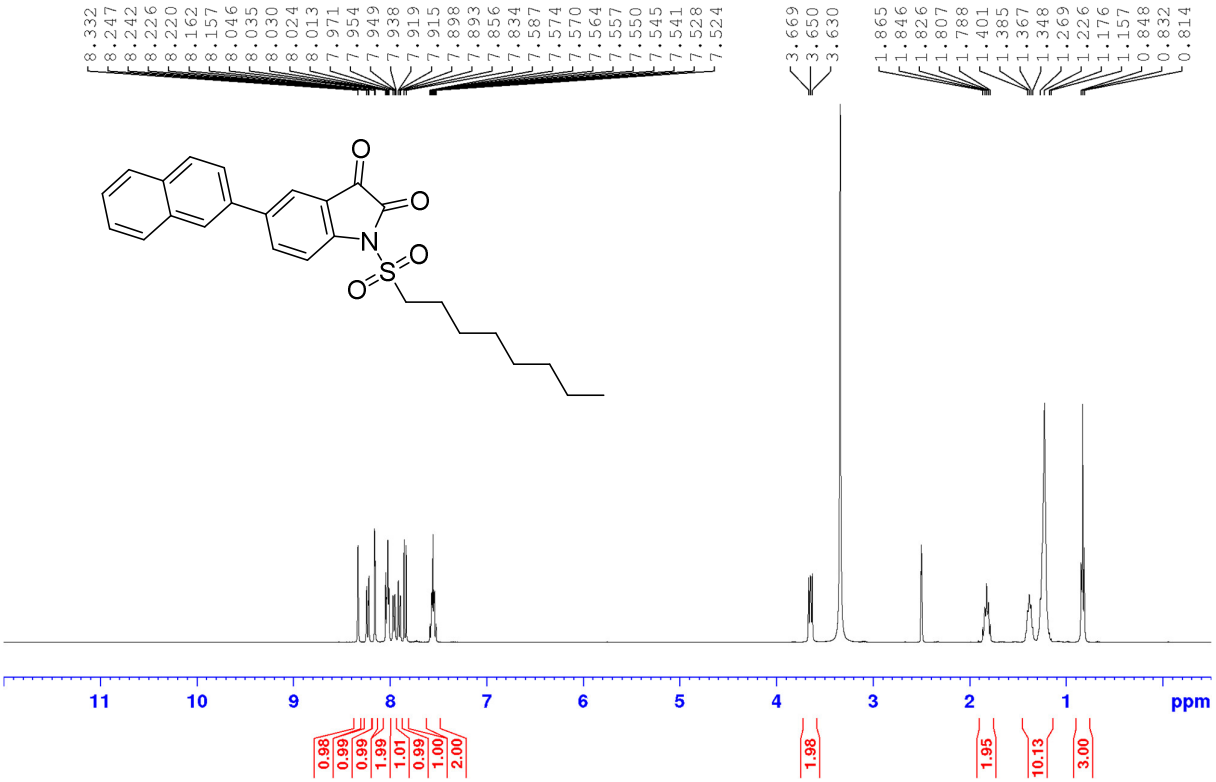


^{13}C NMR (100 MHz, DMSO-d_6):

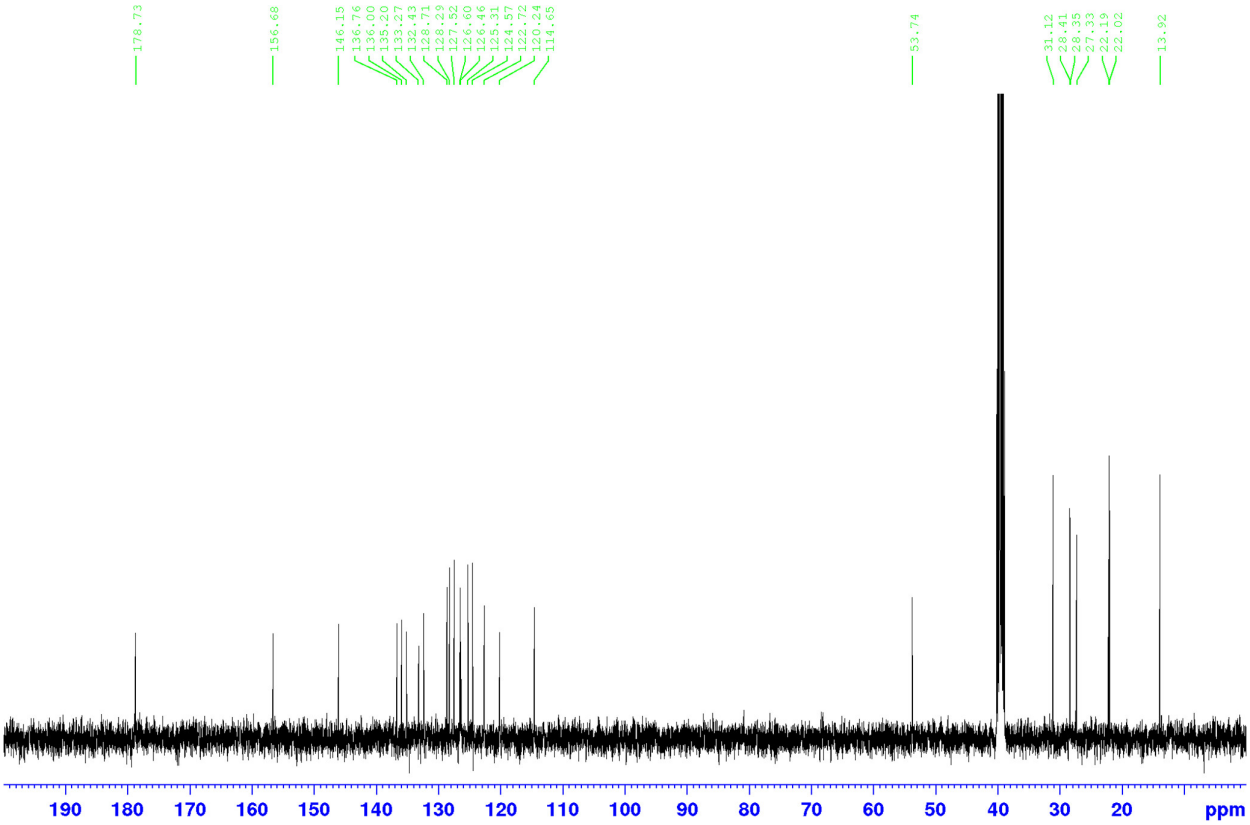


5-(Naphthalen-2-yl)-1-(octylsulfonyl)indoline-2,3-dione (**8d**)

^{1}H NMR (400 MHz, DMSO-d_6):

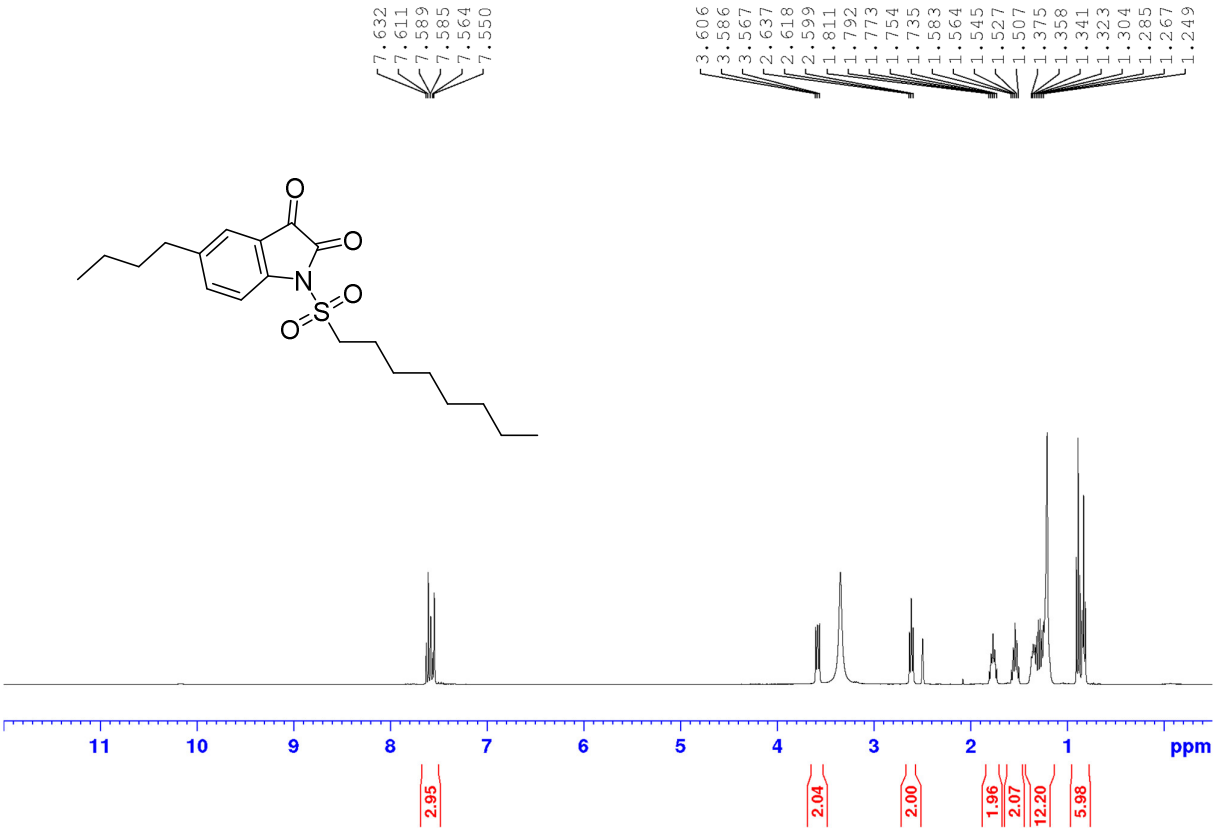


^{13}C NMR (100 MHz, DMSO-d_6):

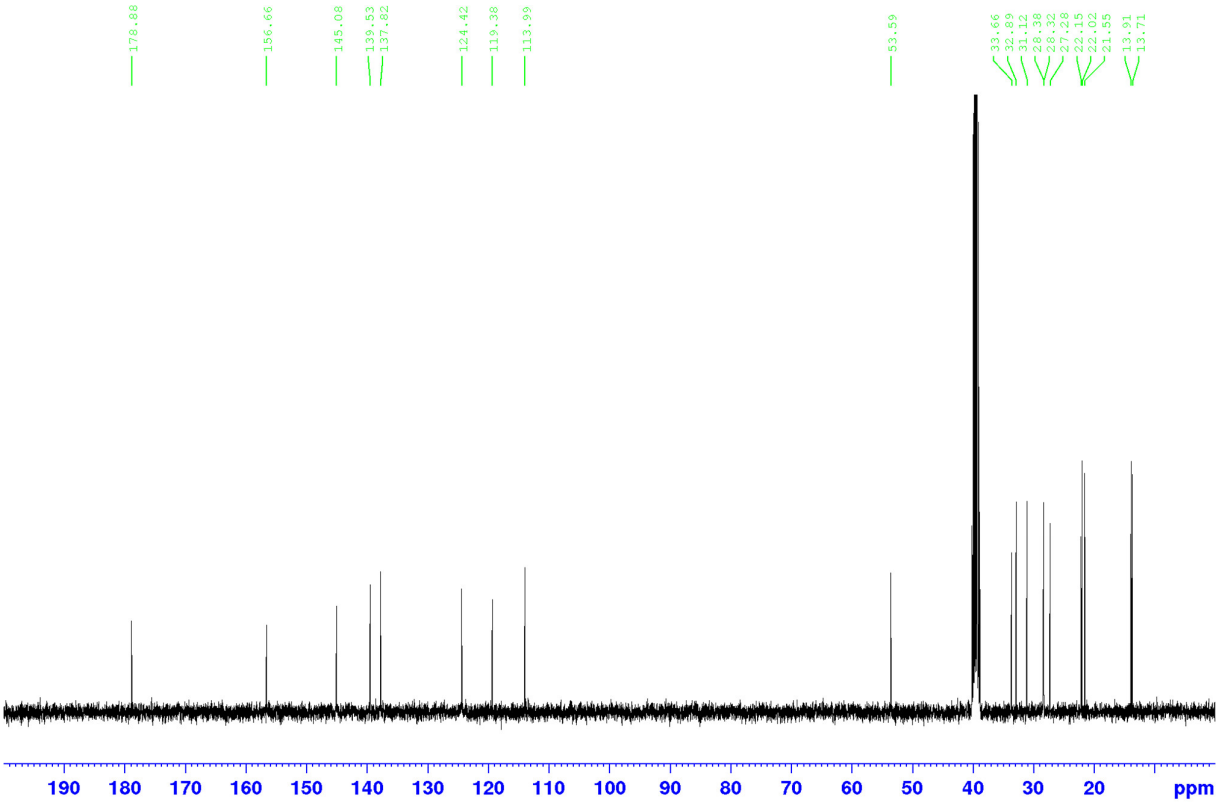


5-Butyl-1-(octylsulfonyl)indoline-2,3-dione (**8e**)

^{1}H NMR (400 MHz, DMSO-d_6):

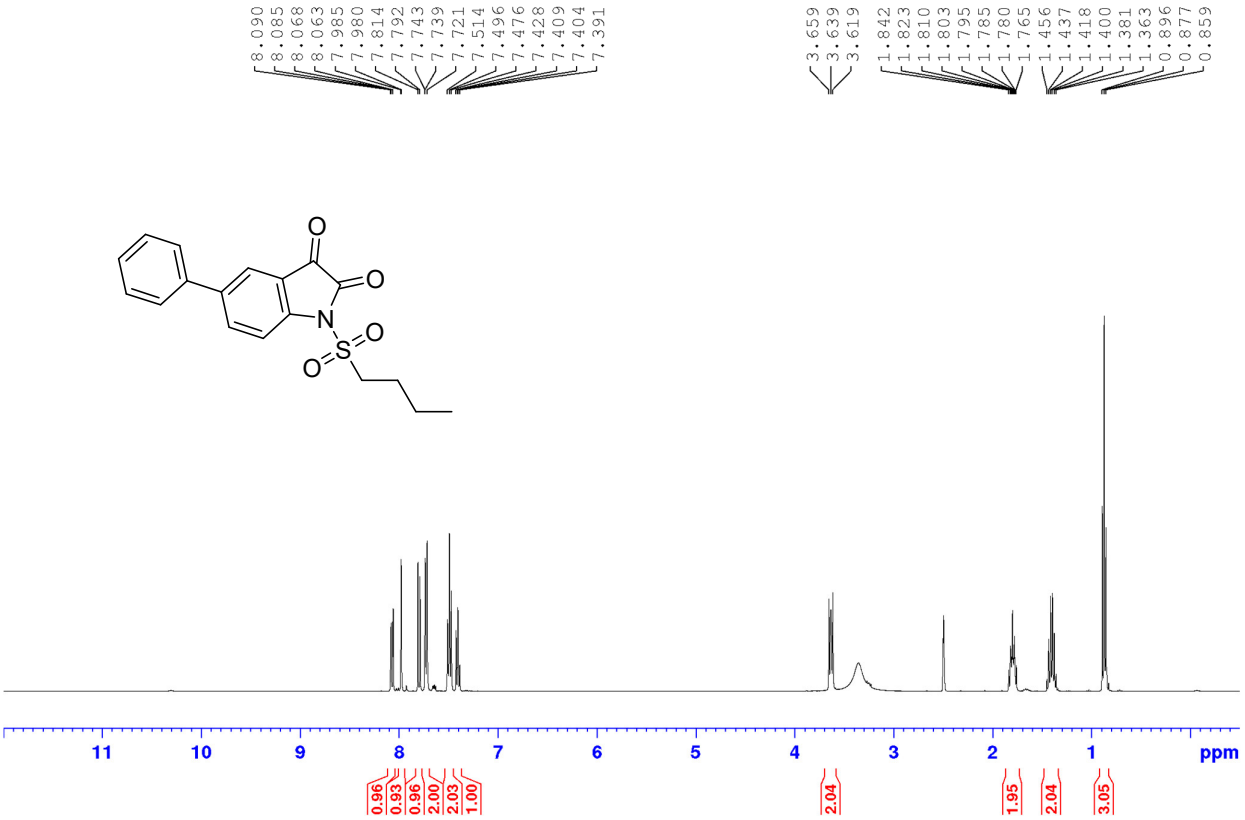


^{13}C NMR (100 MHz, DMSO-d_6):

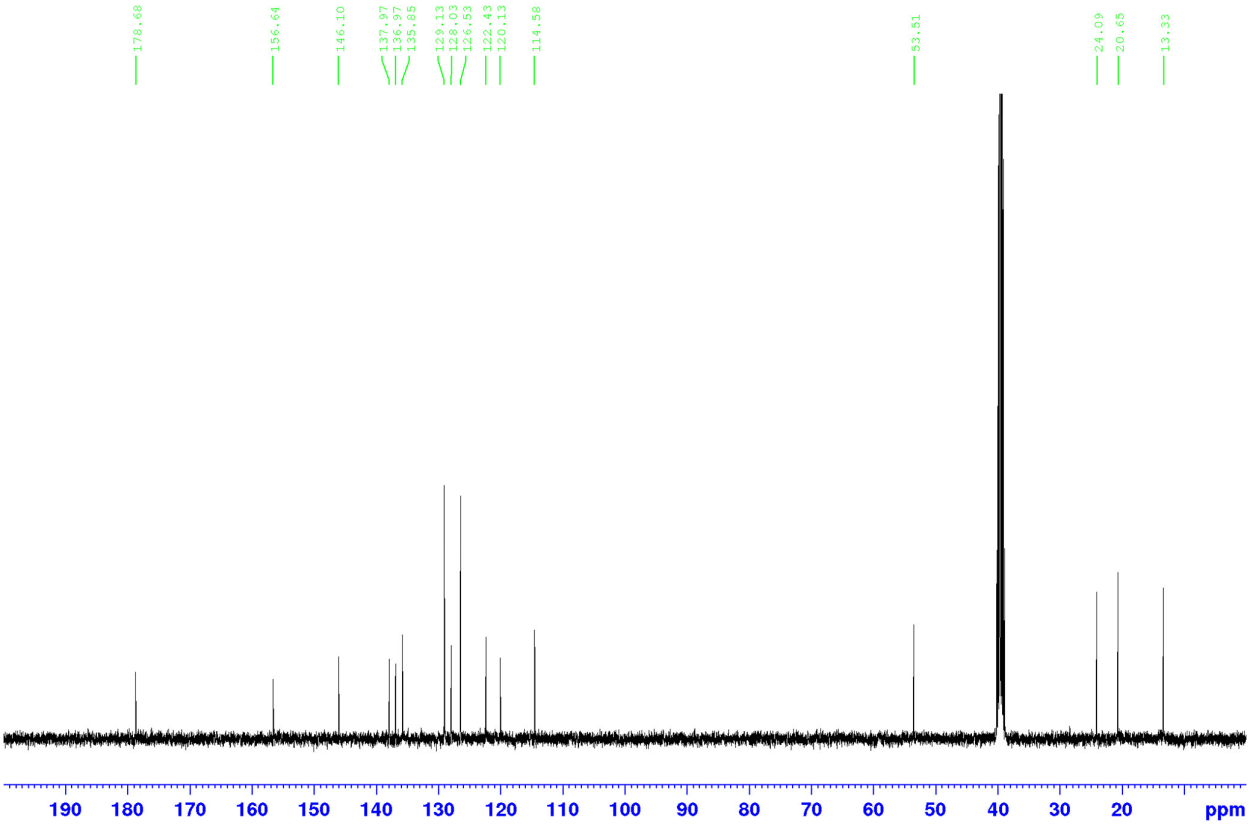


1-(Butylsulfonyl)-5-phenylindoline-2,3-dione (**9a**)

^{1}H NMR (400 MHz, DMSO-d_6):

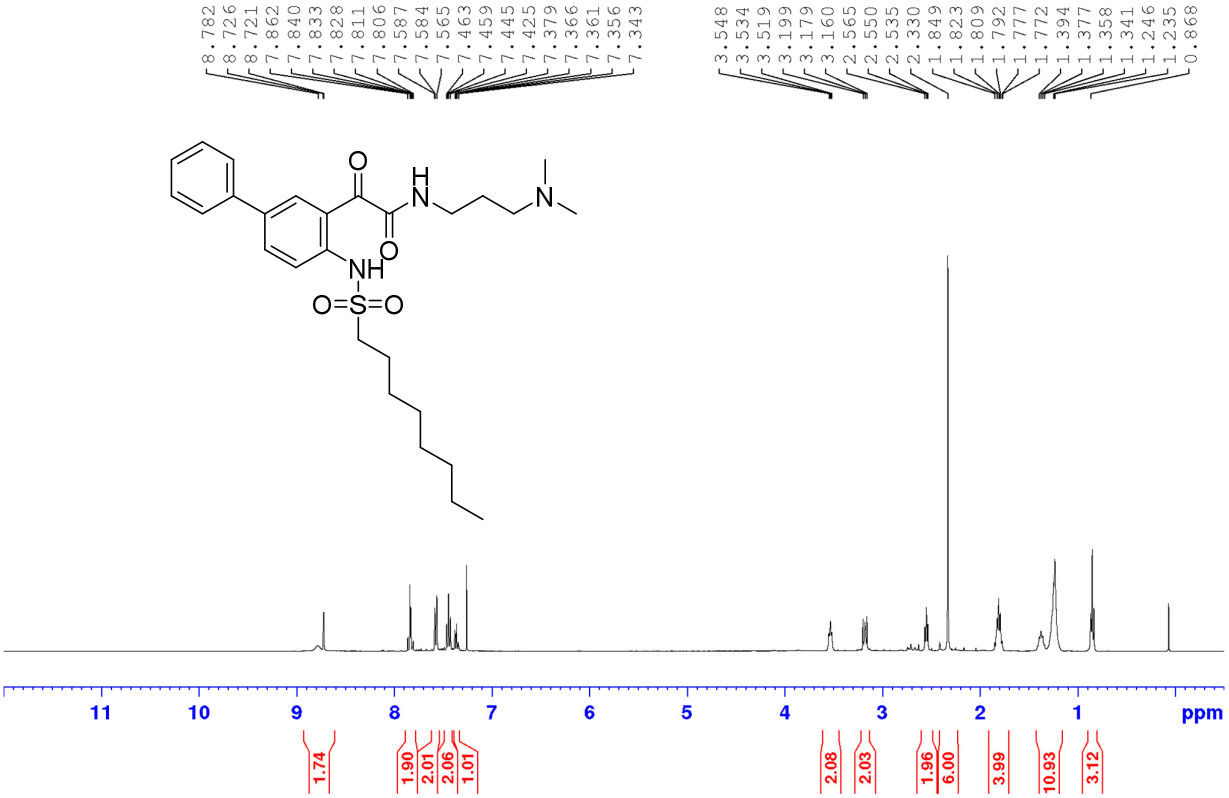


^{13}C NMR (100 MHz, DMSO-d_6):

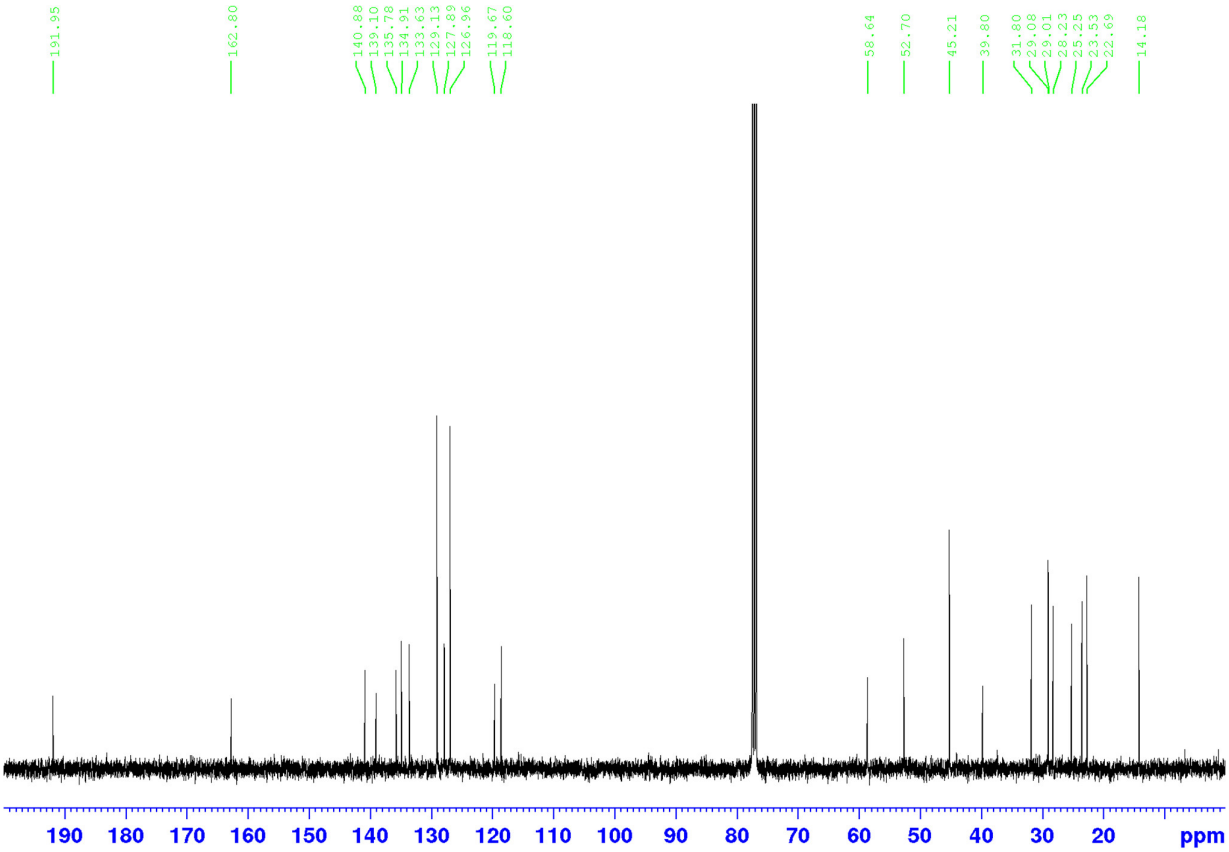


N-(3-(Dimethylamino)propyl)-2-(4-(octylsulfonamido)-[1,1'-biphenyl]-3-yl)-2-oxoacetamide (**11a**)

^{1}H NMR (400 MHz, $CDCl_3$):

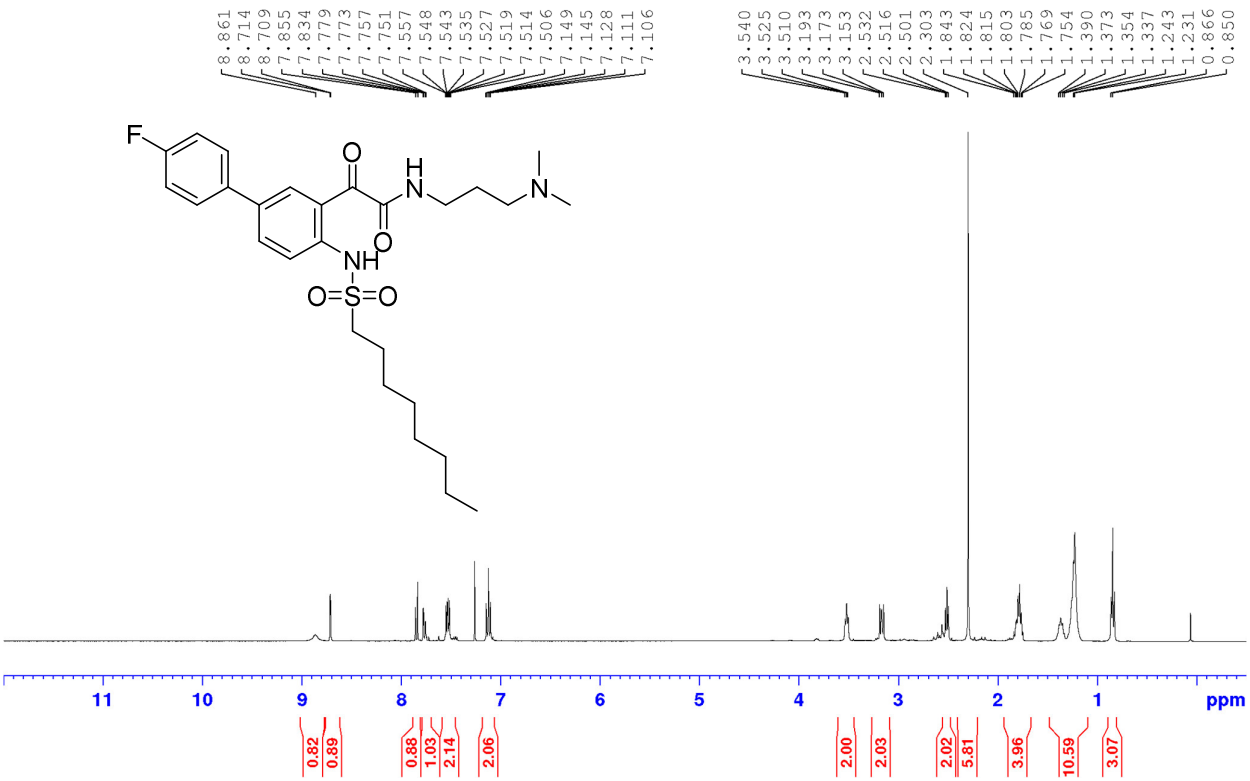


^{13}C NMR (100 MHz, $CDCl_3$):

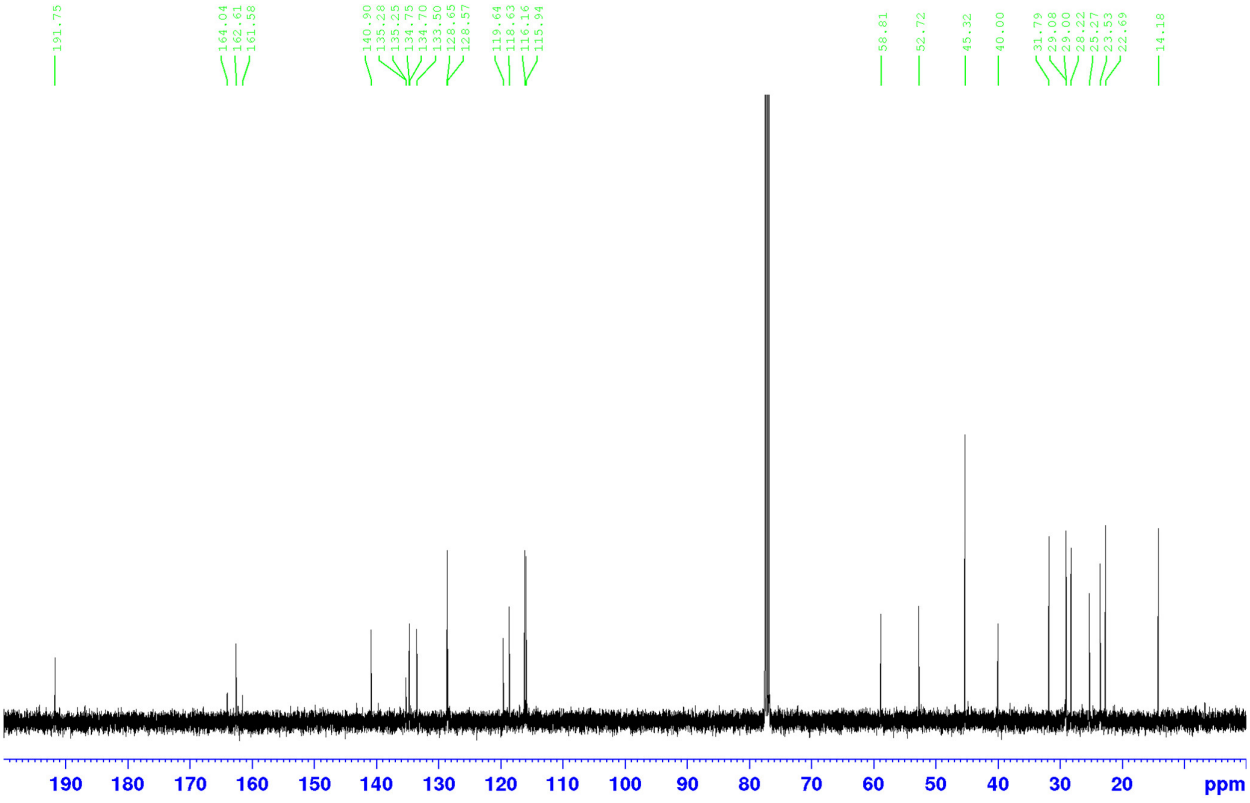


N-(3-(Dimethylamino)propyl)-2-(4'-fluoro-4-(octylsulfonamido)-[1,1'-biphenyl]-3-yl)-2-oxoacetamide (**11b**)

^{1}H NMR (400 MHz, $CDCl_3$):

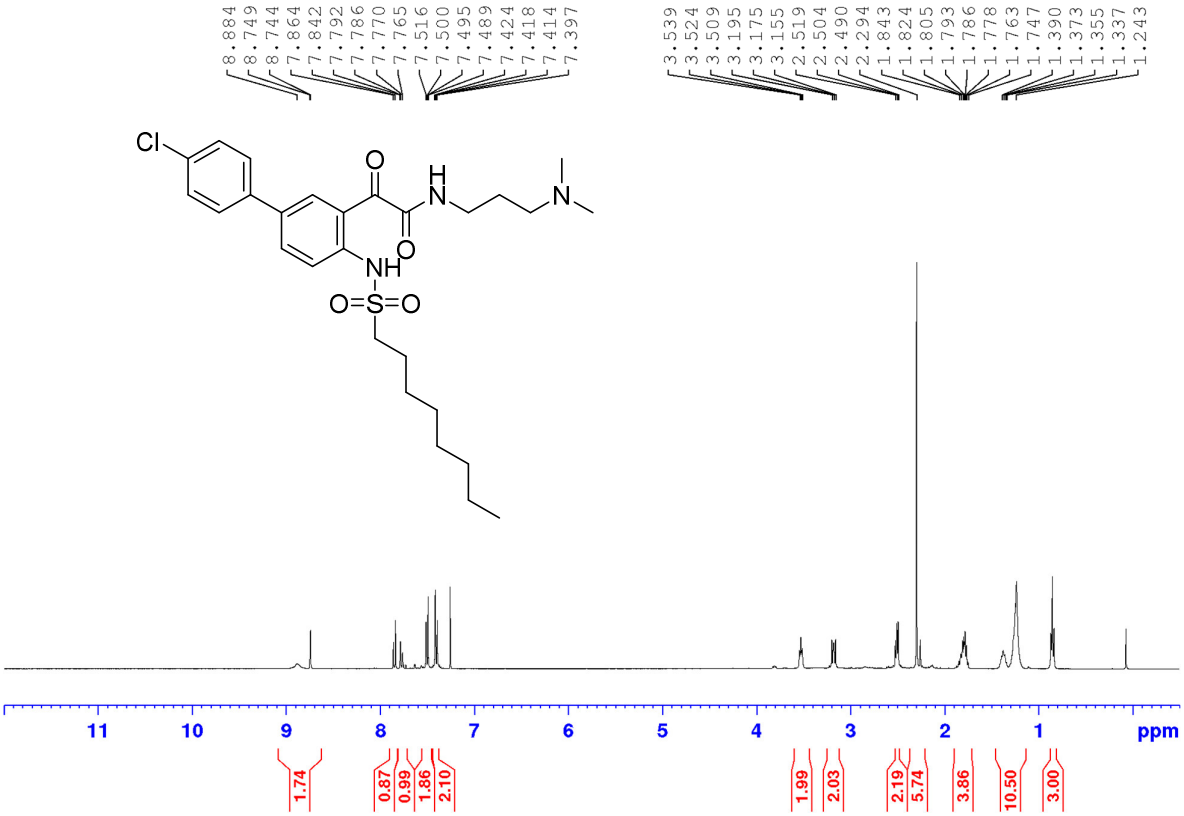


^{13}C NMR (100 MHz, $CDCl_3$):

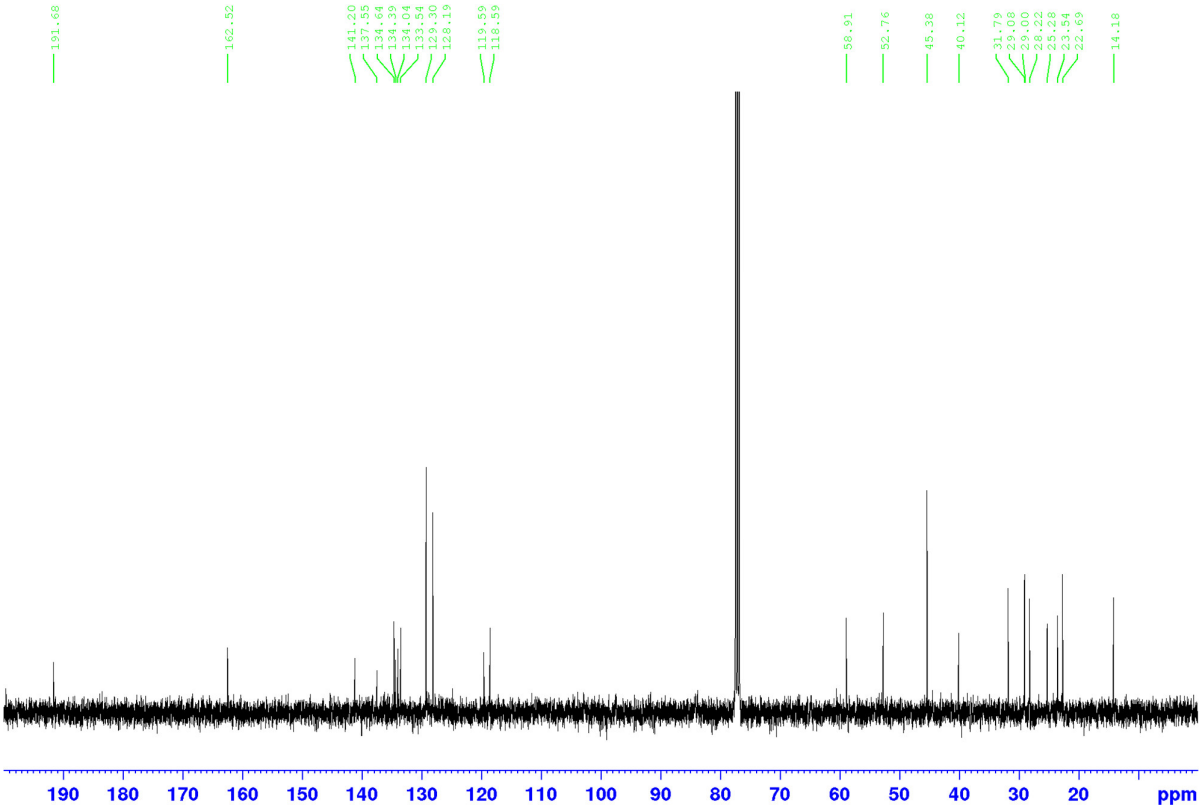


2-(4'-Chloro-4-(octylsulfonamido)-[1,1'-biphenyl]-3-yl)-*N*-(3-(dimethylamino)propyl)-2-oxoacetamide (**11c**)

^{1}H NMR (400 MHz, $CDCl_3$):

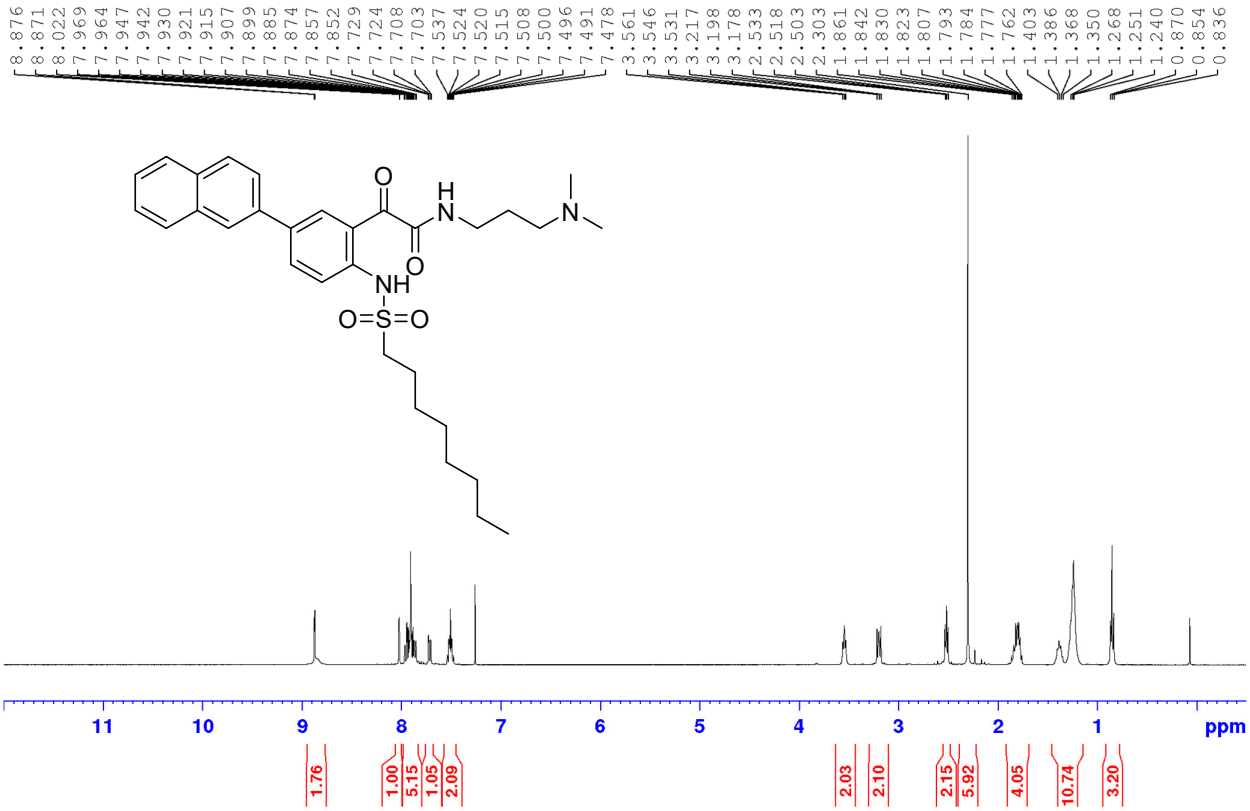


^{13}C NMR (100 MHz, $CDCl_3$):

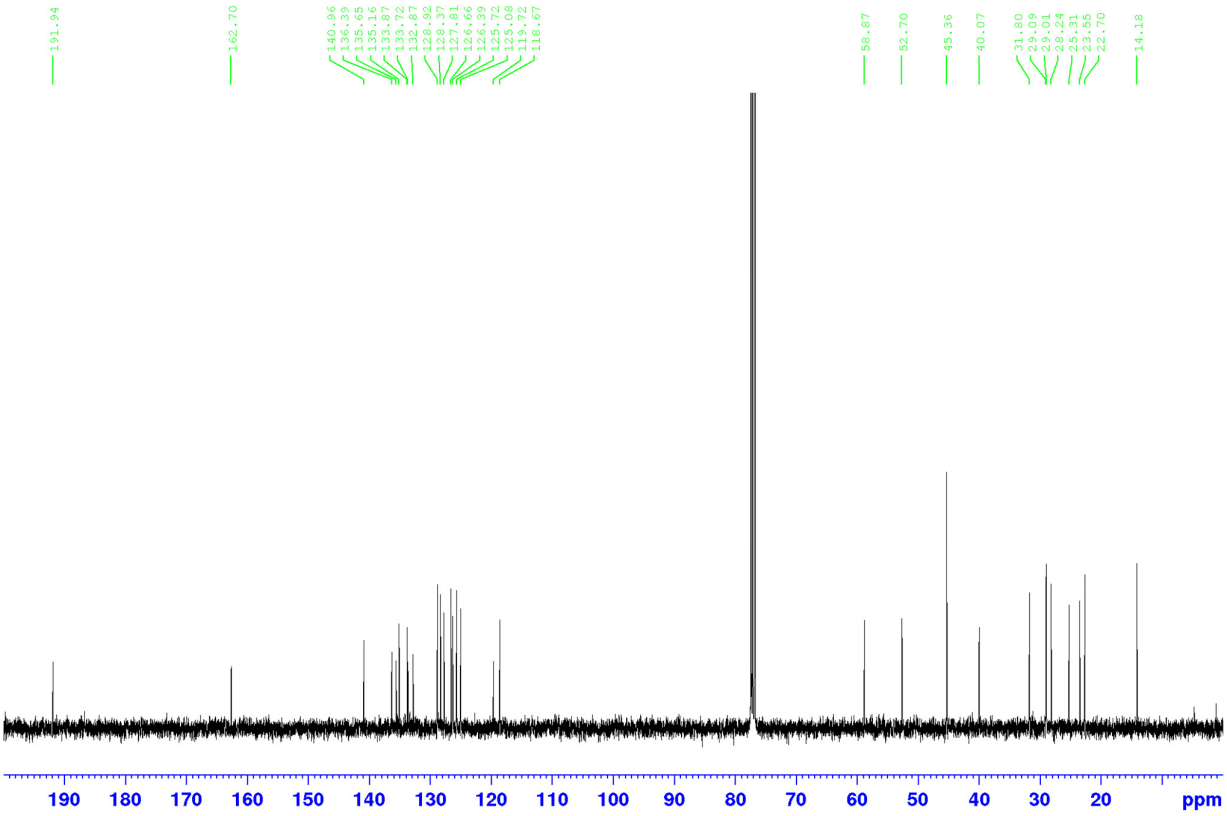


N-(3-(Dimethylamino)propyl)-2-(5-(naphthalen-2-yl)-2-(octylsulfonamido)phenyl)-2-oxoacetamide (**11d**)

^{1}H NMR (400 MHz, $CDCl_3$):

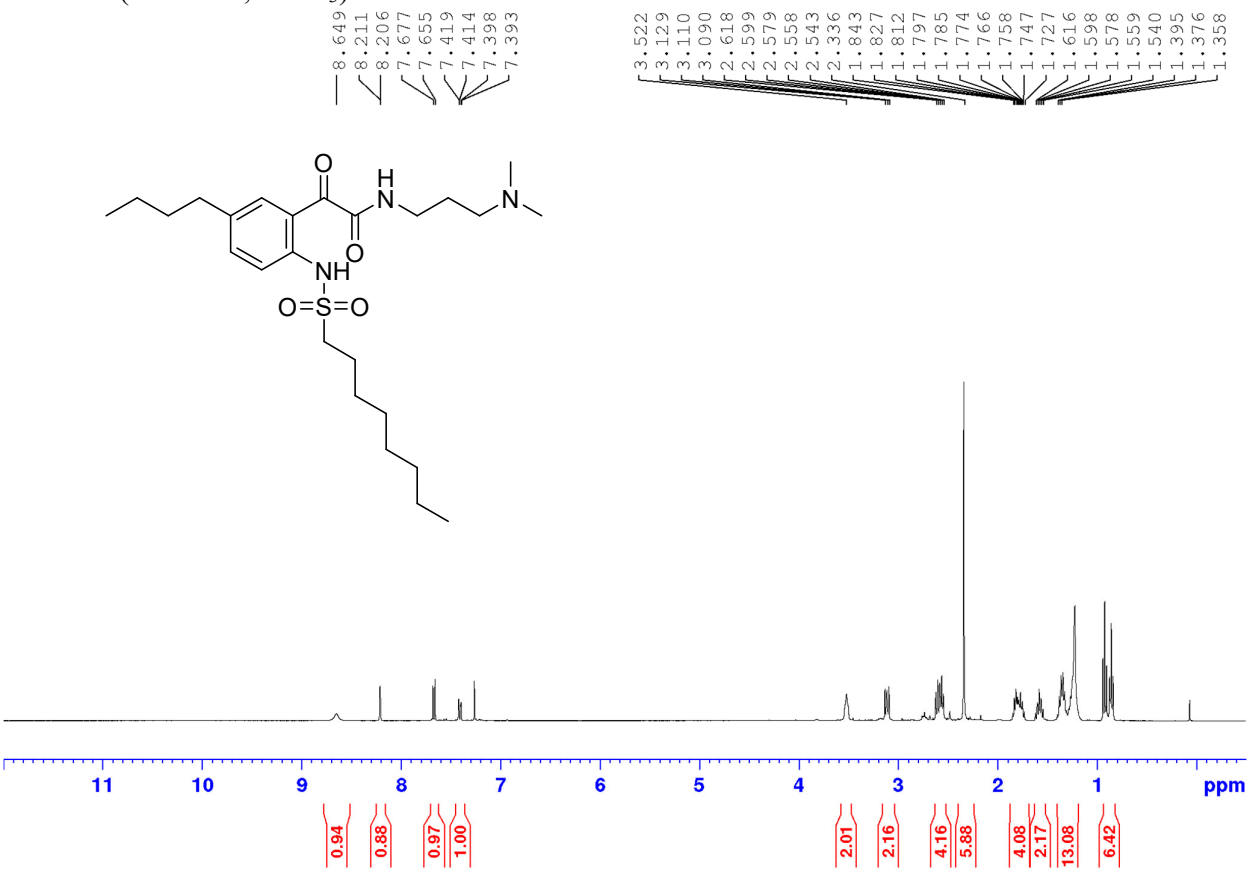


^{13}C NMR (100 MHz, $CDCl_3$):

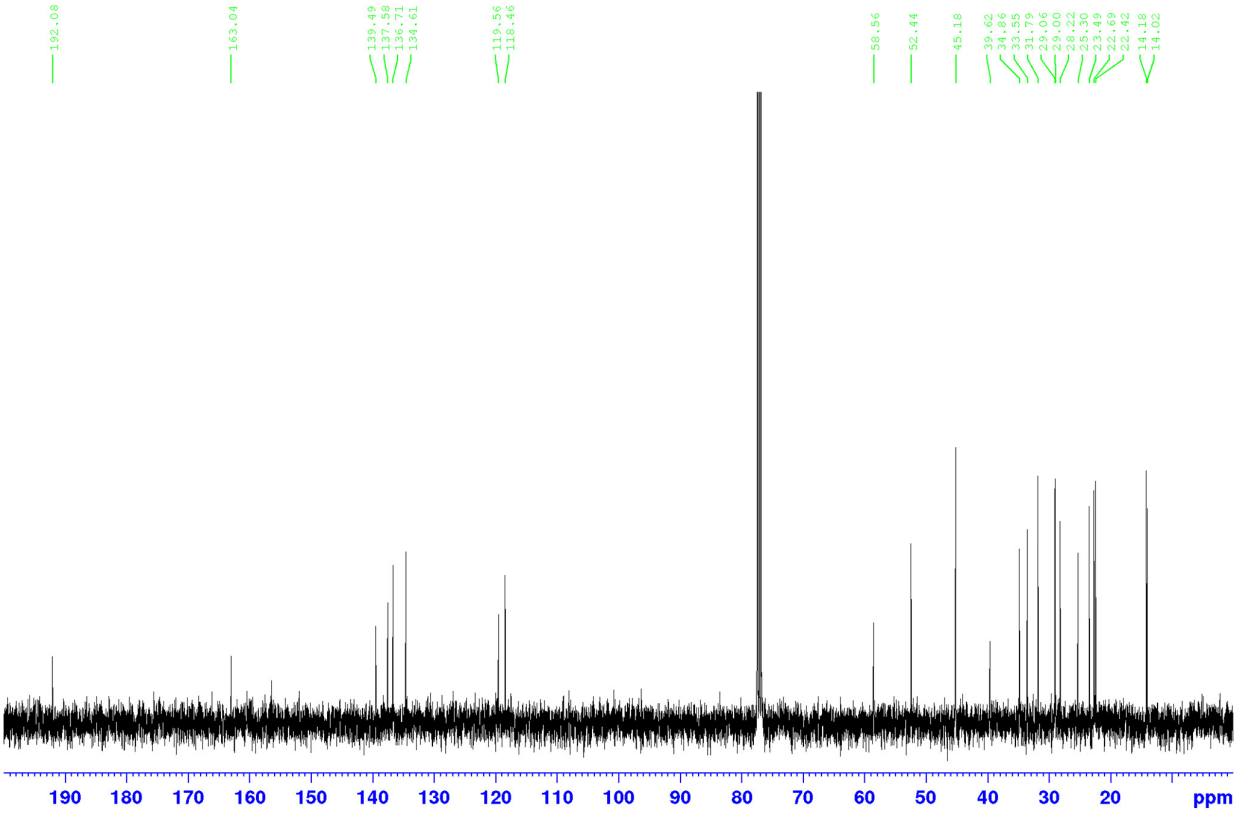


2-(5-Butyl-2-(octylsulfonamido)phenyl)-*N*-(3-(dimethylamino)propyl)-2-oxoacetamide (**11e**)

^{1}H NMR (400 MHz, $CDCl_3$):

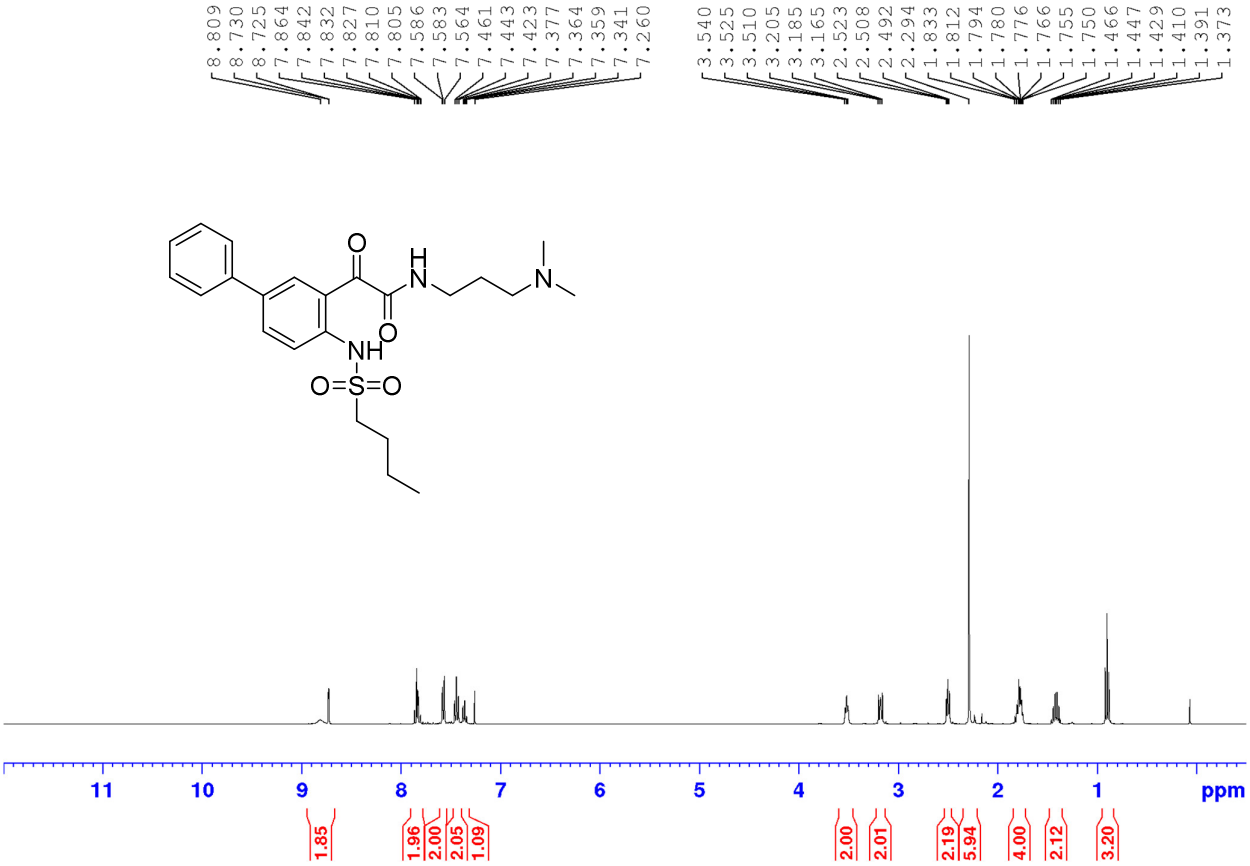


^{13}C NMR (100 MHz, $CDCl_3$):

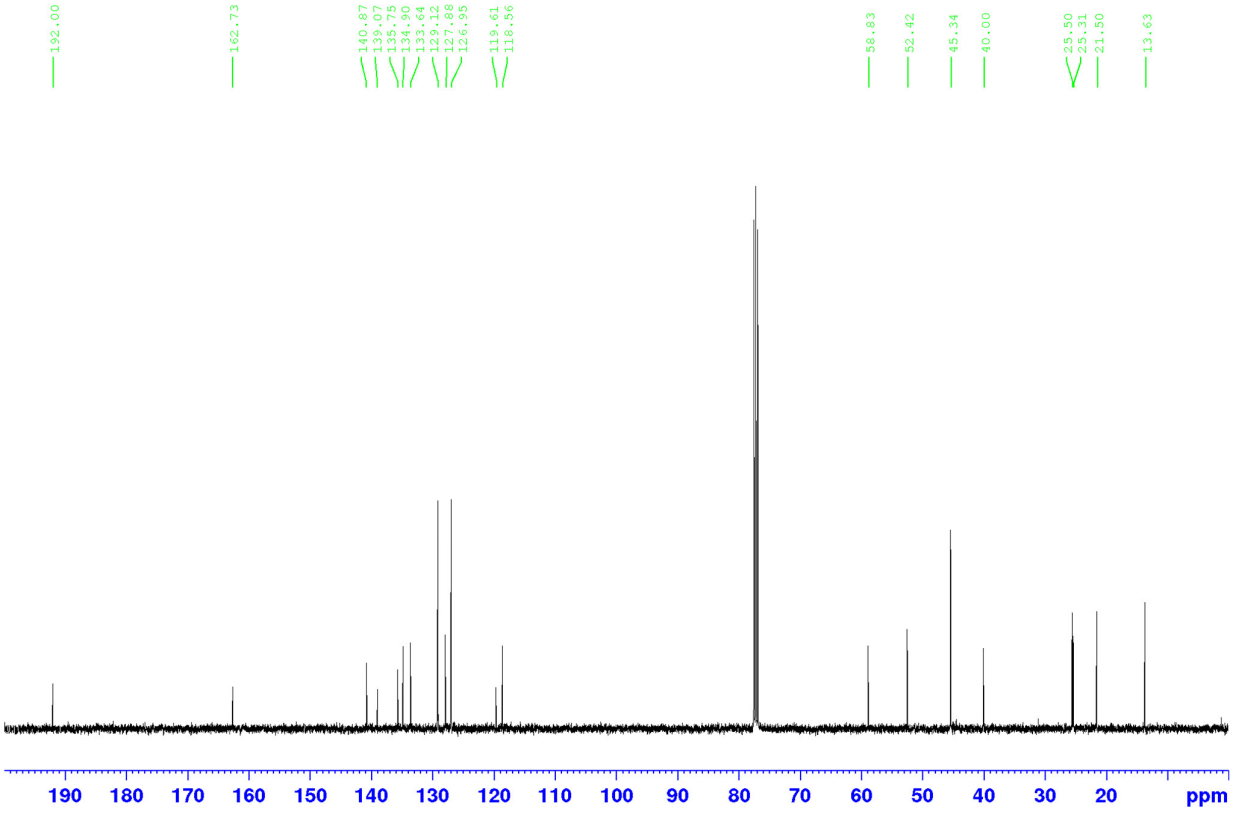


2-(4-(Butylsulfonamido)-[1,1'-biphenyl]-3-yl)-*N*-(3-(dimethylamino)propyl)-2-oxoacetamide (**12a**)

^{1}H NMR (400 MHz, $CDCl_3$):

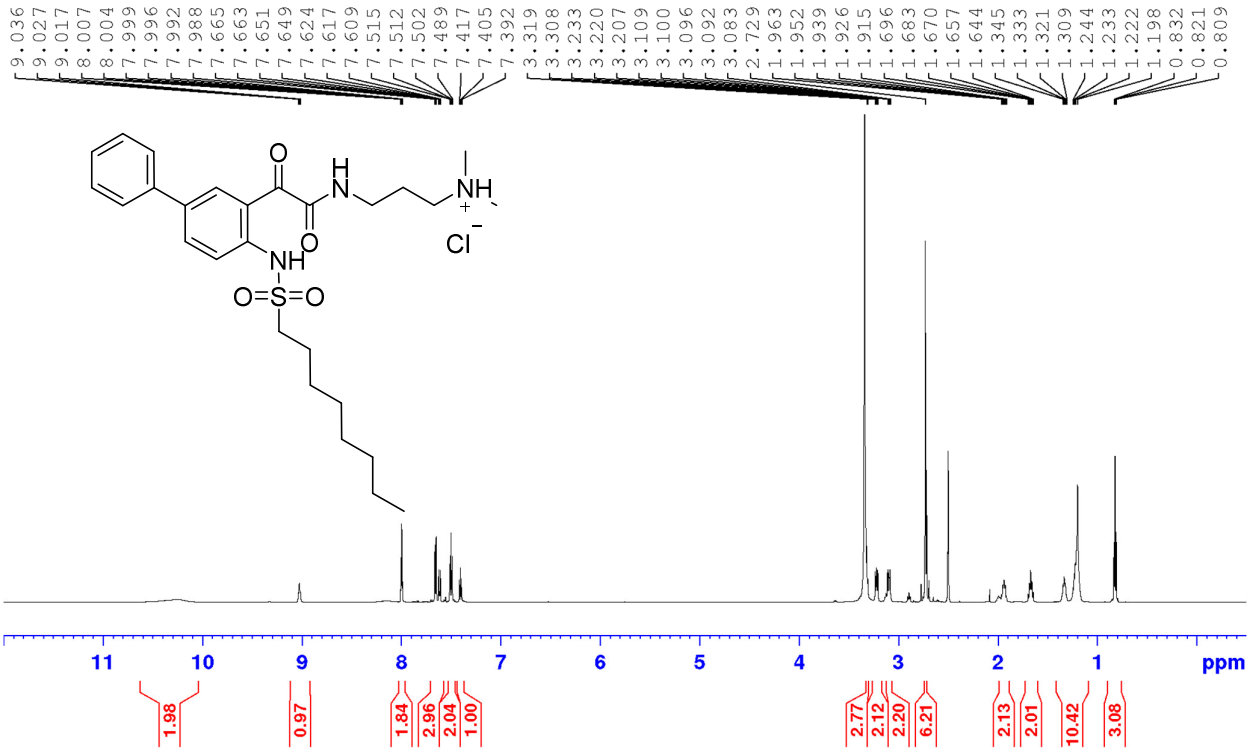


^{13}C NMR (100 MHz, $CDCl_3$):

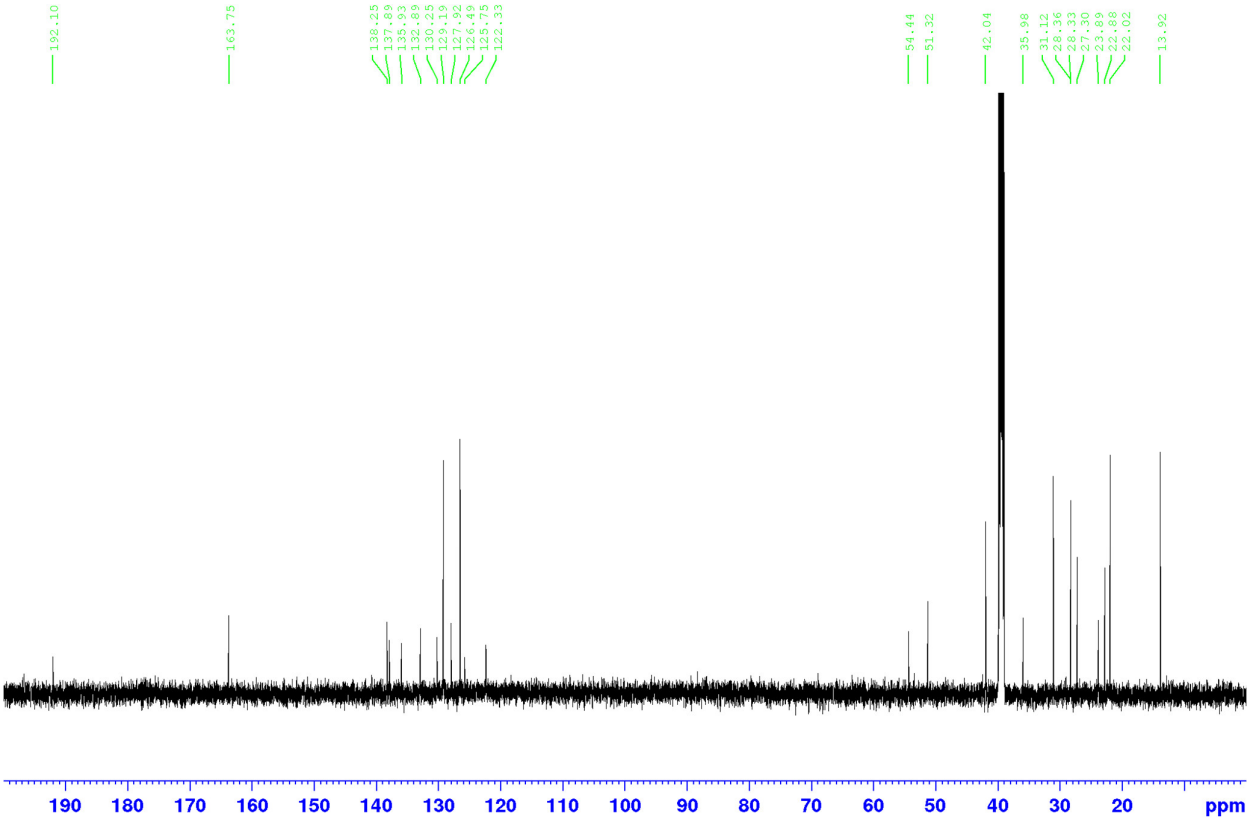


N,*N*-Dimethyl-3-(2-(4-(octylsulfonamido)-[1,1'-biphenyl]-3-yl)-2-oxoacetamido)propan-1-aminium chloride (**13a**)

^{1}H NMR (600 MHz, DMSO-d_6):

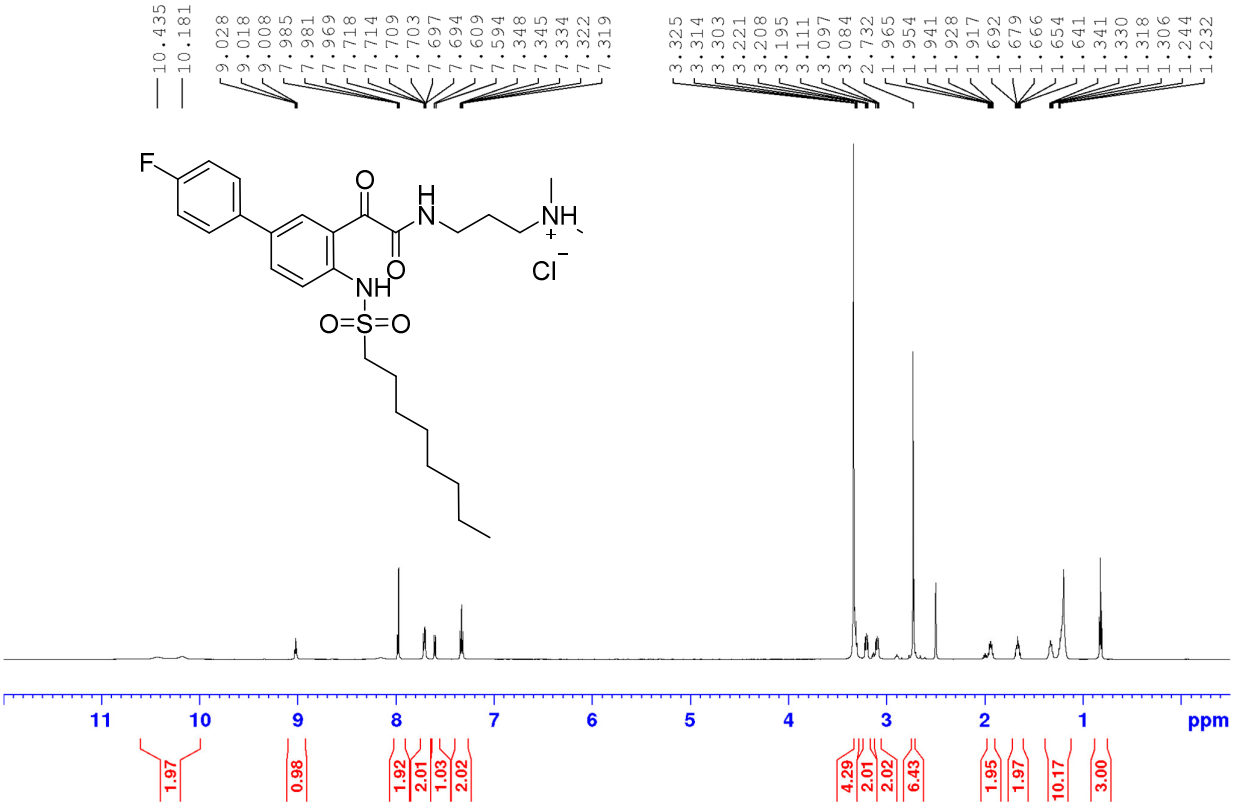


^{13}C NMR (150 MHz, DMSO-d_6):

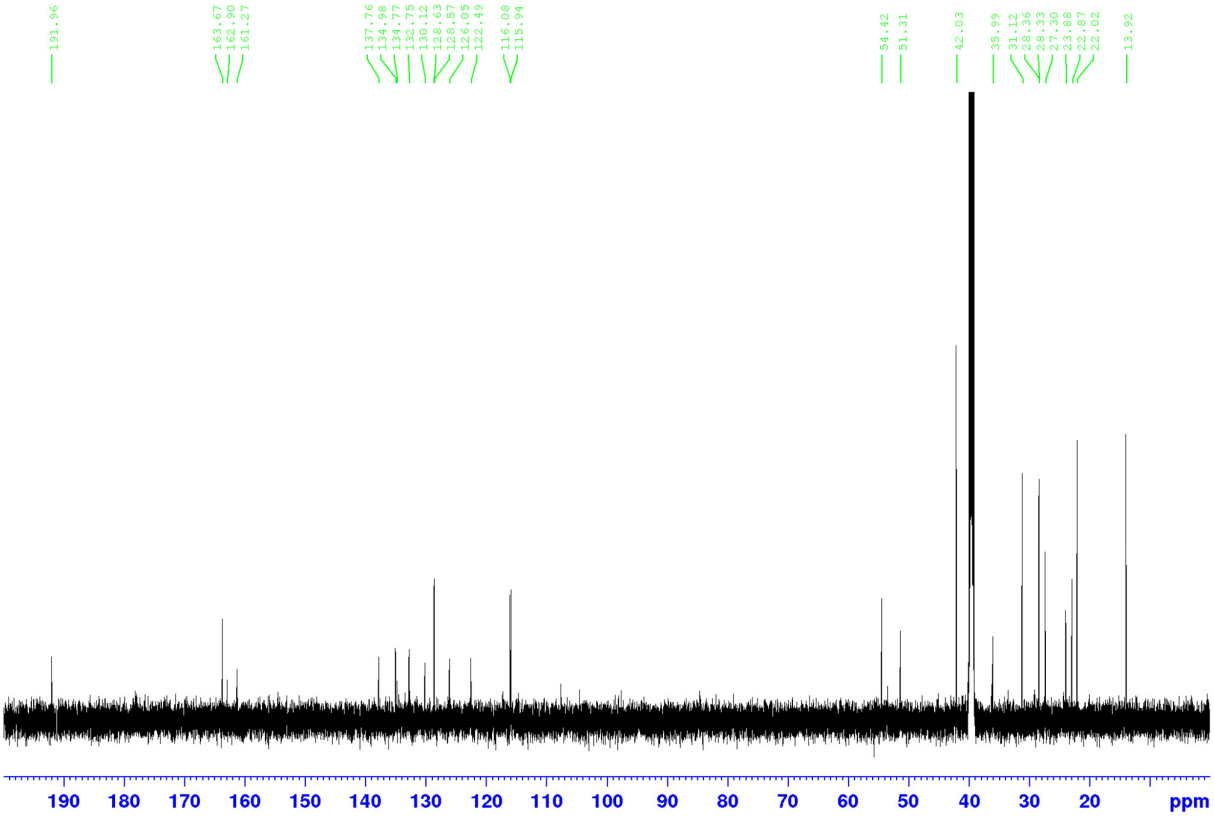


3-(2-(4'-Fluoro-4-(octylsulfonamido)-[1,1'-biphenyl]-3-yl)-2-oxoacetamido)-*N*,*N*-dimethylpropan-1-aminium chloride (**13b**)

^{1}H NMR (600 MHz, DMSO-d_6):

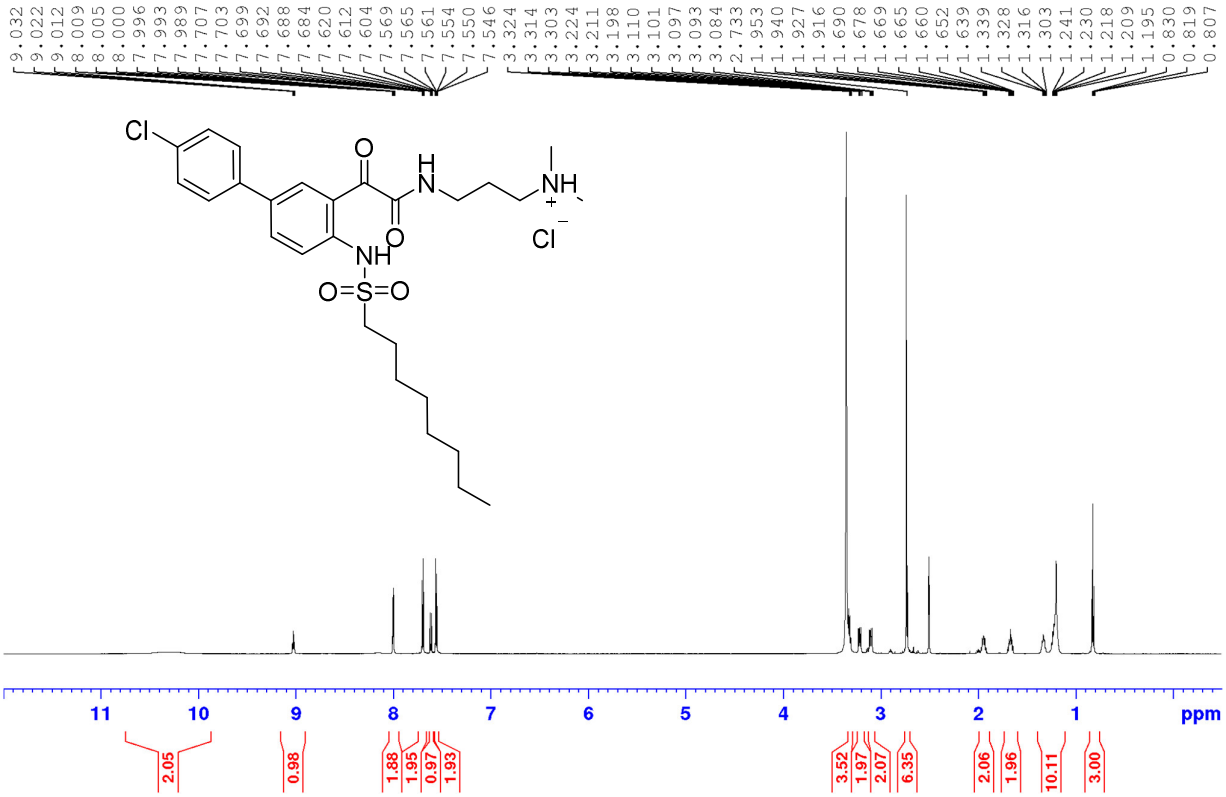


^{13}C NMR (150 MHz, DMSO-d_6):

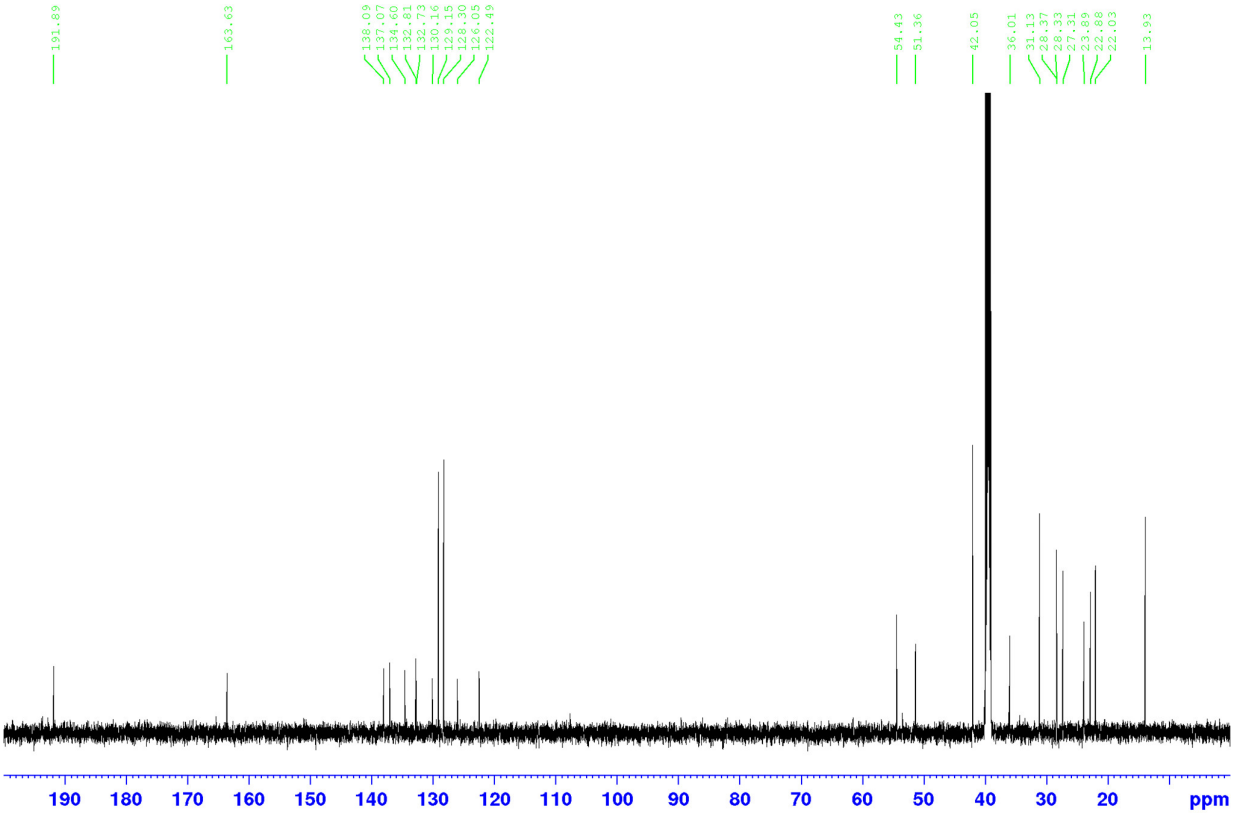


3-(2-(4'-Chloro-4-(octylsulfonamido)-[1,1'-biphenyl]-3-yl)-2-oxoacetamido)-*N*,*N*-dimethylpropan-1-aminium chloride (**13c**)

^{1}H NMR (600 MHz, DMSO-d_6):

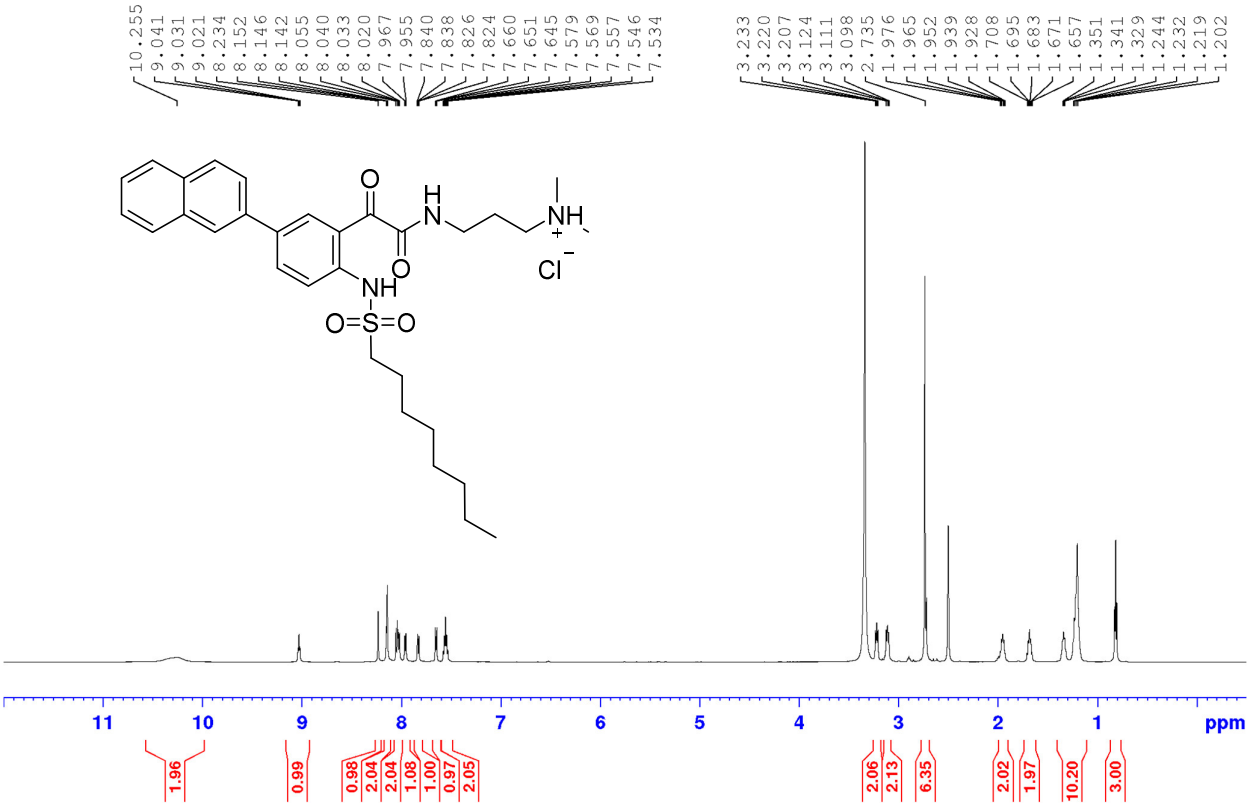


^{13}C NMR (150 MHz, DMSO-d_6):

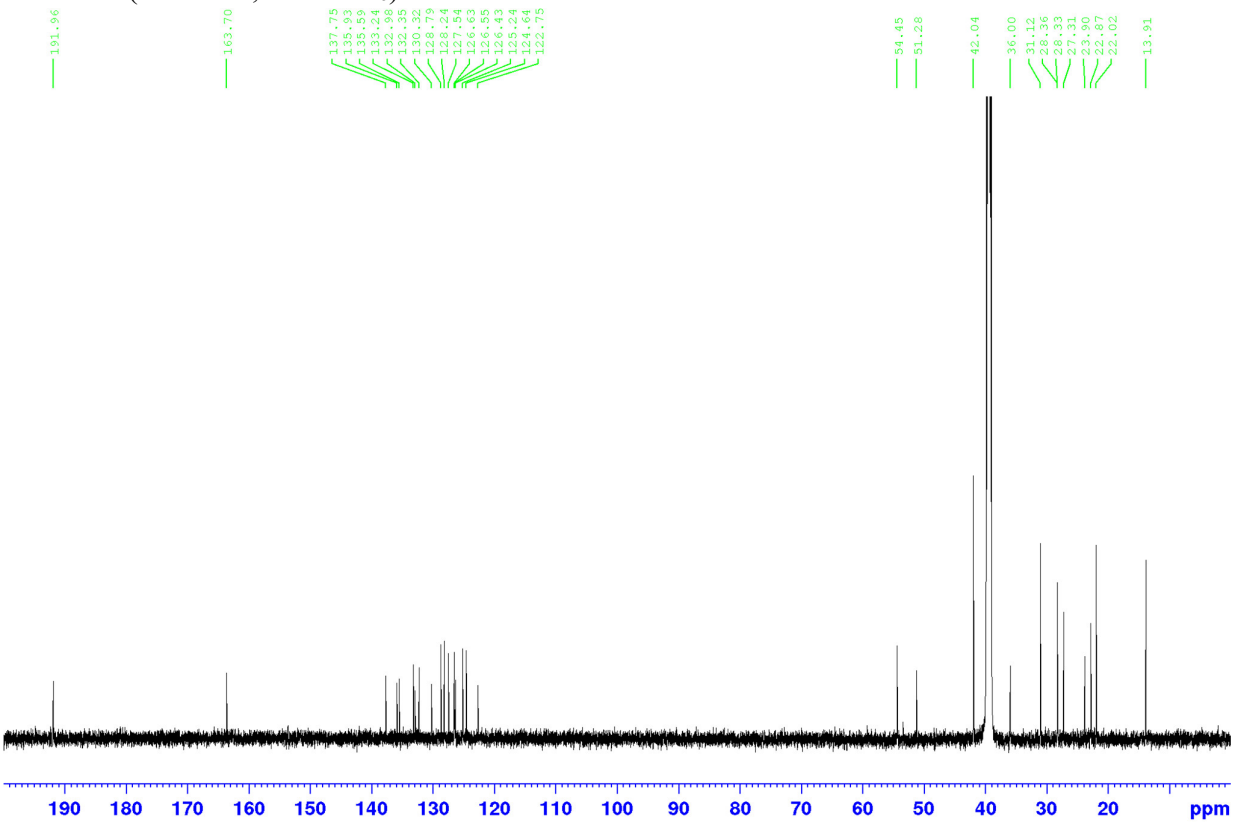


N,*N*-Dimethyl-3-(2-(5-(naphthalen-2-yl)-2-(octylsulfonamido)phenyl)-2-oxoacetamido)propan-1-aminium chloride (**13d**)

^{1}H NMR (600 MHz, DMSO-d_6):

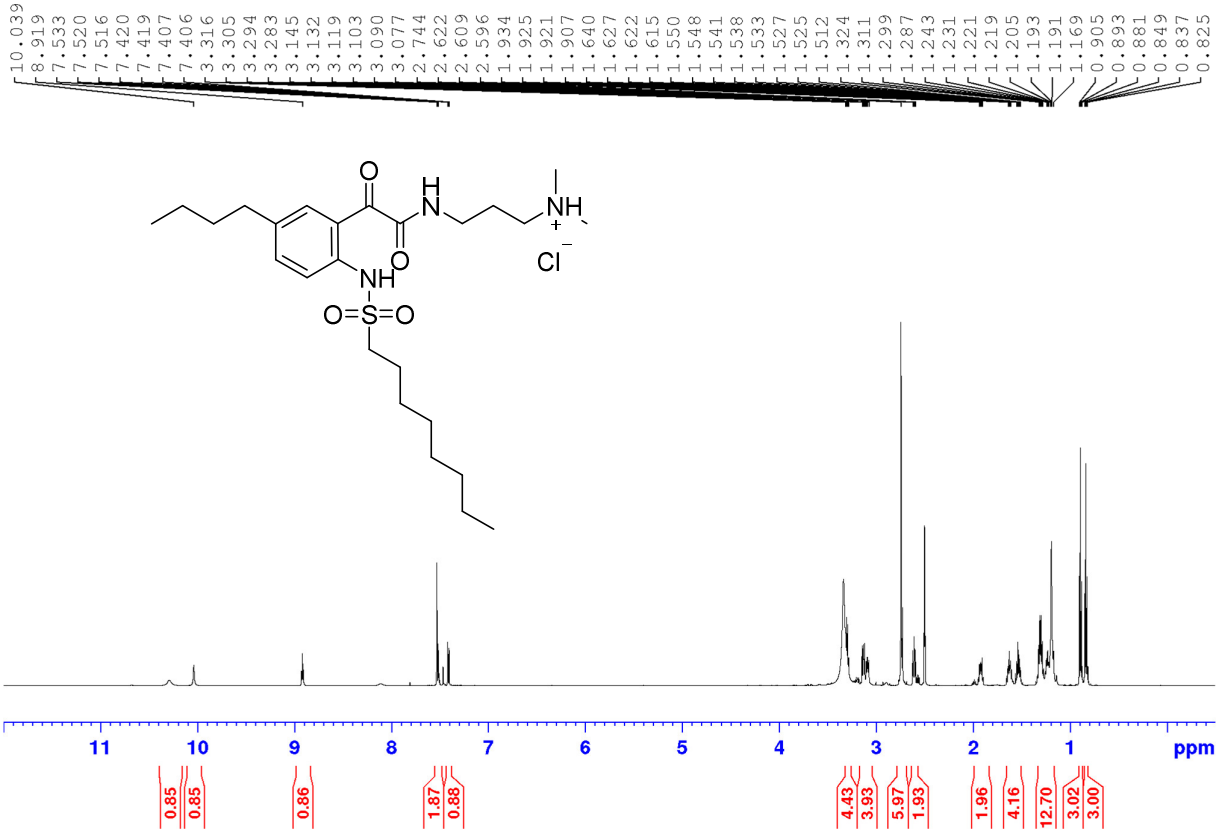


^{13}C NMR (150 MHz, DMSO-d_6):

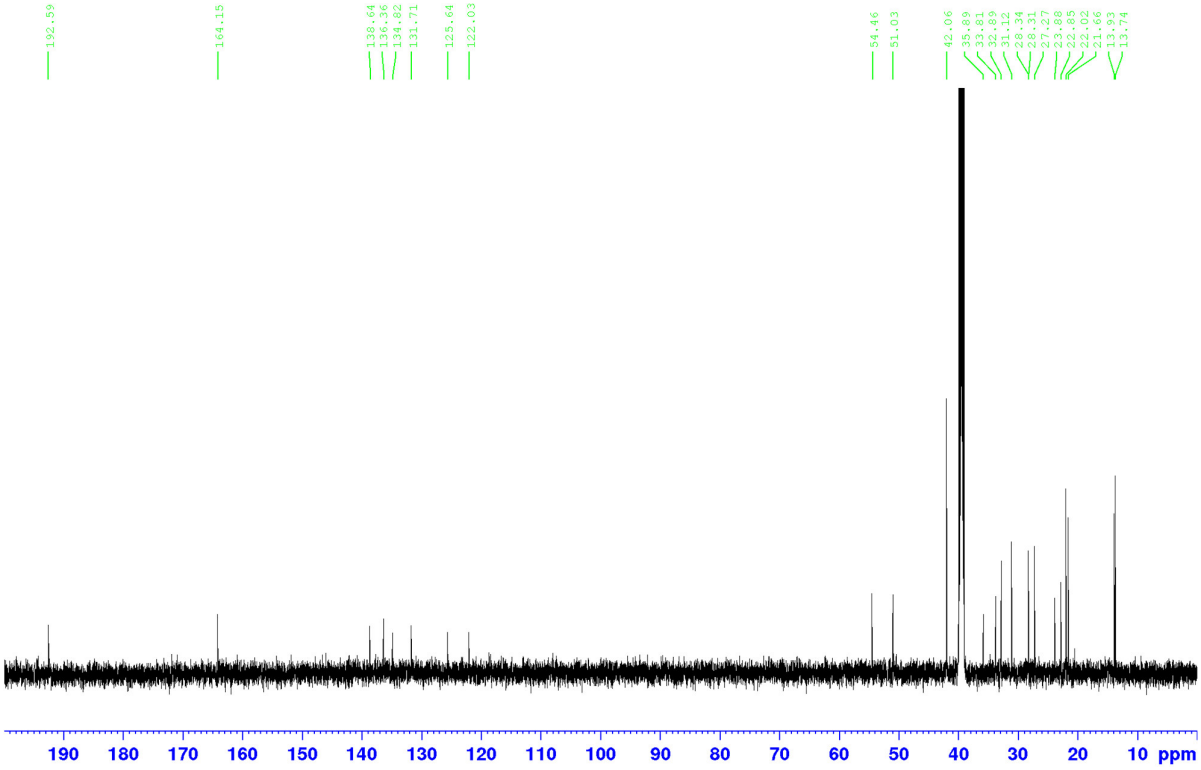


3-(2-(5-Butyl-2-(octylsulfonamido)phenyl)-2-oxoacetamido)-*N*,*N*-dimethylpropan-1-aminium chloride (**13e**)

^{1}H NMR (600 MHz, DMSO-d_6):

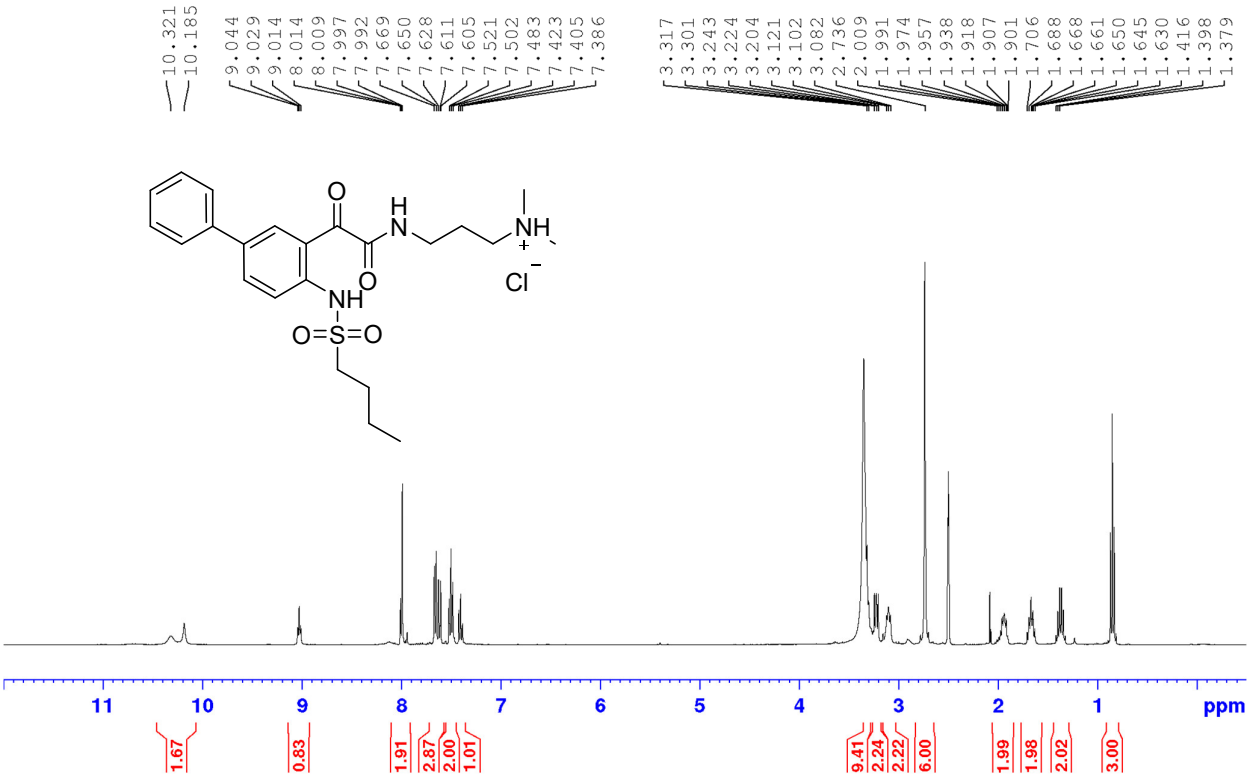


^{13}C NMR (150 MHz, DMSO-d_6):

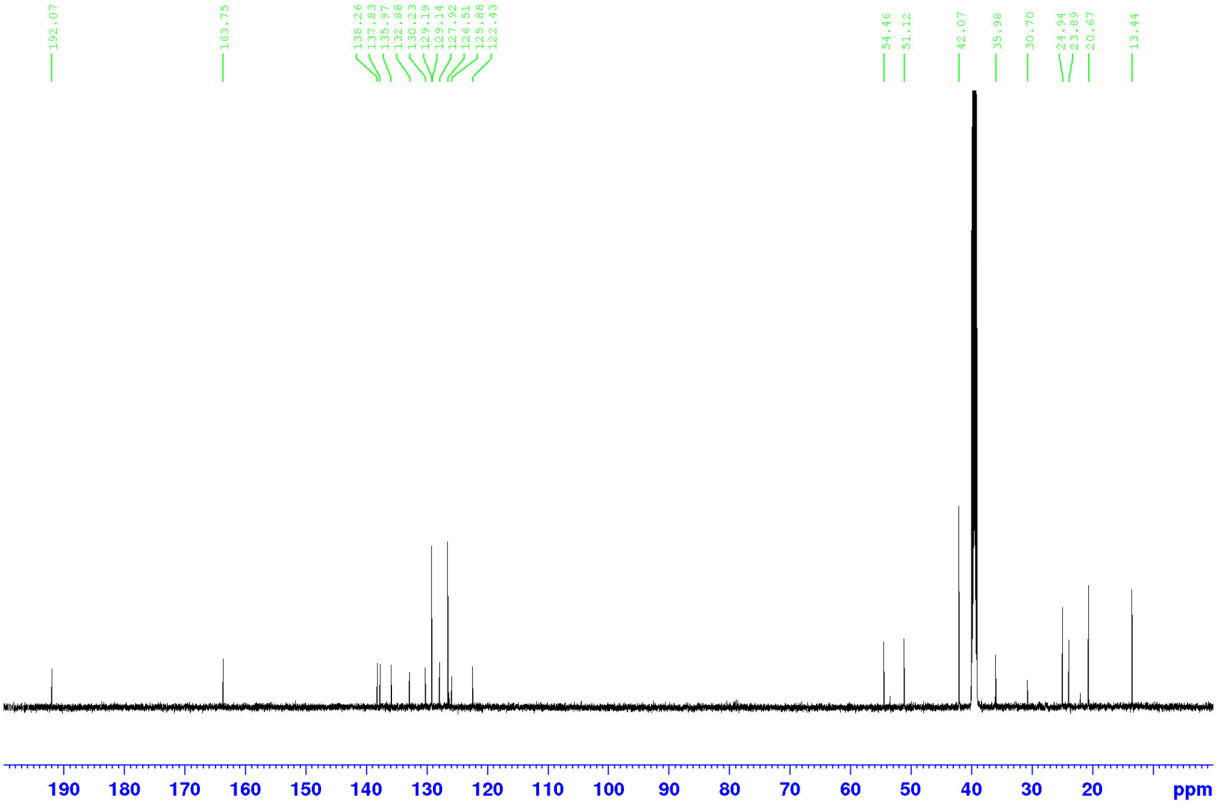


3-(2-(4-(Butylsulfonamido)-[1,1'-biphenyl]-3-yl)-2-oxoacetamido)-*N*,*N*-dimethylpropan-1-aminium chloride (**14a**)

^{1}H NMR (600 MHz, DMSO-d_6):

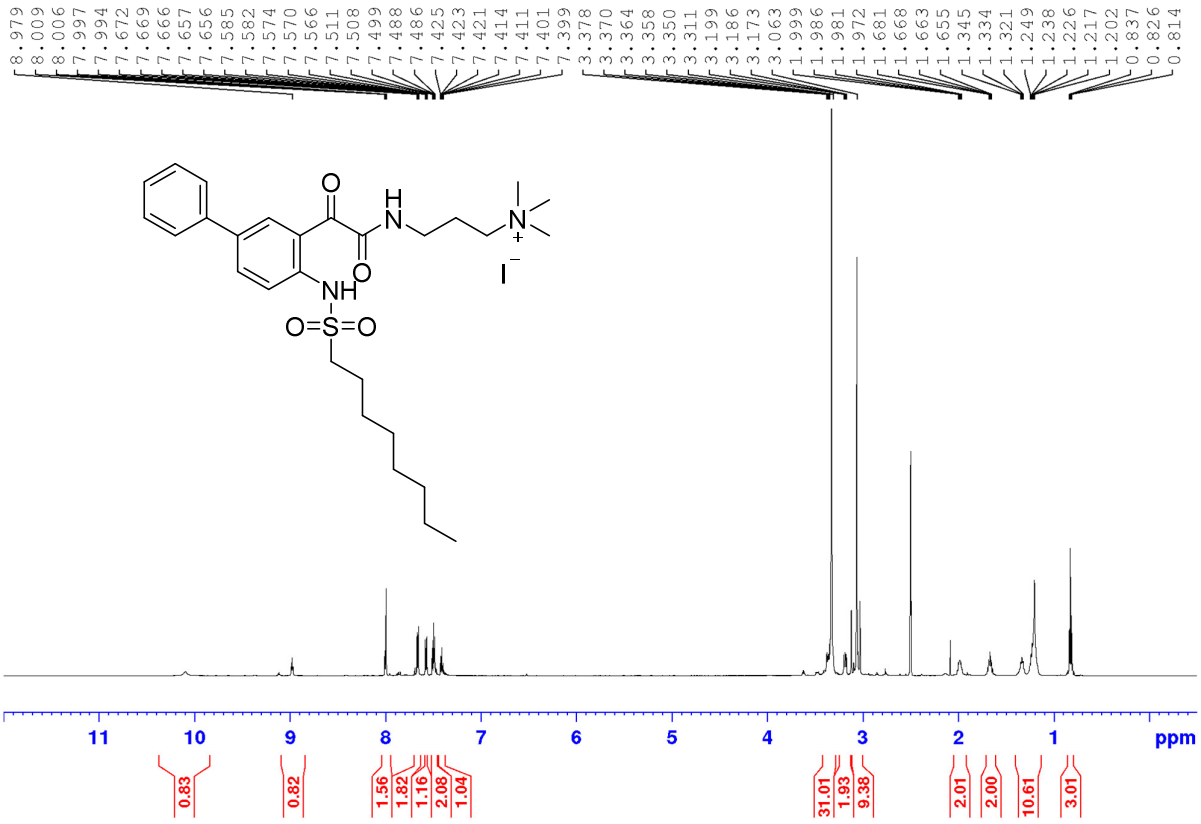


^{13}C NMR (150 MHz, DMSO-d_6):

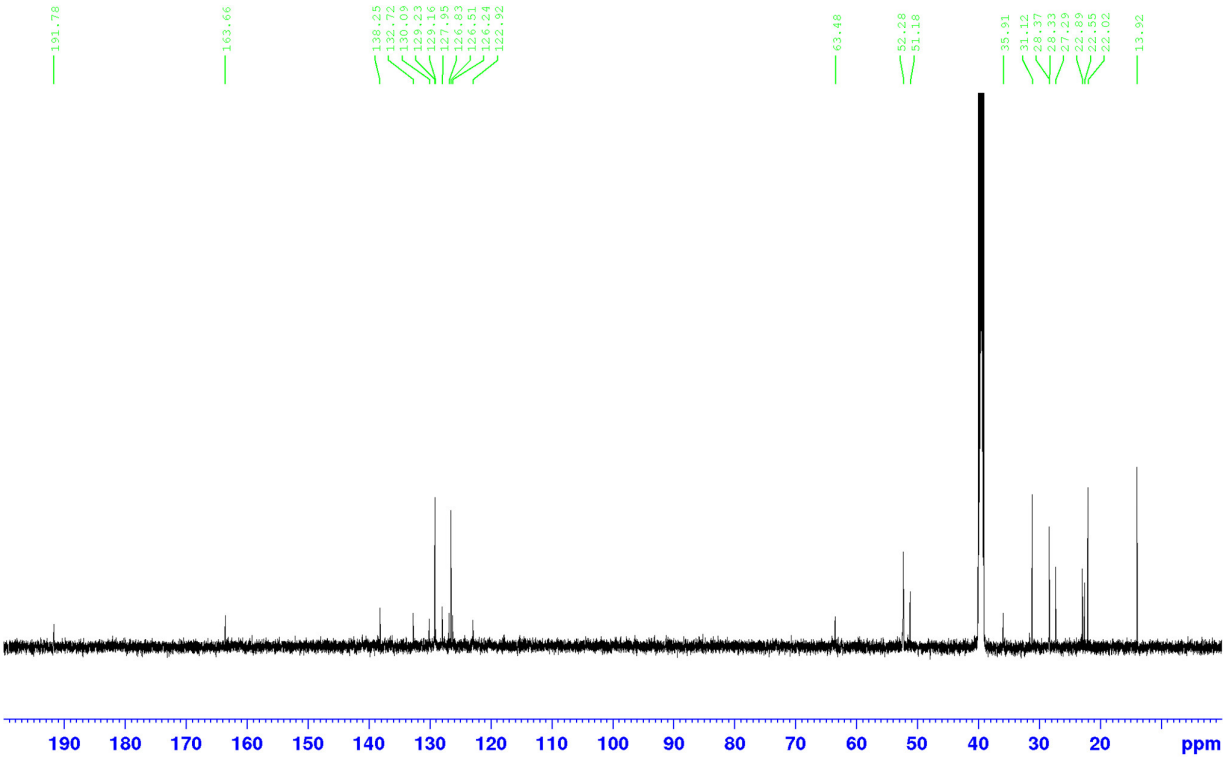


N,*N*,*N*-Trimethyl-3-(2-(4-(octylsulfonamido)-[1,1'-biphenyl]-3-yl)-2-oxoacetamido)propan-1-aminium iodide (**15a**)

^{1}H NMR (600 MHz, DMSO-d_6):

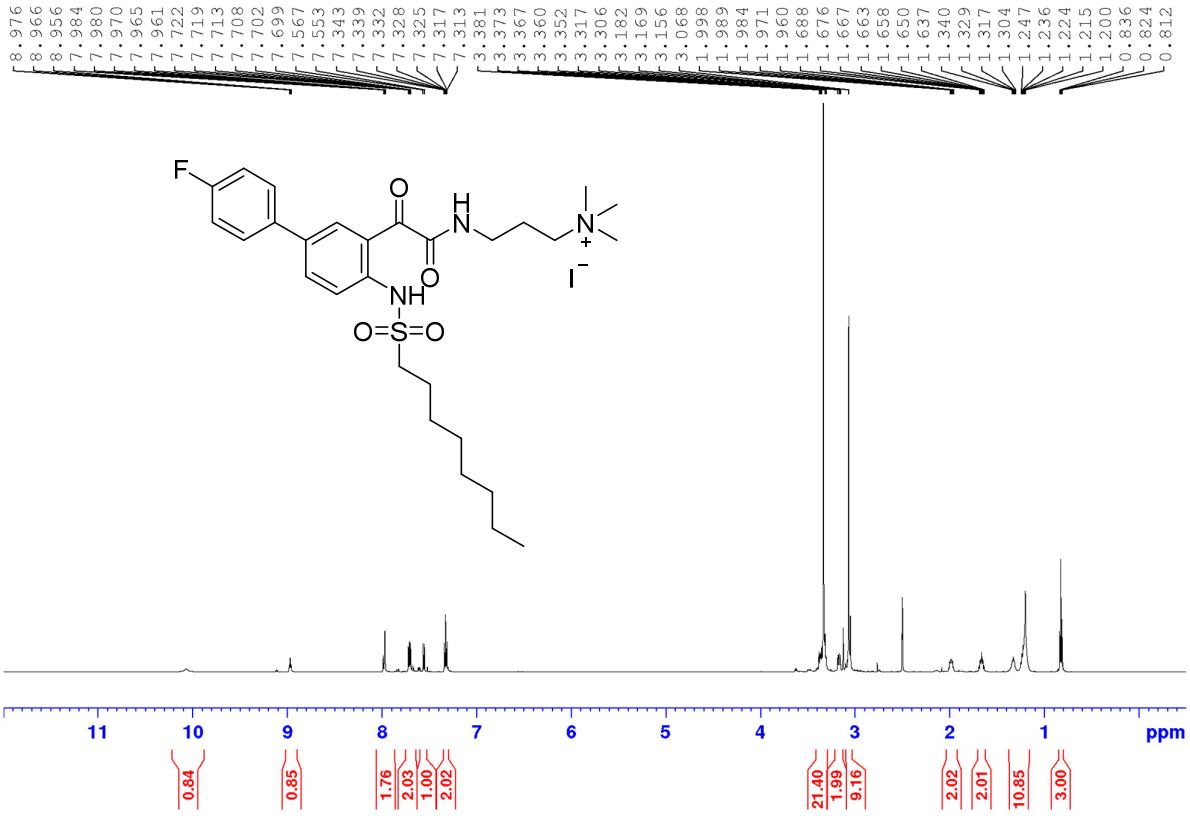


^{13}C NMR (150 MHz, DMSO-d_6):

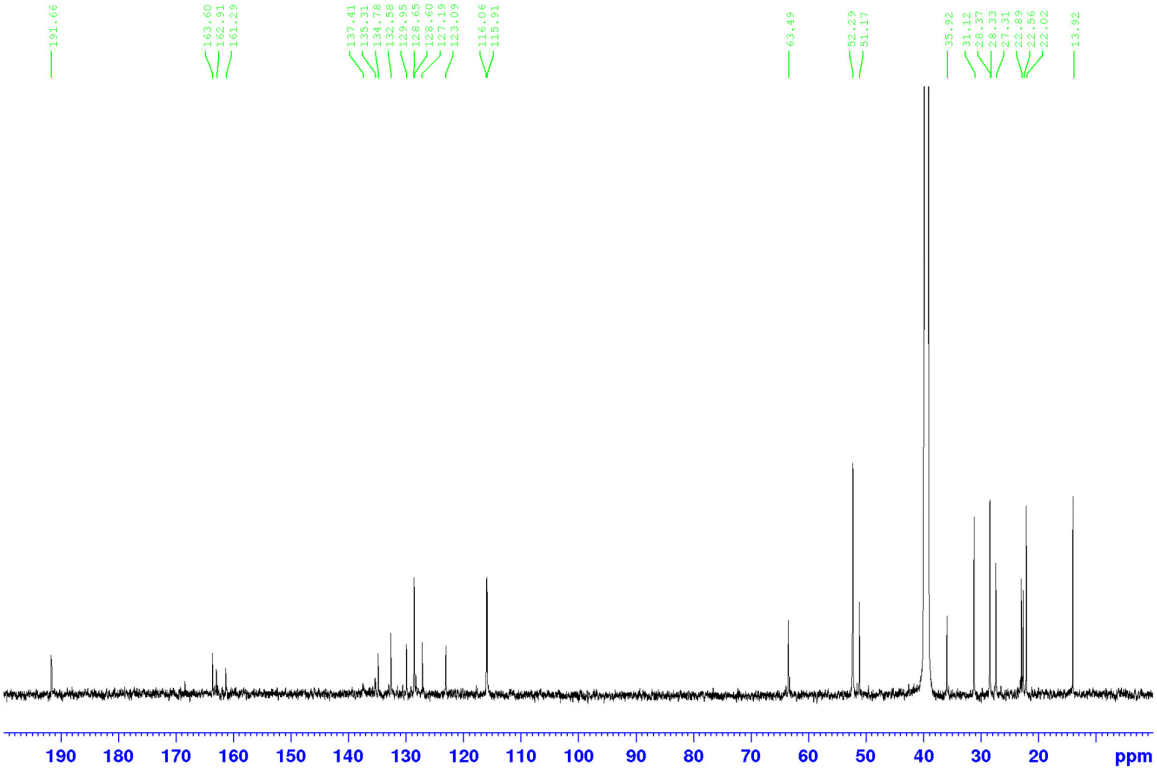


3-(2-(4'-Fluoro-4-(octylsulfonamido)-[1,1'-biphenyl]-3-yl)-2-oxoacetamido)-*N*,*N*,*N*-trimethylpropan-1-aminium iodide (**15b**)

^{1}H NMR (600 MHz, DMSO-d_6):

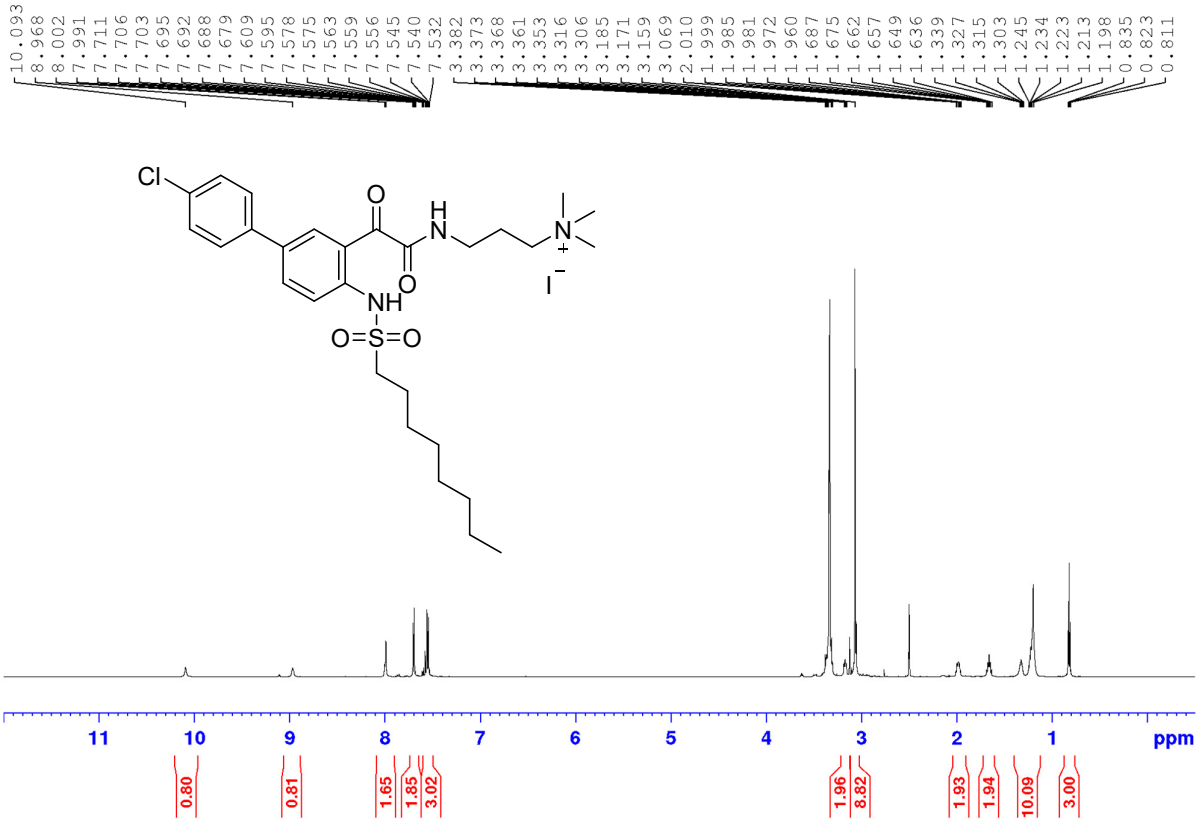


^{13}C NMR (150 MHz, DMSO-d_6):

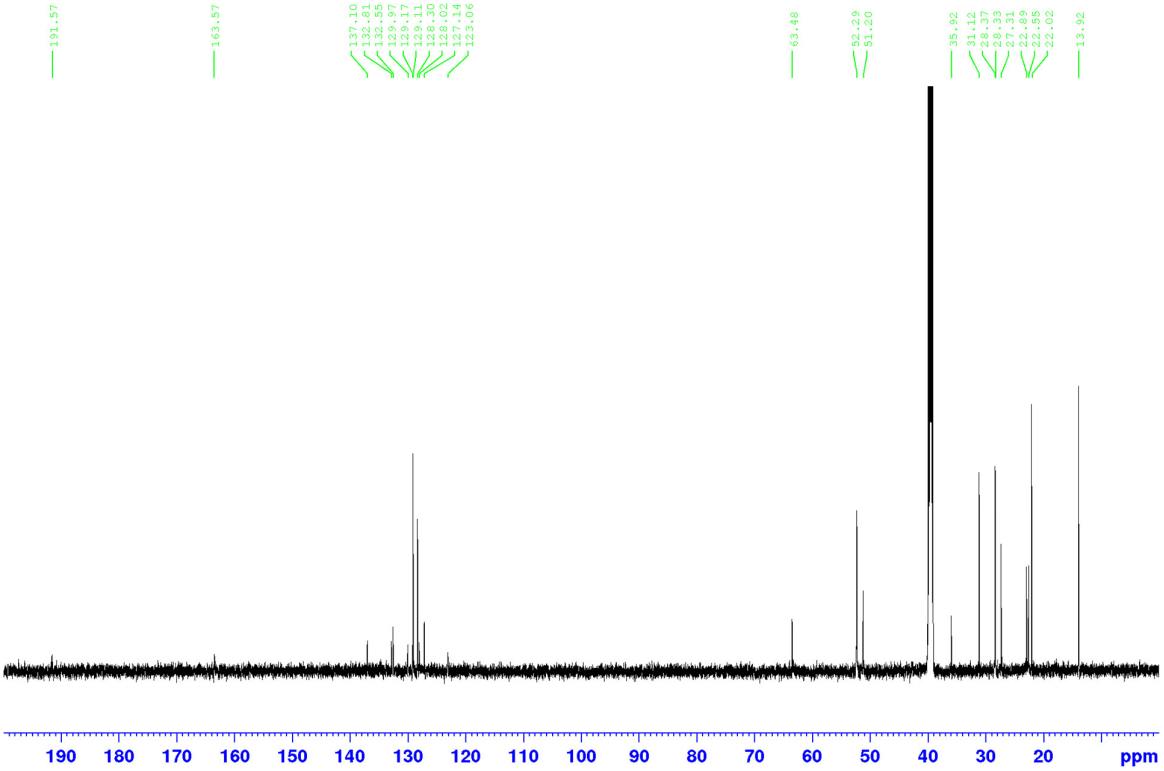


3-(2-(4'-Chloro-4-(octylsulfonamido)-[1,1'-biphenyl]-3-yl)-2-oxoacetamido)-*N*,*N*,*N*-trimethylpropan-1-aminium iodide (**15c**)

^{1}H NMR (600 MHz, DMSO-d_6):

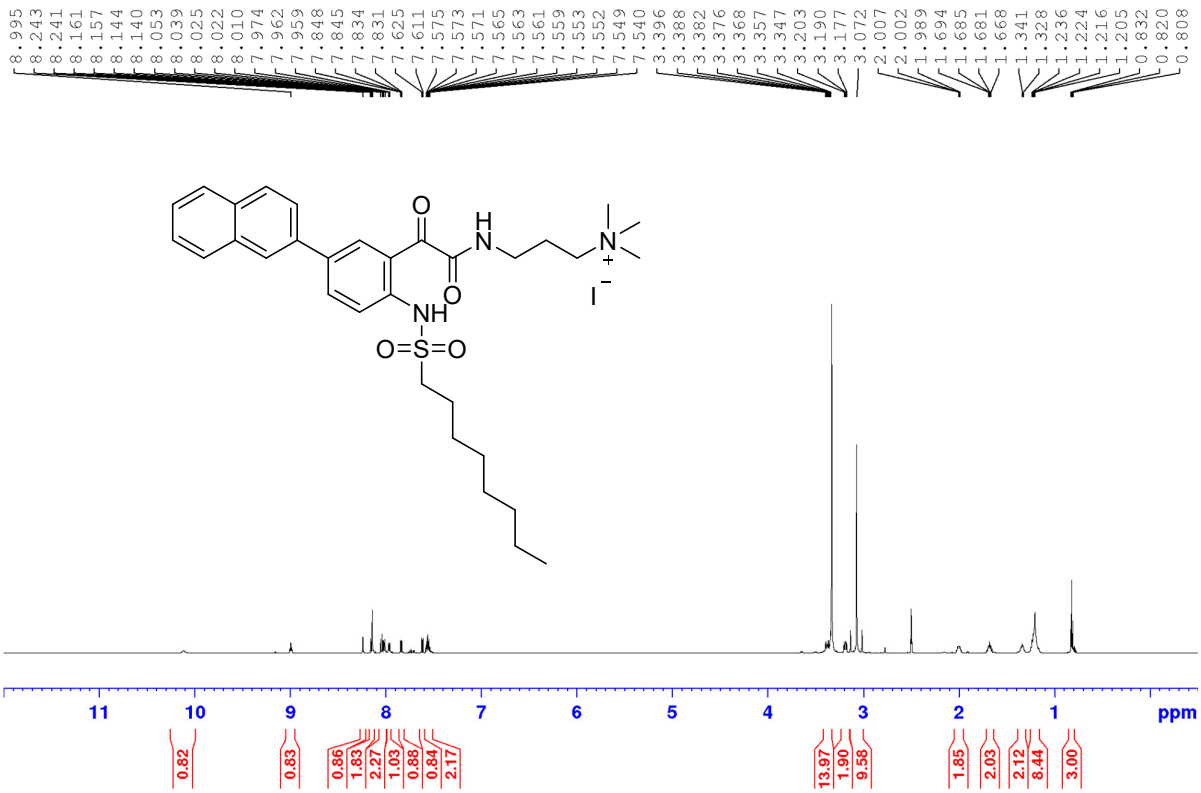


^{13}C NMR (150 MHz, DMSO-d_6):

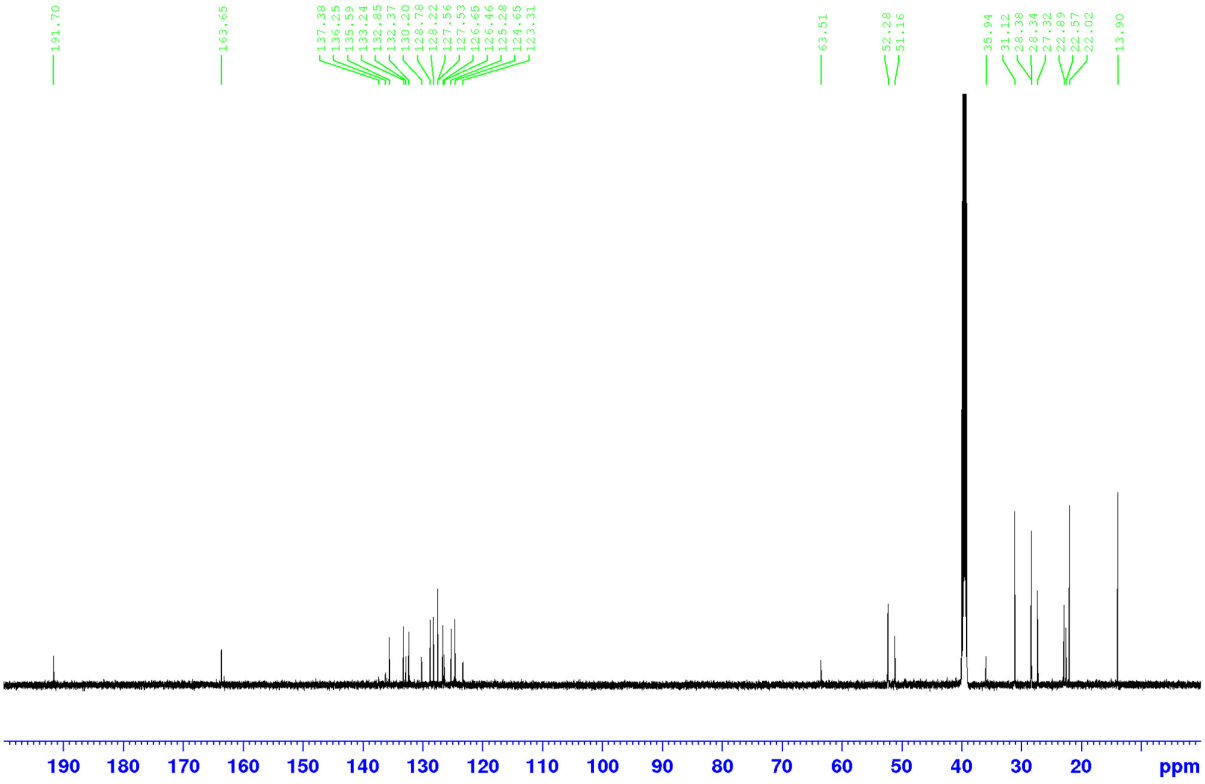


N,*N*,*N*-Trimethyl-3-(2-(5-(naphthalen-2-yl)-2-(octylsulfonamido)phenyl)-2-oxoacetamido)propan-1-aminium iodide (**15d**)

^{1}H NMR (600 MHz, DMSO-d_6):

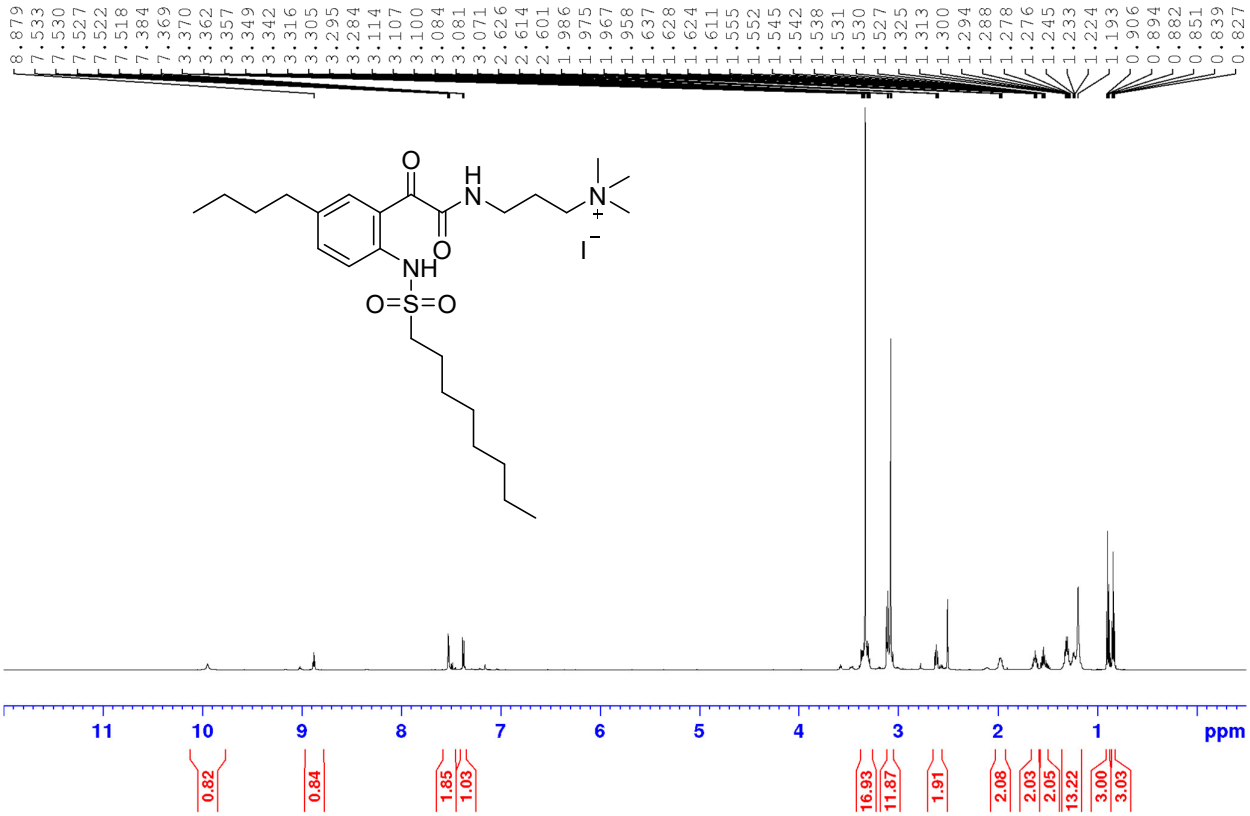


^{13}C NMR (150 MHz, DMSO-d_6):

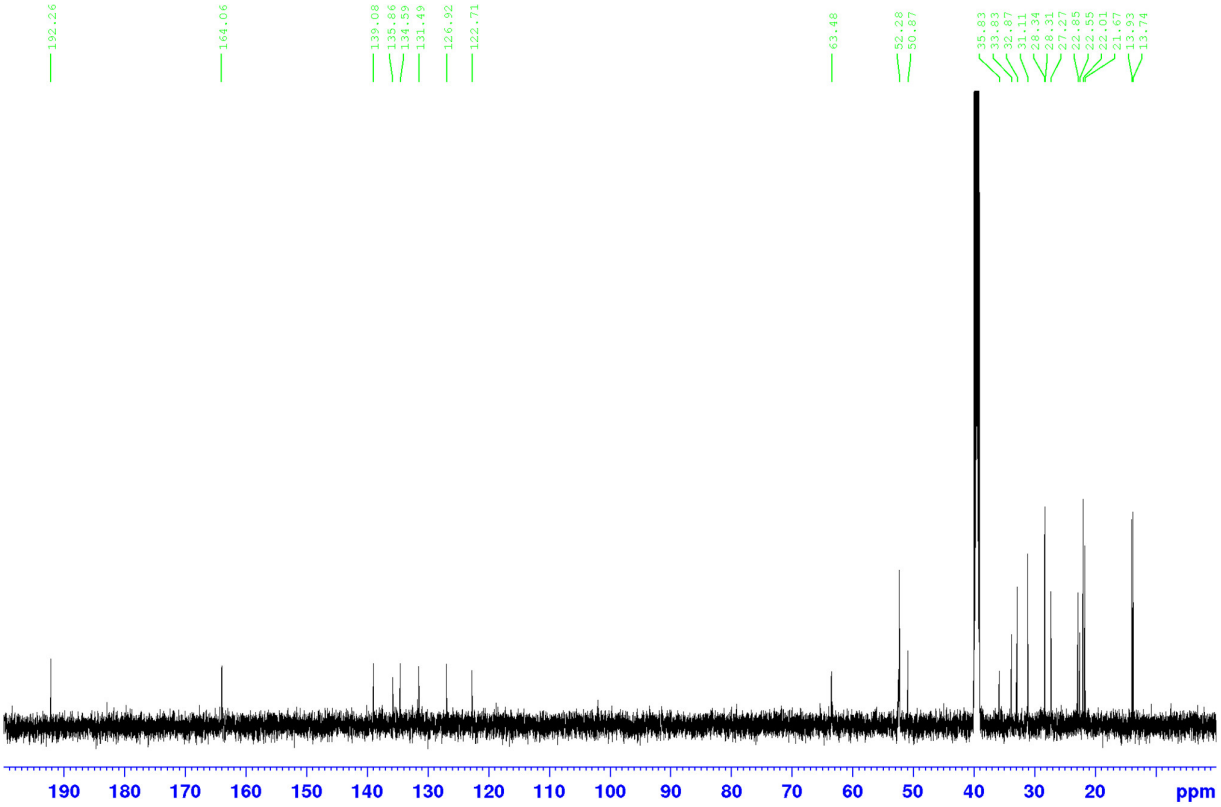


3-(2-(5-Butyl-2-(octylsulfonamido)phenyl)-2-oxoacetamido)-*N*,*N*,*N*-trimethylpropan-1-aminium iodide (**15e**)

^{1}H NMR (600 MHz, DMSO-d_6):

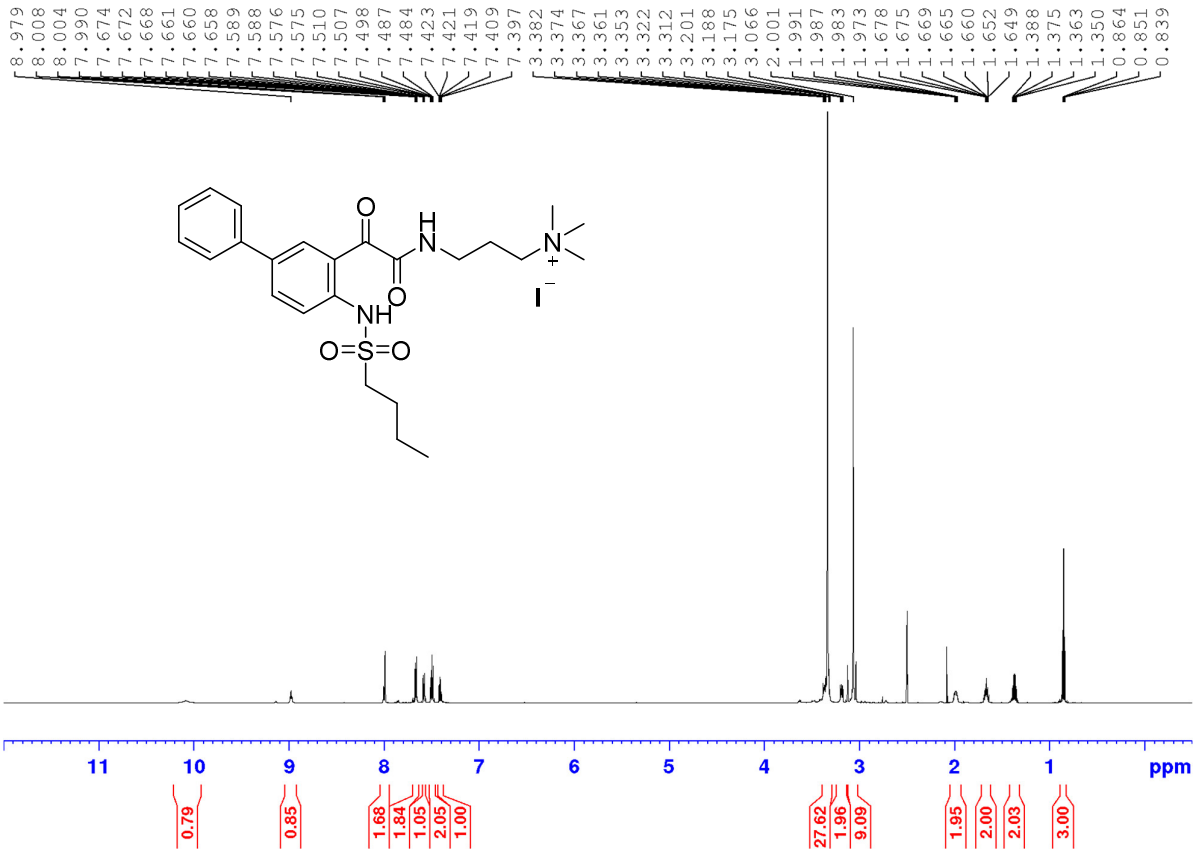


^{13}C NMR (150 MHz, DMSO-d_6):

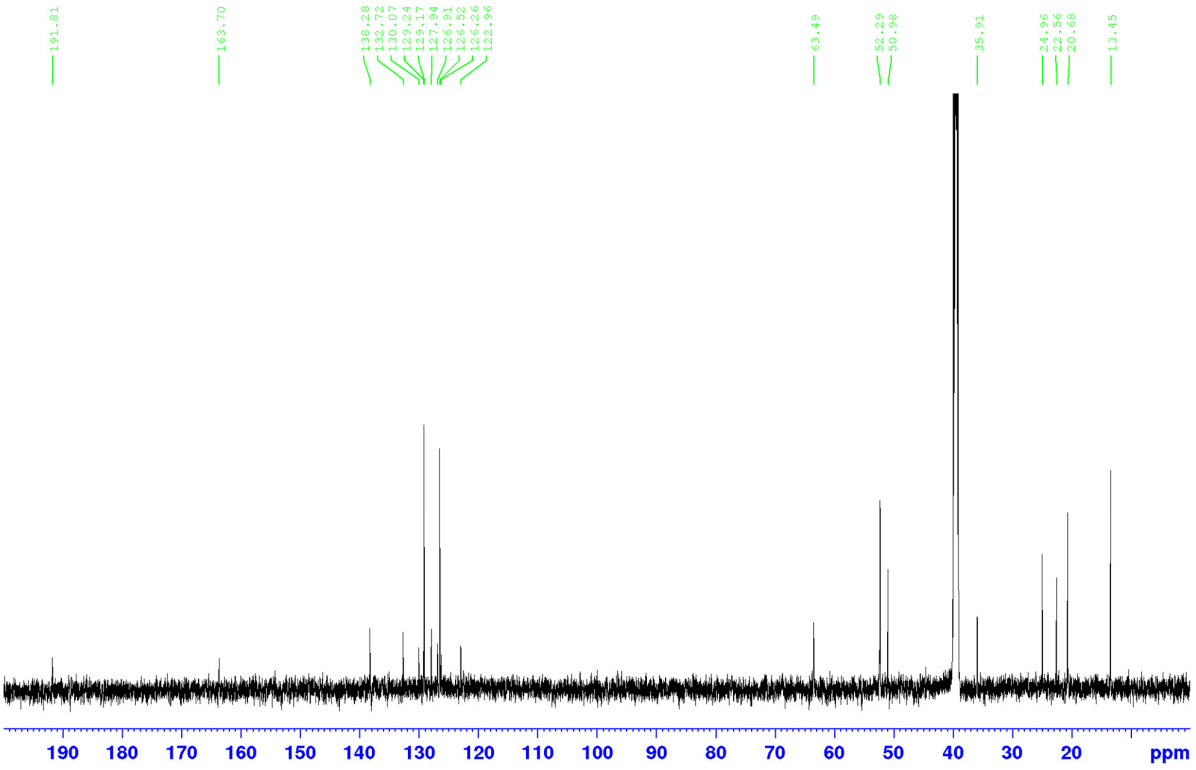


3-(2-(4-(Butylsulfonamido)-[1,1'-biphenyl]-3-yl)-2-oxoacetamido)-*N*,*N*,*N*-trimethylpropan-1-aminium iodide (**16a**)

^{1}H NMR (600 MHz, DMSO-d_6):

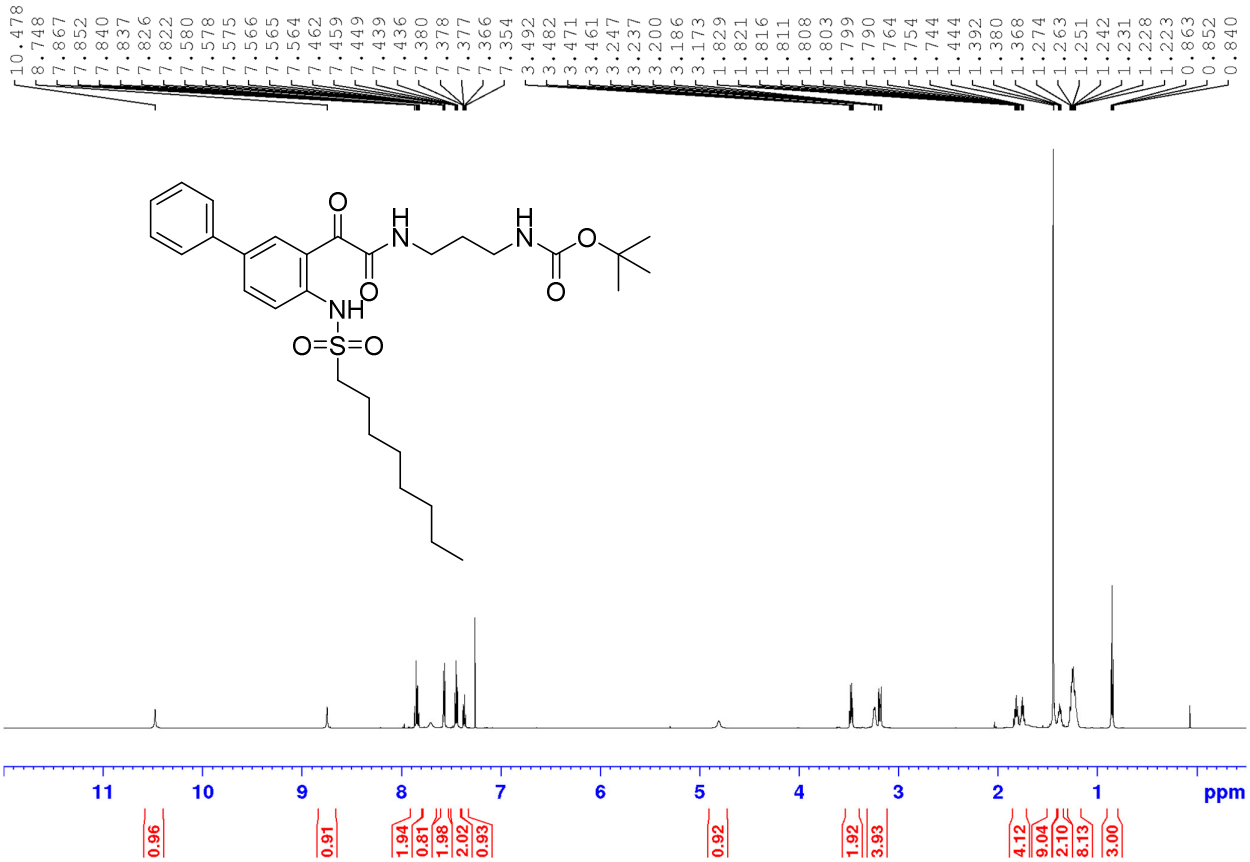


^{13}C NMR (150 MHz, DMSO-d_6):

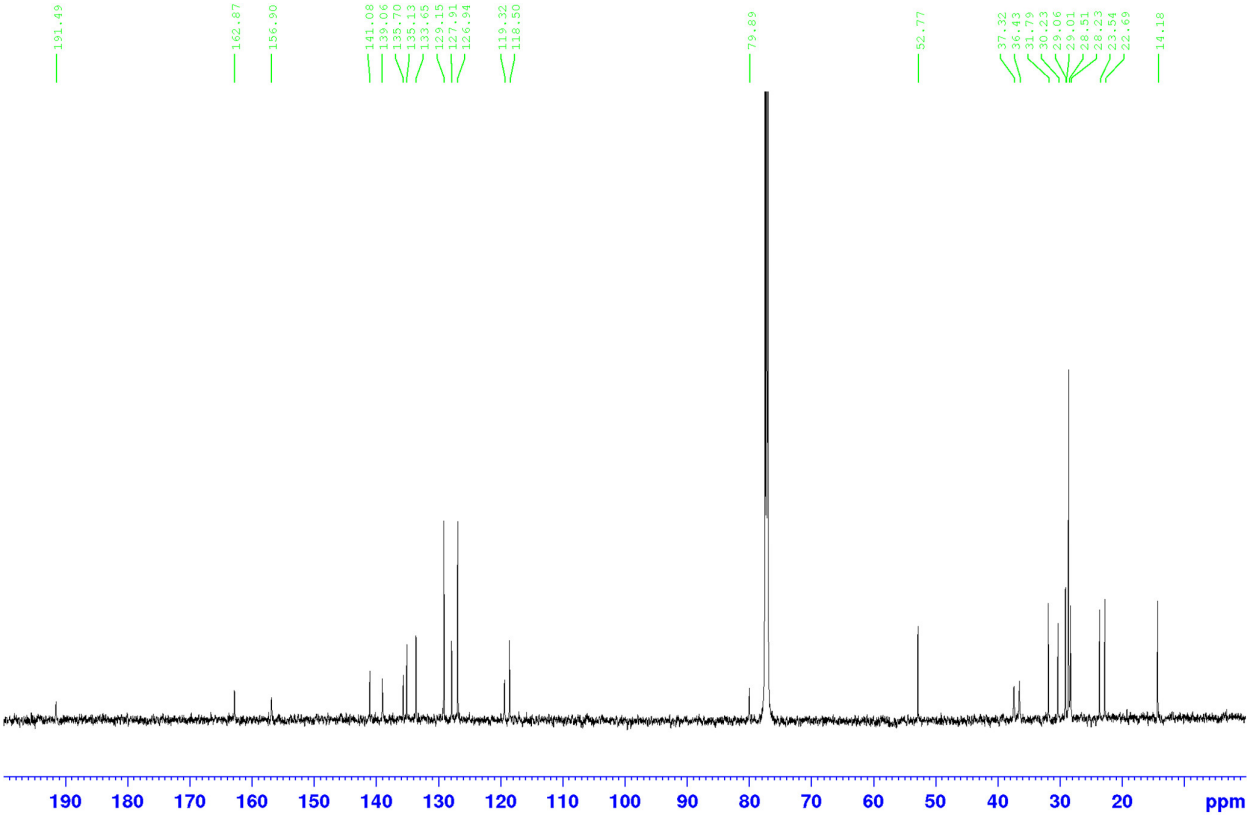


tert-Butyl (3-(2-(4-(octylsulfonamido)-[1,1'-biphenyl]-3-yl)-2-oxoacetamido)propyl)carbamate (**18a**)

^{1}H NMR (600 MHz, $CDCl_3$):

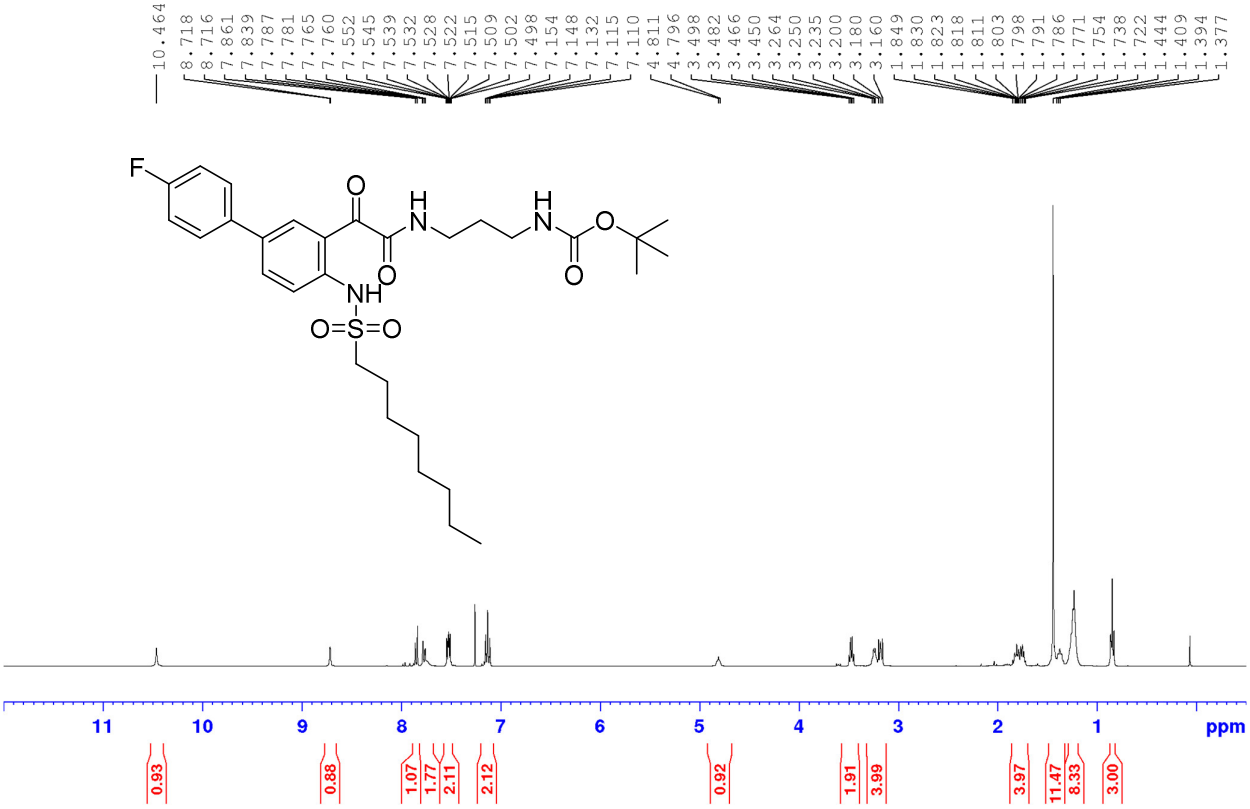


^{13}C NMR (150 MHz, $CDCl_3$):

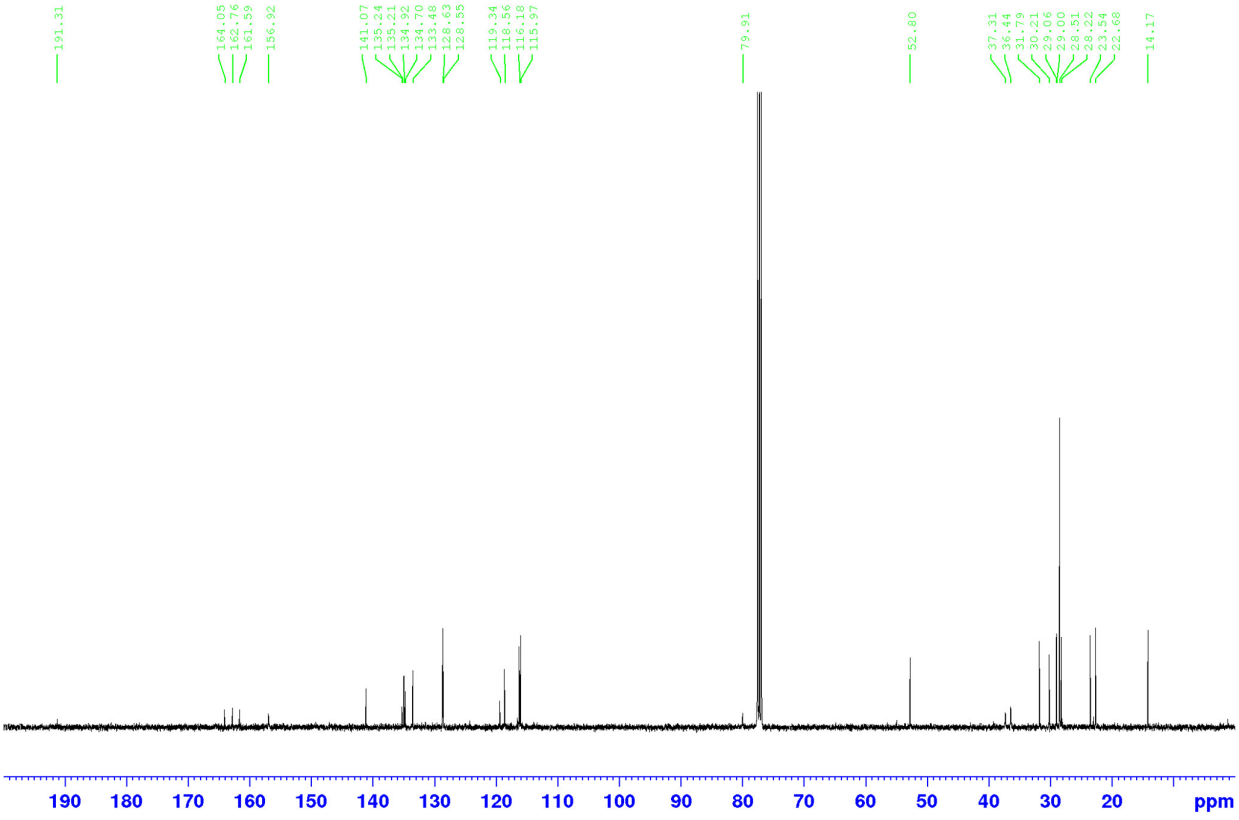


tert-Butyl (3-(2-(4'-fluoro-4-(octylsulfonamido)-[1,1'-biphenyl]-3-yl)-2-oxoacetamido)propyl) carbamate (**18b**)

^{1}H NMR (400 MHz, $CDCl_3$):

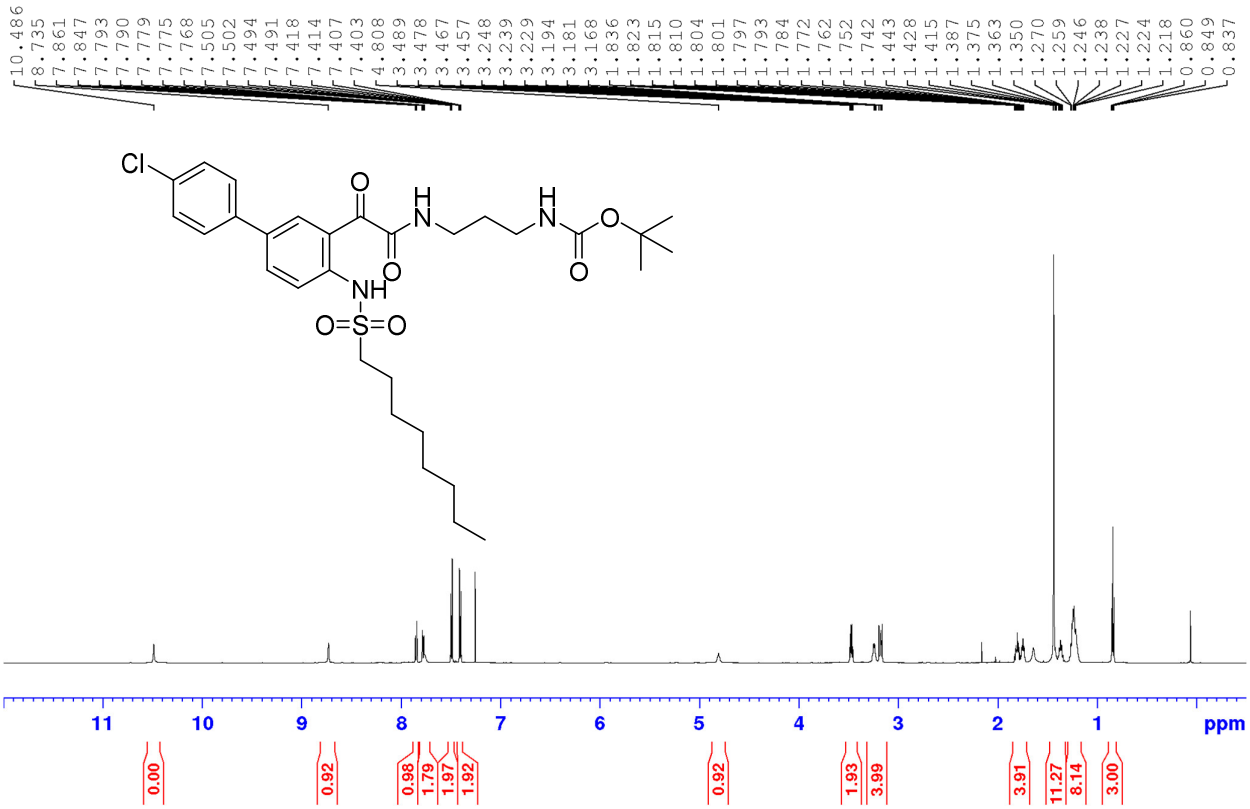


^{13}C NMR (100 MHz, $CDCl_3$):

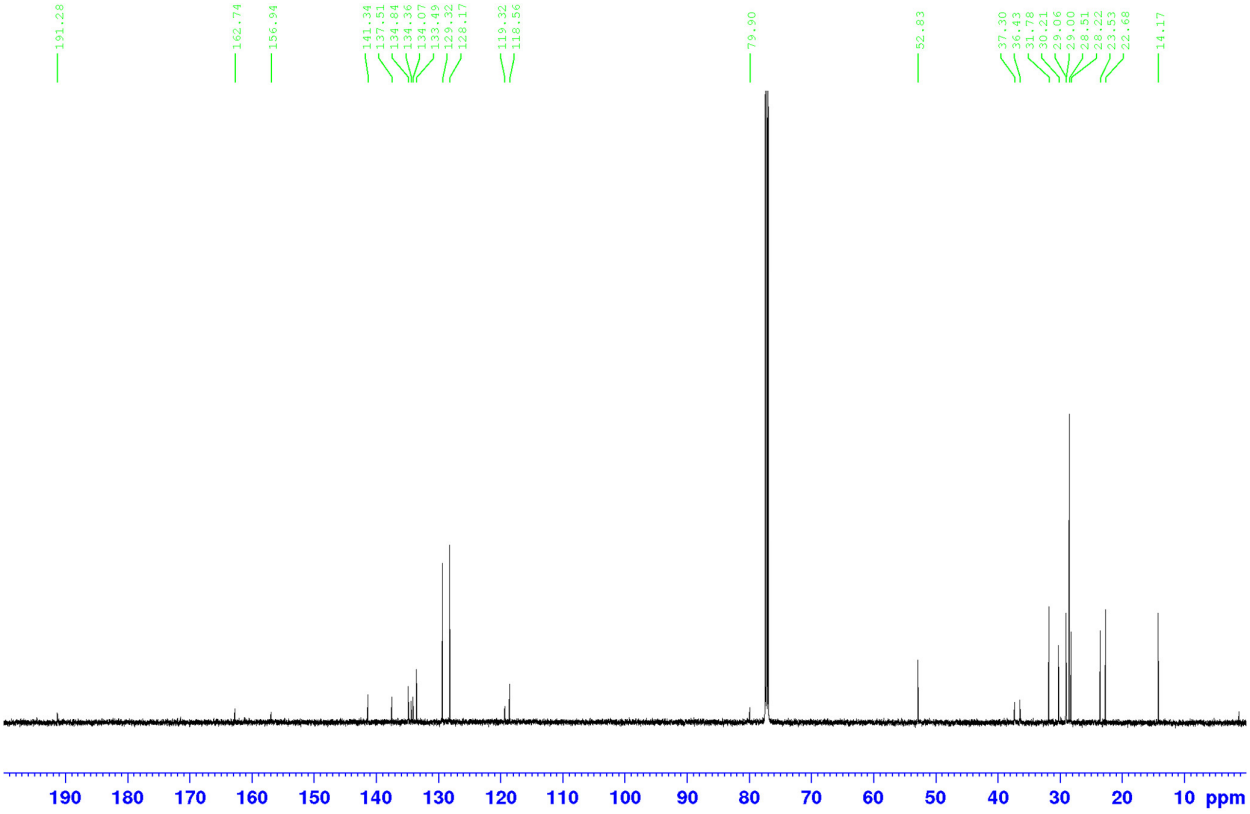


tert-Butyl (3-(2-(4'-Chloro-4-(octylsulfonamido)-[1,1'-biphenyl]-3-yl)-2-oxoacetamido)propyl) carbamate (**18c**)

^{1}H NMR (600 MHz, $CDCl_3$):

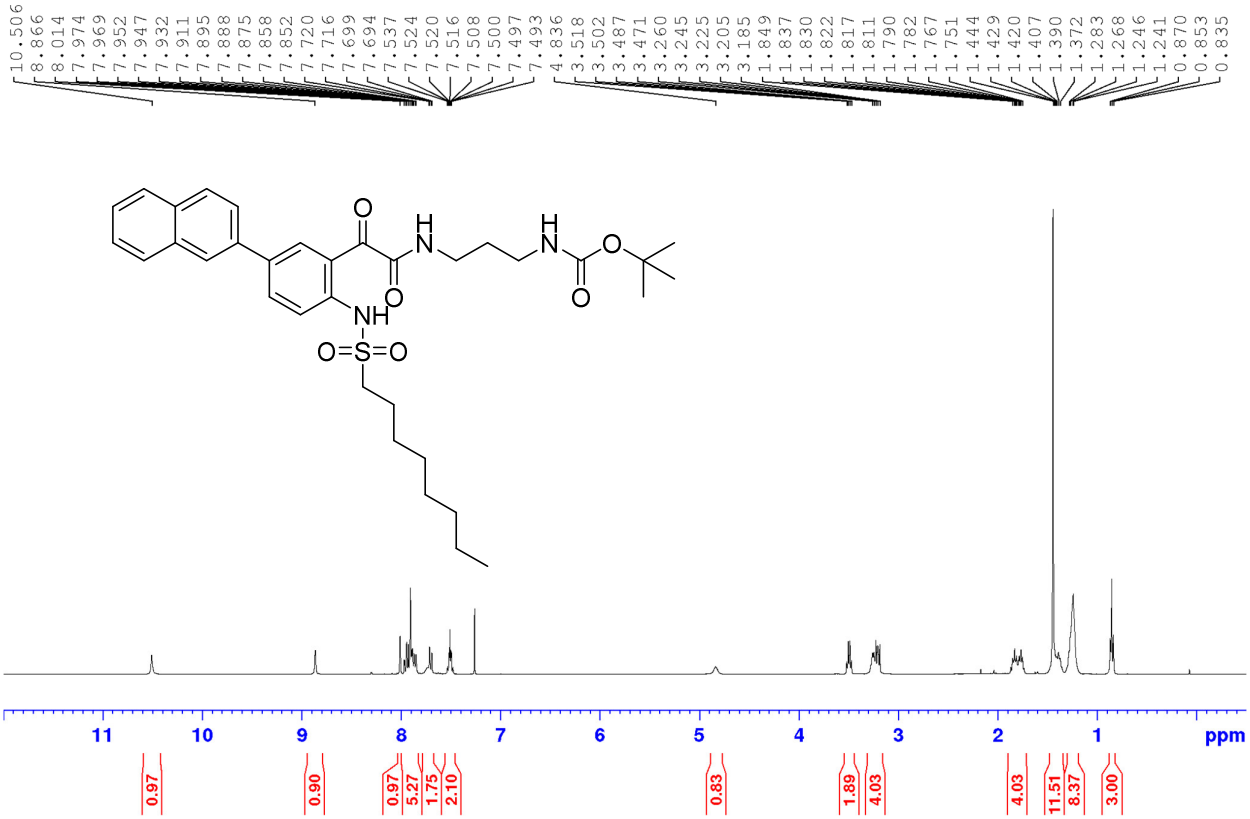


^{13}C NMR (150 MHz, $CDCl_3$):

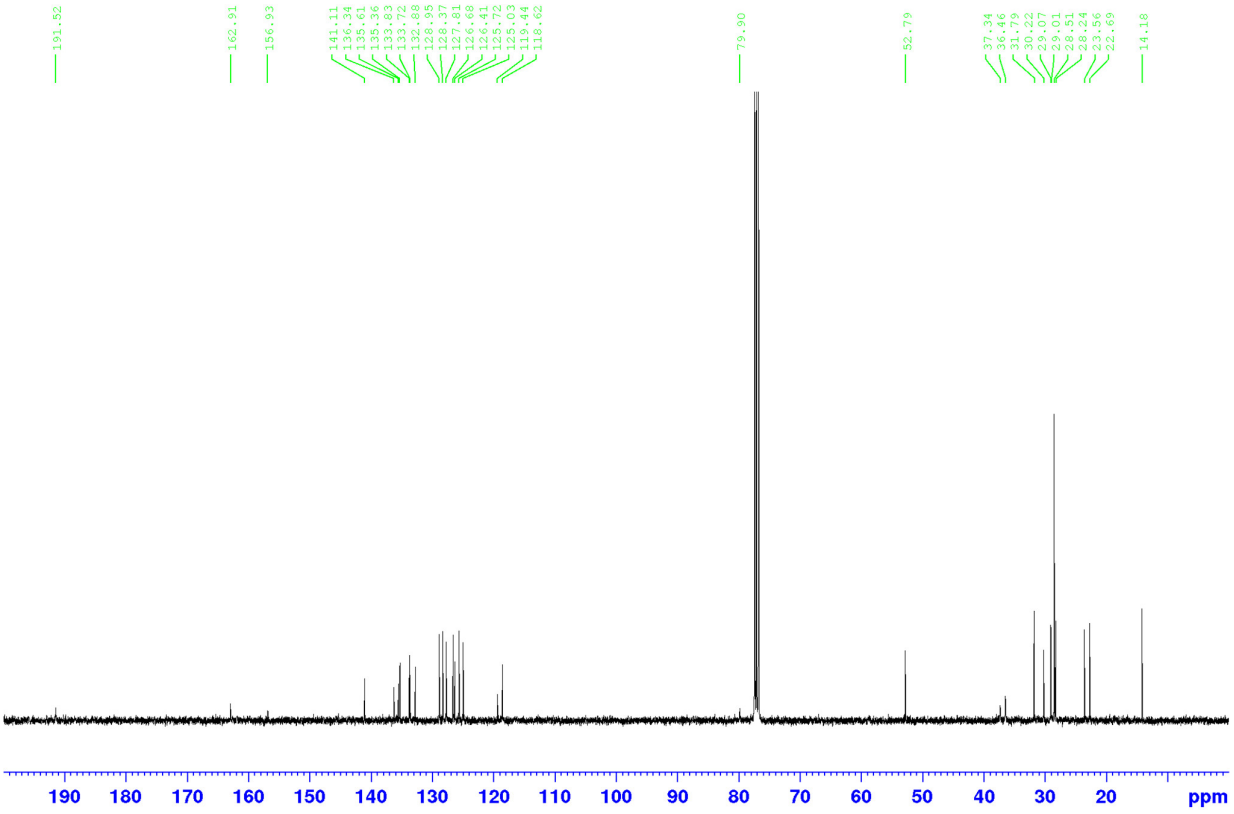


tert-Butyl (3-(2-(5-(naphthalen-2-yl)-2-(octylsulfonamido)phenyl)-2-oxoacetamido)propyl) carbamate (**18d**)

^{1}H NMR (600 MHz, $CDCl_3$):

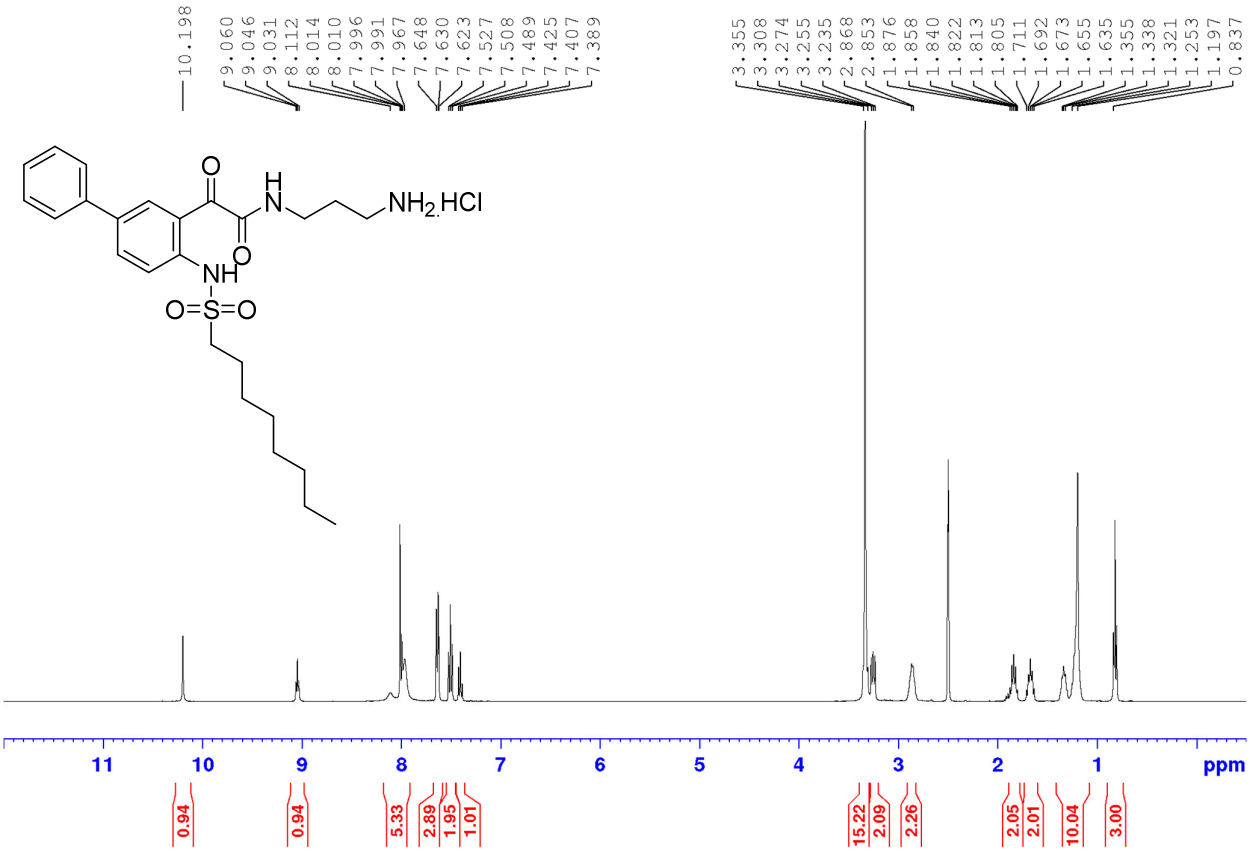


^{13}C NMR (150 MHz, $CDCl_3$):

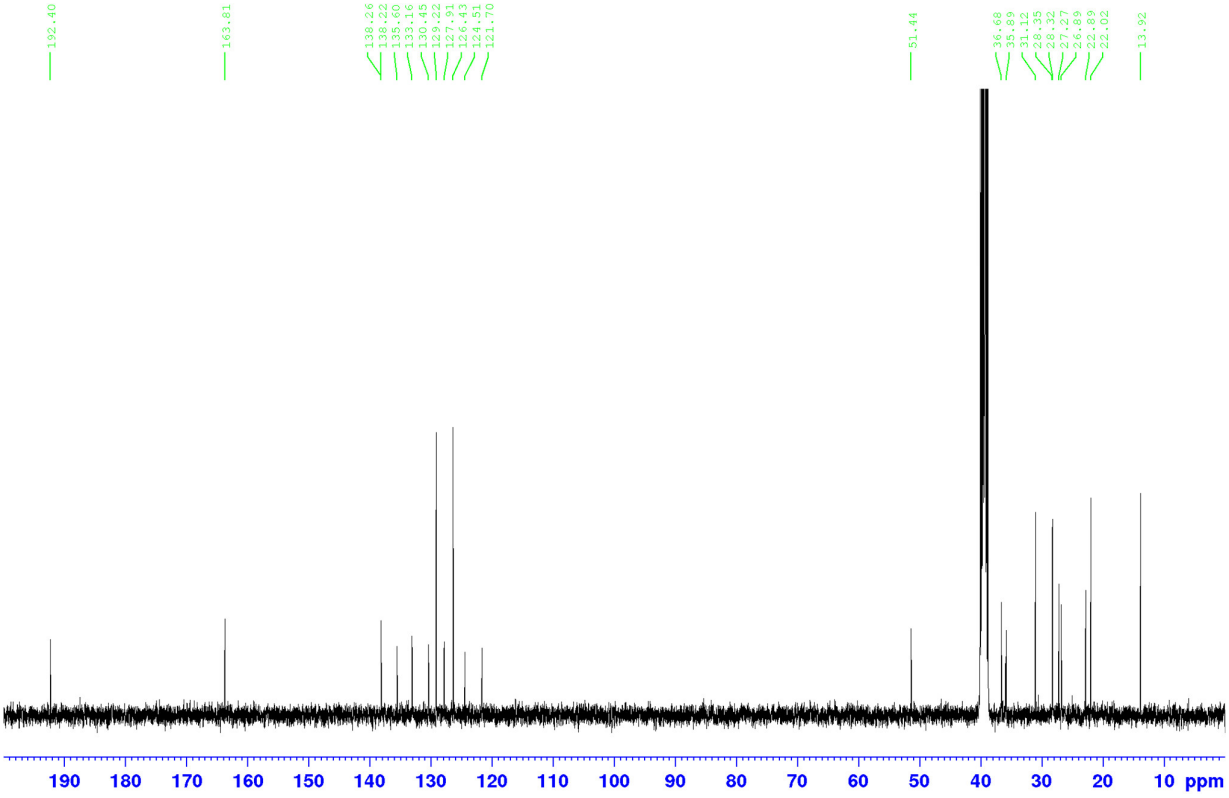


N-(3-Aminopropyl)-2-(4-(octylsulfonamido)-[1,1'-biphenyl]-3-yl)-2-oxoacetamide hydrochloride (**19a**)

^{1}H NMR (400 MHz, DMSO-d_6):

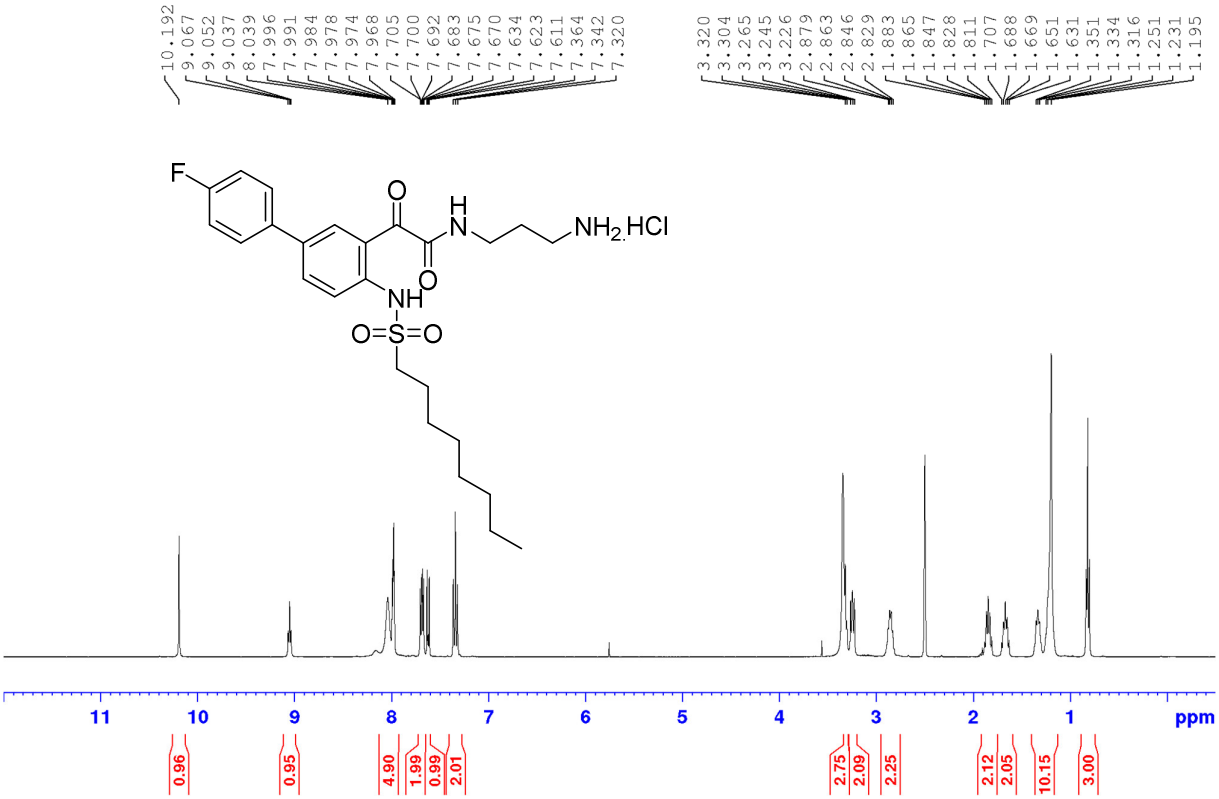


^{13}C NMR (100 MHz, DMSO-d_6):

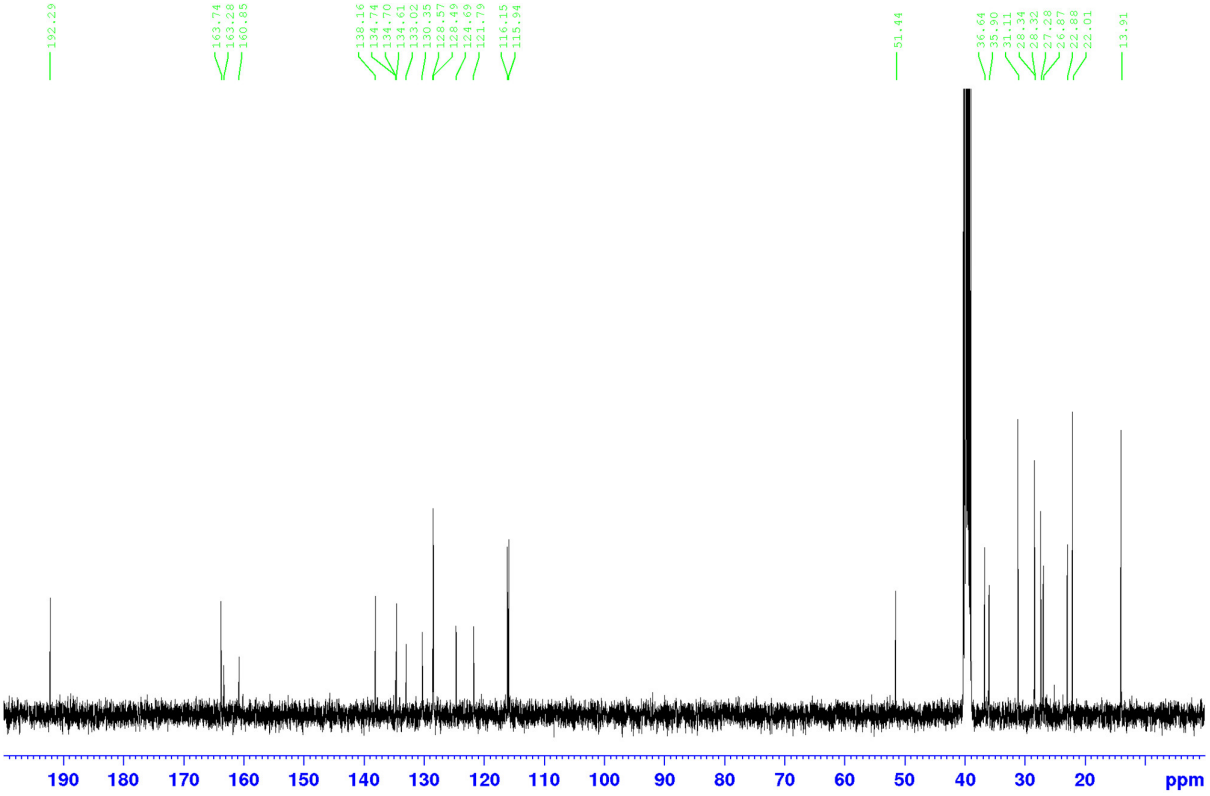


N-(3-Aminopropyl)-2-(4'-fluoro-4-(octylsulfonamido)-[1,1'-biphenyl]-3-yl)-2-oxoacetamide hydrochloride (**19b**)

^{1}H NMR (400 MHz, DMSO-d_6):

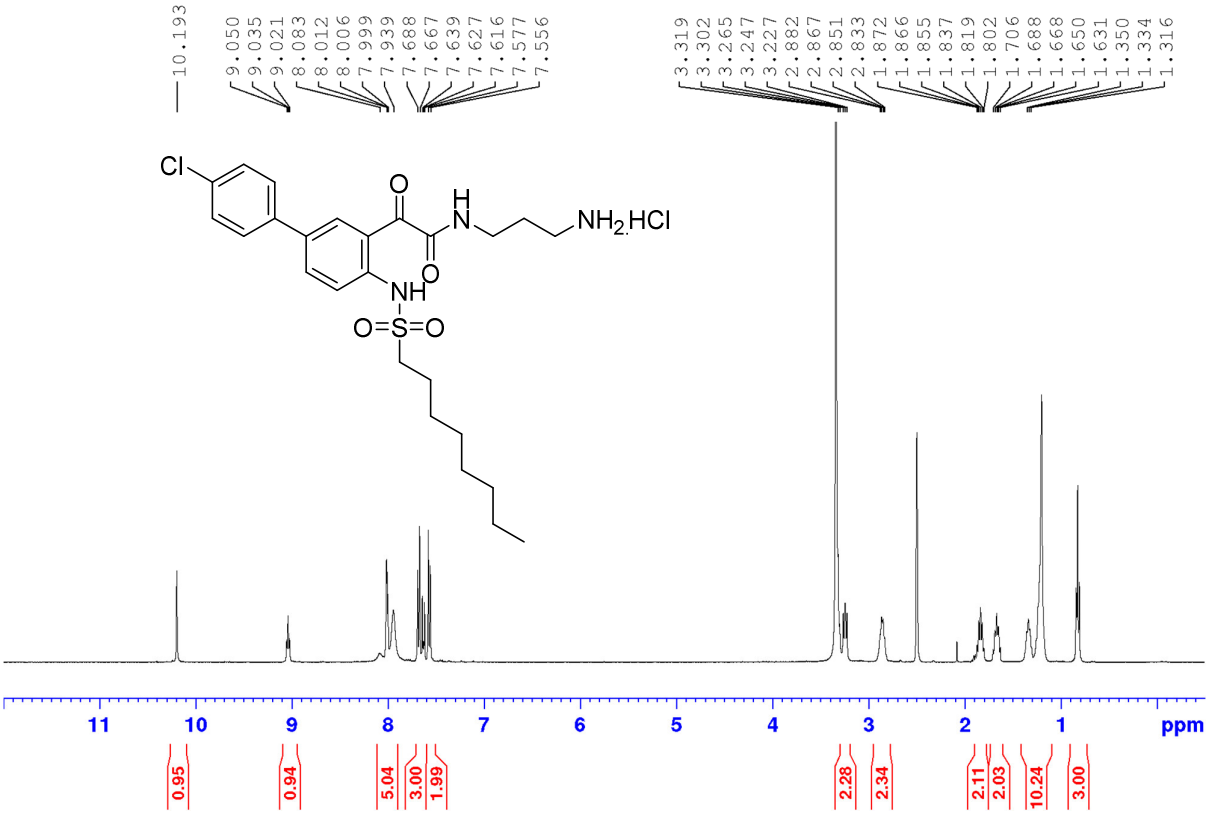


^{13}C NMR (100 MHz, DMSO-d_6):

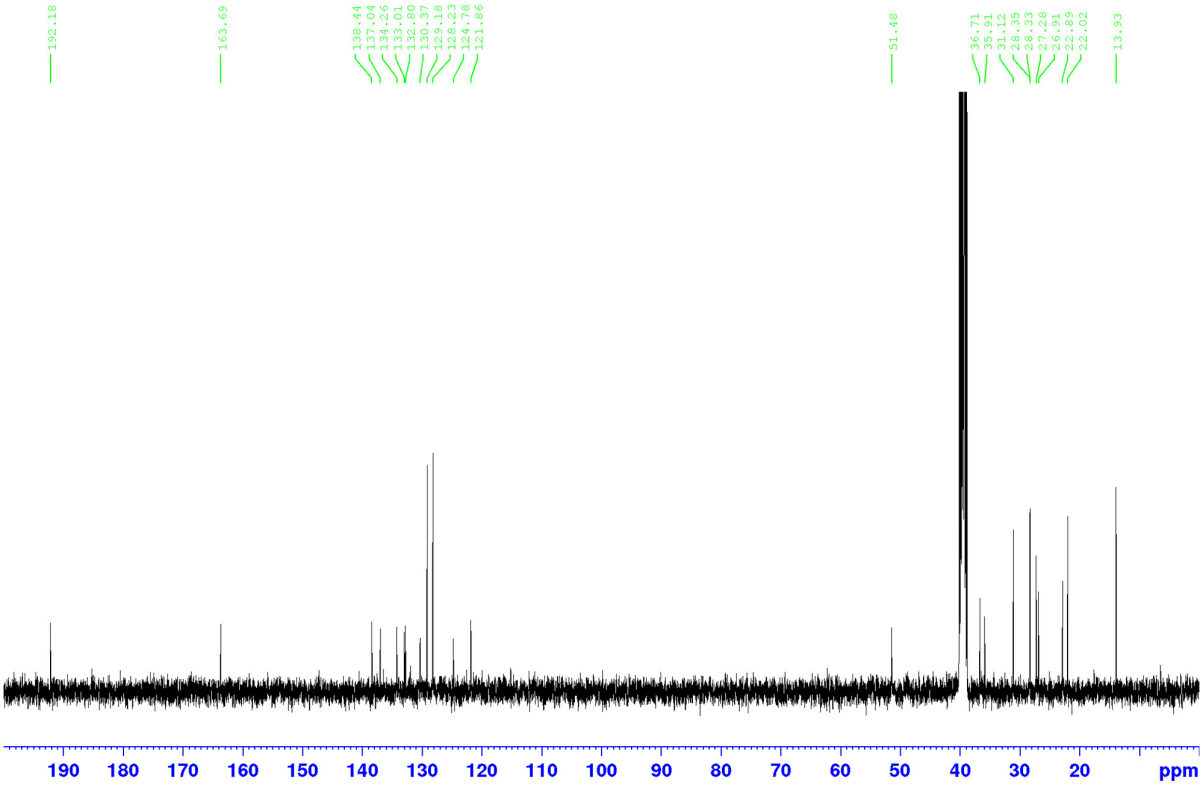


N-(3-Aminopropyl)-2-(4'-chloro-4-(octylsulfonamido)-[1,1'-biphenyl]-3-yl)-2-oxoacetamide hydrochloride (**19c**)

^{1}H NMR (400 MHz, DMSO-d_6):

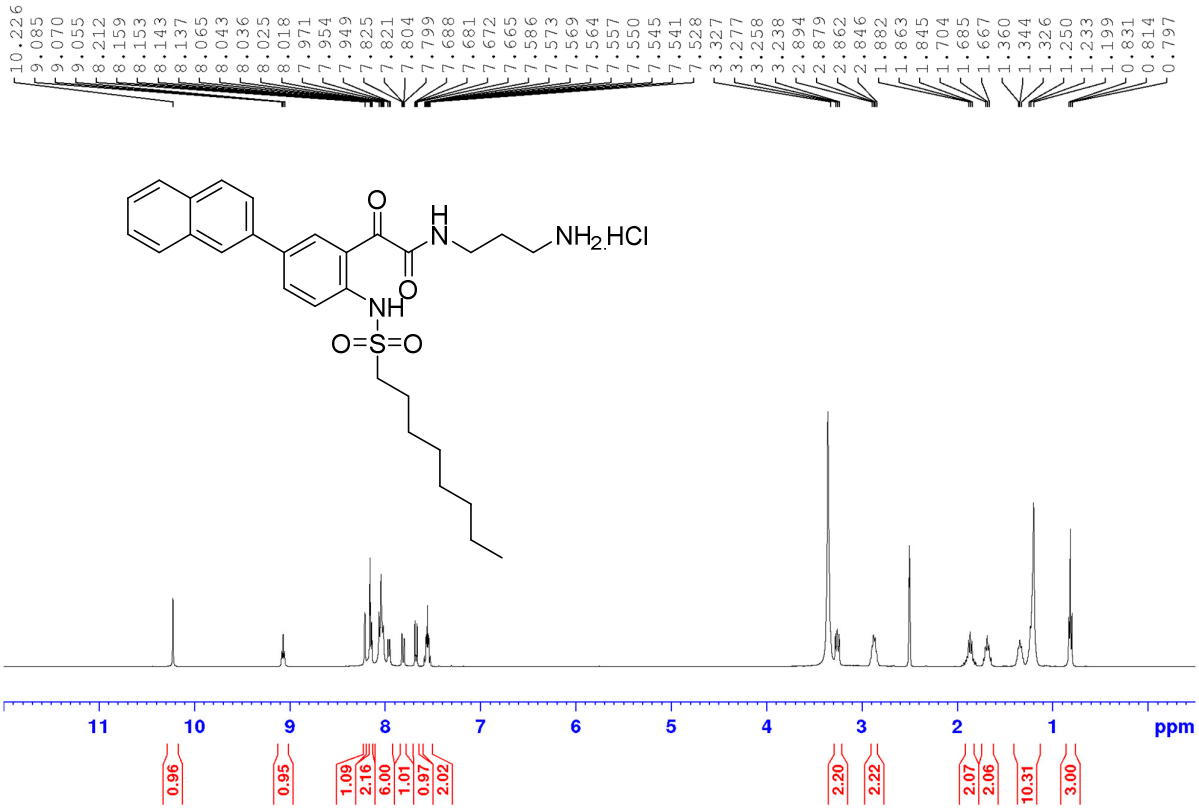


^{13}C NMR (100 MHz, DMSO-d_6):

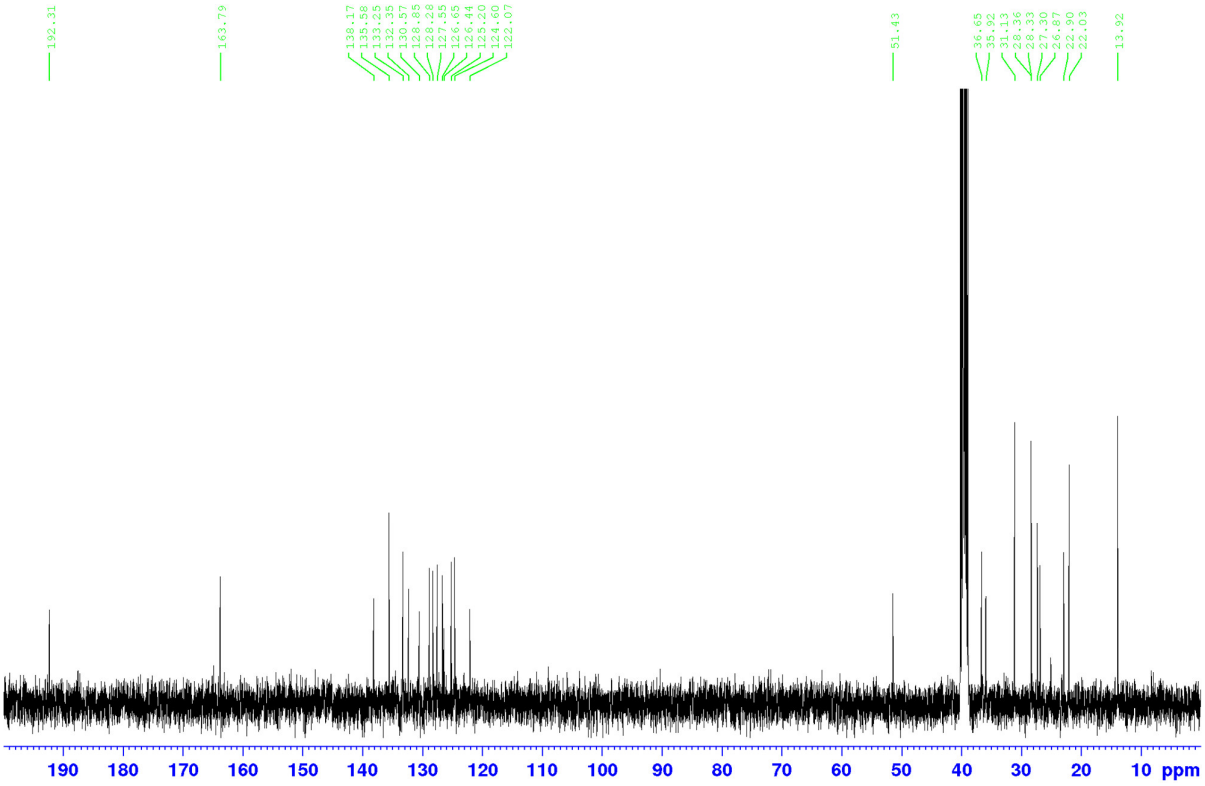


N-(3-Aminopropyl)-2-(5-(naphthalen-2-yl)-2-(octylsulfonamido)phenyl)-2-oxoacetamide hydrochloride (**19d**)

^{1}H NMR (400 MHz, DMSO-d_6):

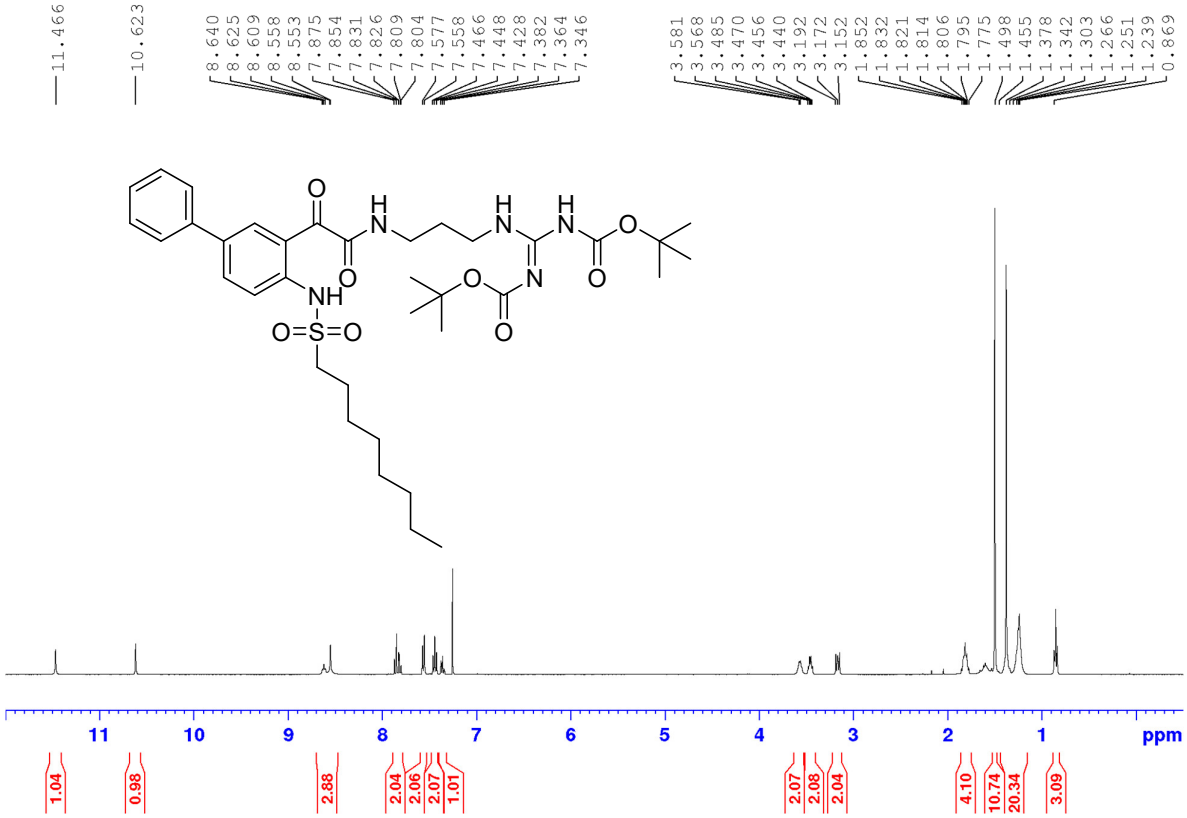


^{13}C NMR (100 MHz, DMSO-d_6):

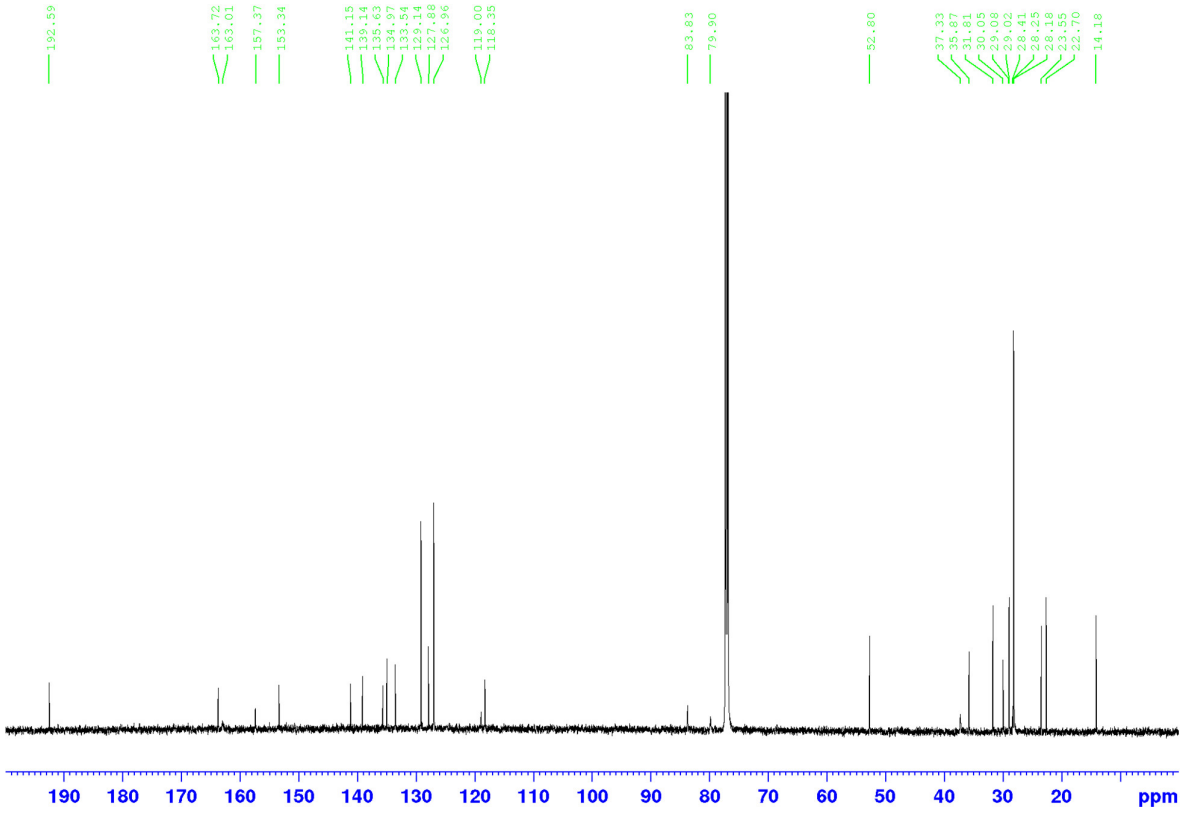


(*E*)-1-tert-Butyl-*N*-(*N*'-((*tert*-butyloxidanyl)carbonyl)-*N*-(3-(2-(4-(octylsulfonamido)-[1,1'-biphenyl]-3-yl)-2-oxoacetamido)propyl)carbamimidoyl)-1-oxidanecarboxamide (**21a**)

^{1}H NMR (400 MHz, $CDCl_3$):

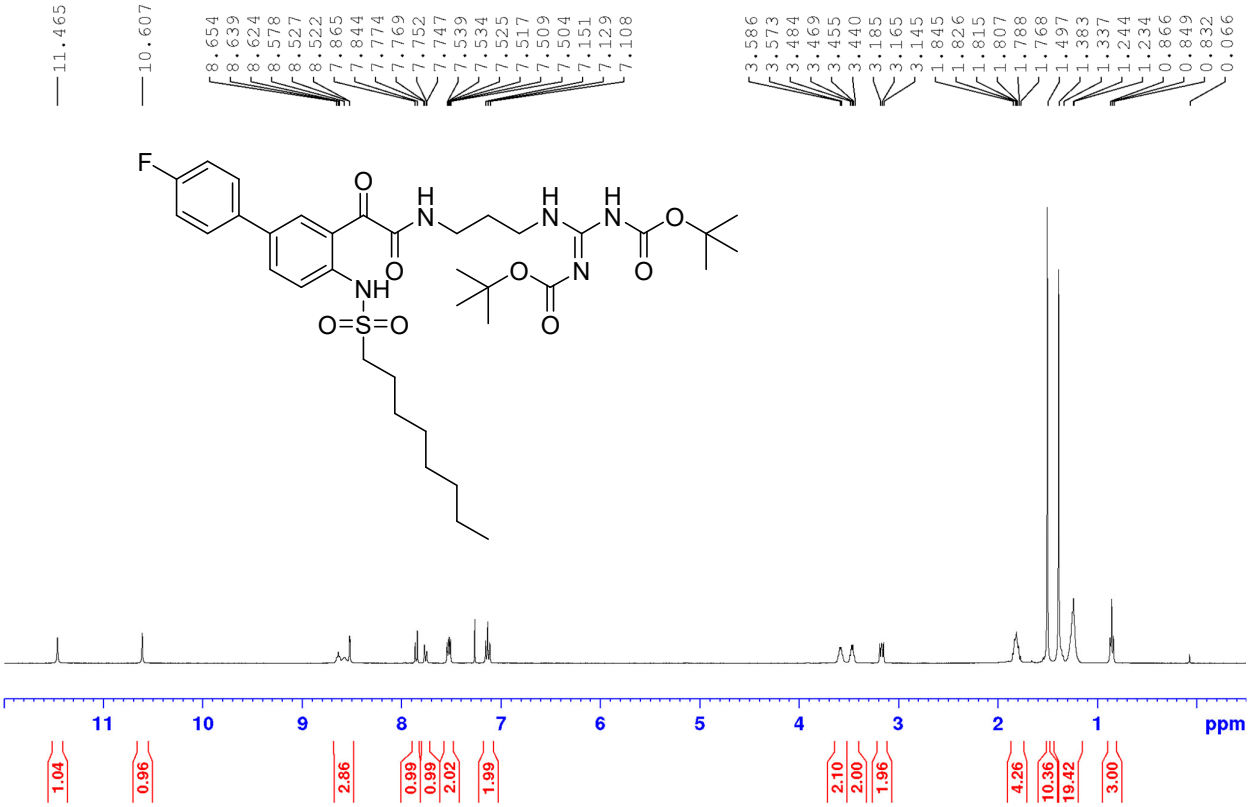


^{13}C NMR (150 MHz, $CDCl_3$):

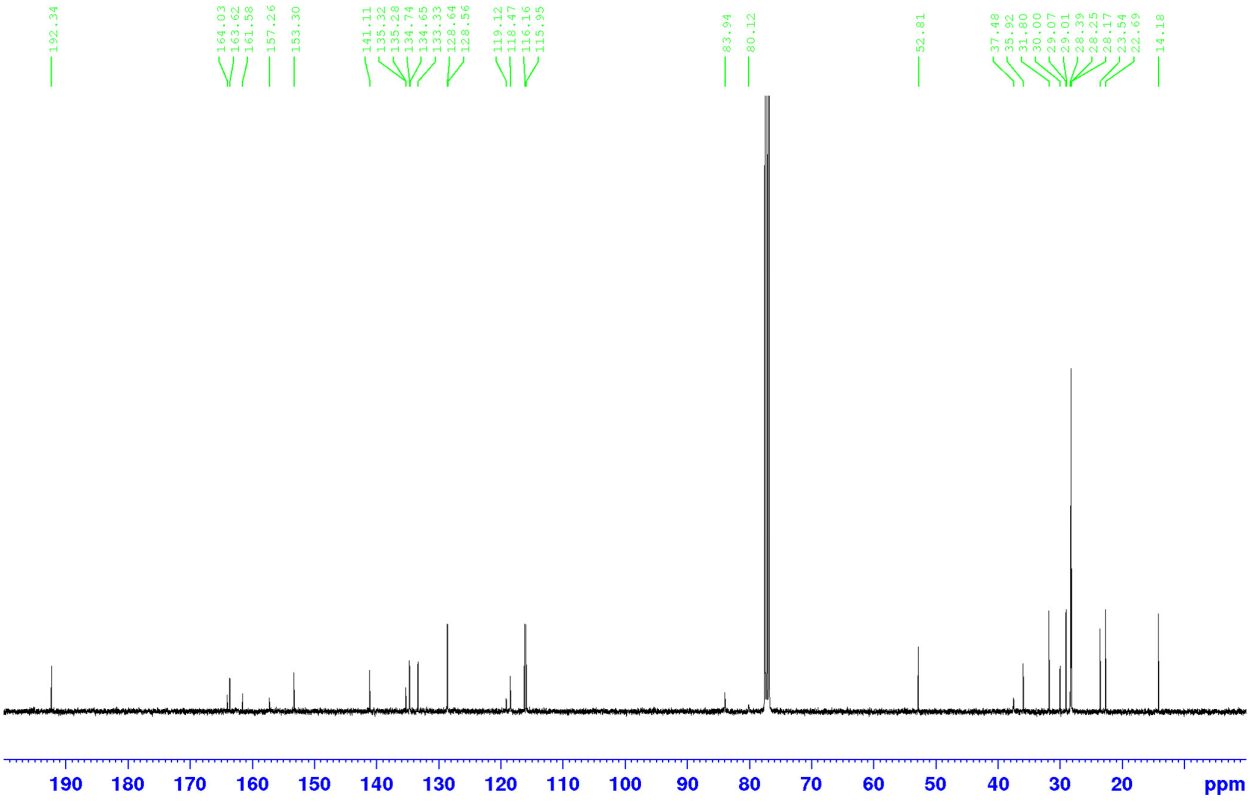


(*E*)-1-*tert*-Butyl-*N*-(*N*'-((*tert*-butyloxidanyl)carbonyl)-*N*-(3-(2-(4'-fluoro-4-(octylsulfonamido)-[1,1'-biphenyl]-3-yl)-2-oxoacetamido)propyl)carbamimidoyl)-1-oxidanecarboxamide (**21b**)

^{1}H NMR (400 MHz, $CDCl_3$):

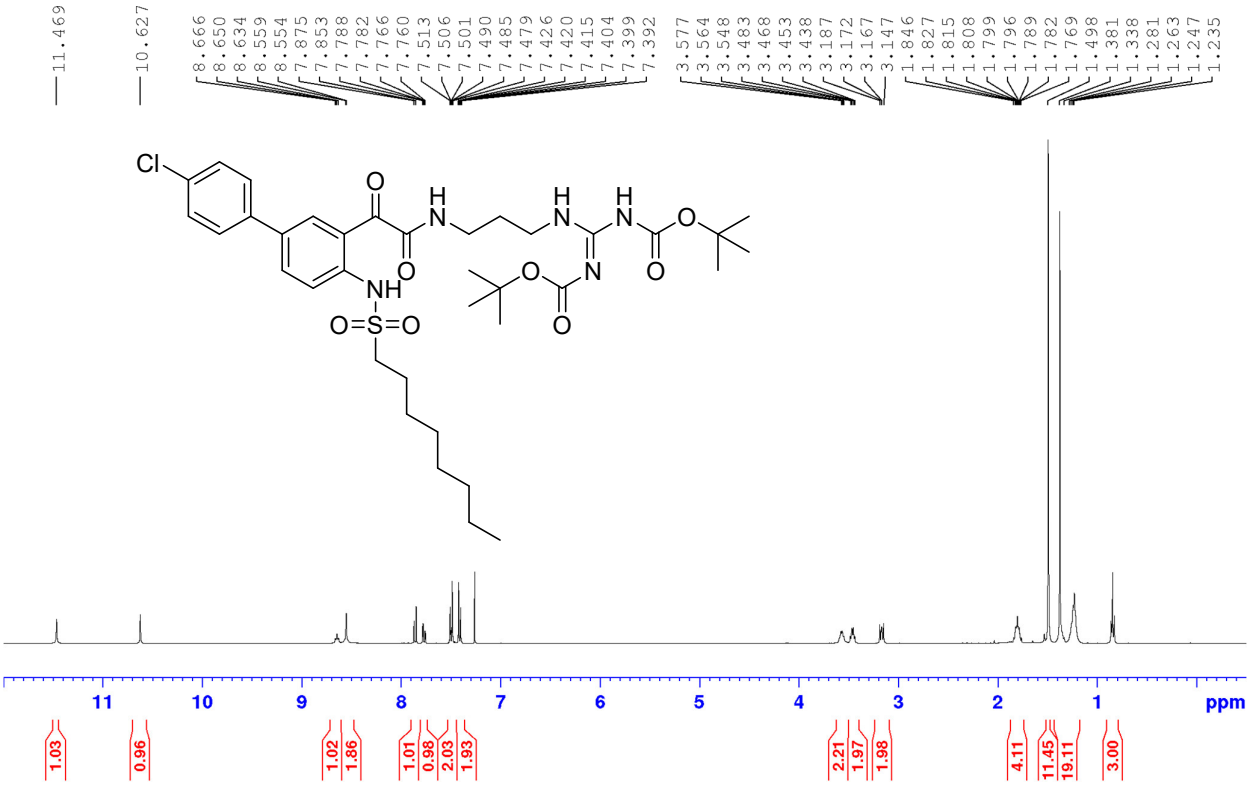


^{13}C NMR (100 MHz, $CDCl_3$):

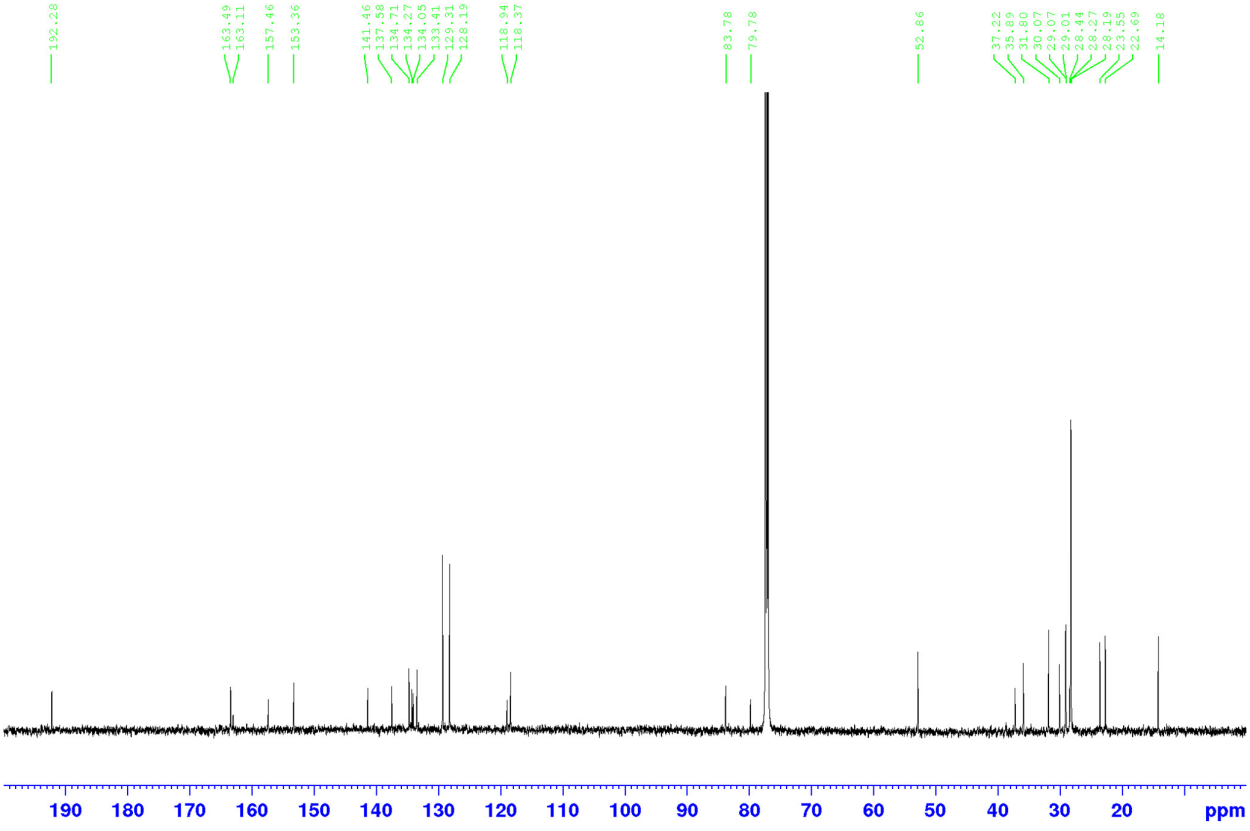


(*E*)-1-*tert*-Butyl-*N*-(*N*'-((*tert*-butyloxidanyl)carbonyl)-*N*-(3-(2-(4'-chloro-4-(octylsulfonamido)-[1,1'-biphenyl]-3-yl)-2-oxoacetamido)propyl)carbamimidoyl)-1-oxidanecarboxamide (**21c**)

^{1}H NMR (400 MHz, $CDCl_3$):

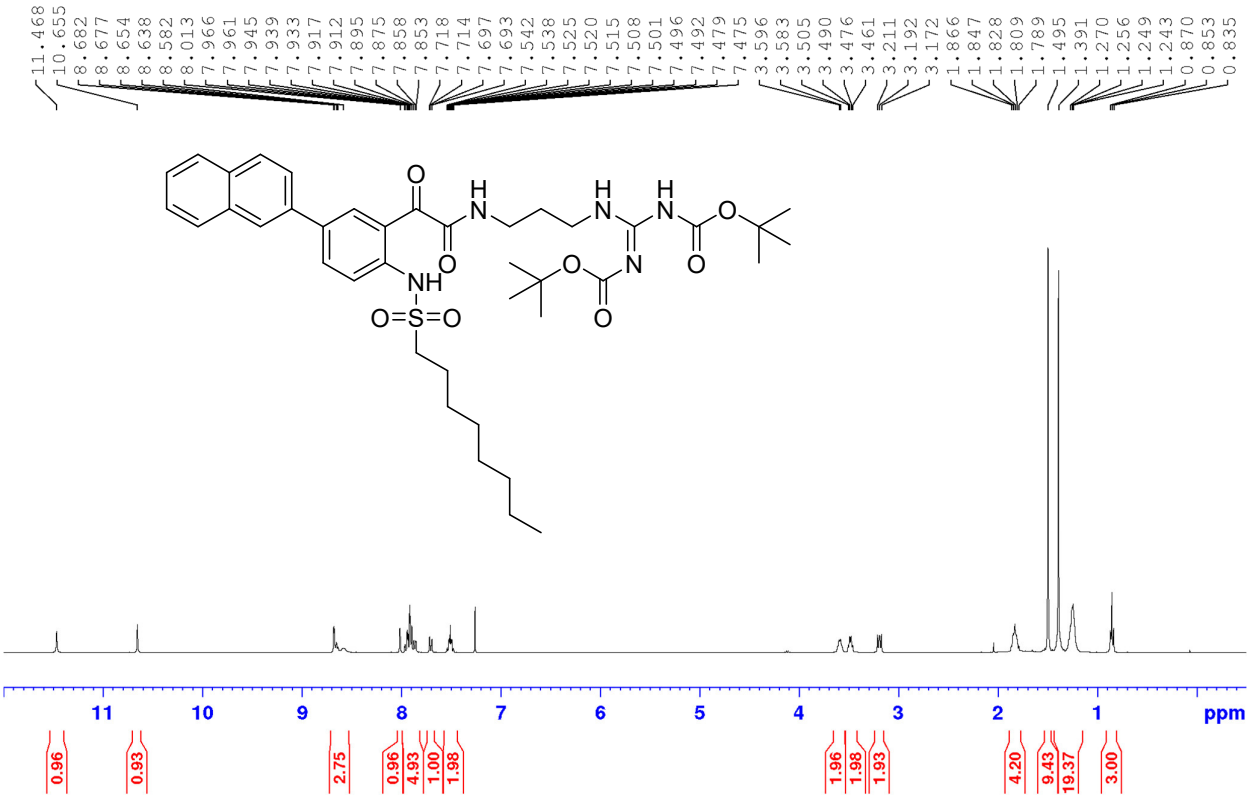


^{13}C NMR (150 MHz, $CDCl_3$):

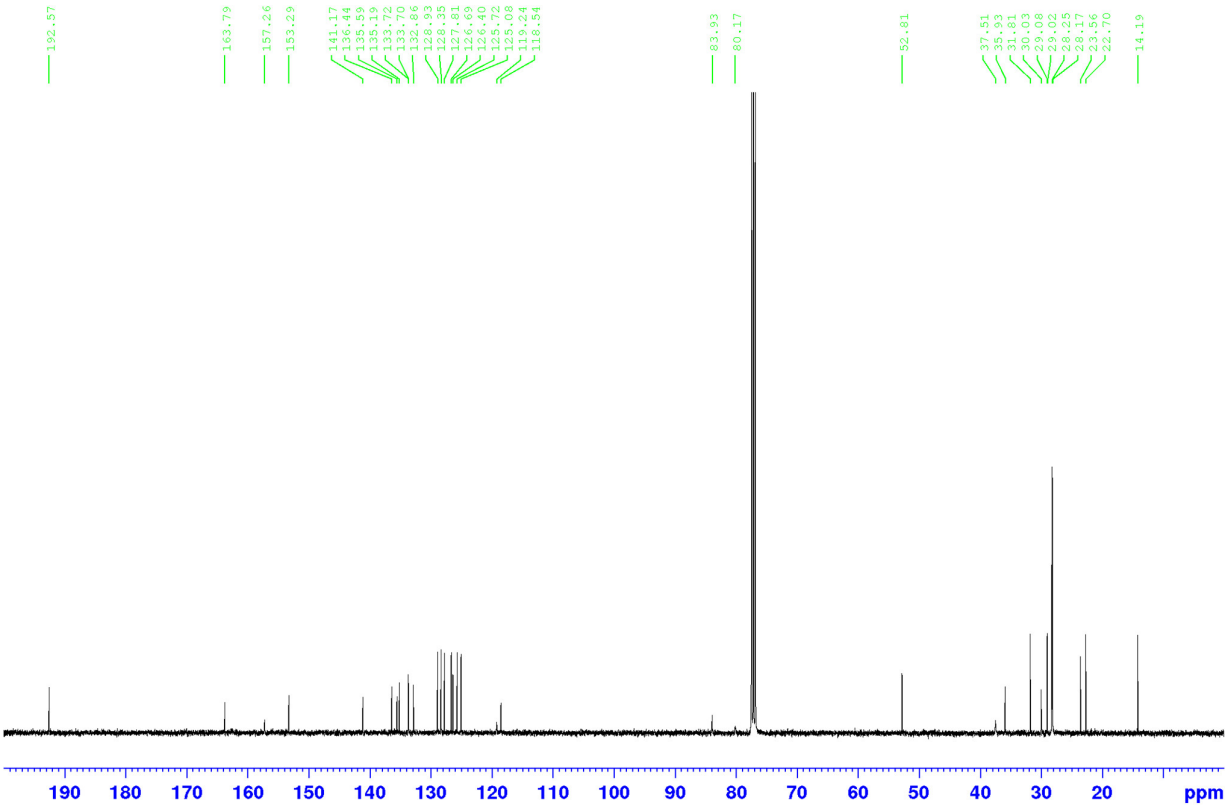


(*E*)-1-*tert*-Butyl-*N*-(*N*'-((*tert*-butyloxidanyl)carbonyl)-*N*-(3-(2-(5-(naphthalen-2-yl)-2-(octylsulfonamido)phenyl)-2-oxoacetamido)propyl)carbamimidoyl)-1-oxidanecarboxamide (**21d**)

^{1}H NMR (400 MHz, $CDCl_3$):

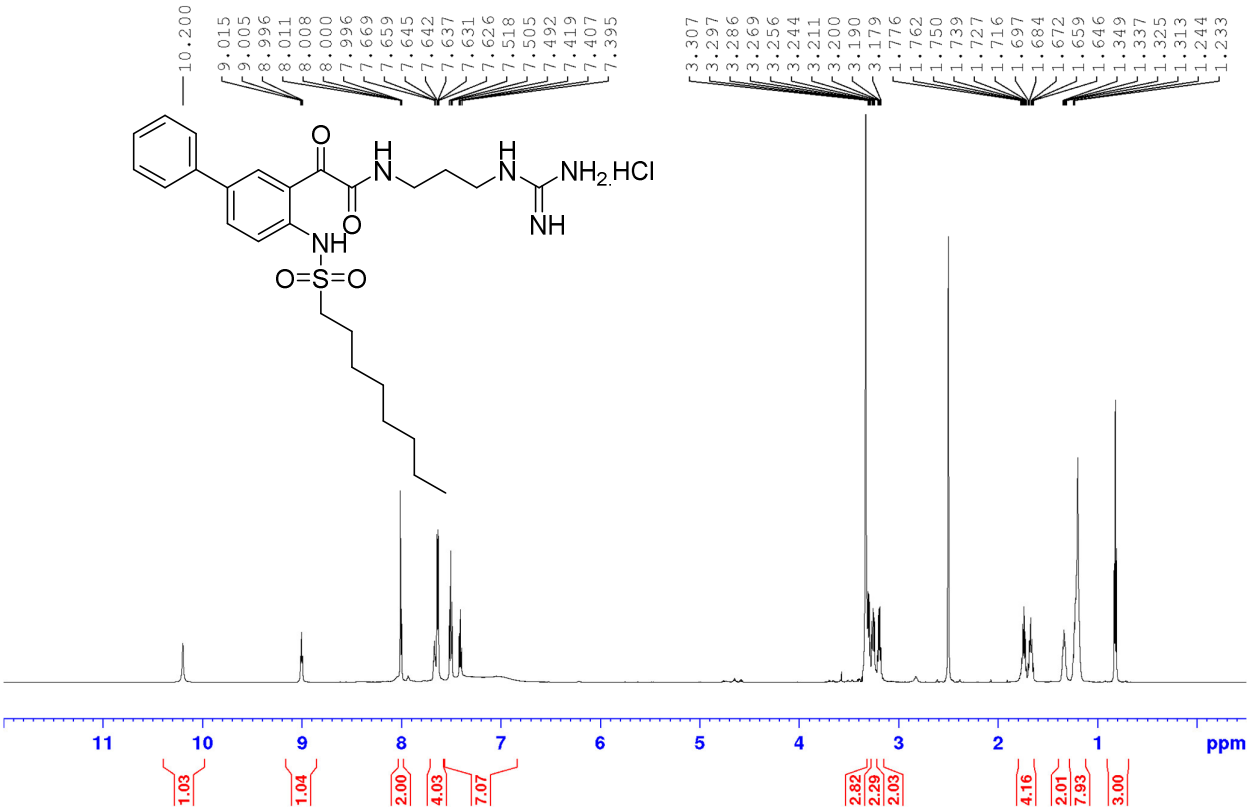


^{13}C NMR (100 MHz, $CDCl_3$):

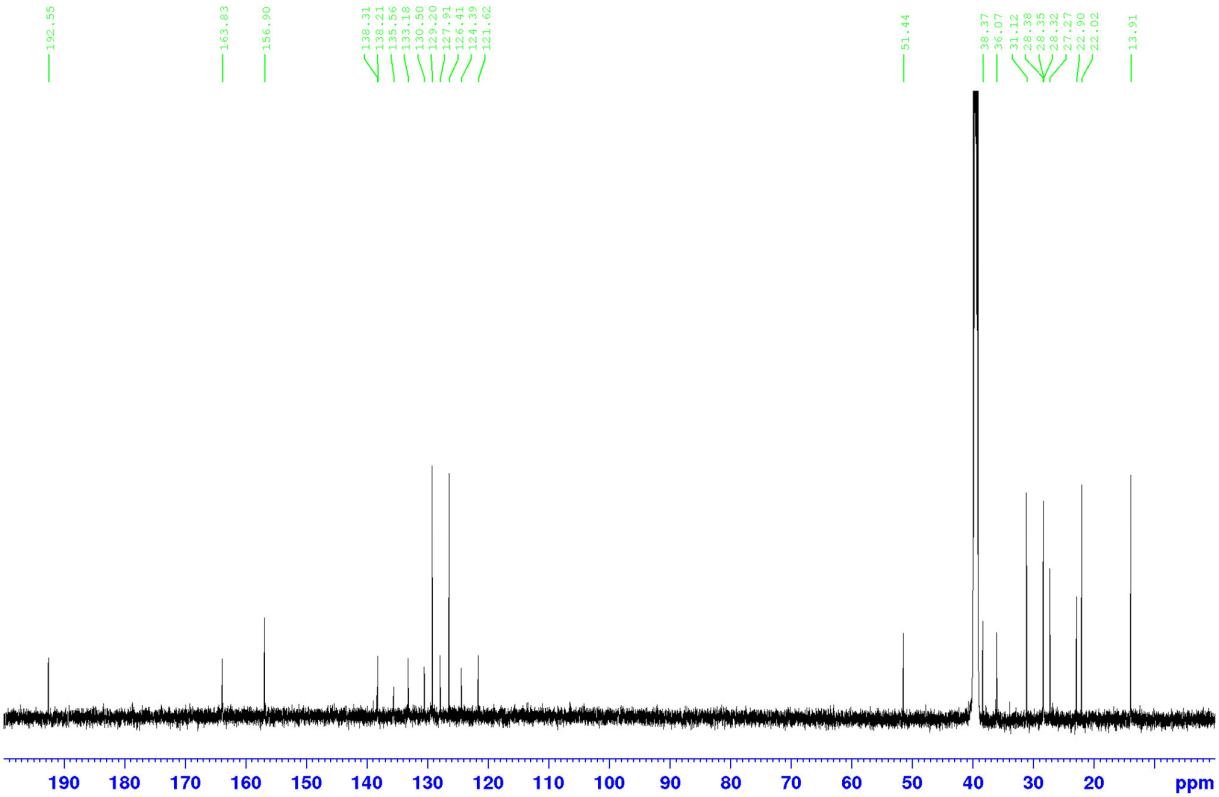


N-(3-Guanidinopropyl)-2-(4-(octylsulfonamido)-[1,1'-biphenyl]-3-yl)-2-oxoacetamide hydrochloride (**22a**)

^{1}H NMR (600 MHz, DMSO-d_6):

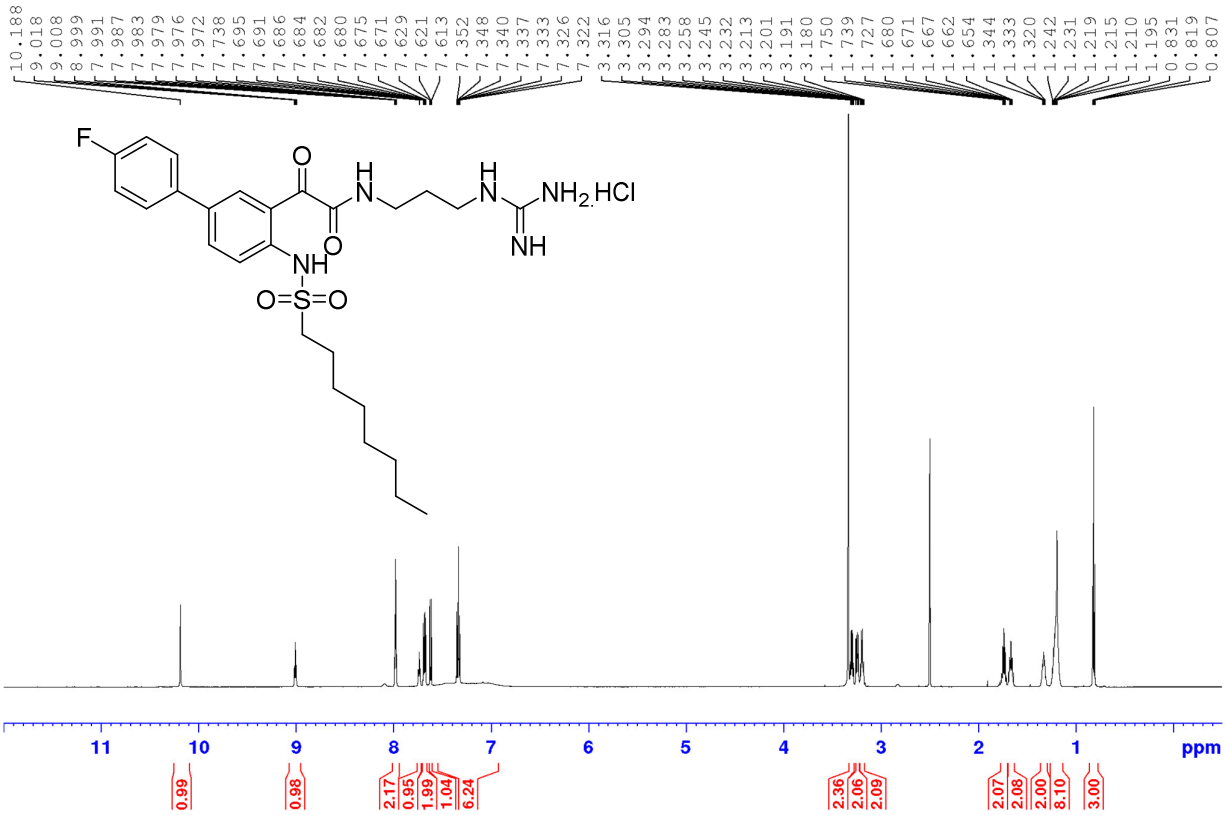


^{13}C NMR (150 MHz, DMSO-d_6):

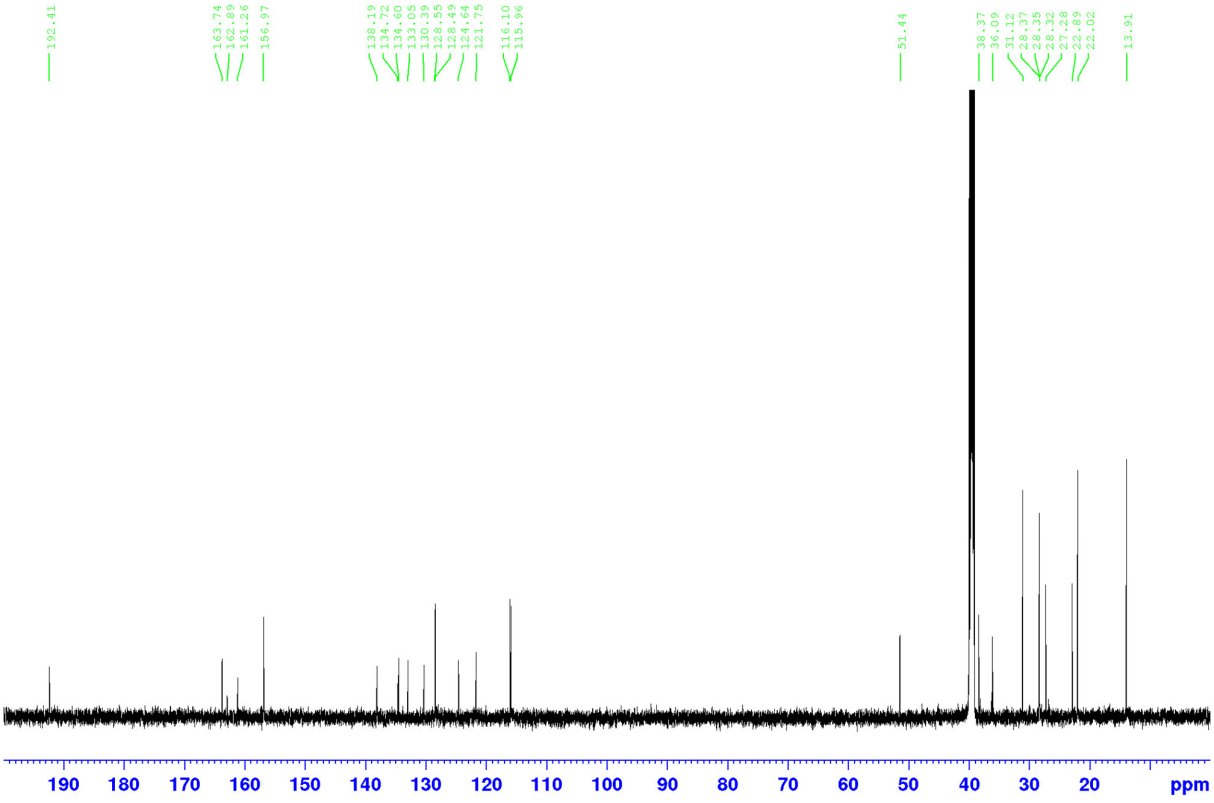


2-(4'-Fluoro-4-(octylsulfonamido)-[1,1'-biphenyl]-3-yl)-*N*-(3-guanidinopropyl)-2-oxoacetamide hydrochloride (**22b**)

^{1}H NMR (600 MHz, DMSO-d_6):

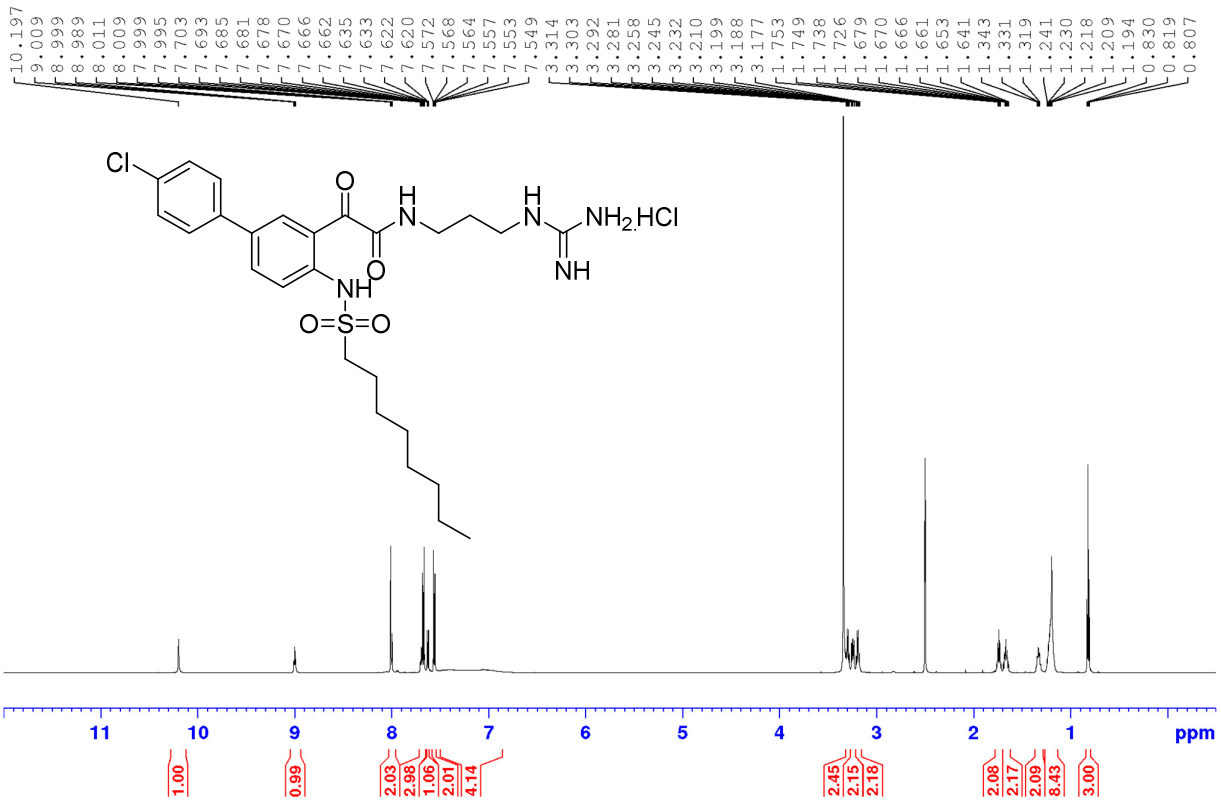


^{13}C NMR (150 MHz, DMSO-d_6):

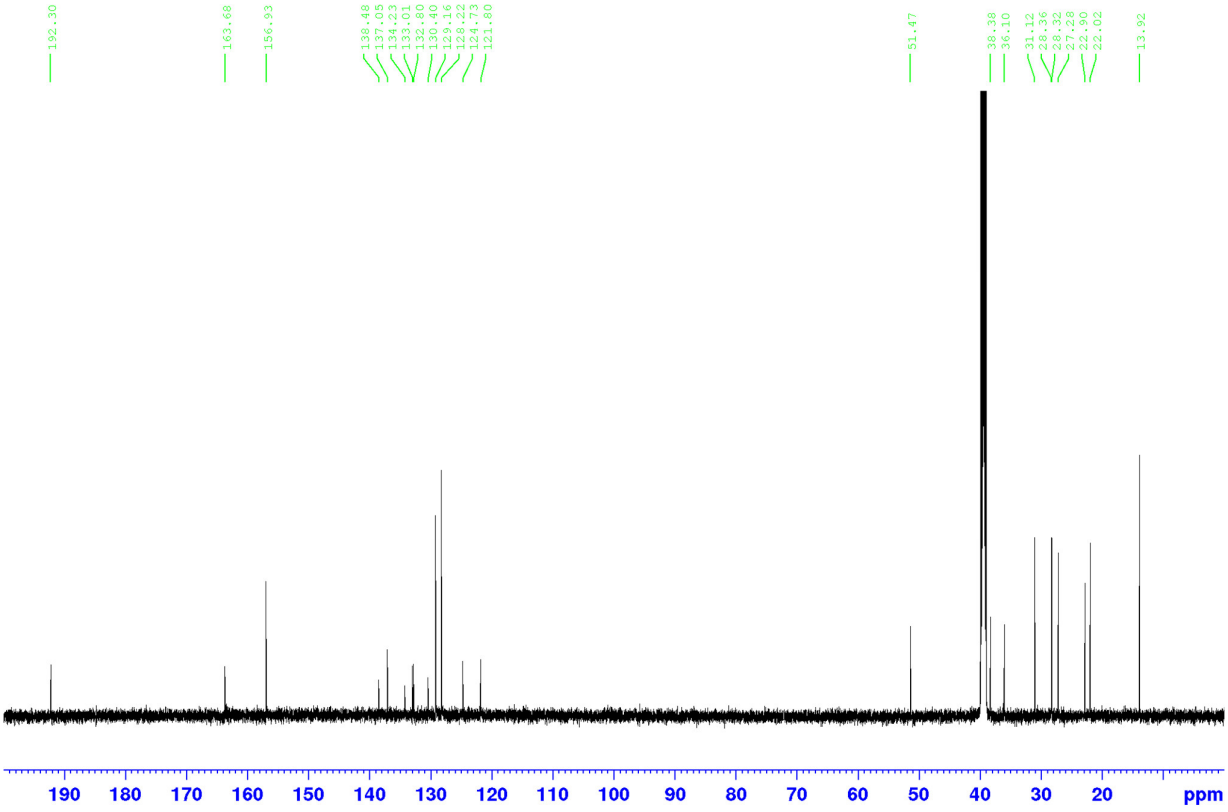


2-(4'-Chloro-4-(octylsulfonamido)-[1,1'-biphenyl]-3-yl)-*N*-(3-guanidinopropyl)-2-oxoacetamide hydrochloride (**22c**)

^{1}H NMR (600 MHz, DMSO-d_6):

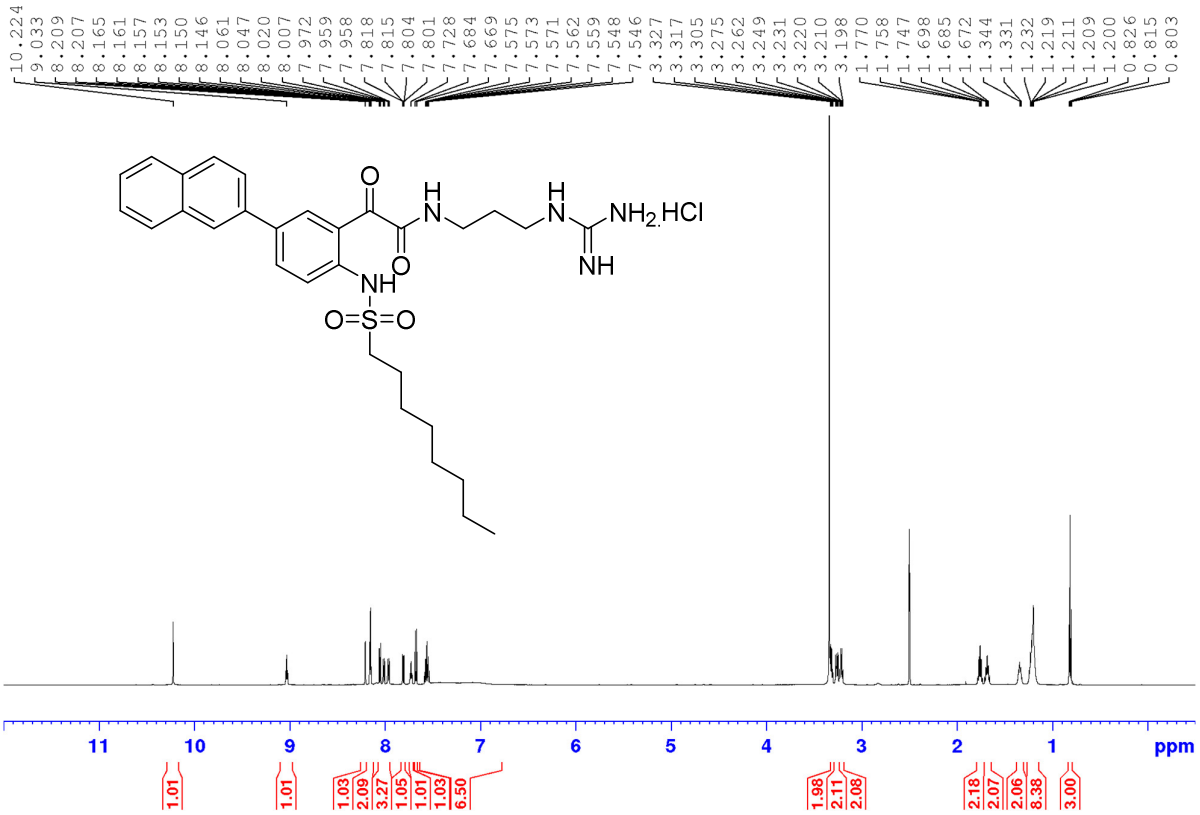


^{13}C NMR (150 MHz, DMSO-d_6):

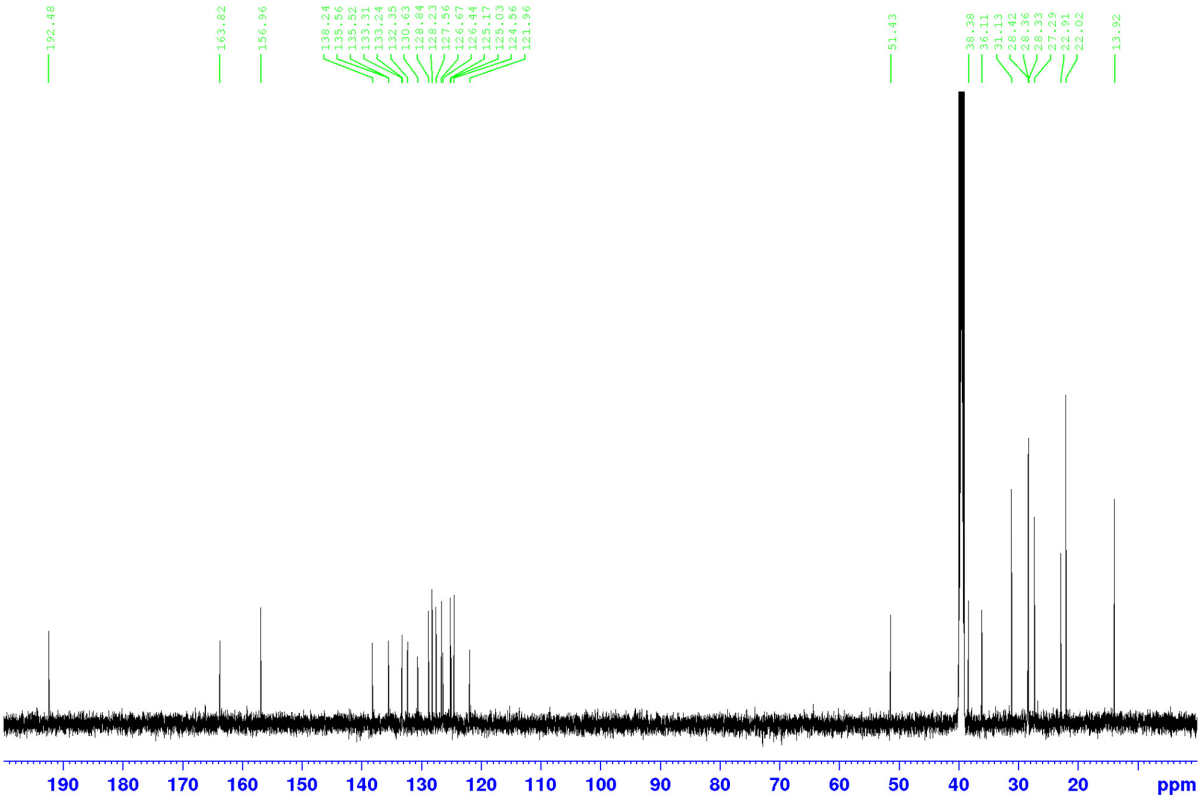


N-(3-Guanidinopropyl)-2-(5-(naphthalen-2-yl)-2-(octylsulfonamido)phenyl)-2-oxoacetamide hydrochloride (**22d**)

^{1}H NMR (600 MHz, DMSO-d_6):

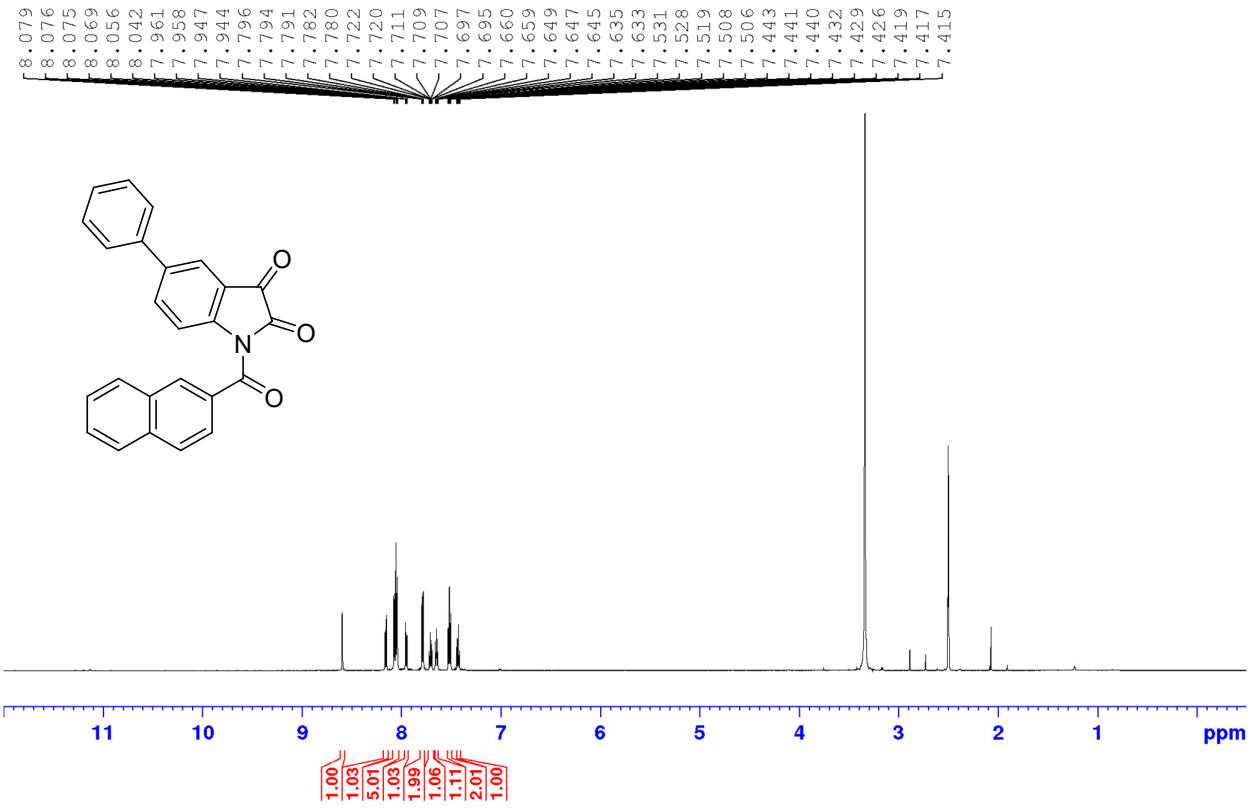


^{13}C NMR (150 MHz, DMSO-d_6):

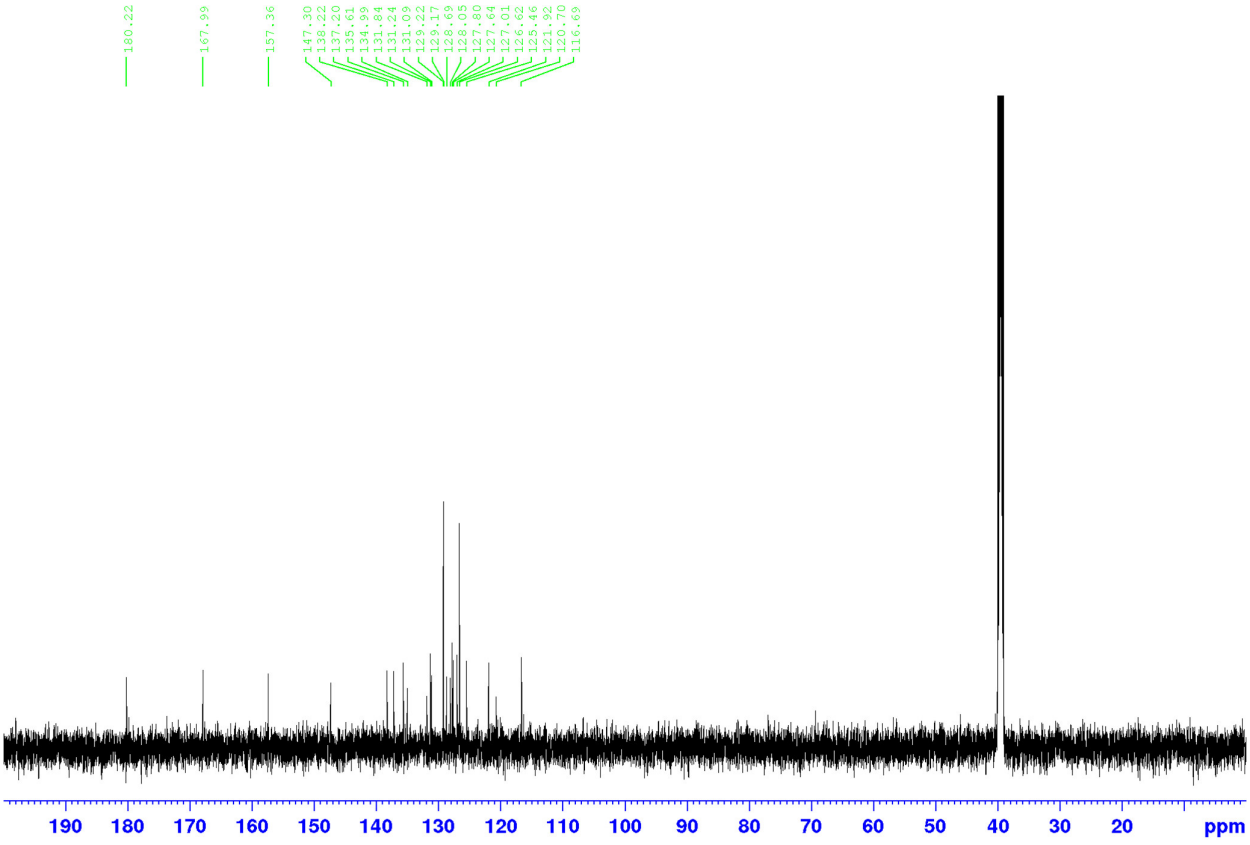


1-(2-Naphthoyl)-5-phenylindoline-2,3-dione (**24**)

^{1}H NMR (600 MHz, DMSO-d_6):

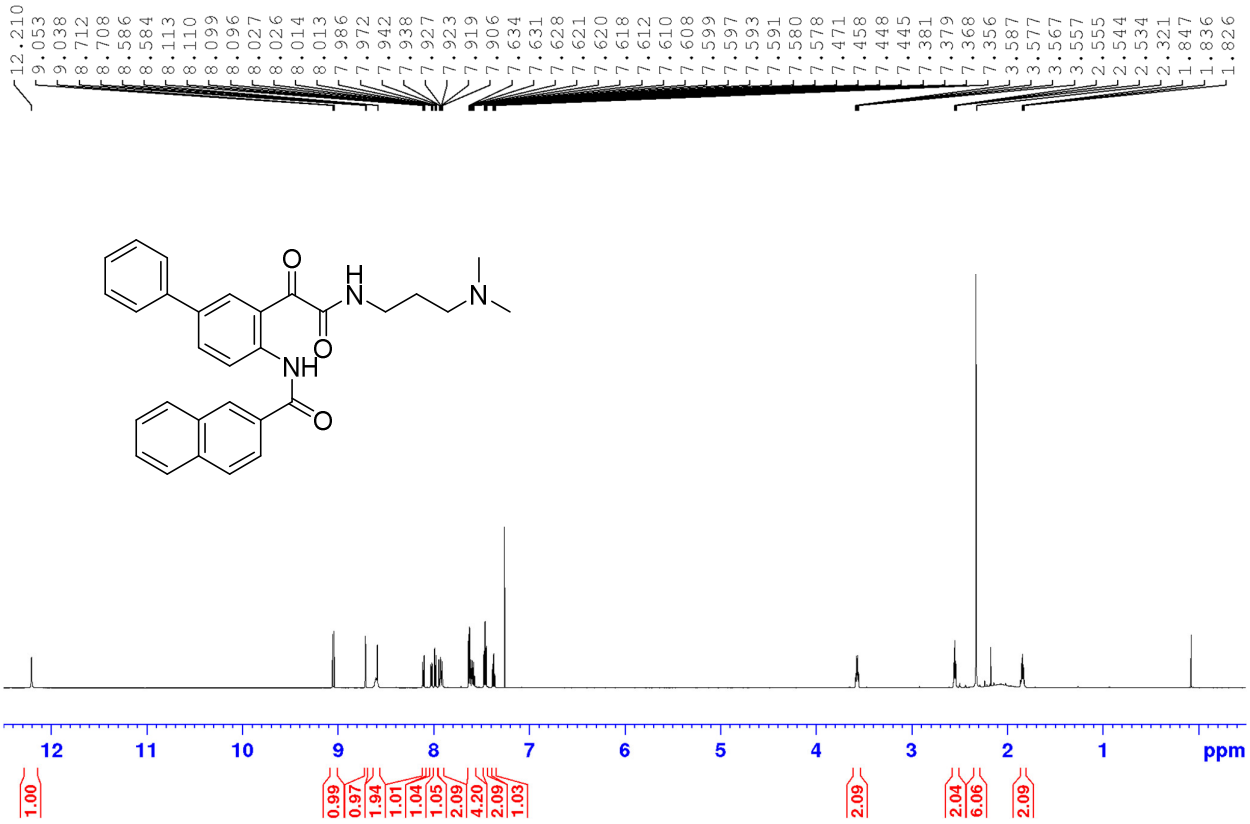


^{13}C NMR (150 MHz, DMSO-d_6):

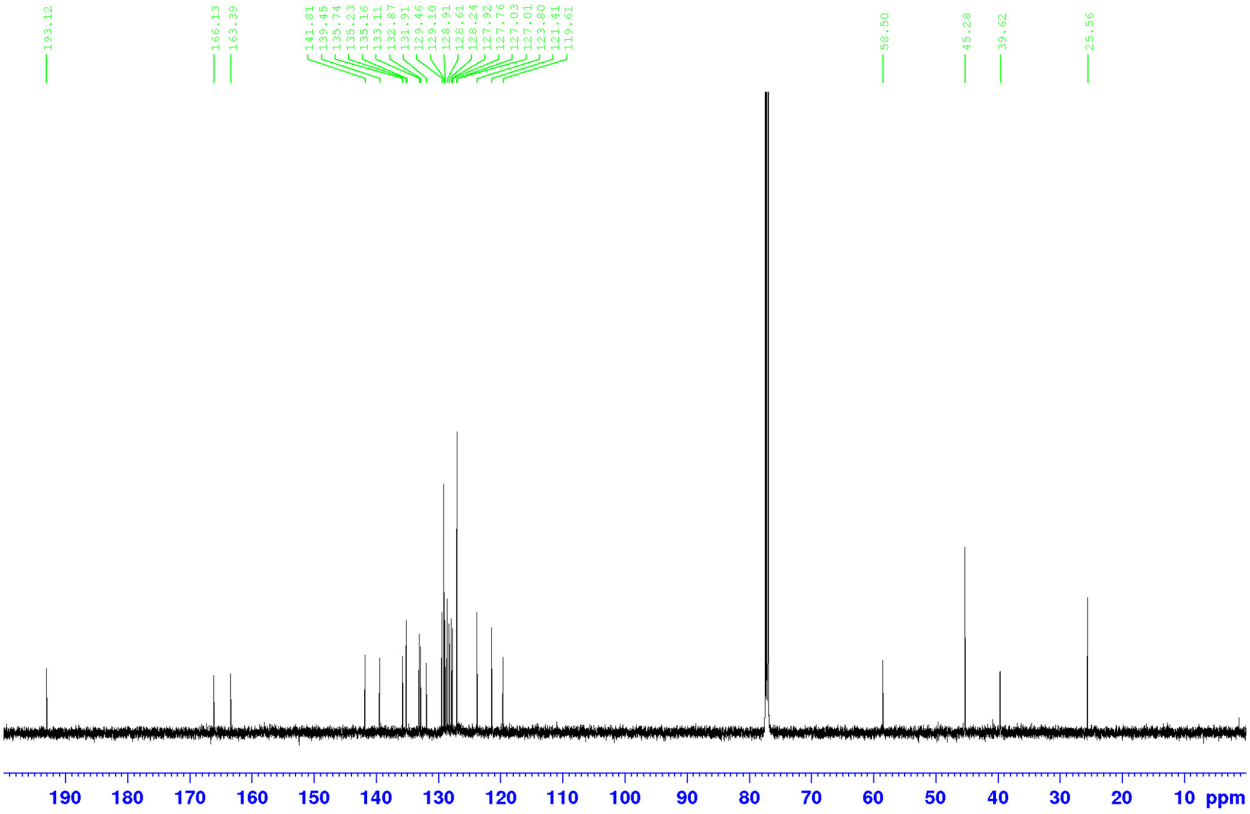


N-(3-(2-((3-(Dimethylamino)propyl)amino)-2-oxoacetyl)-[1,1'-biphenyl]-4-yl)-2-naphthamide (**25**)

^{1}H NMR (600 MHz, $CDCl_3$):

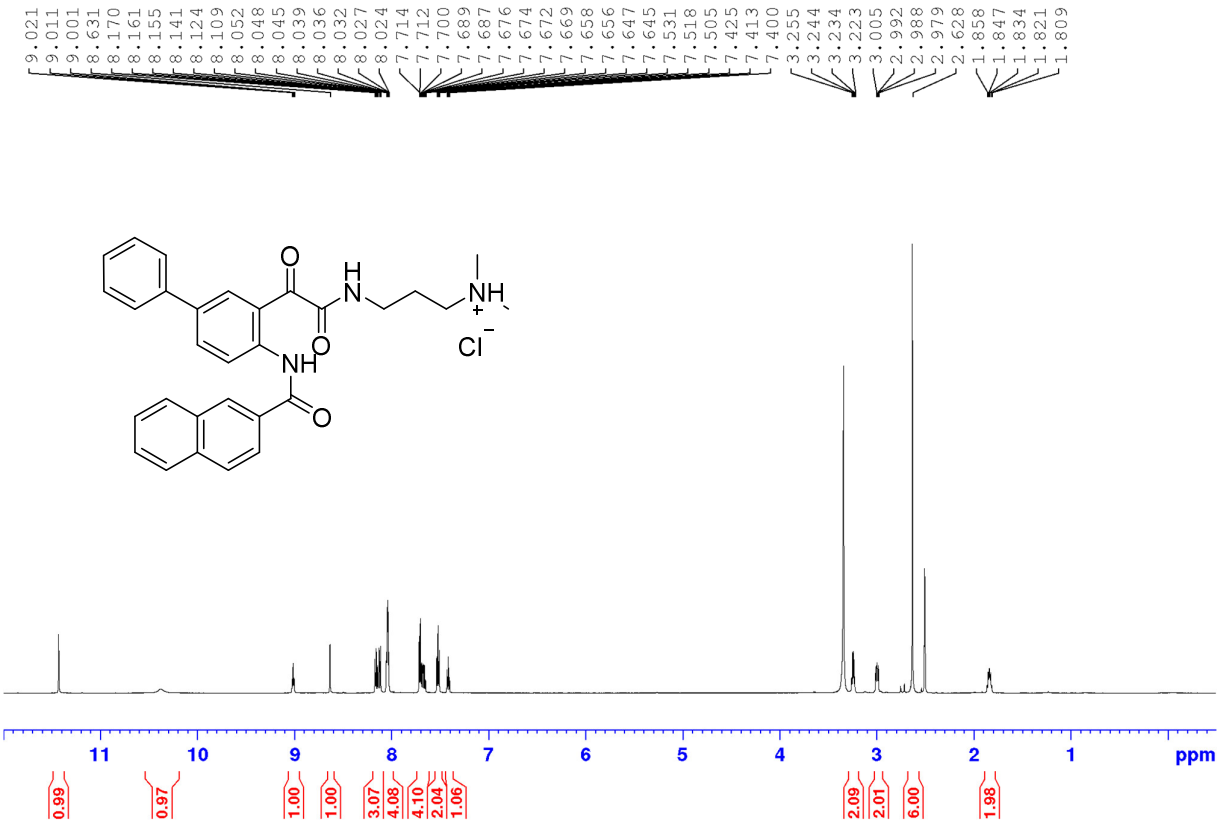


^{13}C NMR (150 MHz, $CDCl_3$):

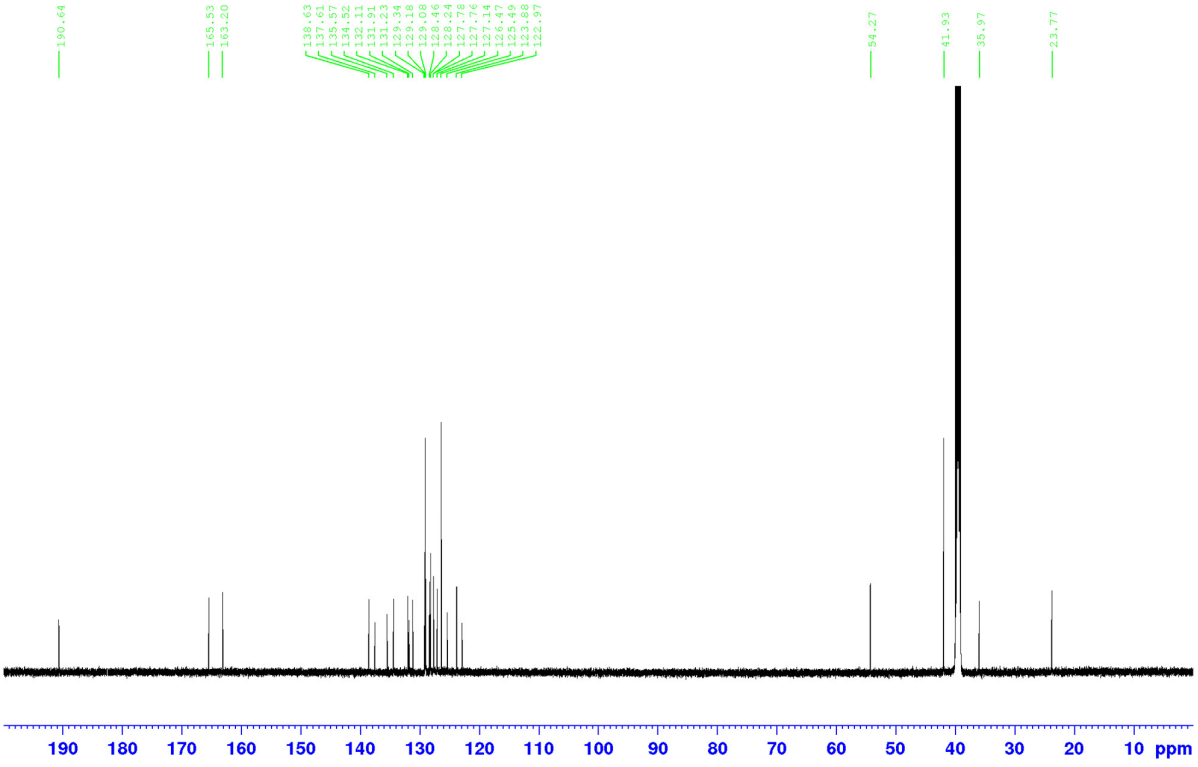


3-(2-(4-(2-Naphthamido)-[1,1'-biphenyl]-3-yl)-2-oxoacetamido)-*N*,*N*-dimethylpropan-1-aminium chloride (**26**)

^{1}H NMR (600 MHz, DMSO-d_6):

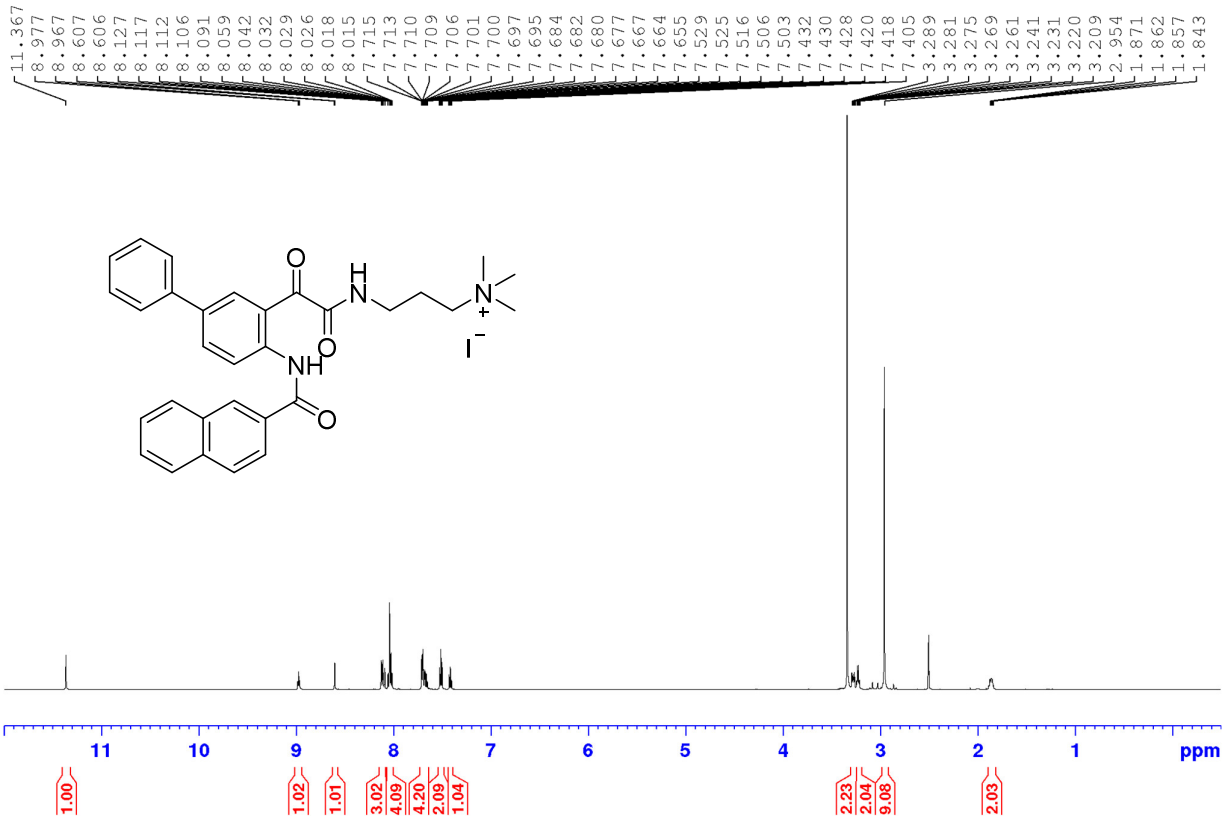


^{13}C NMR (150 MHz, DMSO-d_6):



3-(2-(4-(2-Naphthamido)-[1,1'-biphenyl]-3-yl)-2-oxoacetamido)-*N*,*N*,*N*-trimethylpropan-1-aminium iodide (**27**)

^{1}H NMR (600 MHz, DMSO-d_6):



^{13}C NMR (150 MHz, DMSO-d_6):