

***N*-Benzyl-6-Chloro-4-Hydroxy-2-Quinolone-3-Carboxamides: Synthesis, Computational Studies, and Biological Investigation as Anticancer Agents**

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Abushaikh⁵, Kamal Sweidan⁶, Swapnaa Balaji⁷, Amit K. Tiwari⁷, Dima A. Sabbah^{1*}

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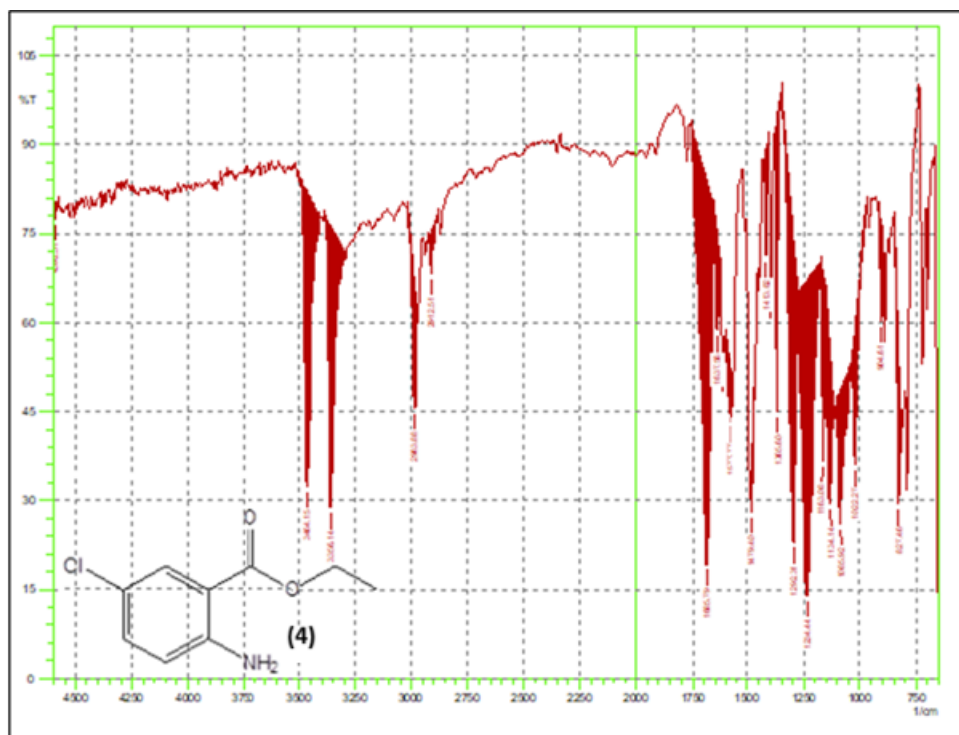
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⁵Department of Medicinal and Biological Chemistry, College of Pharmacy and Pharmaceutical Sciences, University of Toledo, Toledo, Ohio 43606-3390, USA; email address: Ghassan.Abushaikh@utoledo.edu

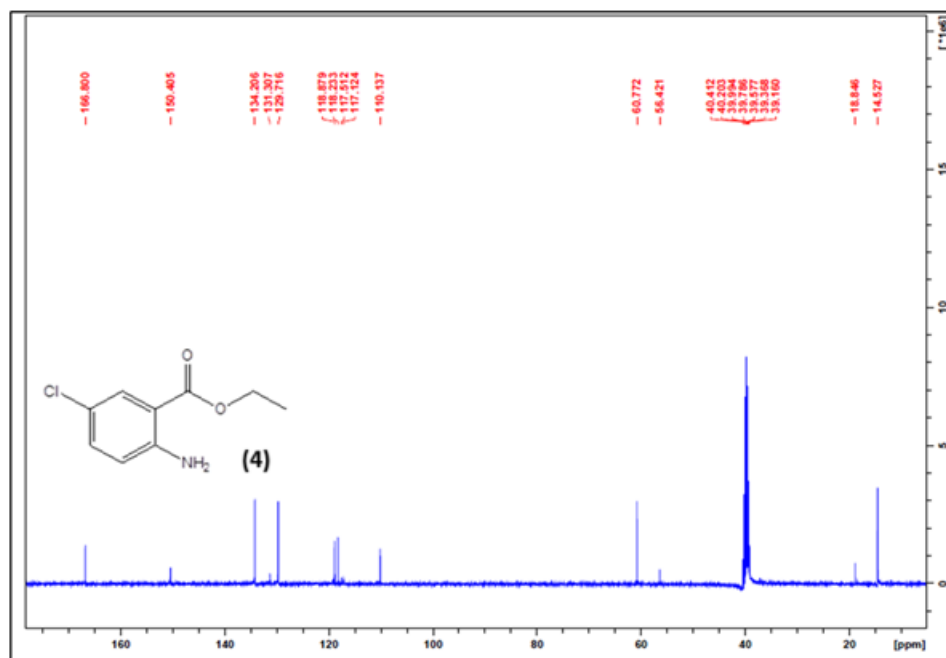
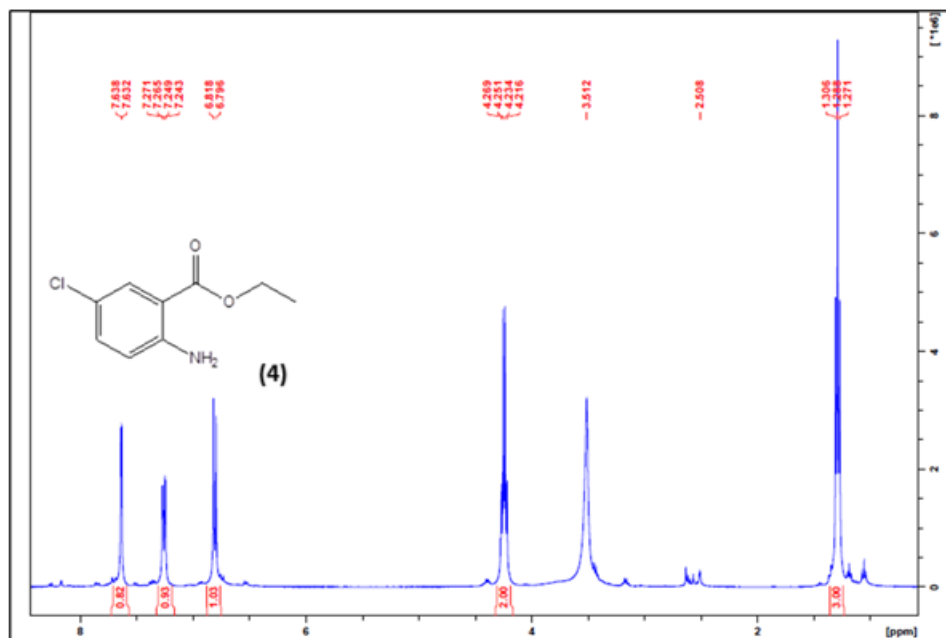
⁶Department of Chemistry, The University of Jordan, Amman 11942, Jordan; email address: k.sweidan@ju.edu.jo

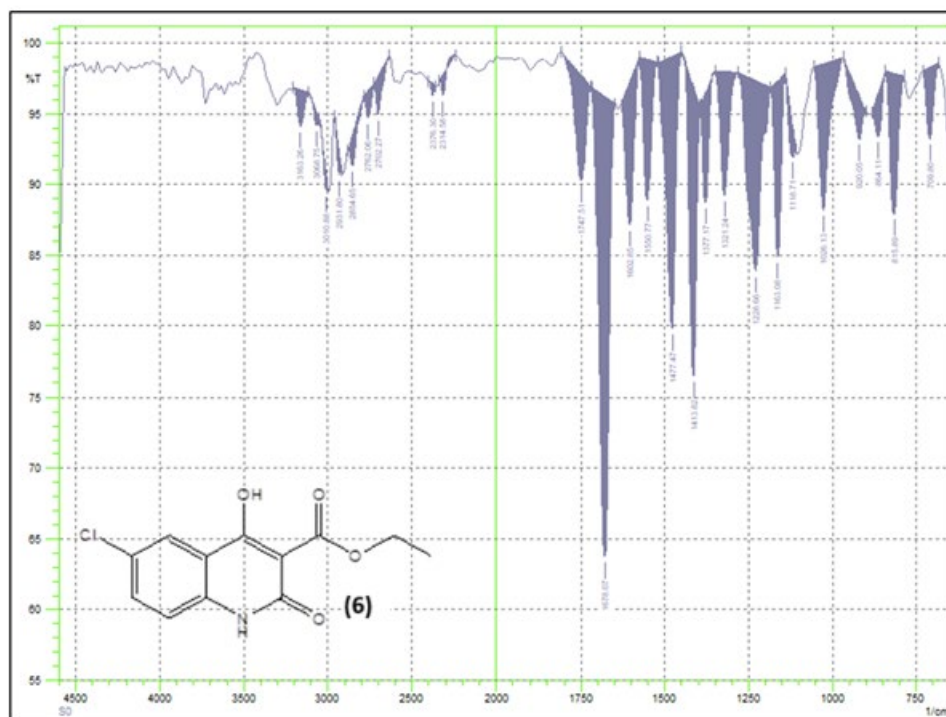
⁷Department of Pharmacology and Experimental Therapeutics, College of Pharmacy and Pharmaceutical Sciences, University of Toledo, Toledo, Ohio 43614, USA; email address: (SB) swapnaa.balaji@rockets.utoledo.edu sbalaji@cambiumoncology.com; (AKT) amit.tiwari@utoledo.edu atiwari@uams.edu

FT-IR, ¹H and ¹³C-NMR Spectra of the compounds (4, 6, and 8-21)

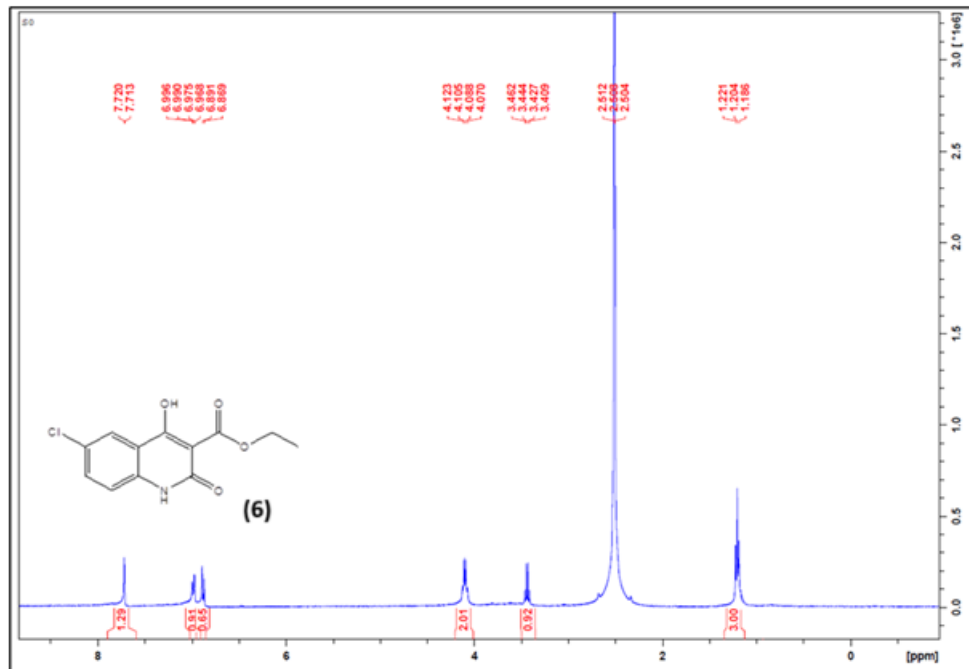


IR (KBr disc) spectrum of Ethyl 2-amino-5-Chlorobenzoate (4).

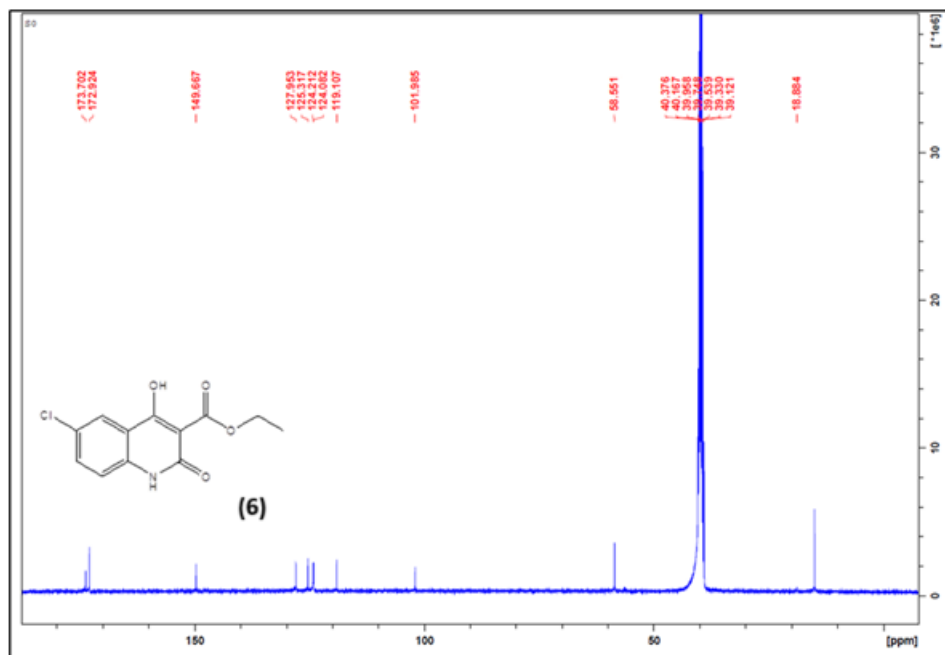




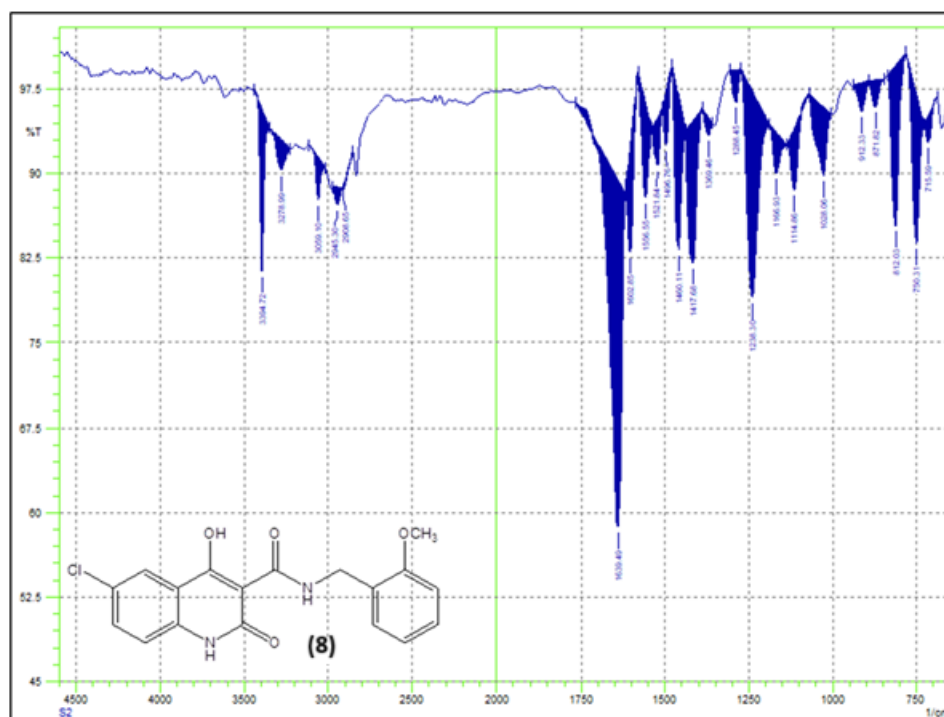
IR (KBr disc) spectrum of ethyl 6-chloro-4-hydroxy-2-quinolone 3-carboxylate (6).



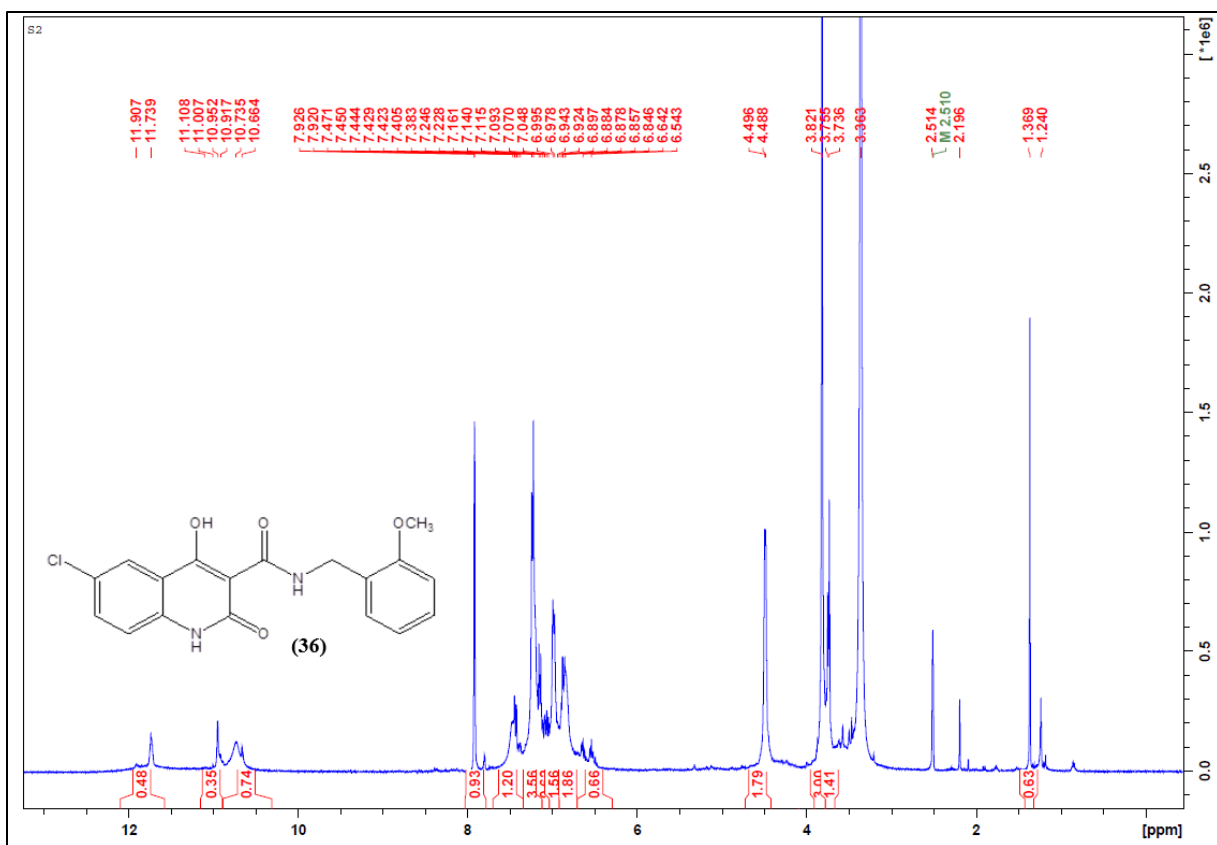
¹H-NMR (DMSO-*d*₆) spectrum of ethyl 6-chloro-4-hydroxy-2-quinolone 3-carboxylate (6).



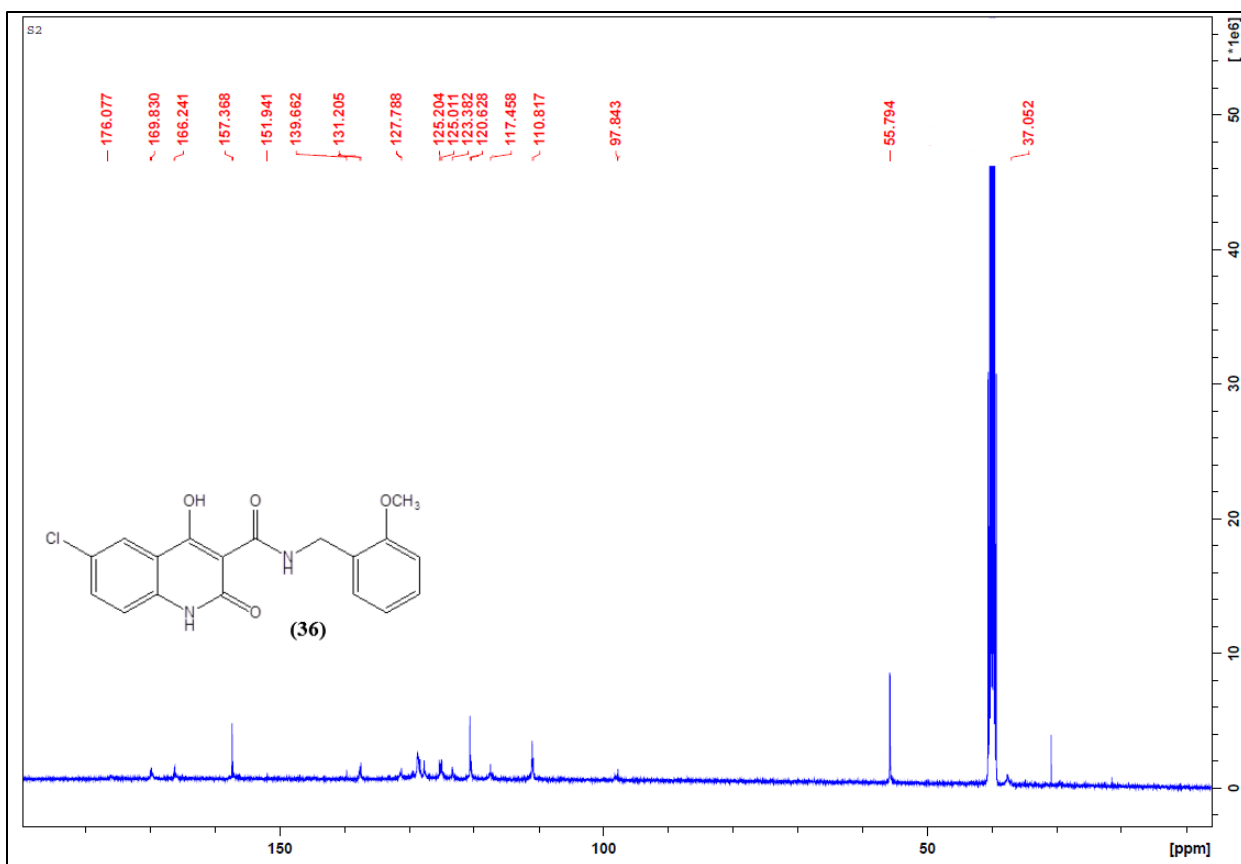
¹³C-NMR (DMSO-*d*₆) Spectrum of ethyl 6-chloro-4-hydroxy-2-quinolone 3-carboxylate (6).



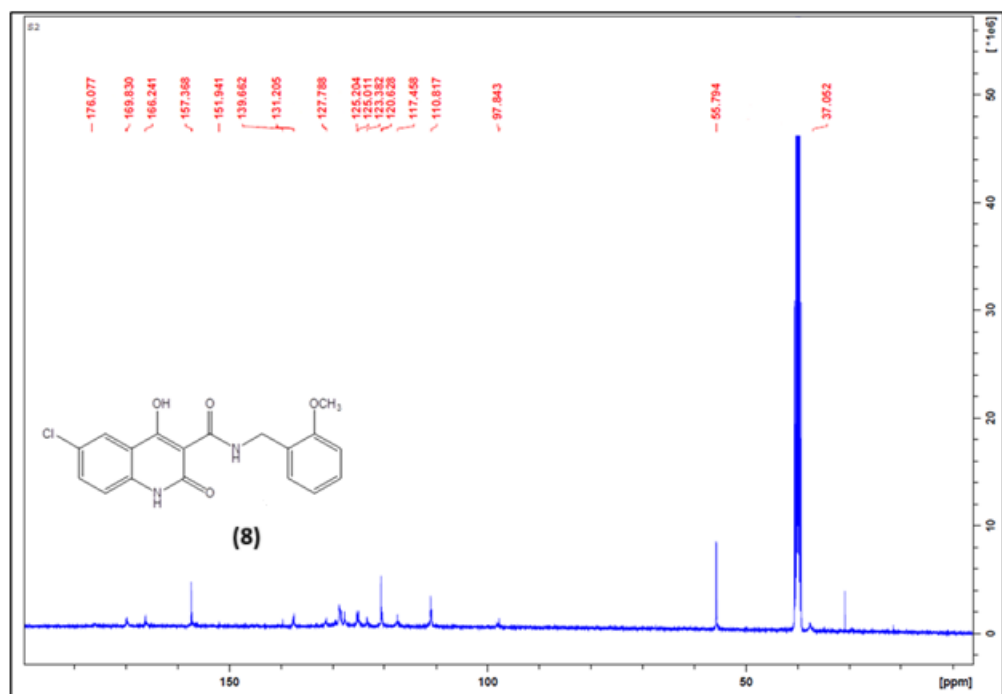
IR (KBr disc) spectrum of *N*-(2-methoxybenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (8).



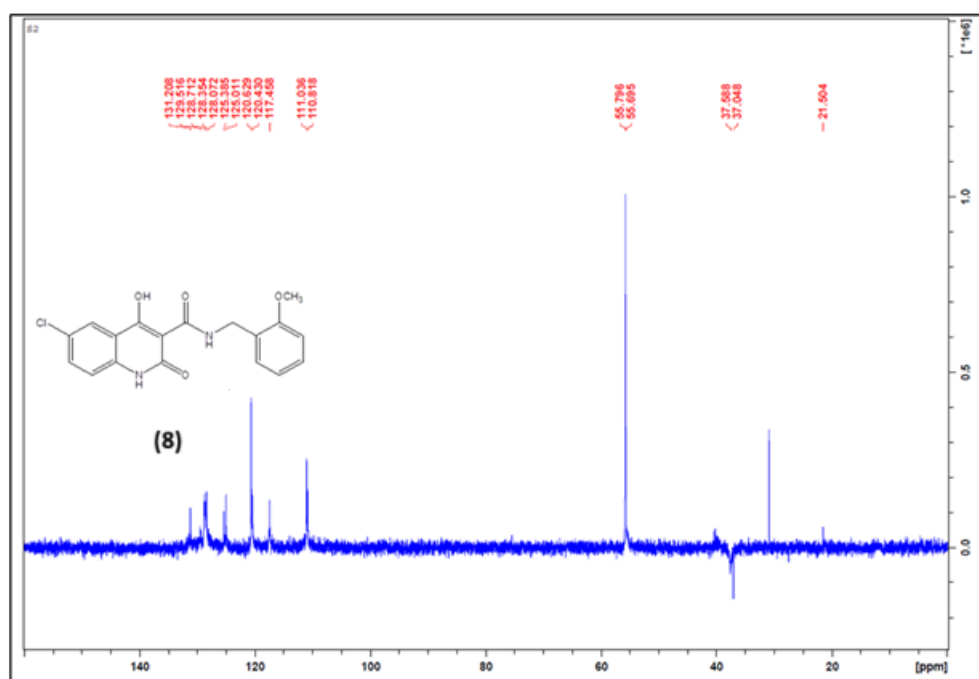
^1H -NMR(DMSO- d_6) Spectrum of *N*-(2-methoxybenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**8**).



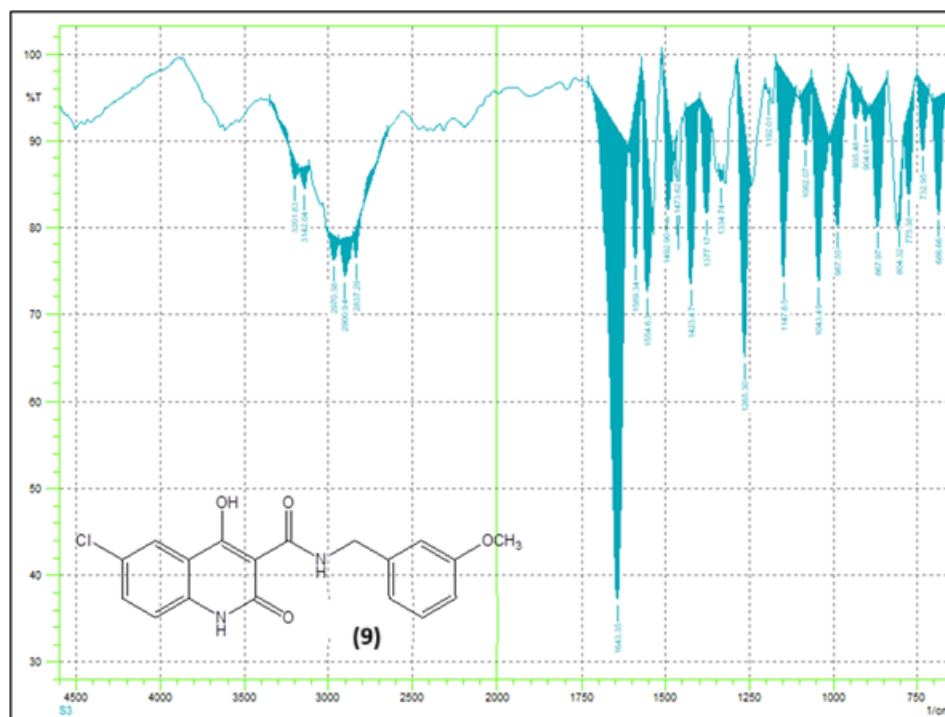
^{13}C -NMR ($\text{DMSO-}d_6$) Spectrum of *N*-(2-methoxybenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**8**).



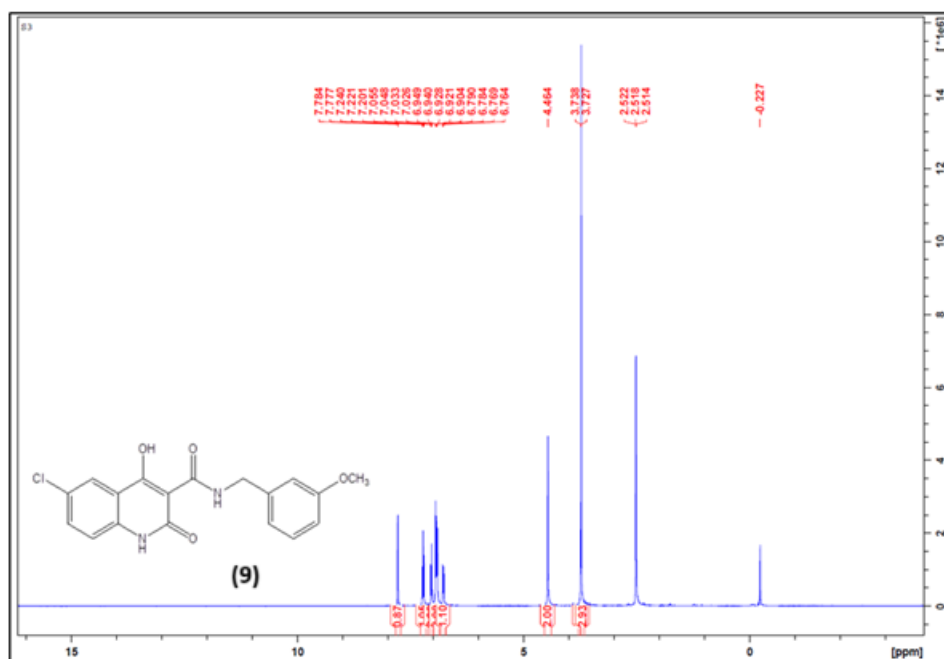
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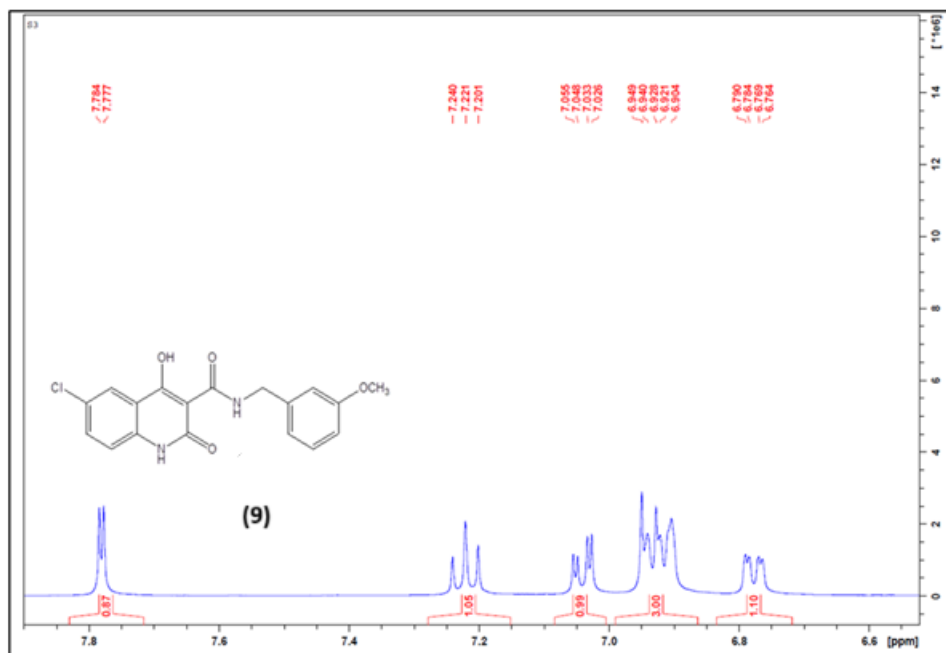
¹³C-DEPT-135-NMR (DMSO-*d*₆) Spectrum of *N*-(2-methoxybenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**8**).



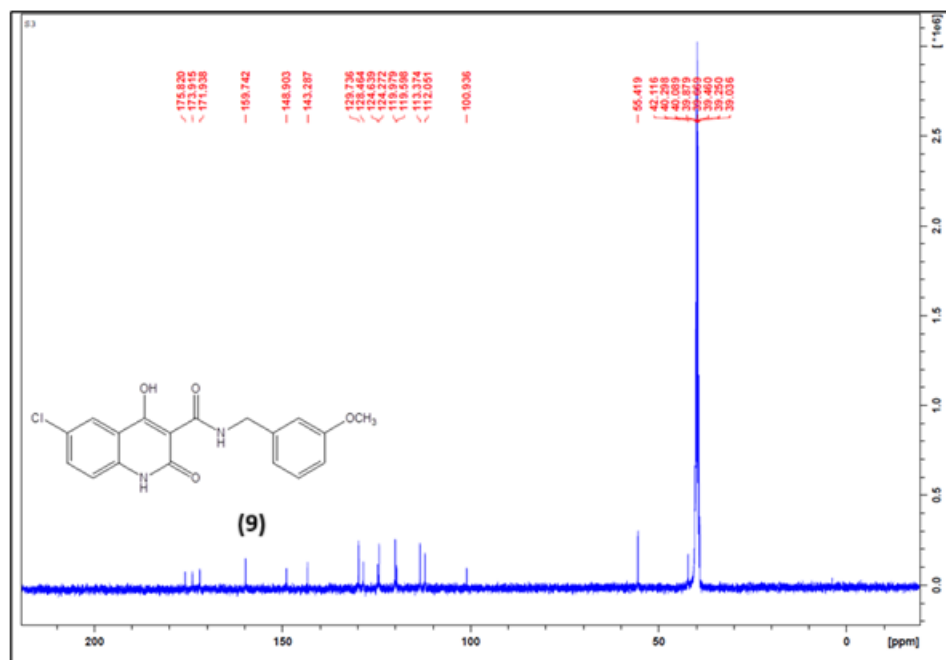
IR (KBr disc) spectrum of *N*-(3-methoxybenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**9**).



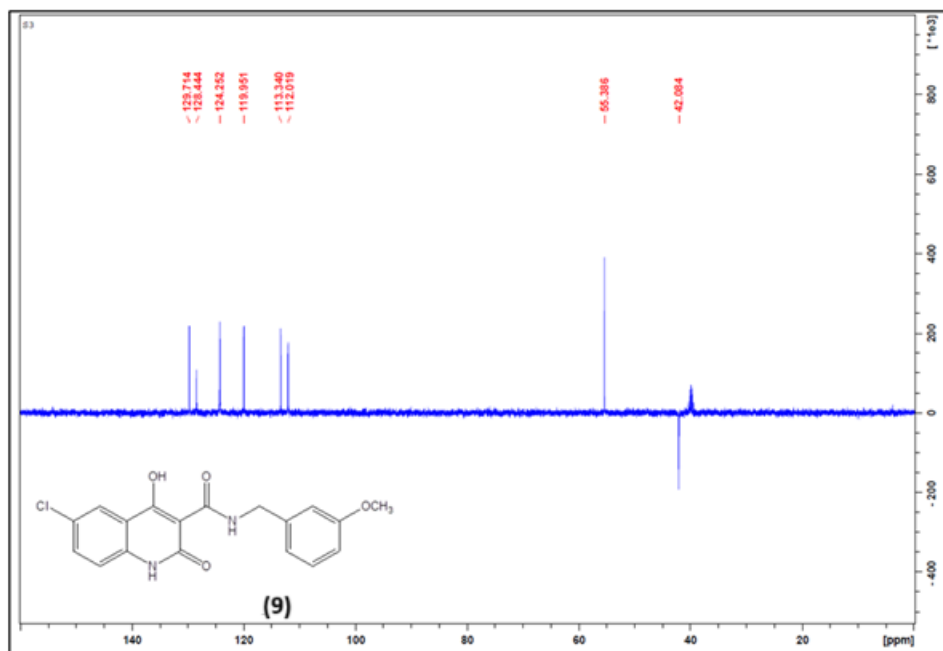
¹H-NMR(DMSO-*d*₆+NaOD) spectrum of *N*-(3-methoxybenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**9**).



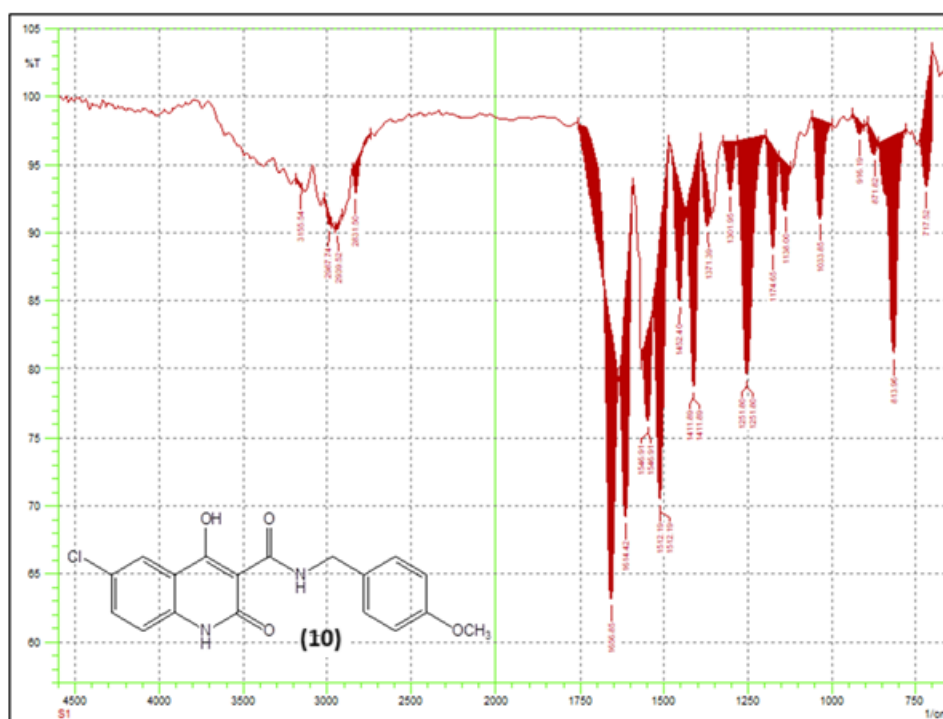
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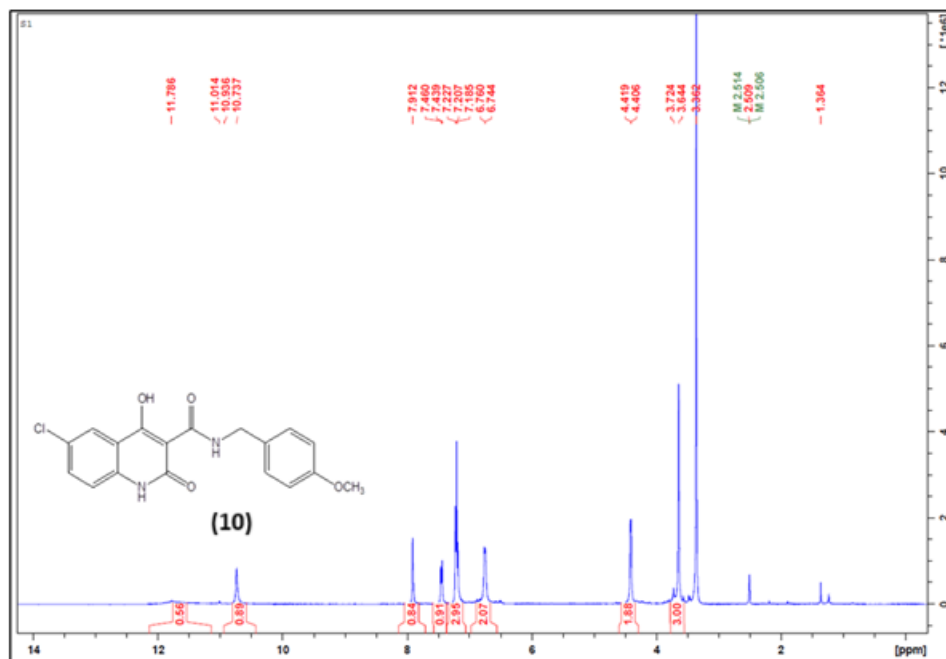
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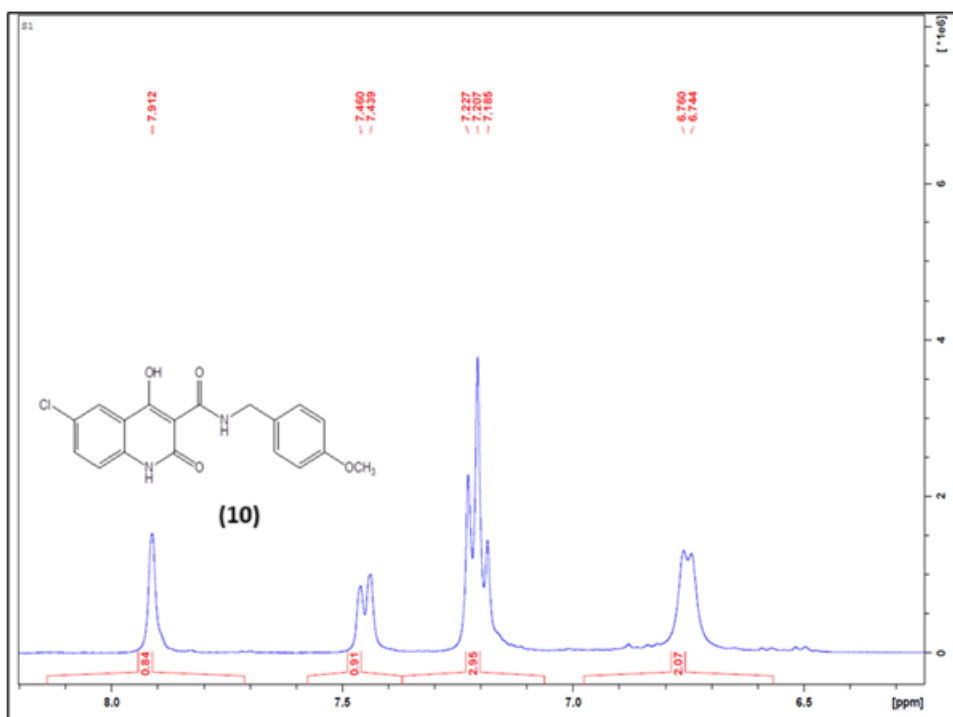
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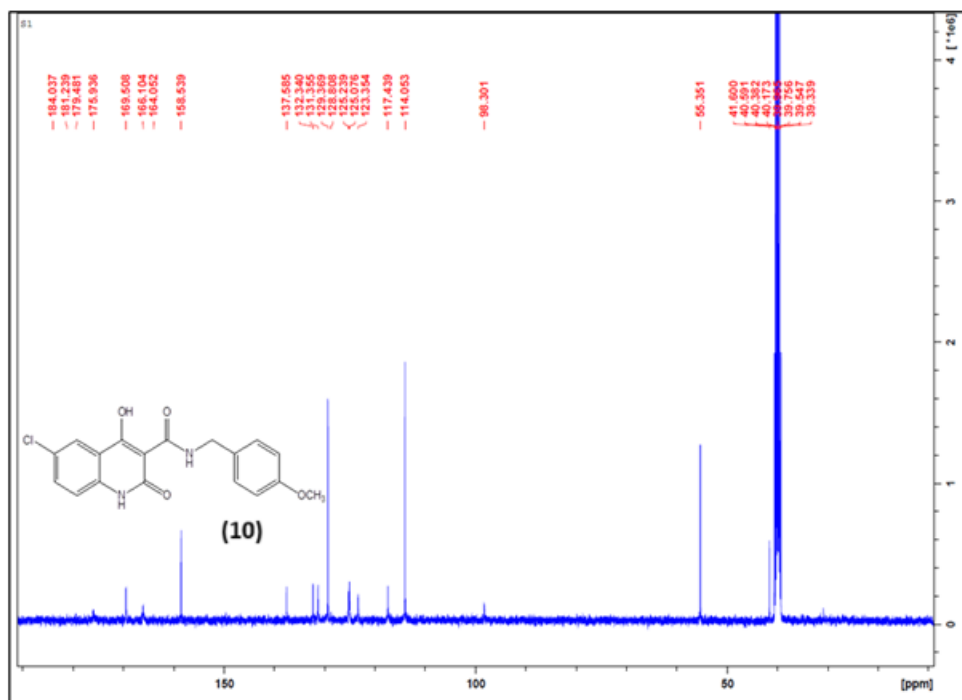
IR (KBr disc) spectrum of *N*-(4-methoxybenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**10**).



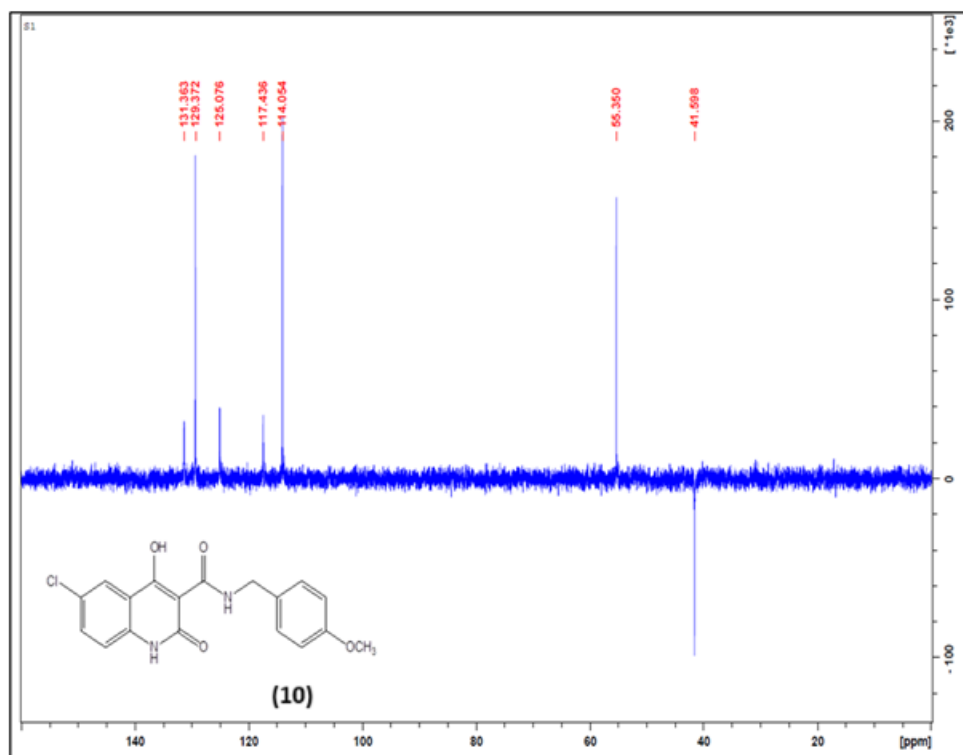
¹H-NMR(DMSO-*d*₆) Spectrum of *N*-(4-methoxybenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide **(10)**.



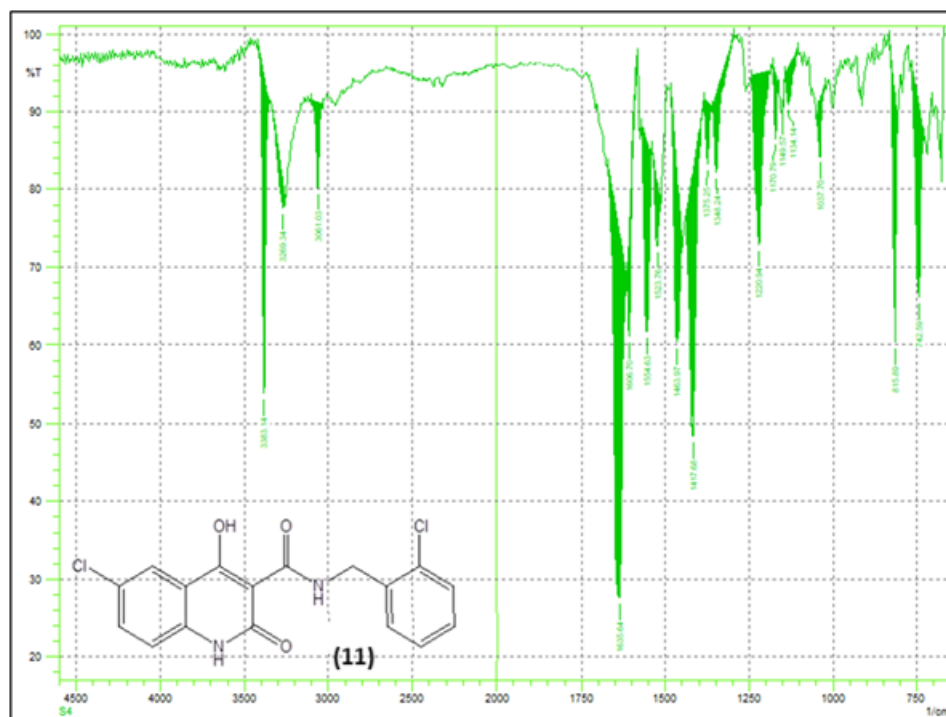
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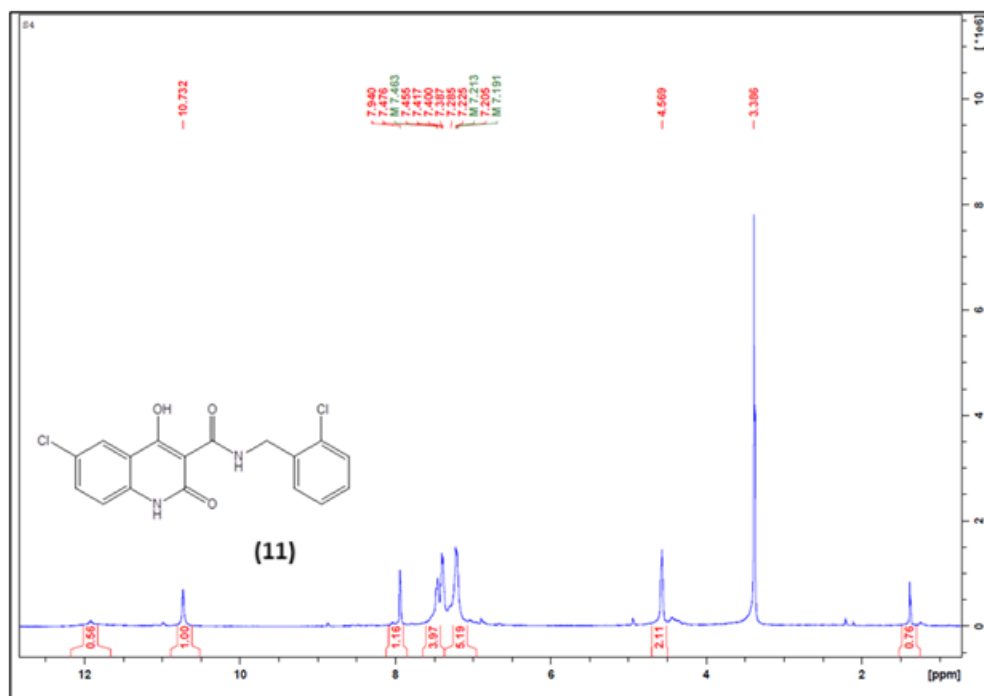
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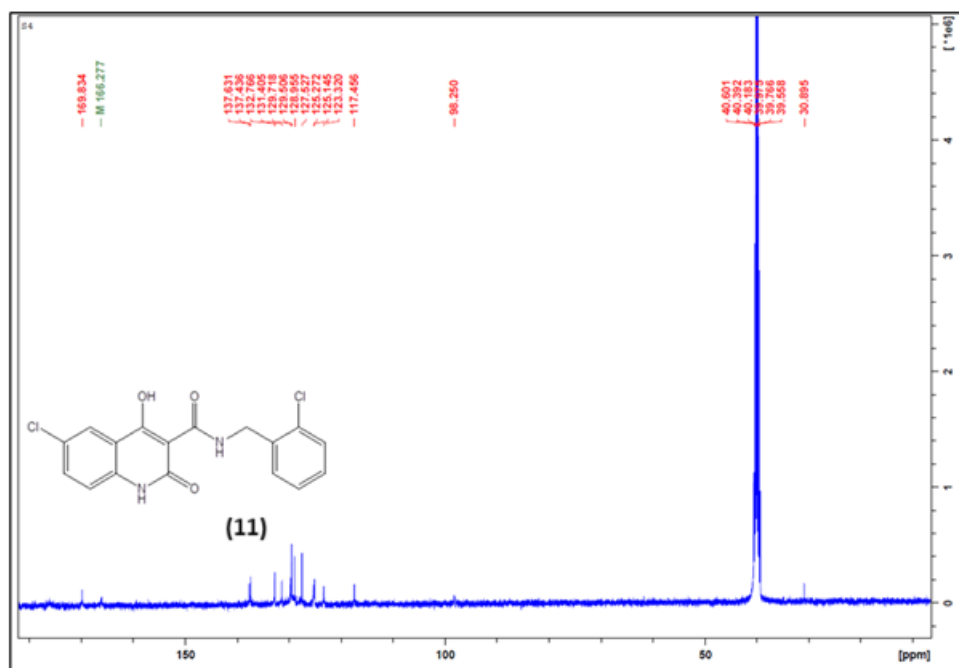
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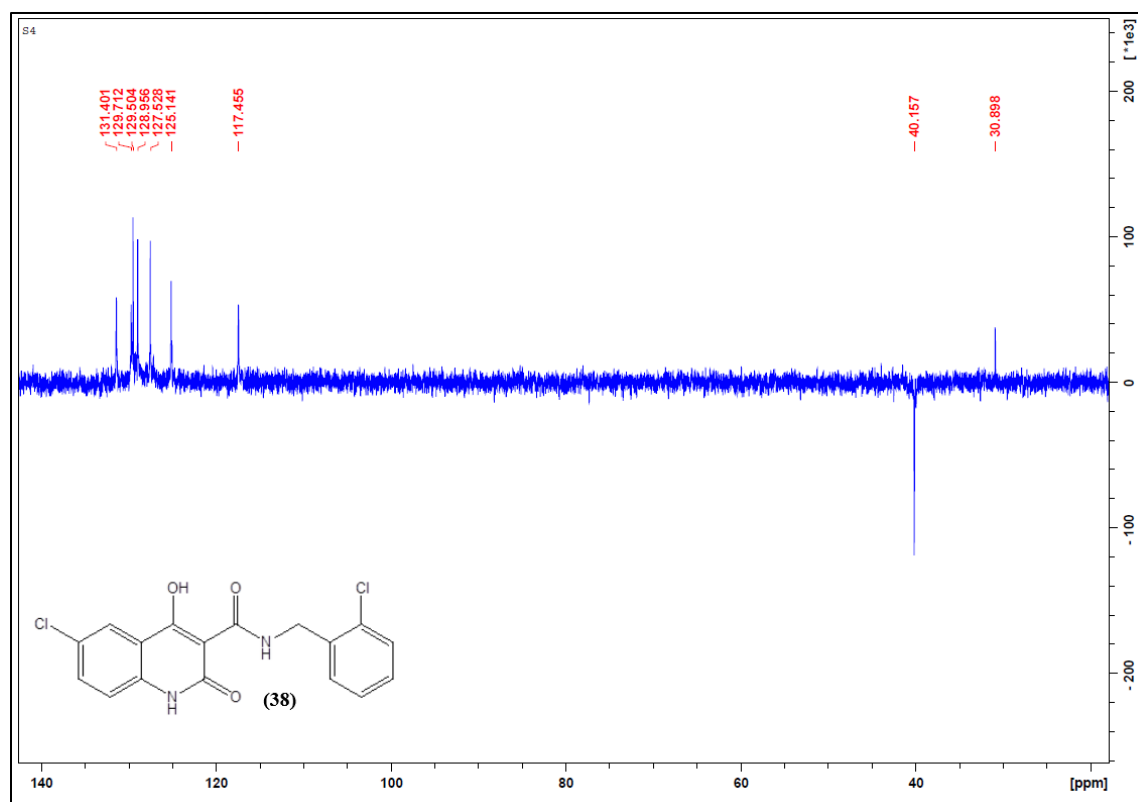
IR (KBr disc) spectrum of *N*-(2-chlorobenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**11**).



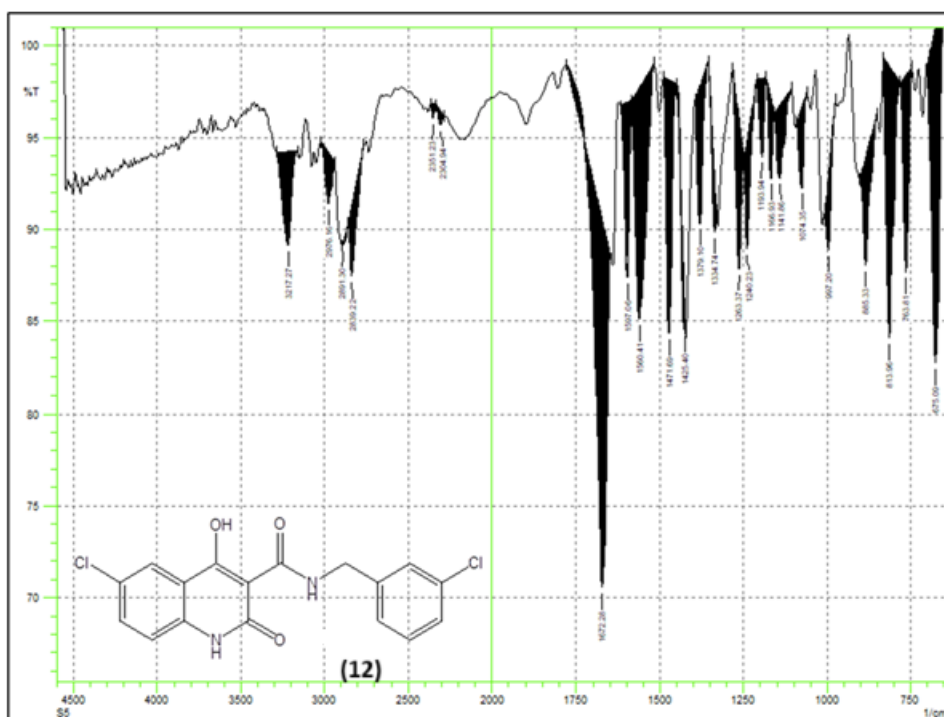
^1H -NMR(DMSO- d_6) spectrum of *N*-(2-chlorobenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**11**).



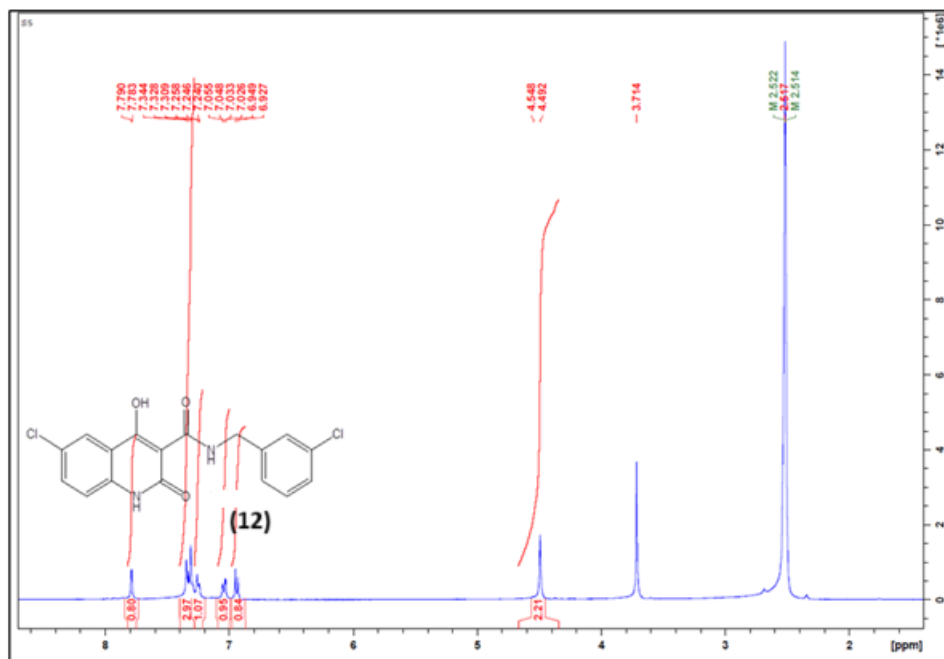
^{13}C -NMR ($\text{DMSO-}d_6$) spectrum of *N*-(2-chlorobenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**11**).



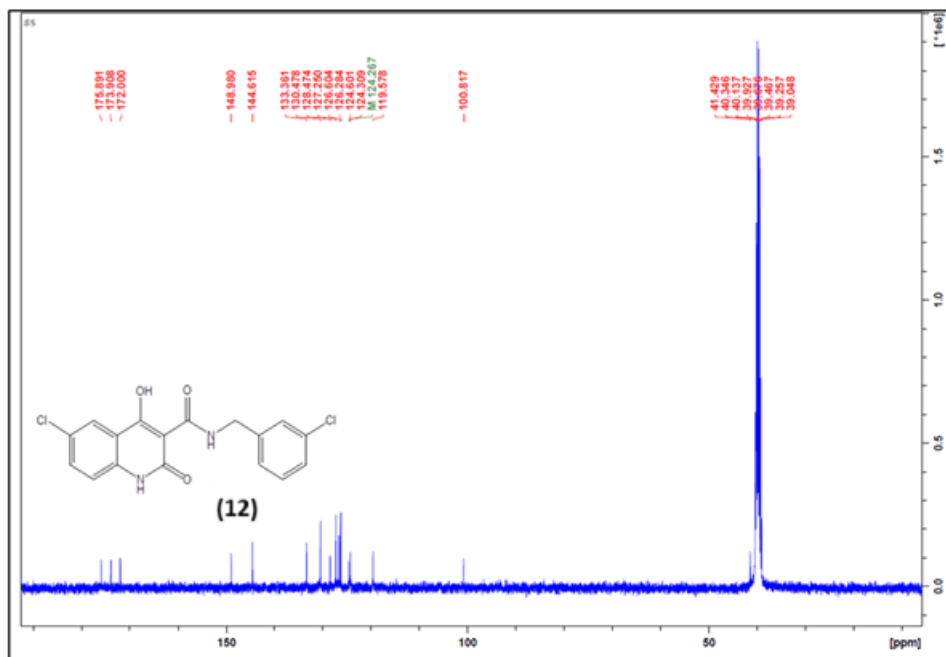
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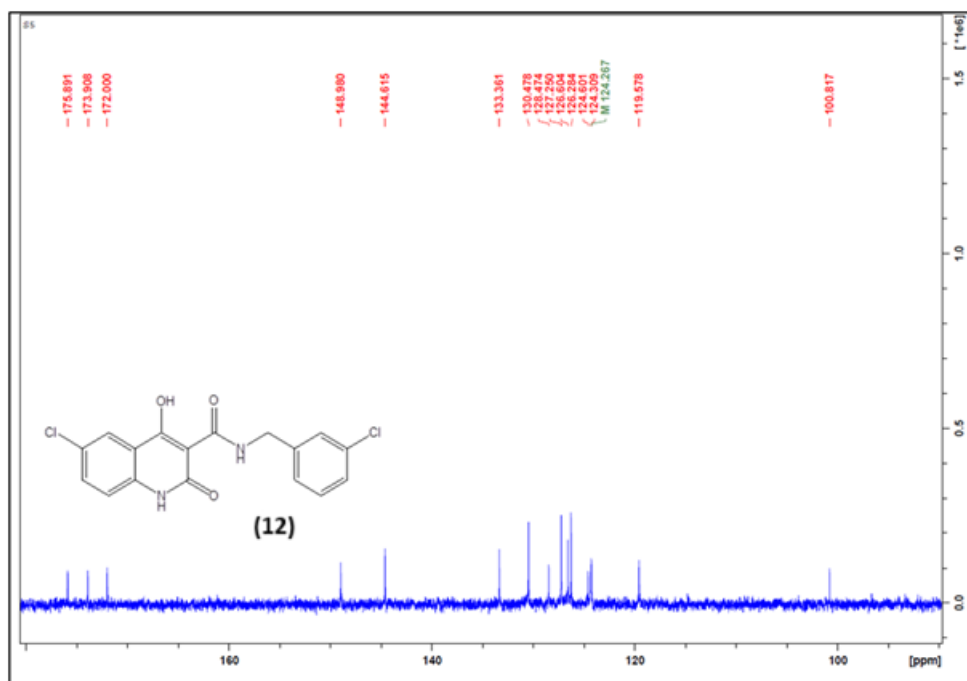
IR (KBr disc) spectrum of *N*-(3-chlorobenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**12**).



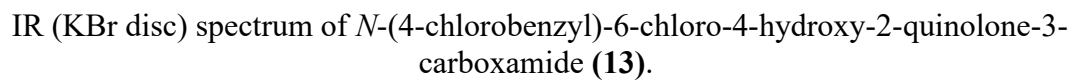
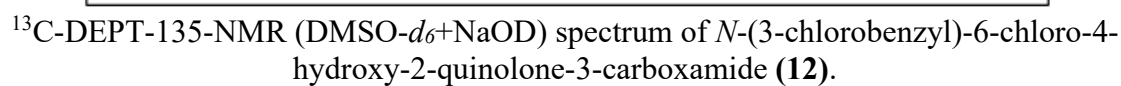
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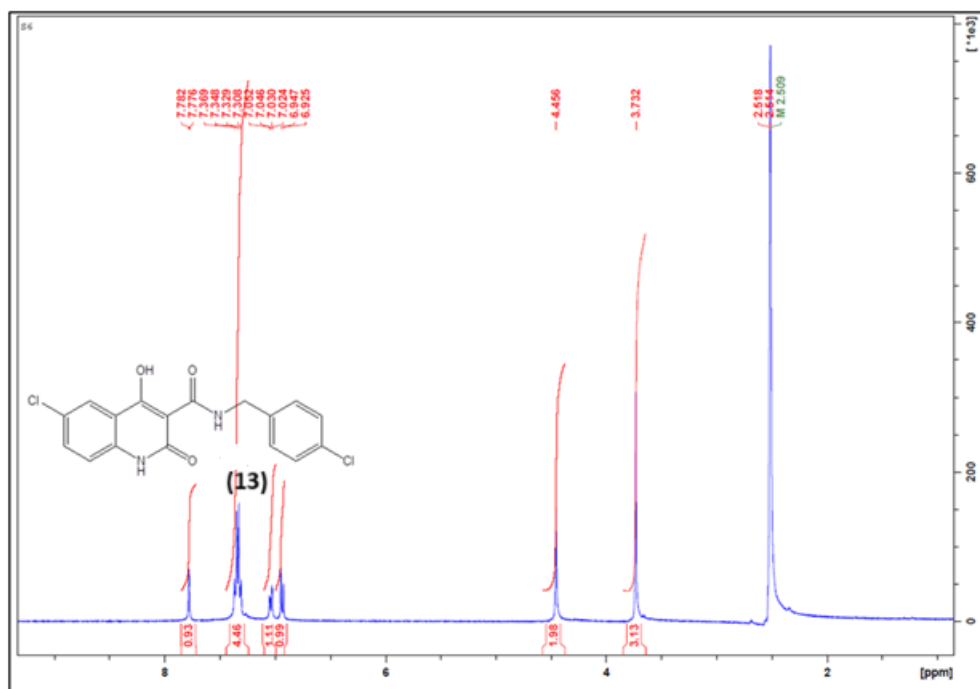


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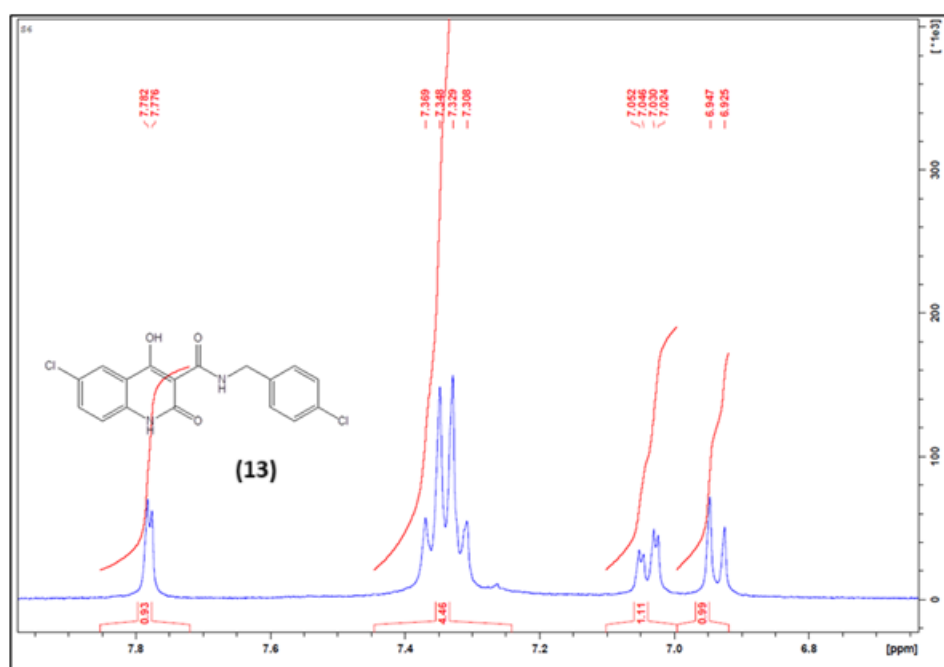


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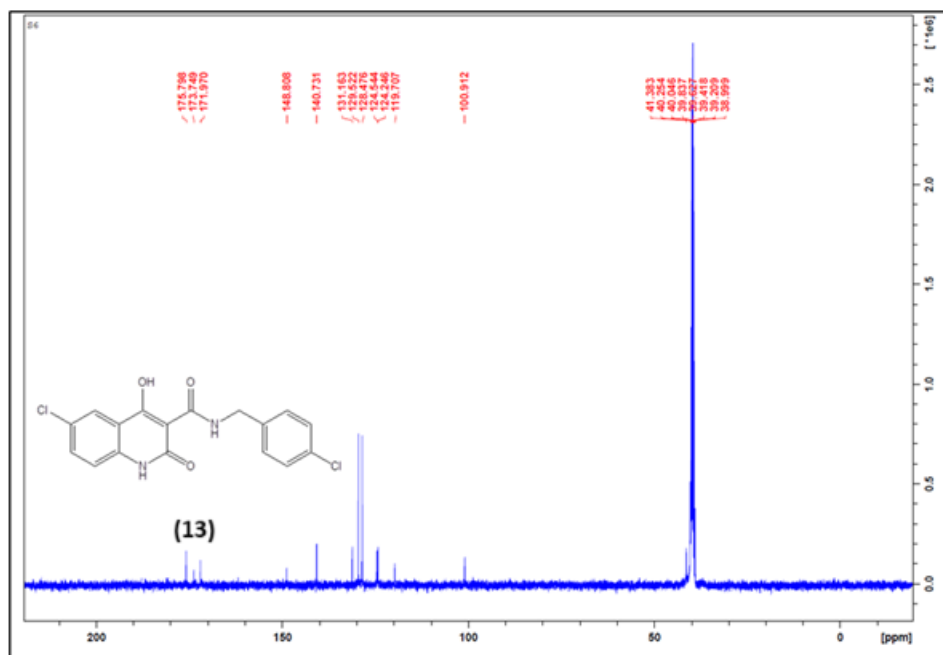




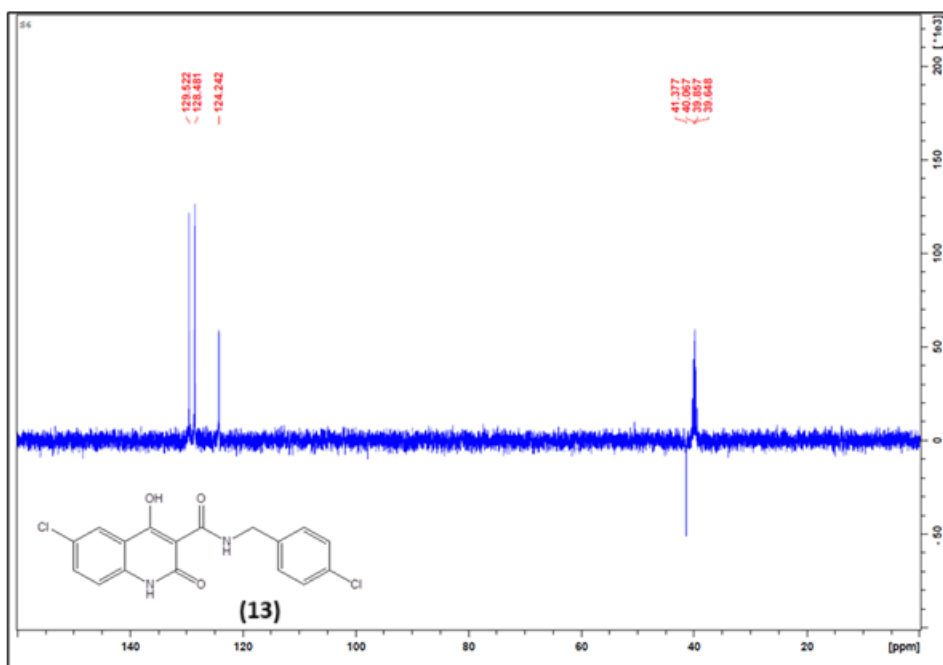
¹H-NMR(DMSO-*d*₆+NaOD) spectrum of *N*-(4-chlorobenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide **(13)**.



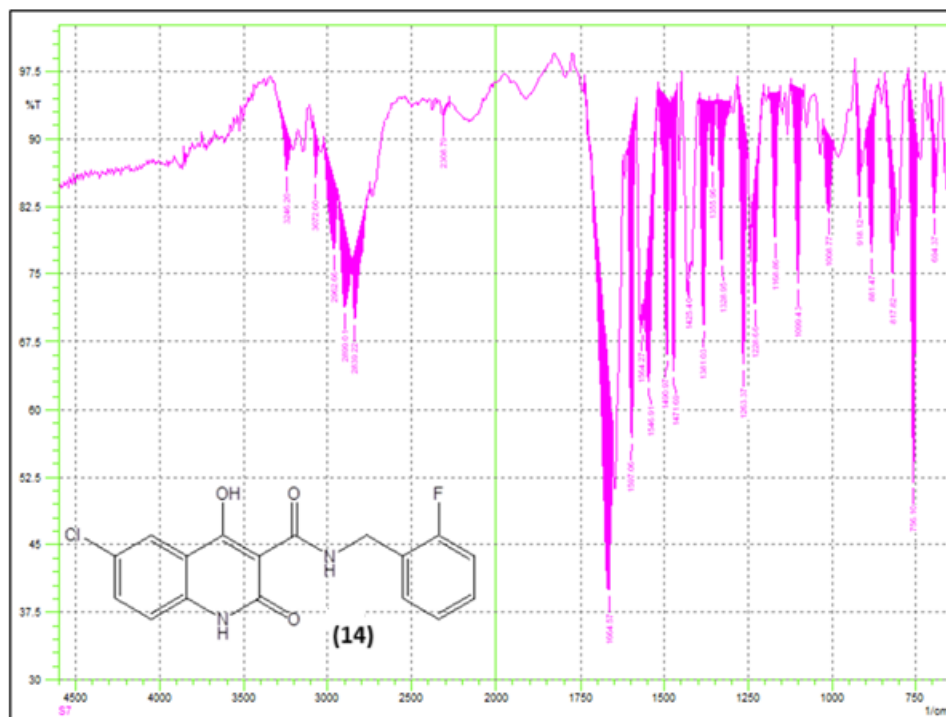
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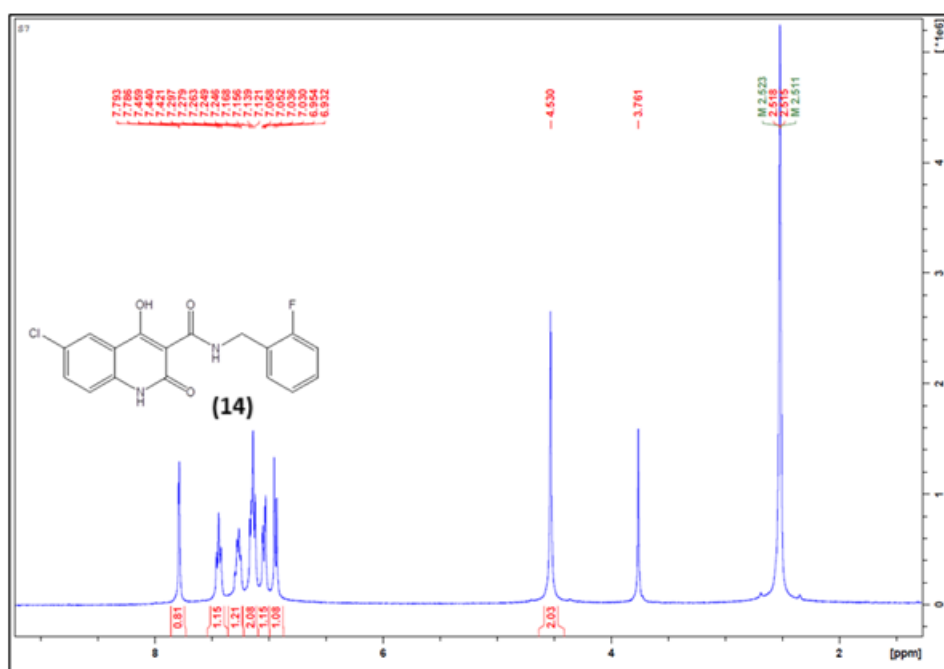
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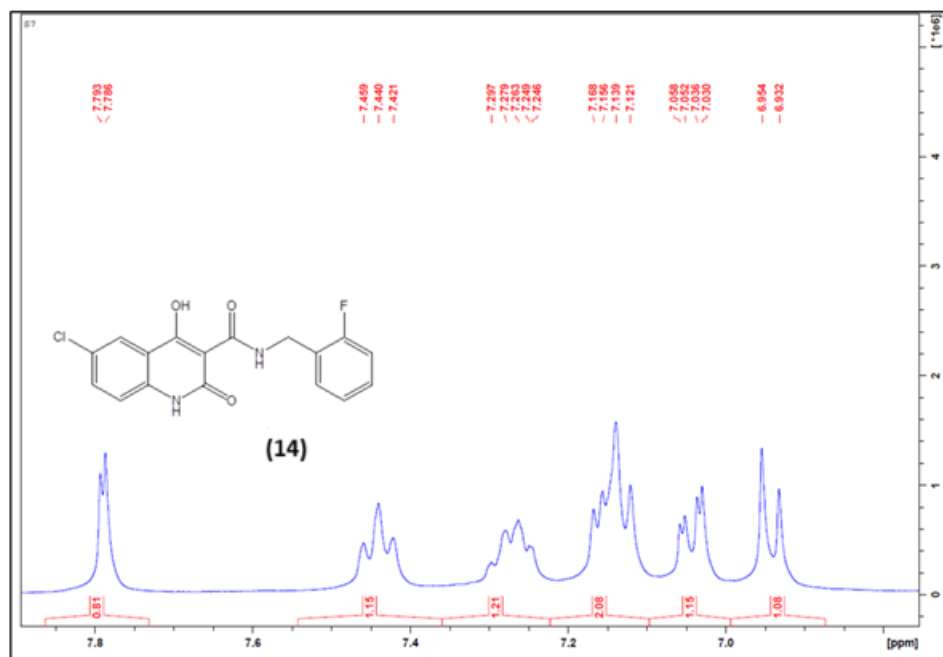
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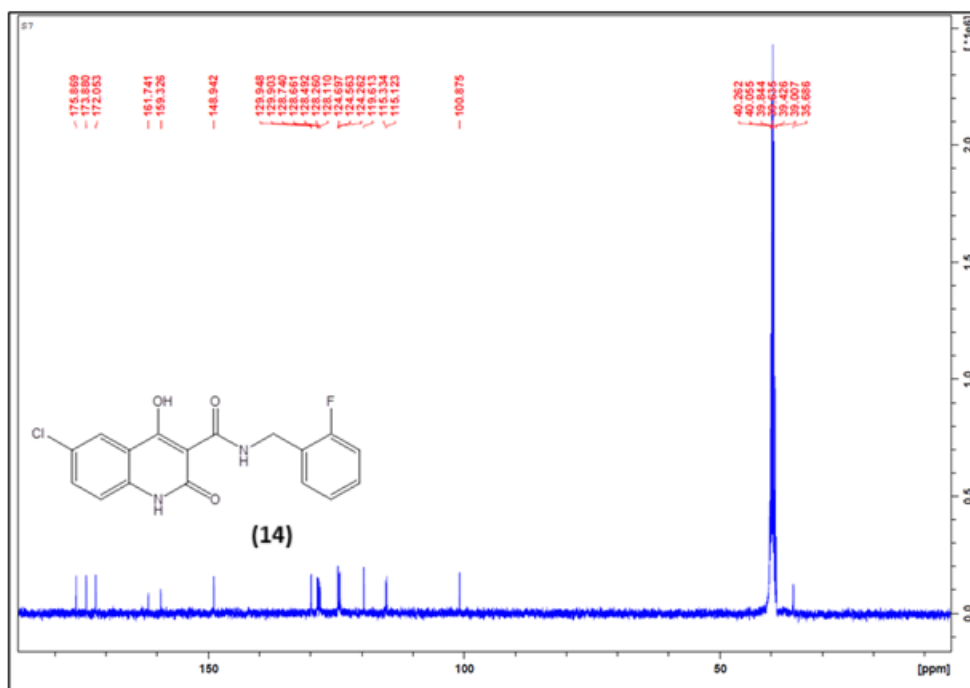
IR (KBr disc) spectrum of *N*-(2-fluorobenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**14**).



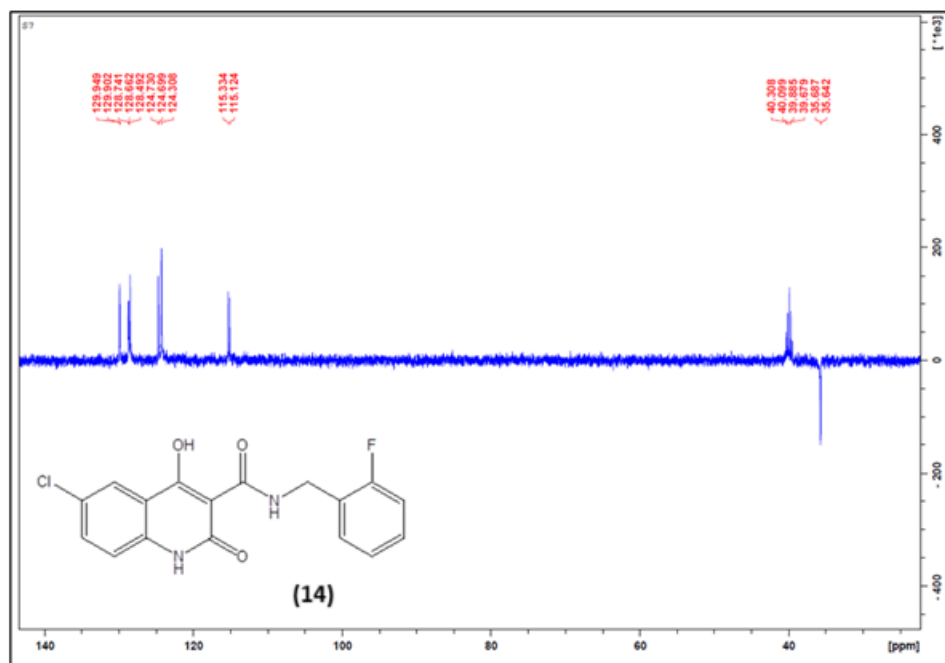
^1H -NMR(DMSO- d_6 +NaOD) spectrum of *N*-(2-fluorobenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**14**).



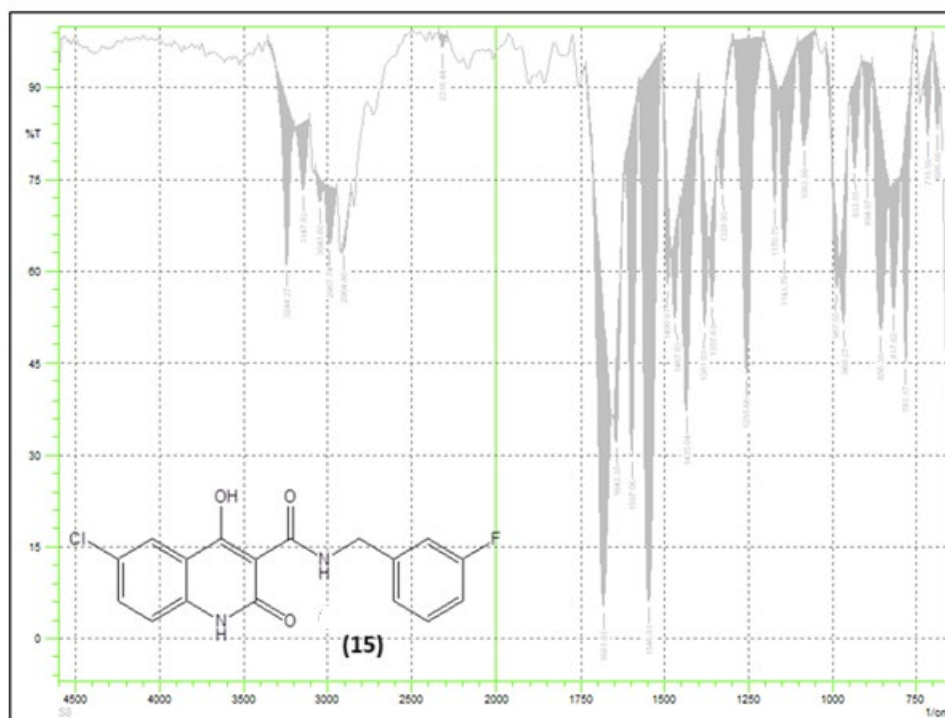
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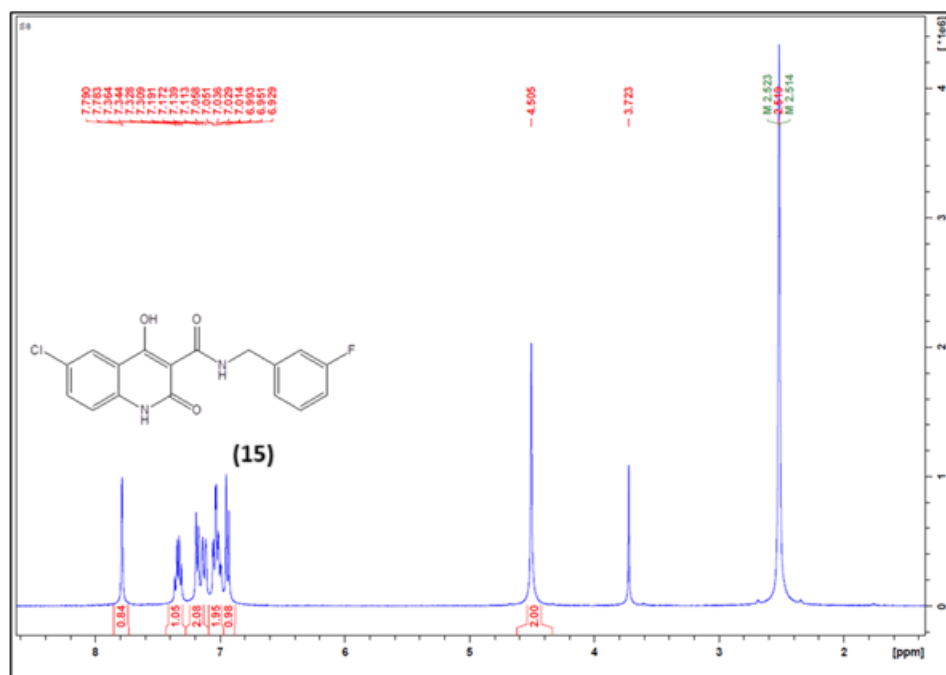
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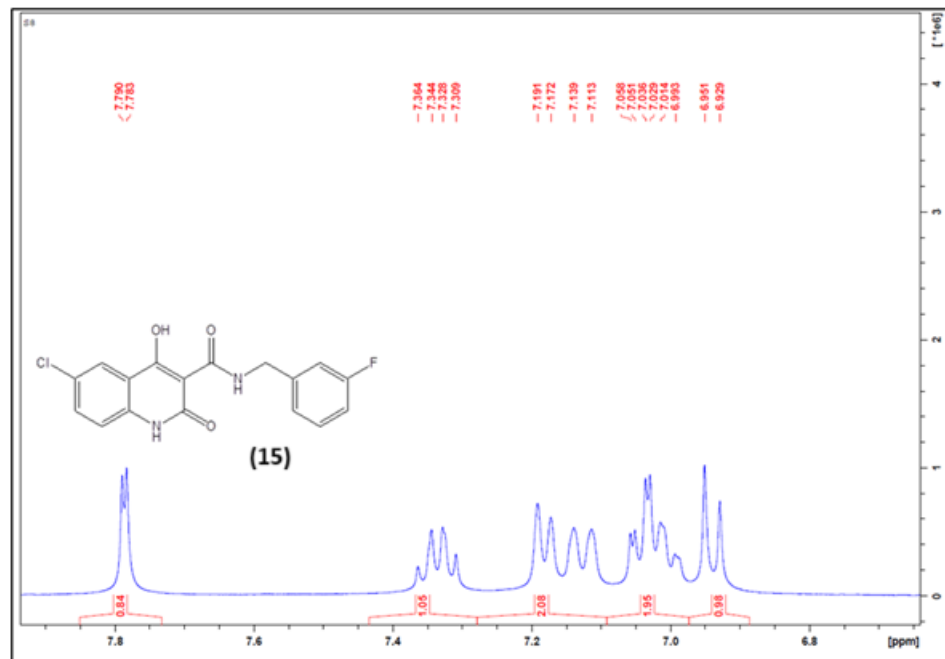
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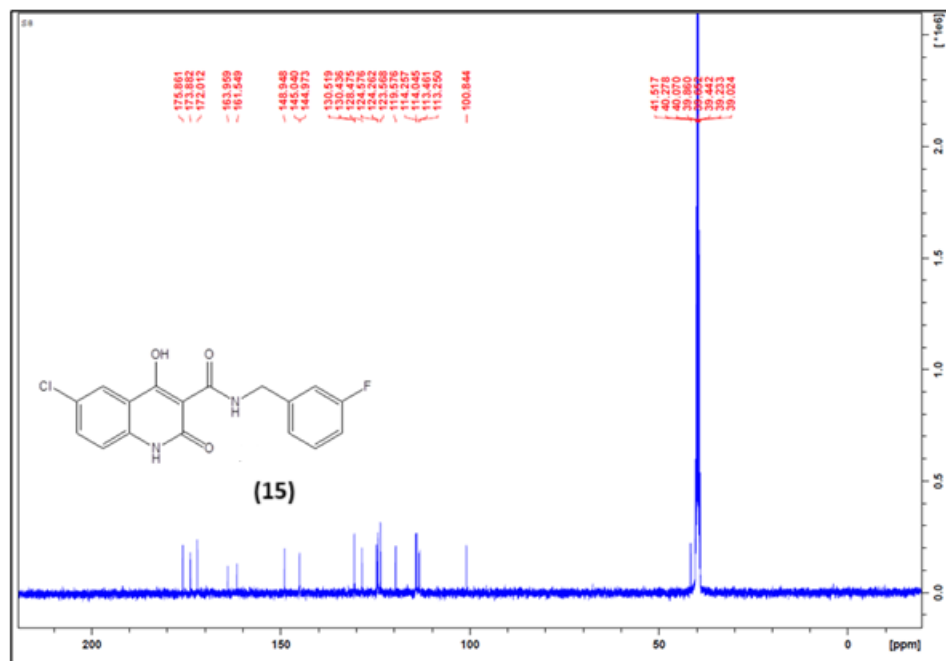
IR (KBr disc) spectrum of *N*-(3-fluorobenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**15**).



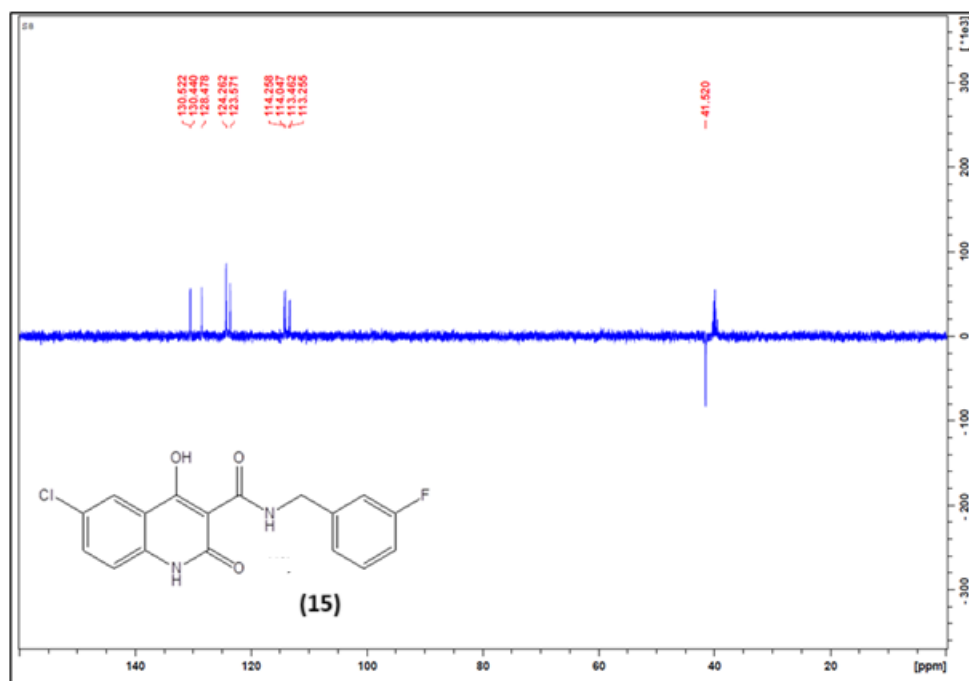
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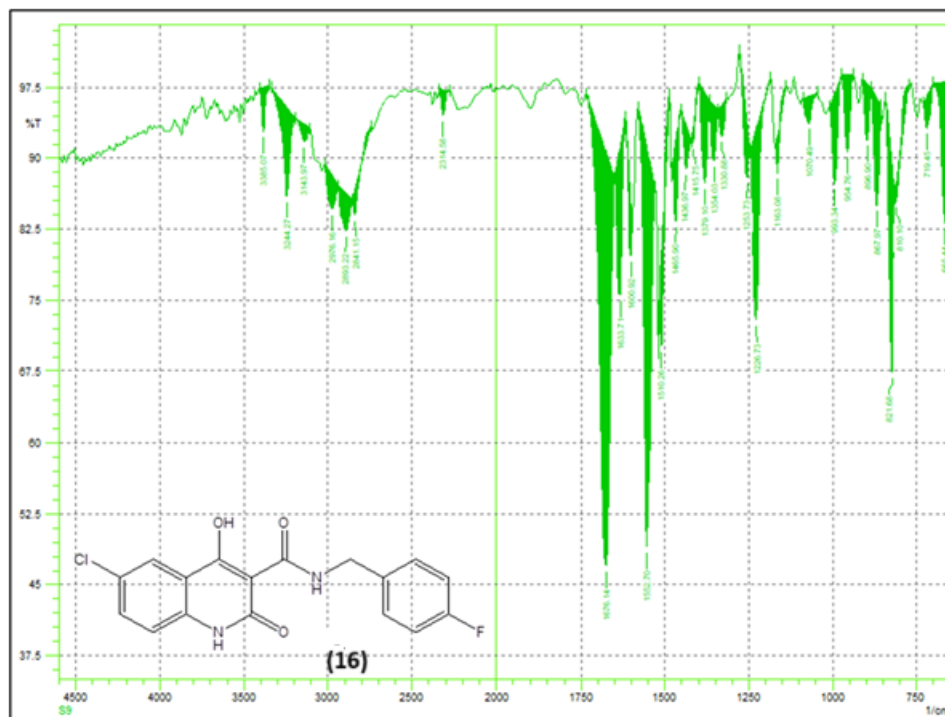
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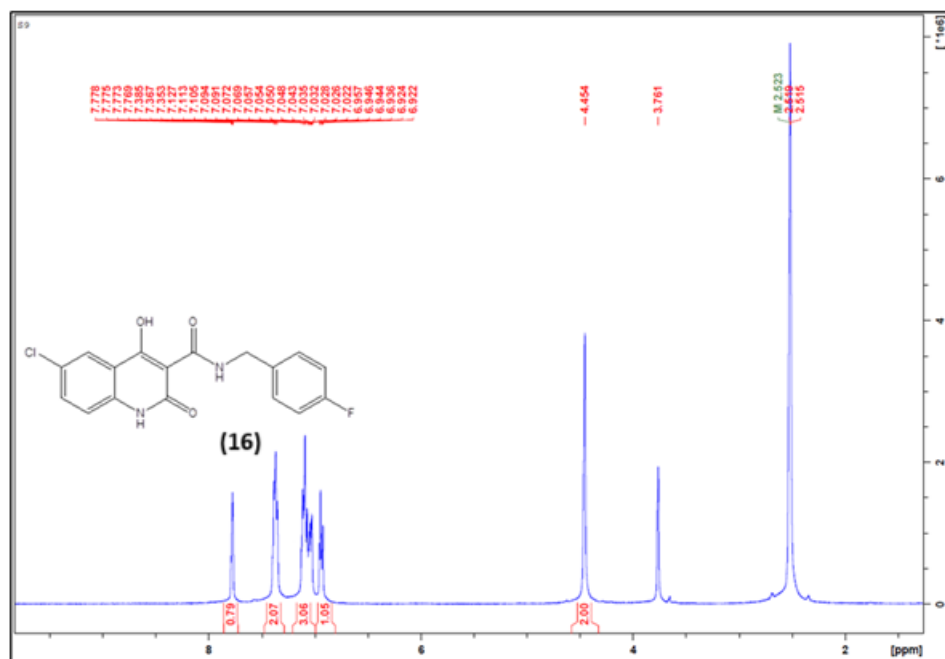
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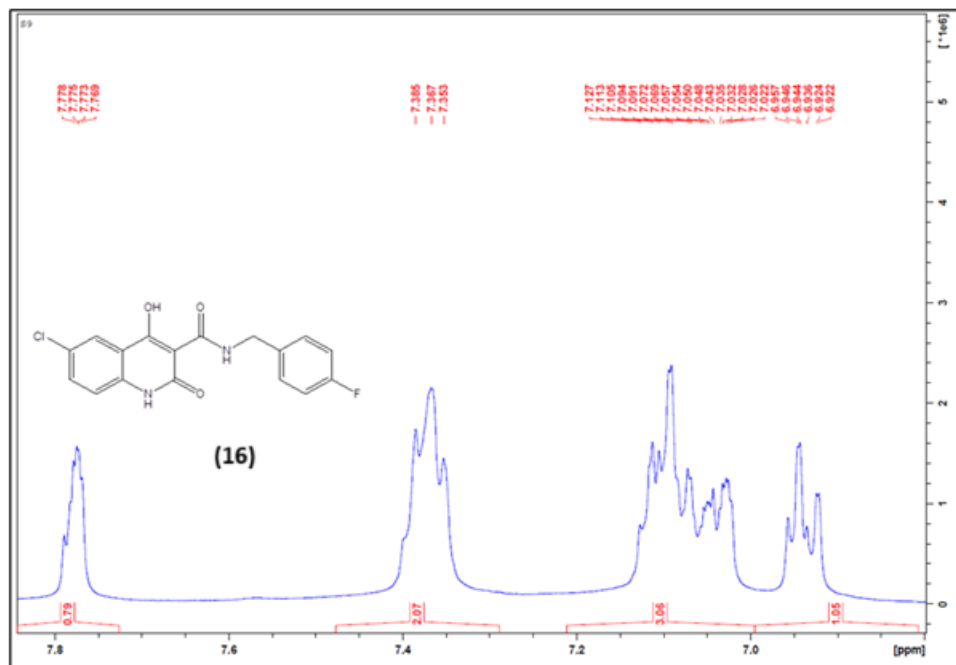
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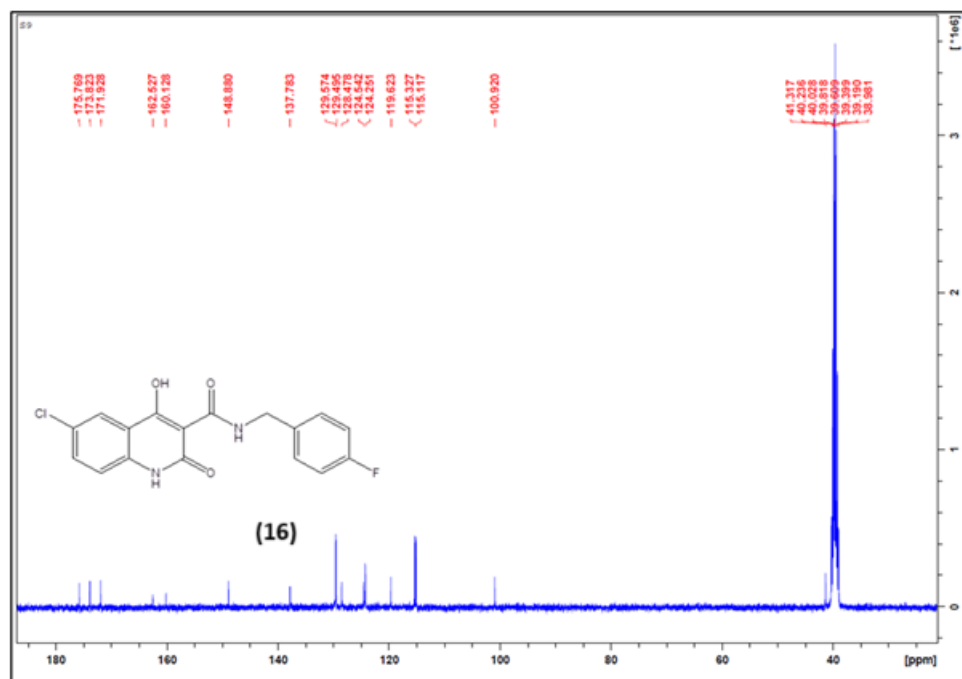
IR (KBr disc) spectrum of *N*-(4-fluorobenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide **(16)**.



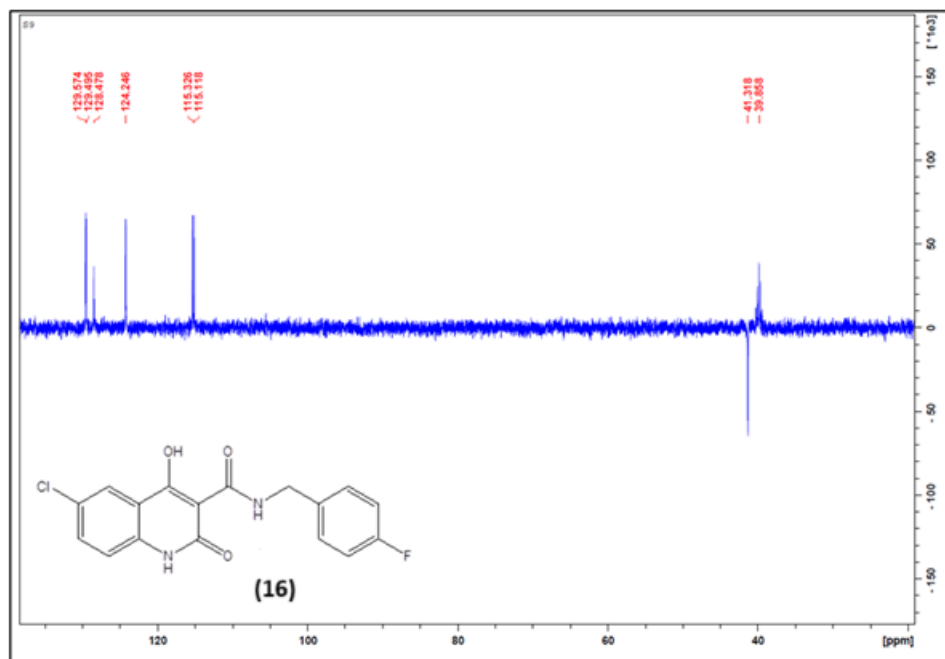
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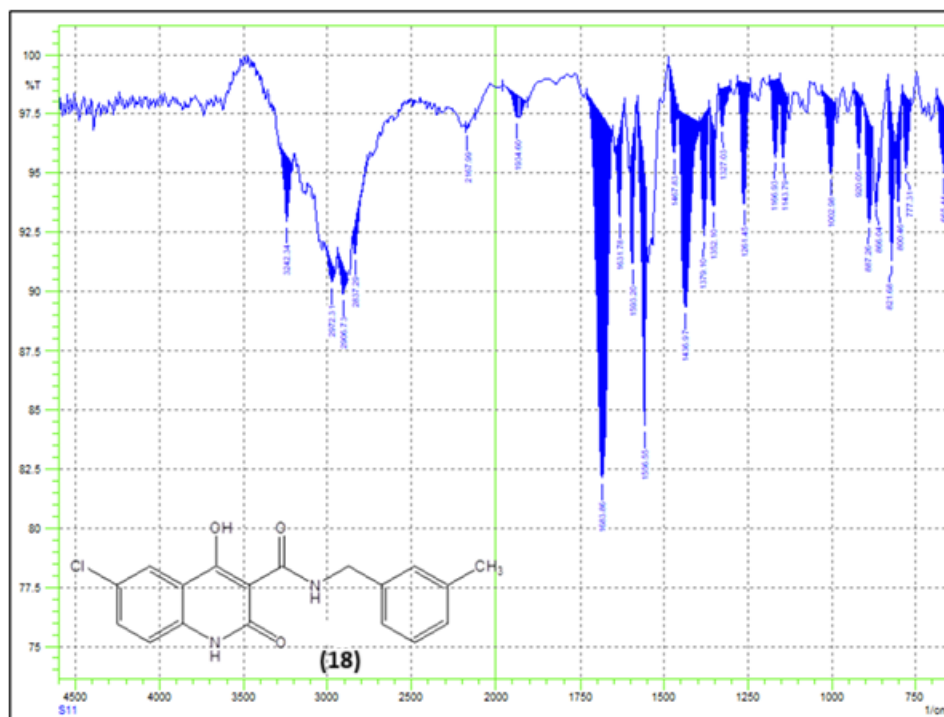
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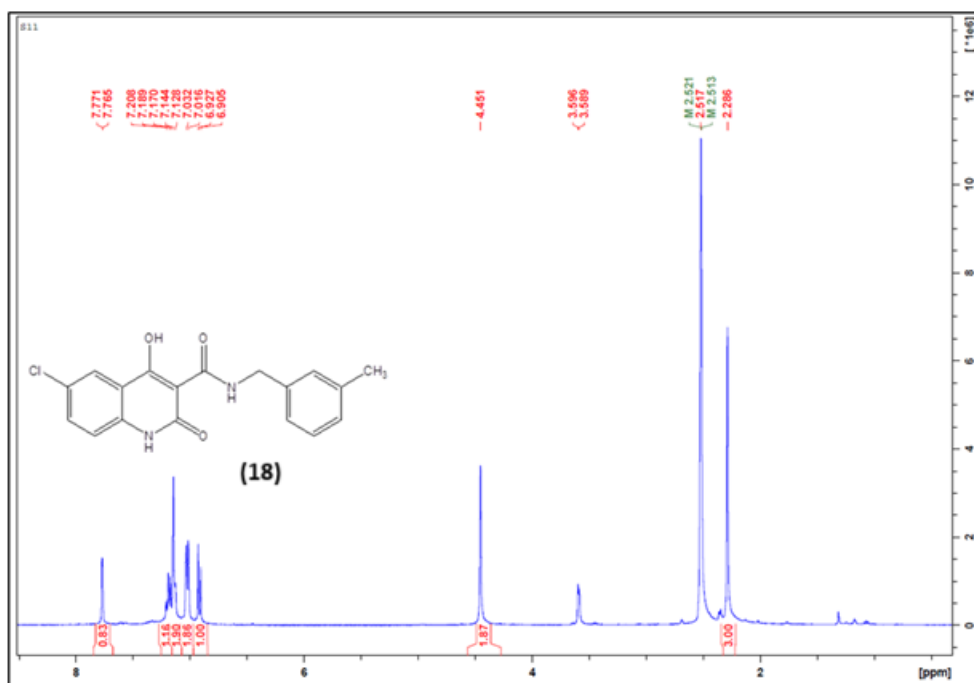
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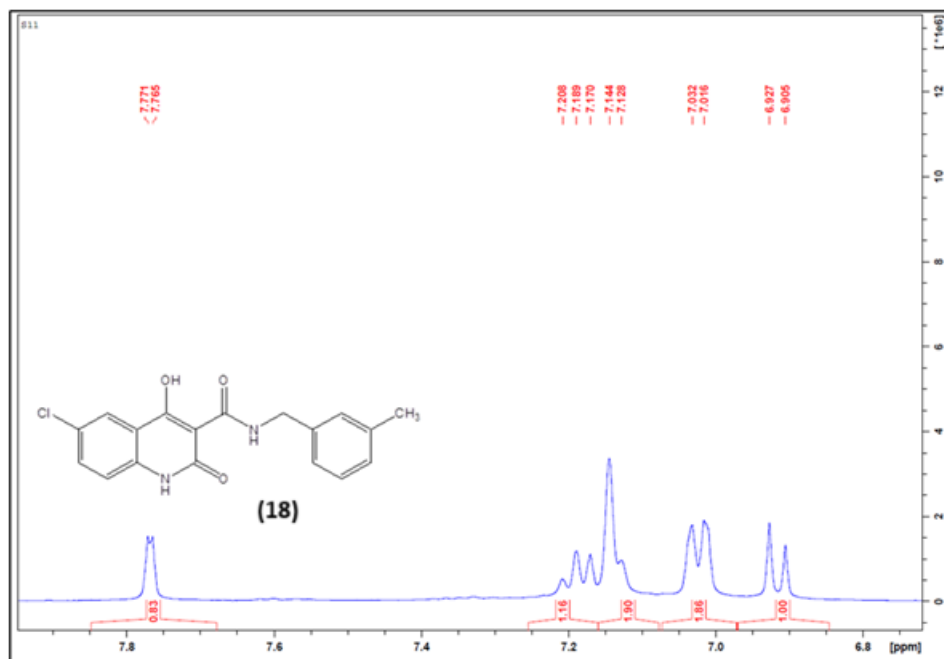
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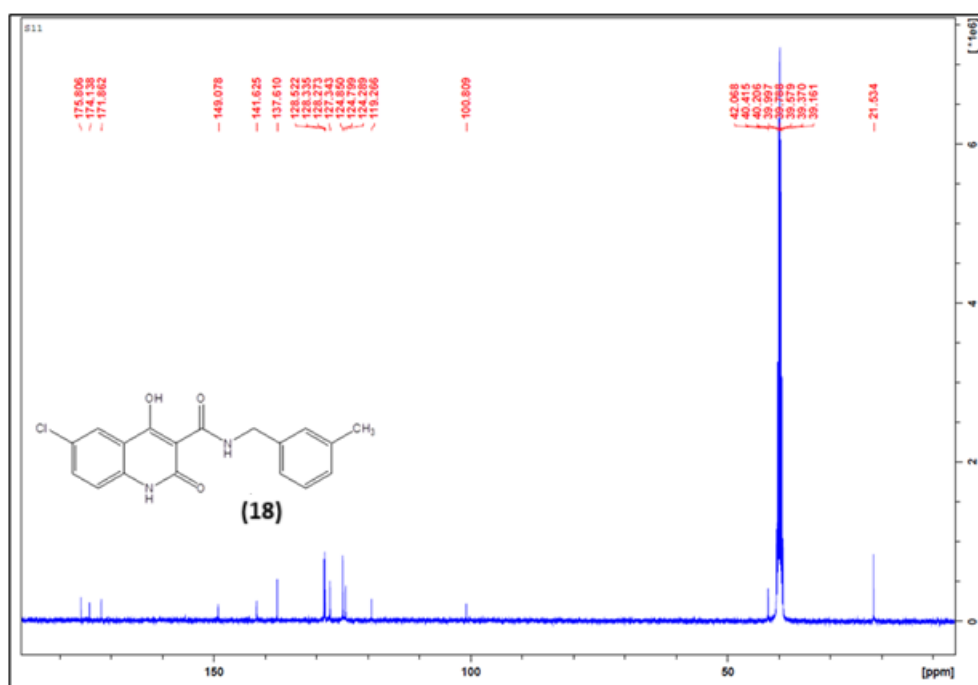
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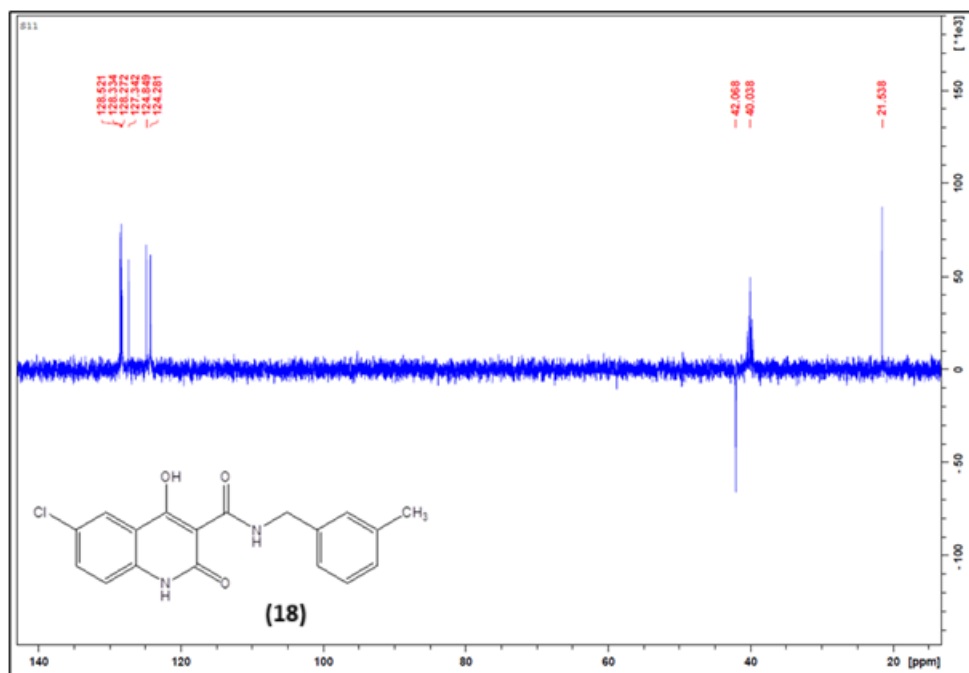
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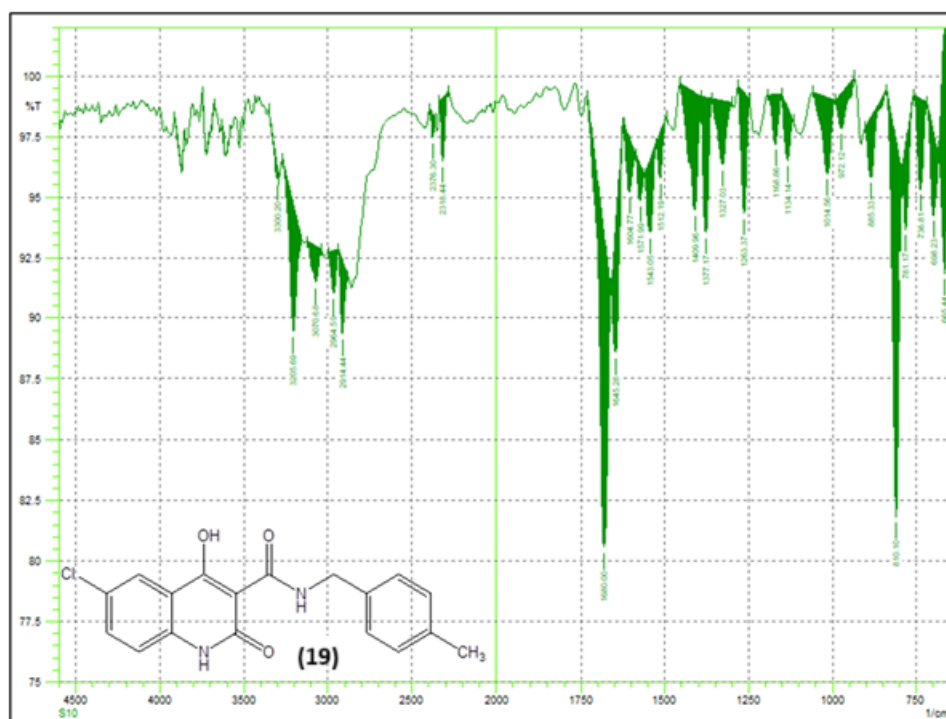
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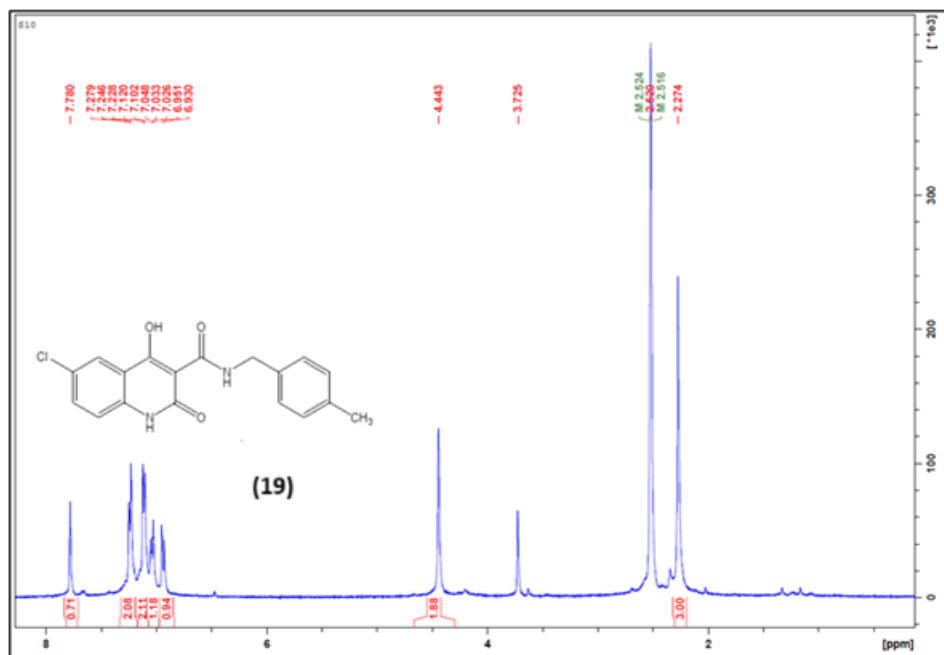
¹³C-NMR (DMSO-*d*₆+NaOD) spectrum of *N*-(3-methylbenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**18**).



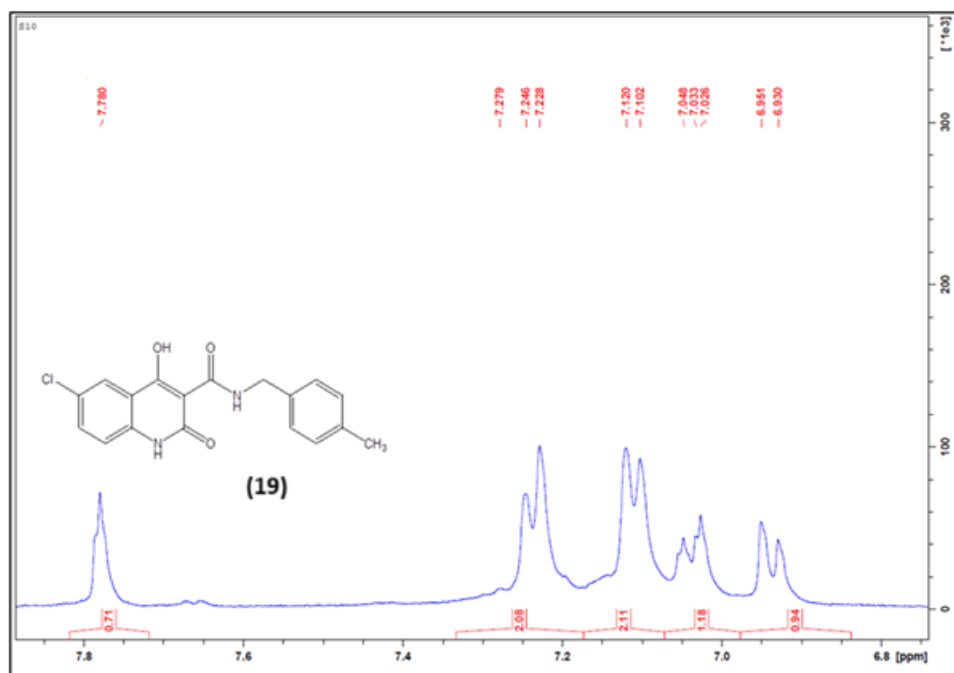
¹³C-DEPT-135-NMR (DMSO-*d*₆+NaOD) spectrum of *N*-(3-methylbenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**18**).



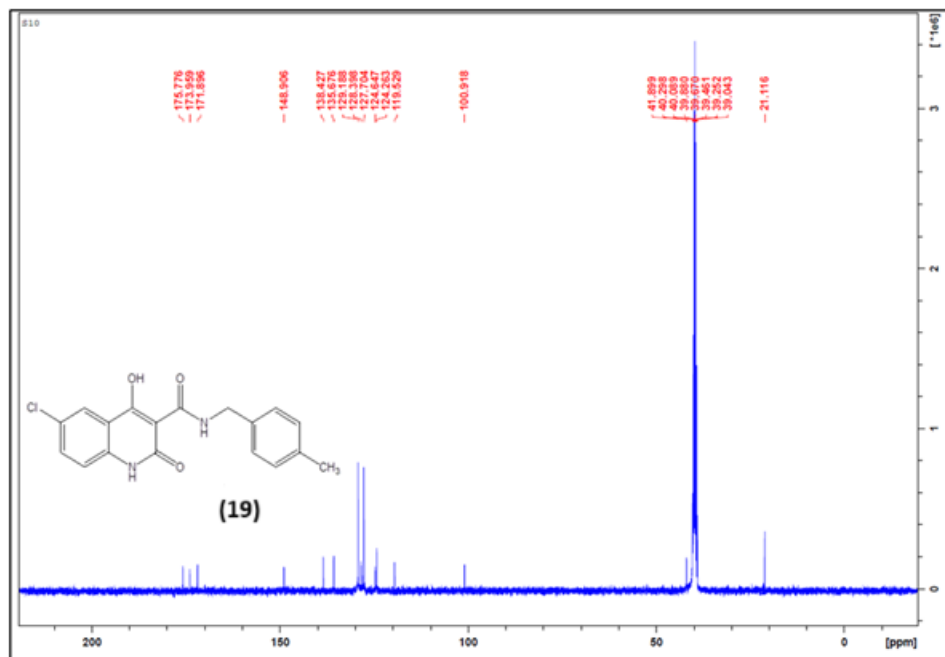
IR (KBr disc) spectrum of *N*-(4-methylbenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**19**).



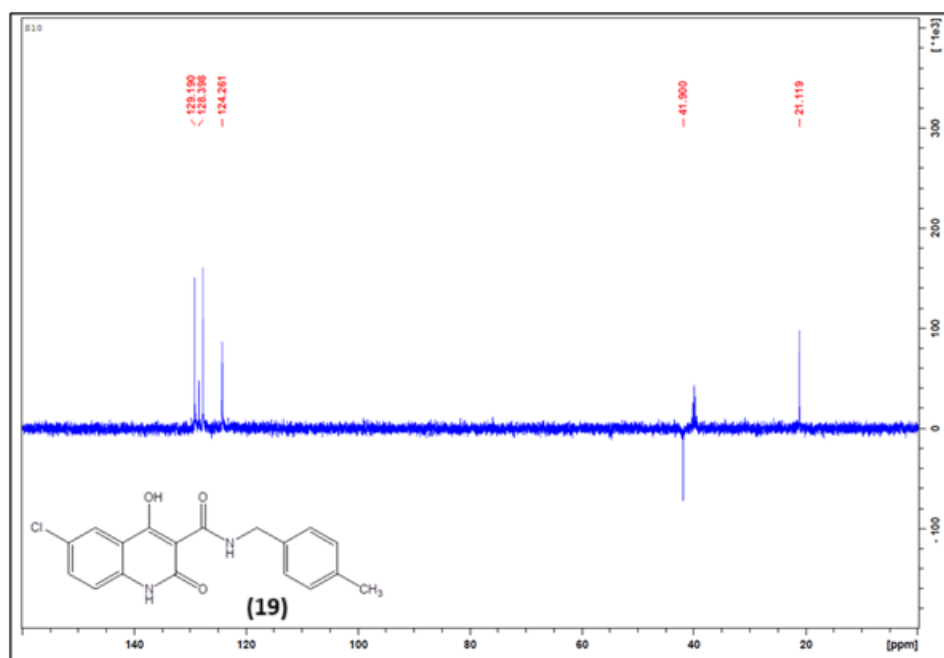
¹H-NMR(DMSO-*d*₆+NaOD) spectrum of *N*-(4-methylbenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide **(19)**.



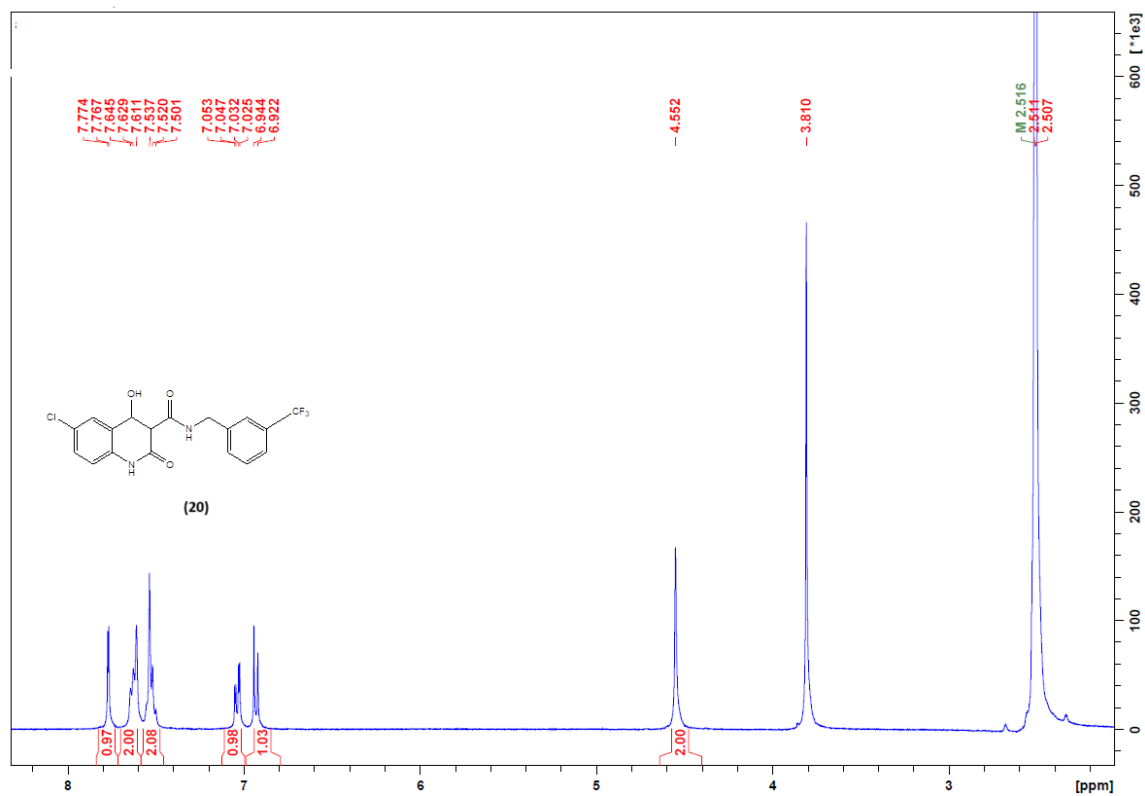
¹H-NMR(DMSO-*d*₆+NaOD) spectrum of *N*-(4-methylbenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide **(19)**.



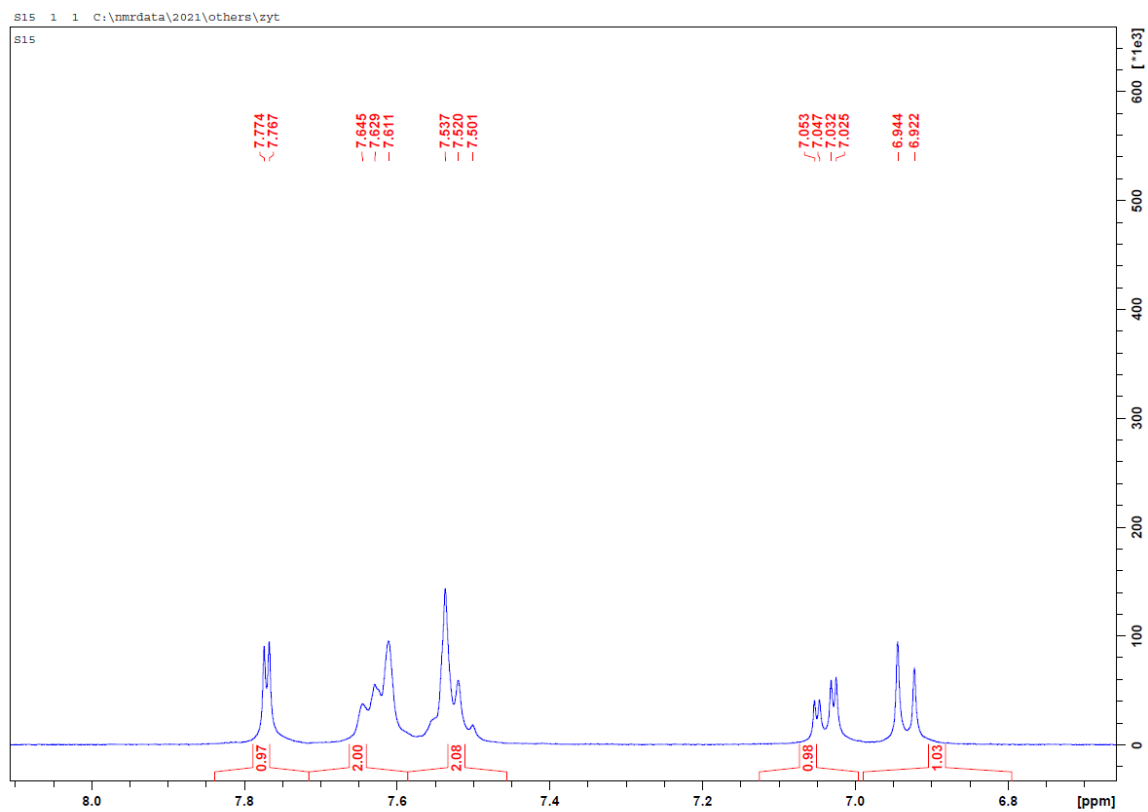
¹³C-NMR (DMSO-*d*₆+NaOD) spectrum of *N*-(4-methylbenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide **(19)**.



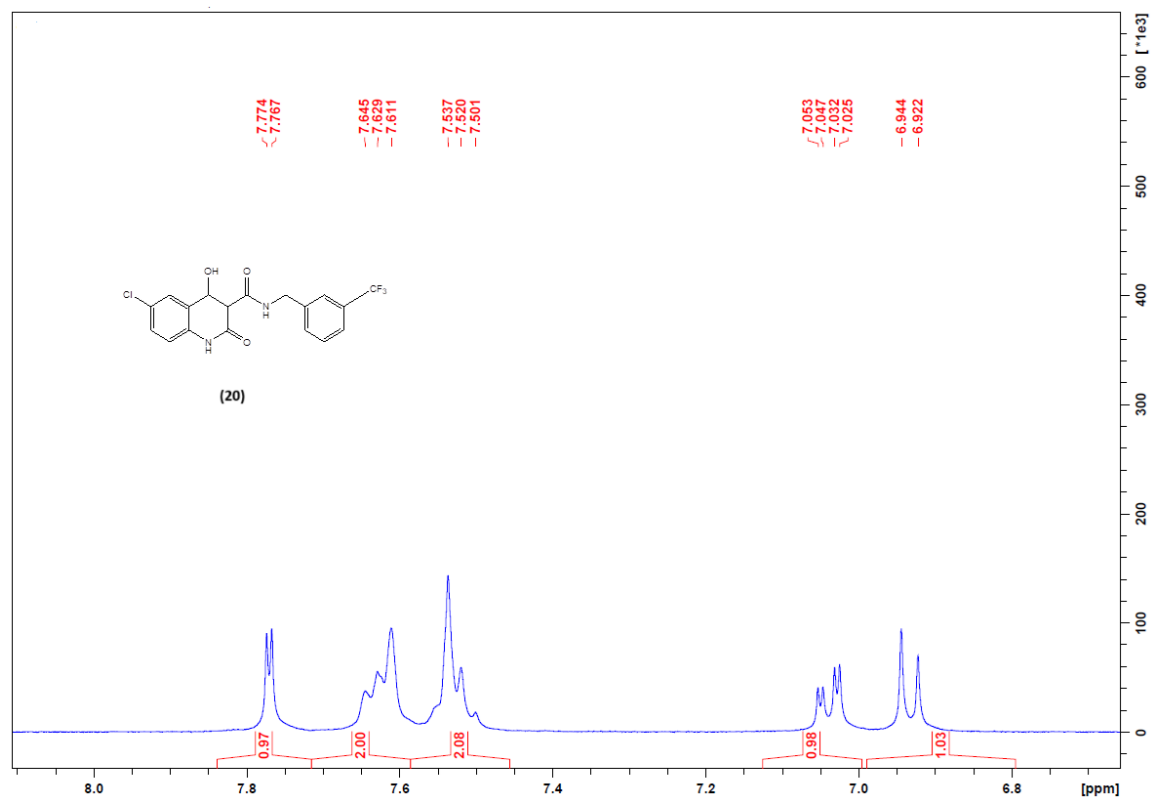
¹³C-DEPT-135-NMR (DMSO-*d*₆+NaOD) spectrum of *N*-(4-methylbenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide **(19)**.



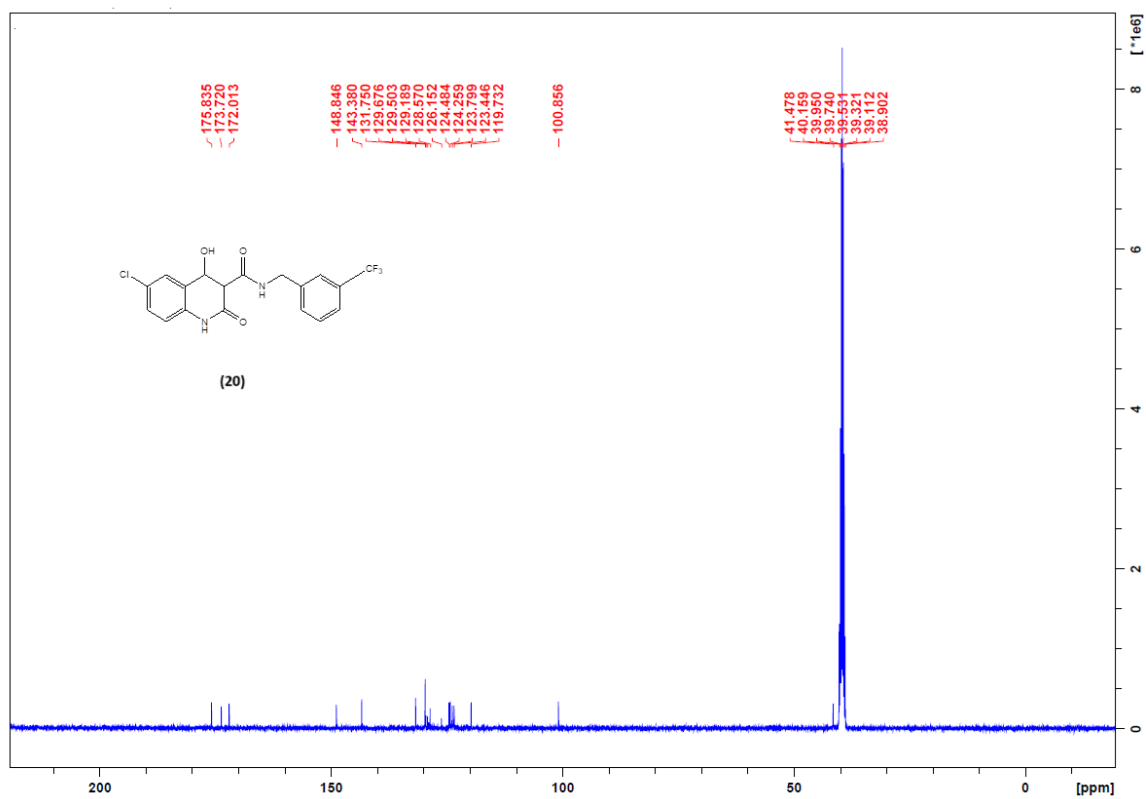
¹H-NMR (DMSO-*d*₆+NaOD) spectrum of *N*-(3-(trifluoromethyl) benzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**20**).



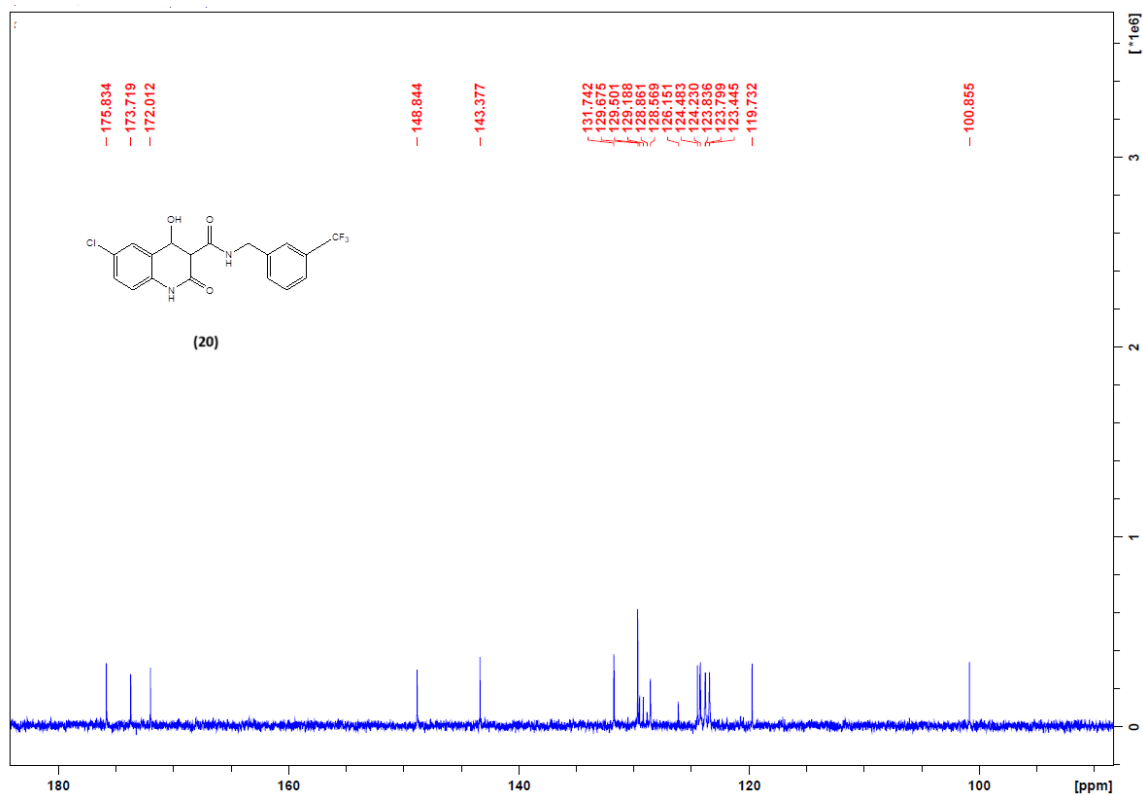
^1H -NMR (DMSO- d_6 +NaOD) spectrum of *N*-(3-(trifluoromethyl) benzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**20**).



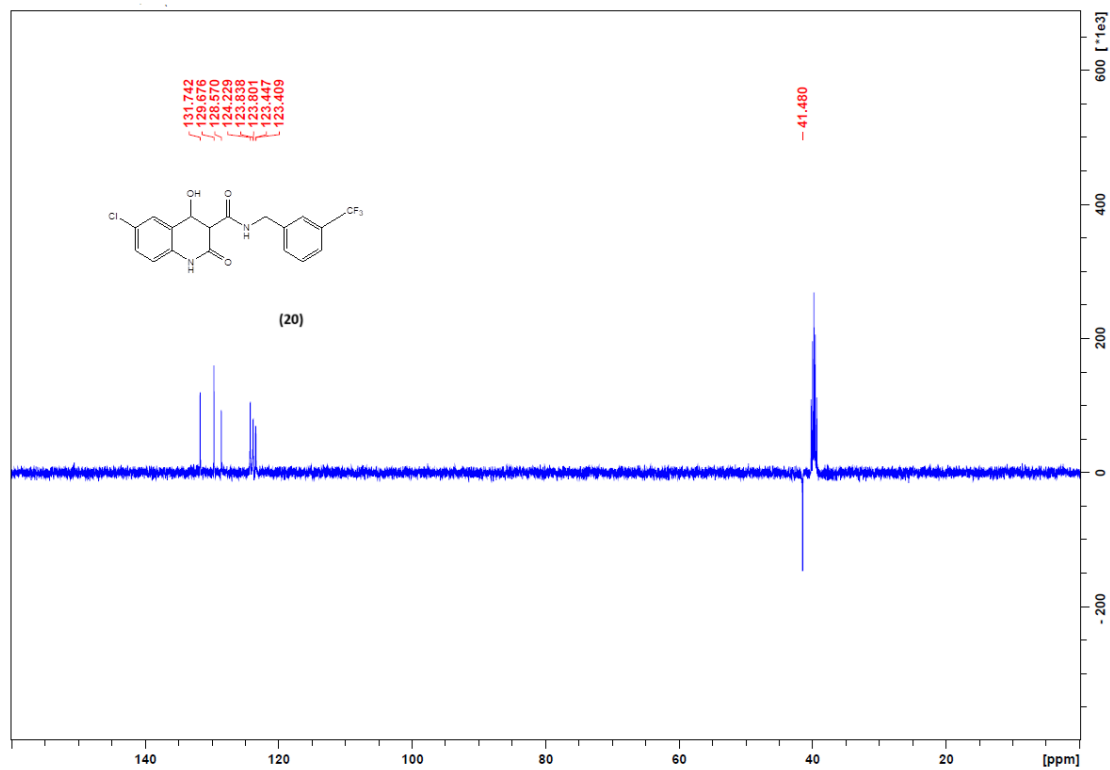
¹H-NMR (DMSO-*d*₆+NaOD) spectrum of *N*-(3-(trifluoromethyl) benzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**20**).



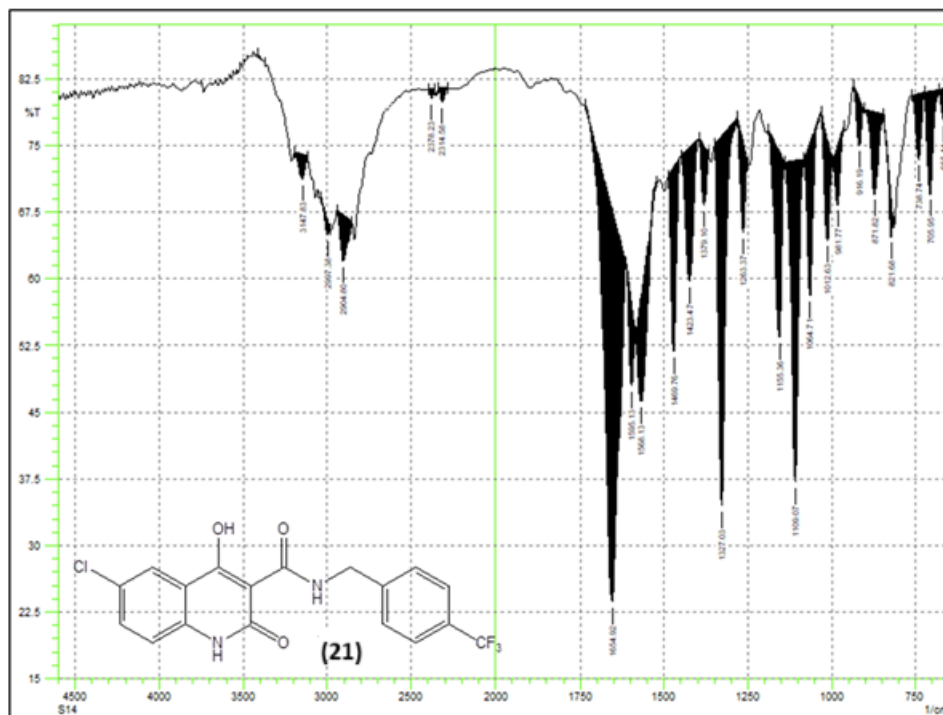
¹³C-NMR (DMSO-*d*₆+NaOD) spectrum of *N*-(3-(trifluoromethyl) benzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**20**).



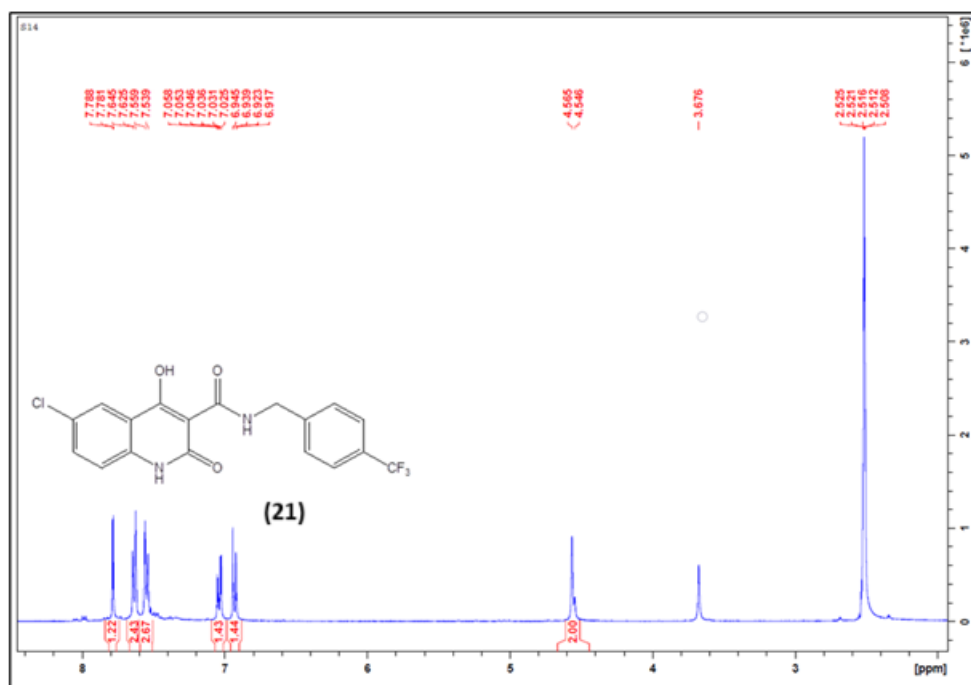
¹³C-NMR (DMSO-*d*₆+NaOD) spectrum of *N*-(3-(trifluoromethyl) benzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**(20)**).



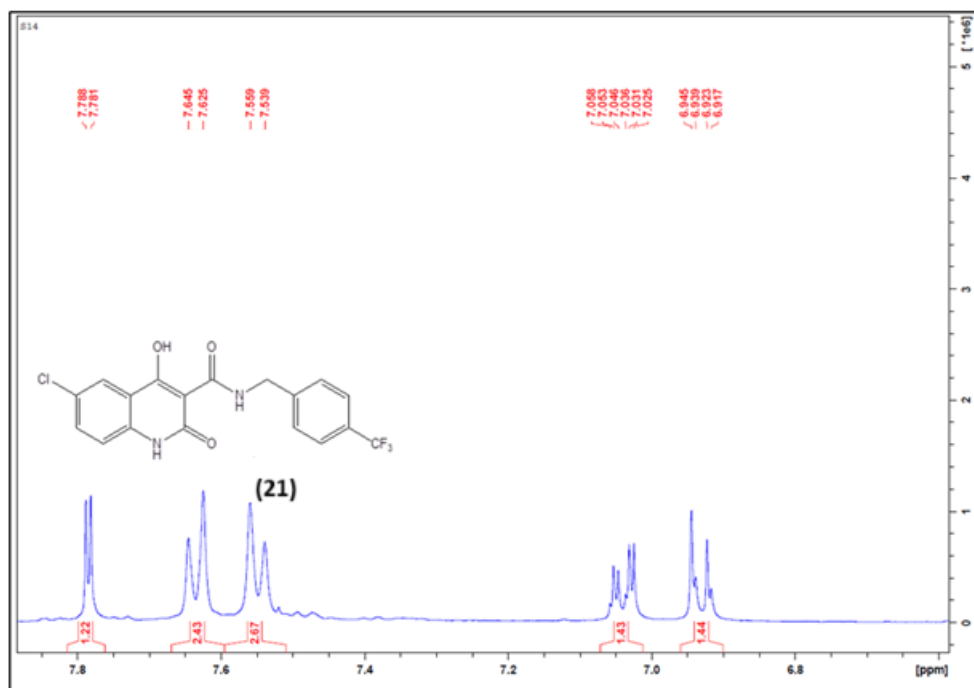
¹³C-DEPT-135-NMR (DMSO-*d*₆+NaOD) spectrum of *N*-(3-(trifluoromethyl) benzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**(20)**).



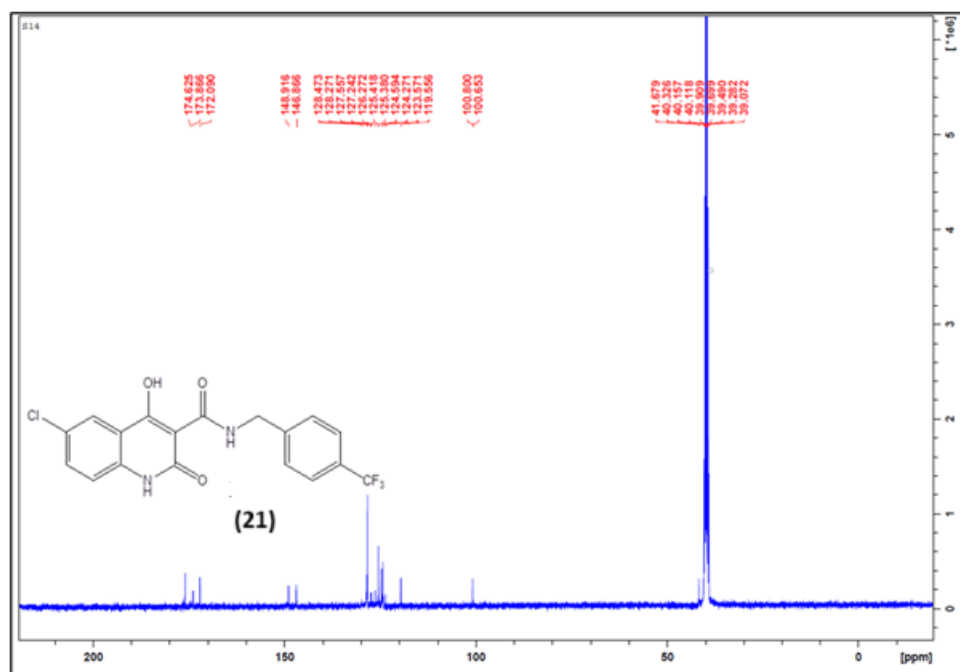
IR (KBr disc) spectrum of *N*-(4-(trifluoromethyl) benzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**21**).



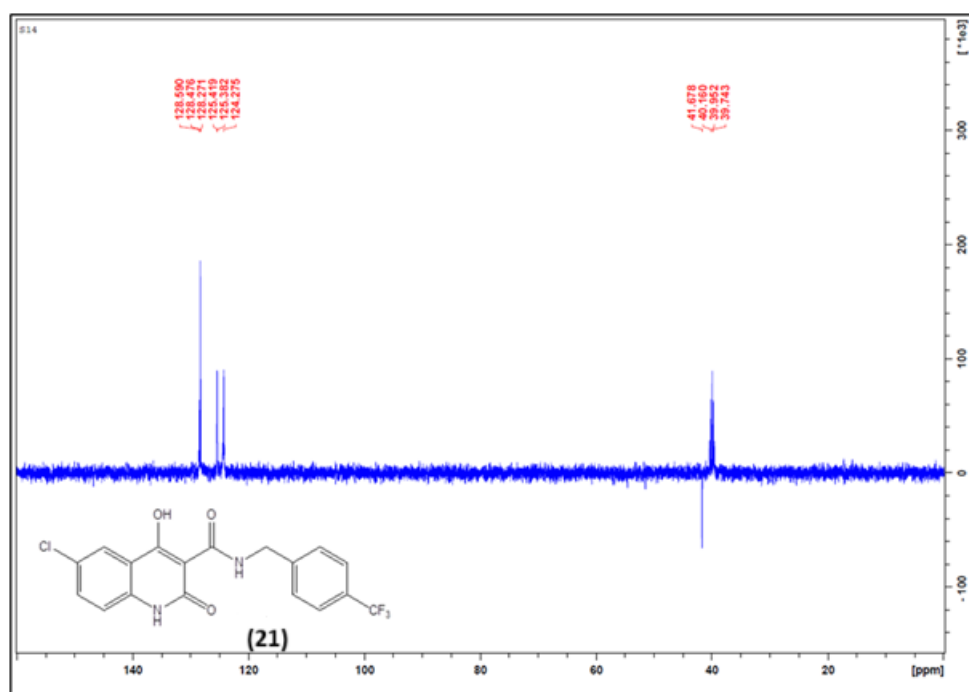
¹H-NMR (DMSO-*d*₆+NaOD) spectrum of *N*-(4-(trifluoromethyl) benzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**21**).



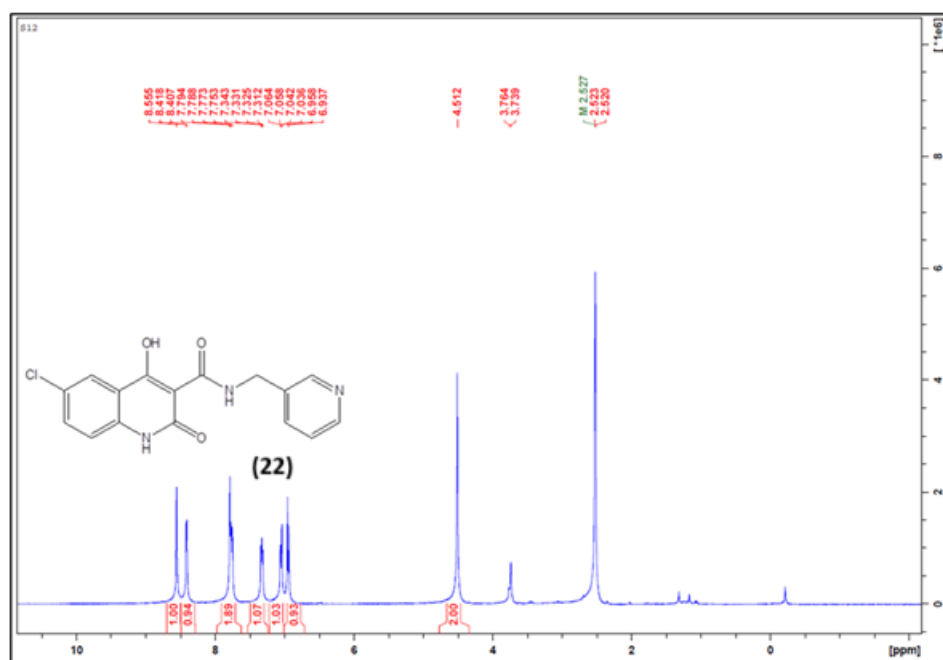
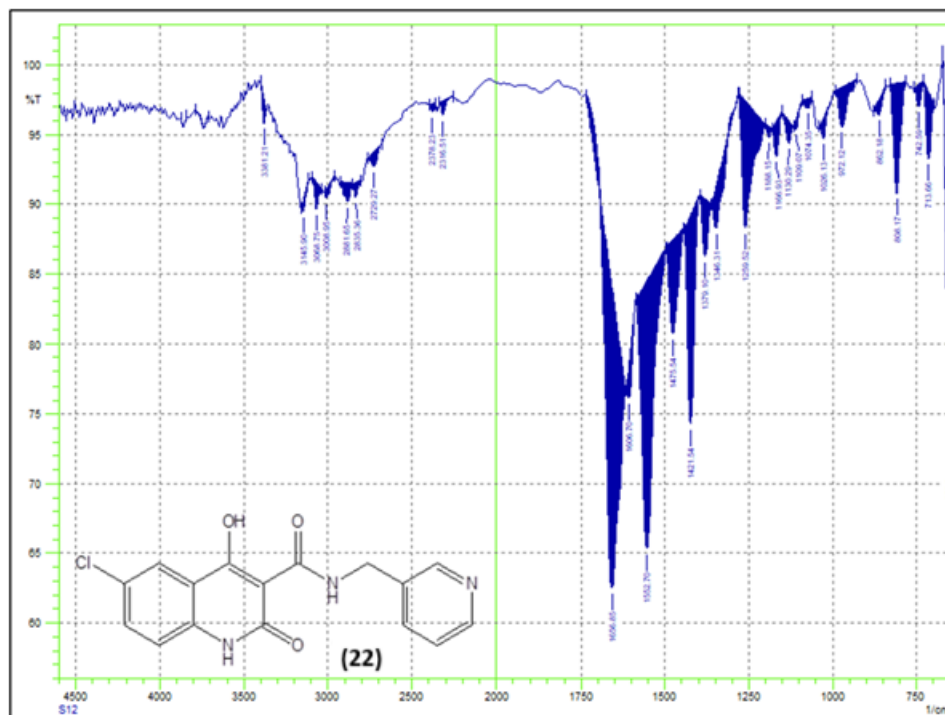
¹H-NMR (DMSO-*d*₆+NaOD) spectrum of *N*-(4-(trifluoromethyl) benzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**21**).

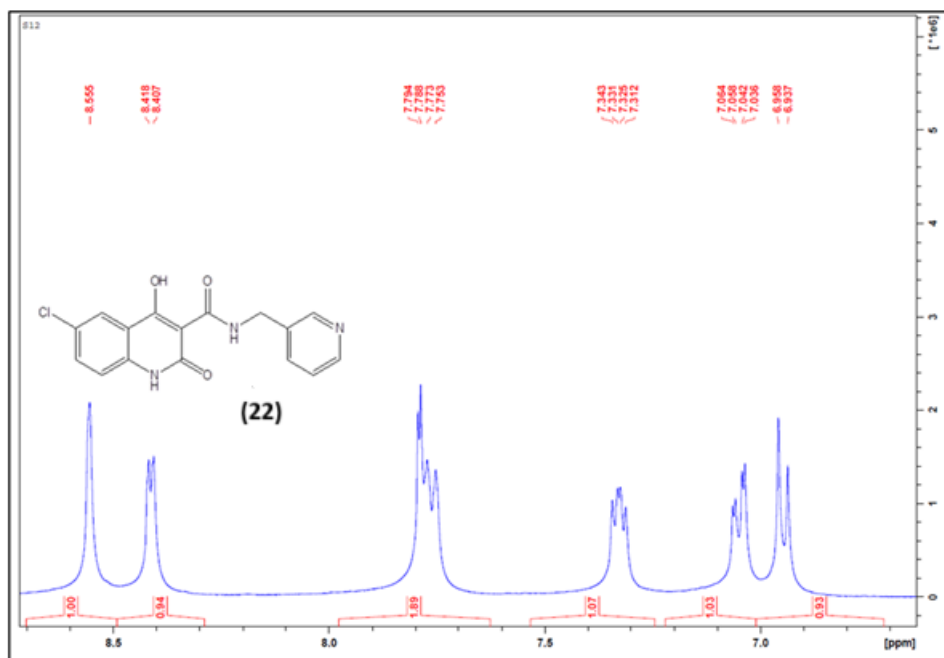


¹³C-NMR (DMSO-*d*₆+NaOD) spectrum of *N*-(4-(trifluoromethyl) benzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**21**).

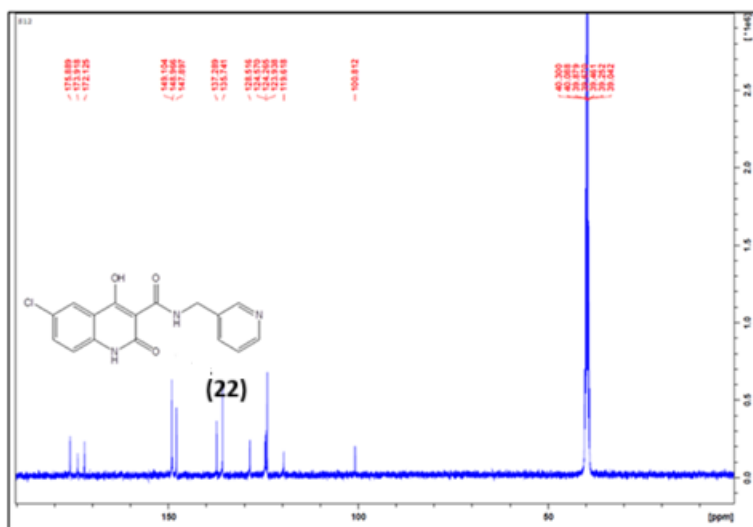


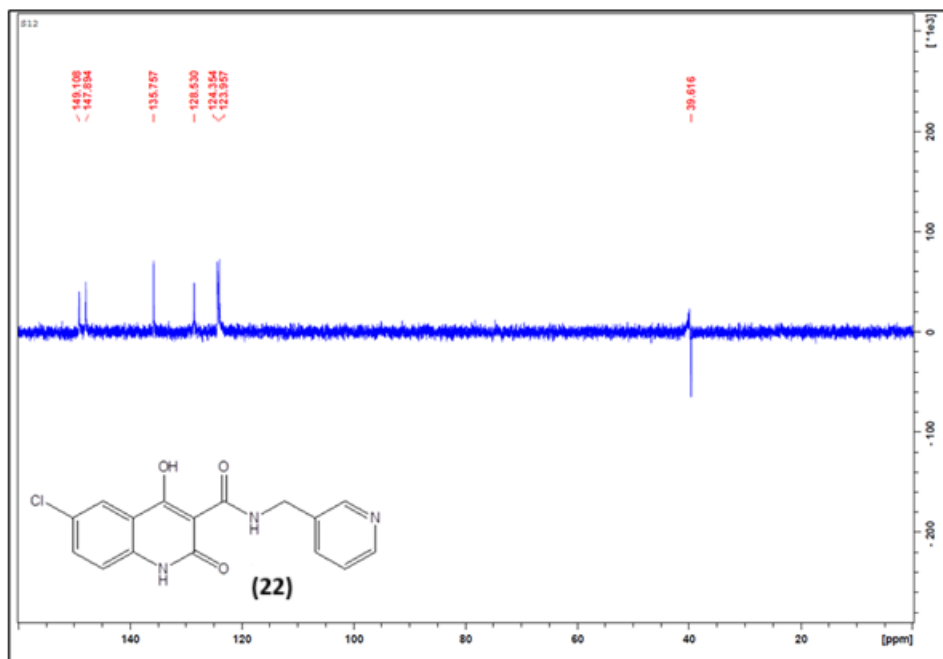
^{13}C -DEPT-135-NMR ($\text{DMSO-}d_6 + \text{NaOD}$) spectrum of *N*-(4-(trifluoromethyl) benzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**21**).



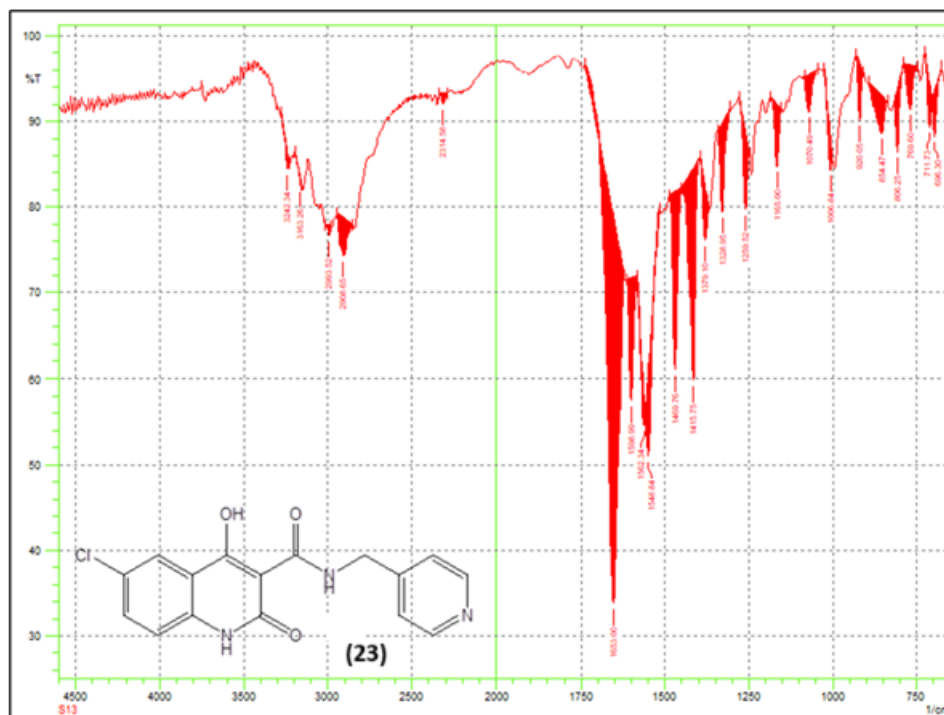


¹H-NMR(DMSO-*d*₆+NaOD) spectrum of *N*-(pyridine-3-ylmethyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**22**).

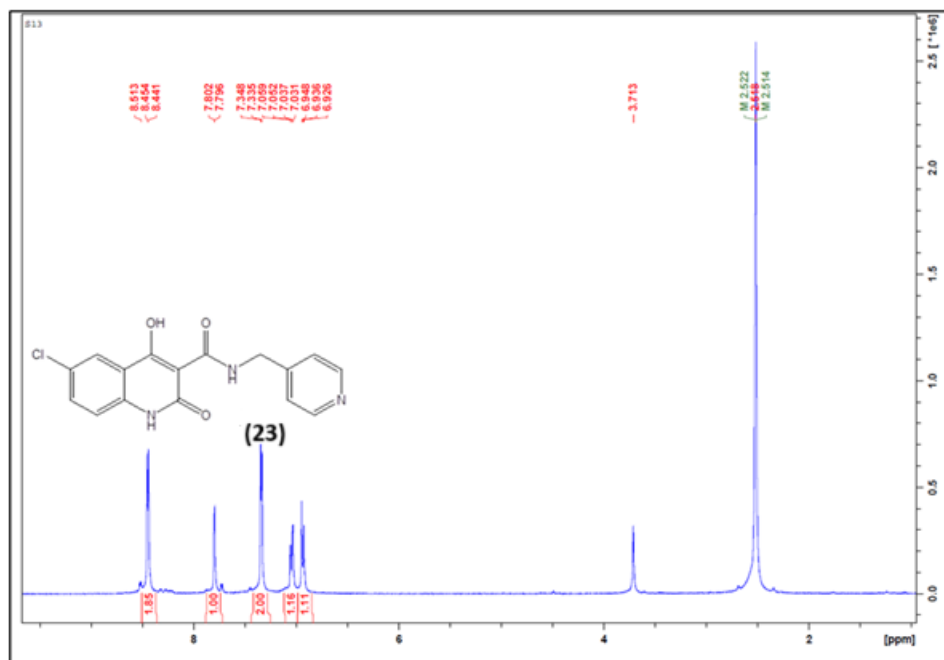




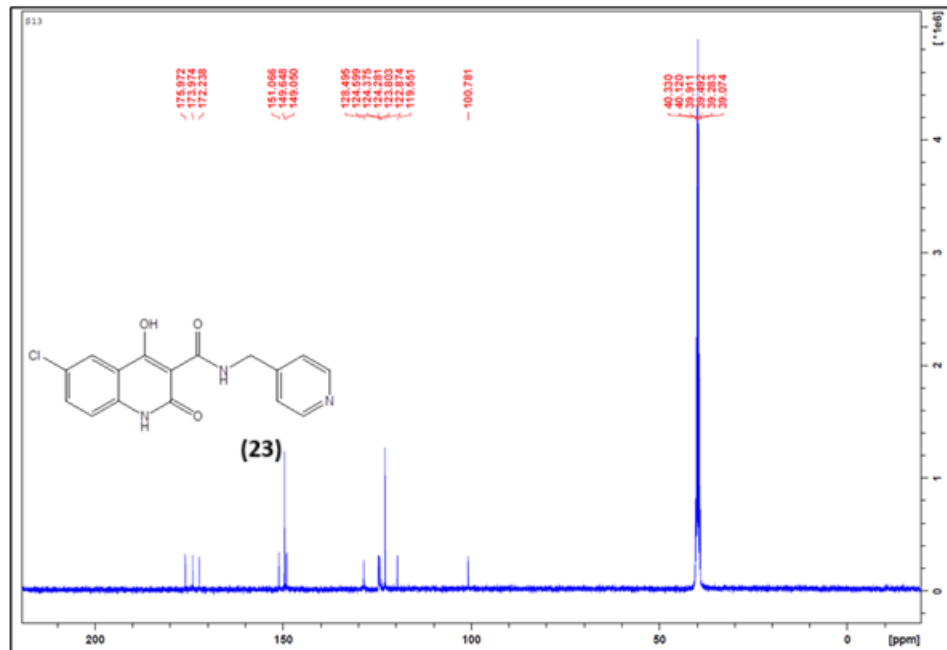
^{13}C -DEPT-NMR ($\text{DMSO-}d_6 + \text{NaOD}$) spectrum of *N*-(pyridine-3-ylmethyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**22**).



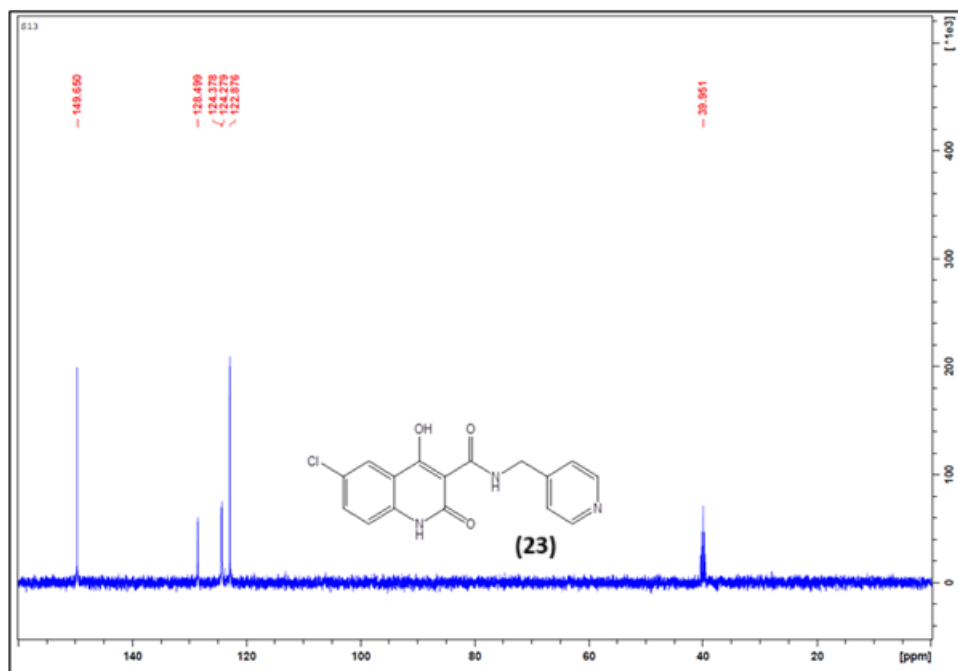
IR (KBr disc) spectrum of *N*-(pyridine-4-ylmethyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**23**).



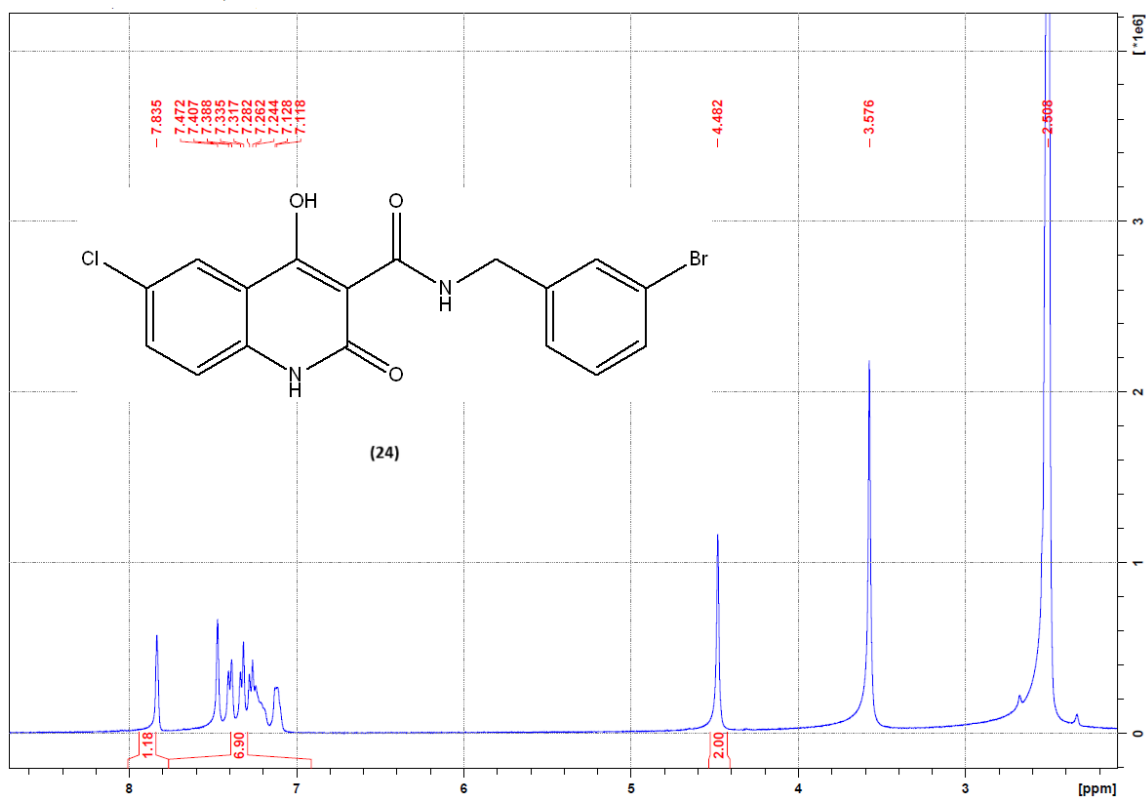
¹H-NMR(DMSO-*d*₆+NaOD) spectrum of *N*-(pyridine-4-ylmethyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**23**).



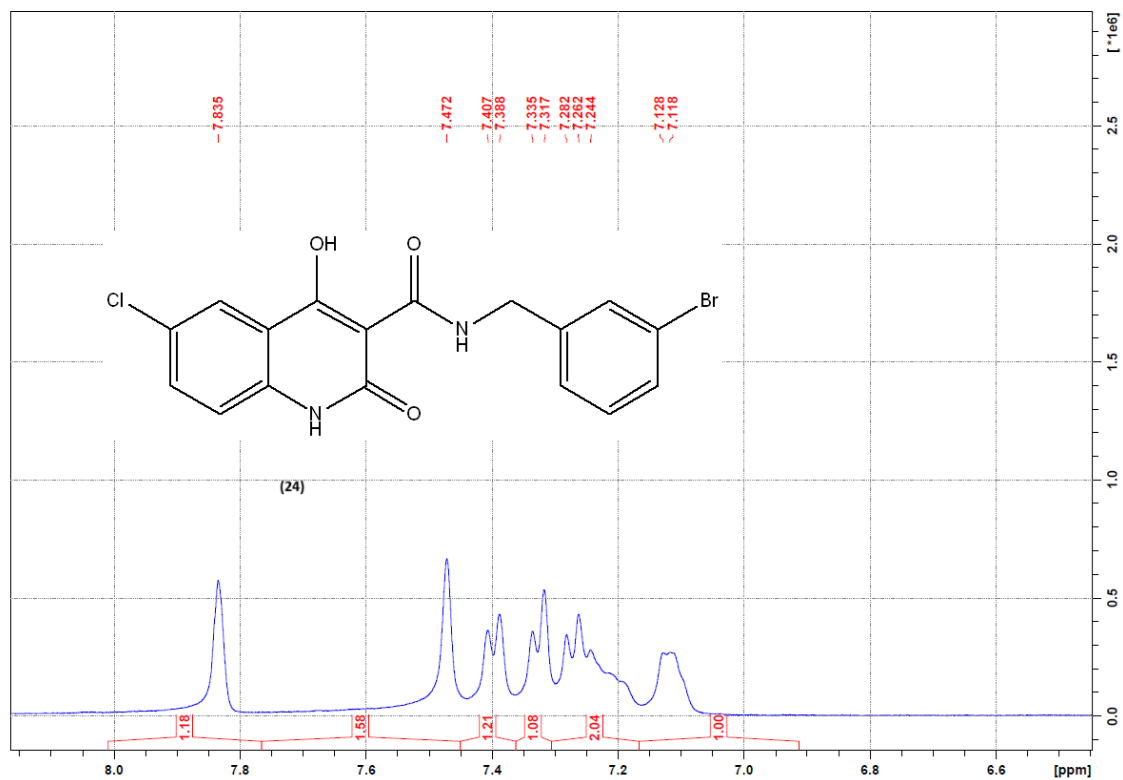
¹³C-NMR (DMSO-*d*₆+NaOD) spectrum of *N*-(pyridine-4-ylmethyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**23**).



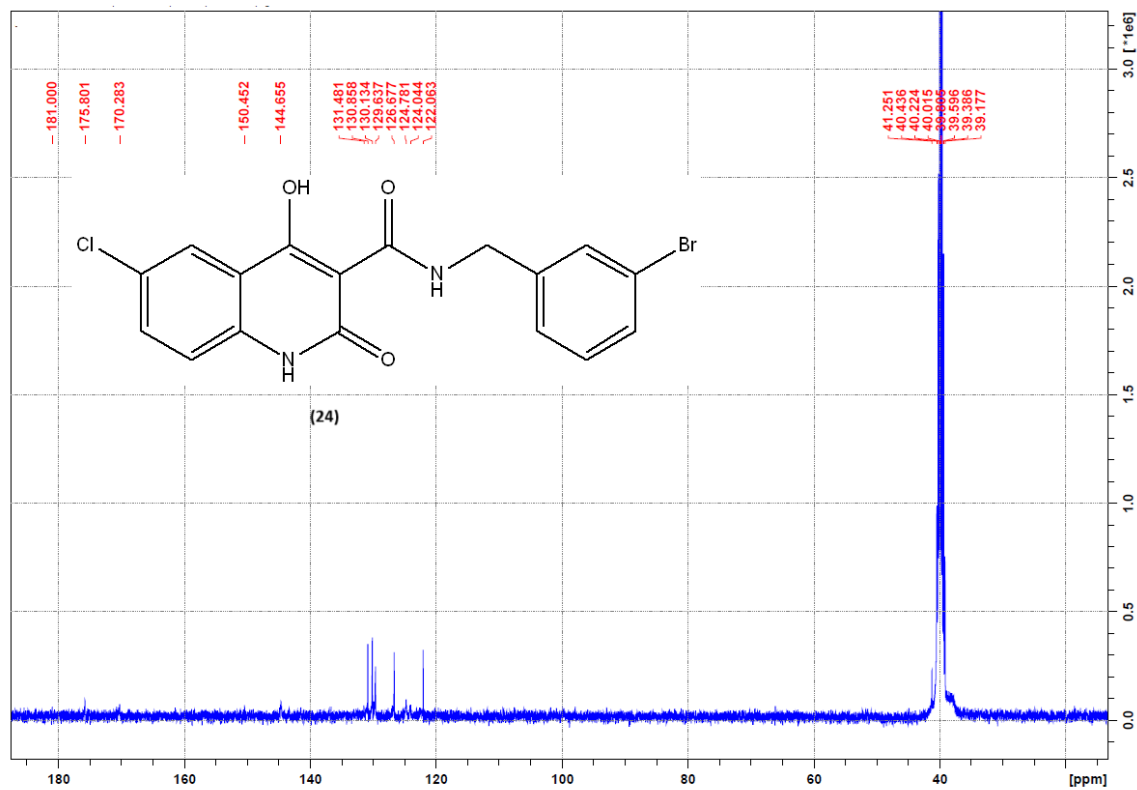
¹³C-DEPT-135-NMR (DMSO-*d*₆+NaOD) spectrum of *N*-(pyridine-4-ylmethyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**23**).



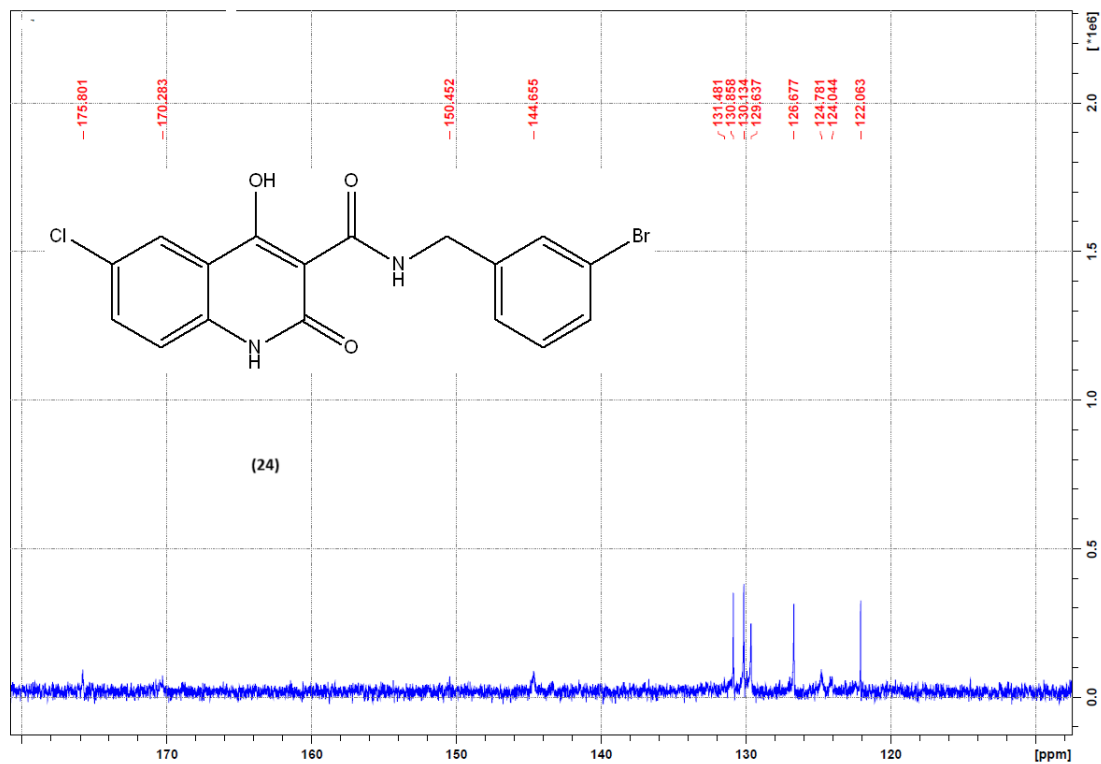
¹H-NMR(DMSO-*d*₆+NaOD) spectrum of *N*-(3-bromobenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**24**).



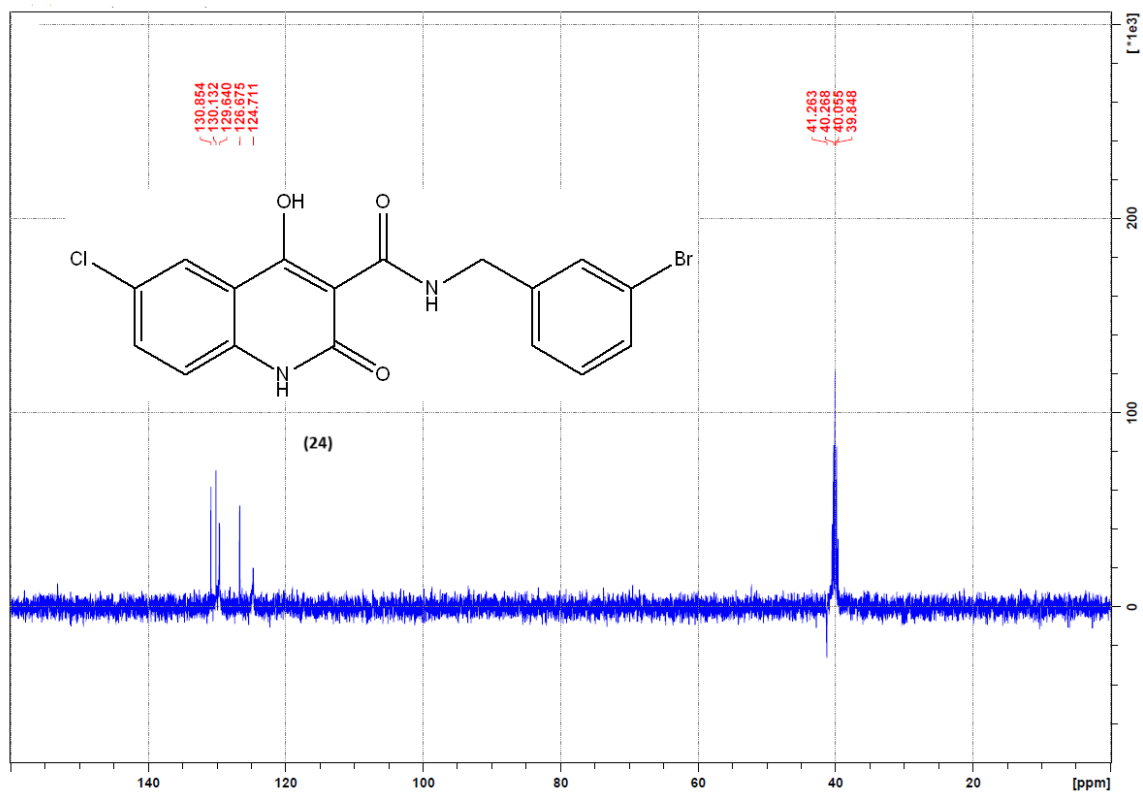
¹H-NMR(DMSO-*d*₆+NaOD) spectrum of *N*-(3-bromobenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**24**).



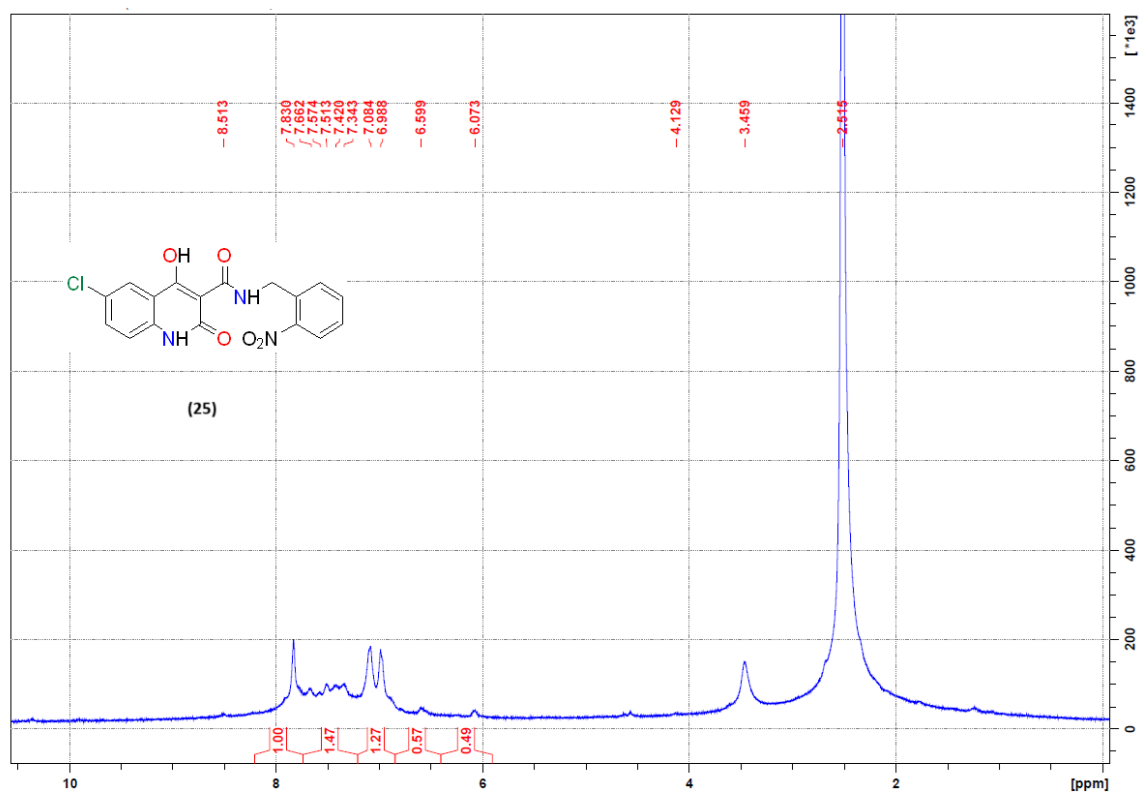
¹³C-NMR(DMSO-*d*₆+NaOD) spectrum of *N*-(3-bromobenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**24**).



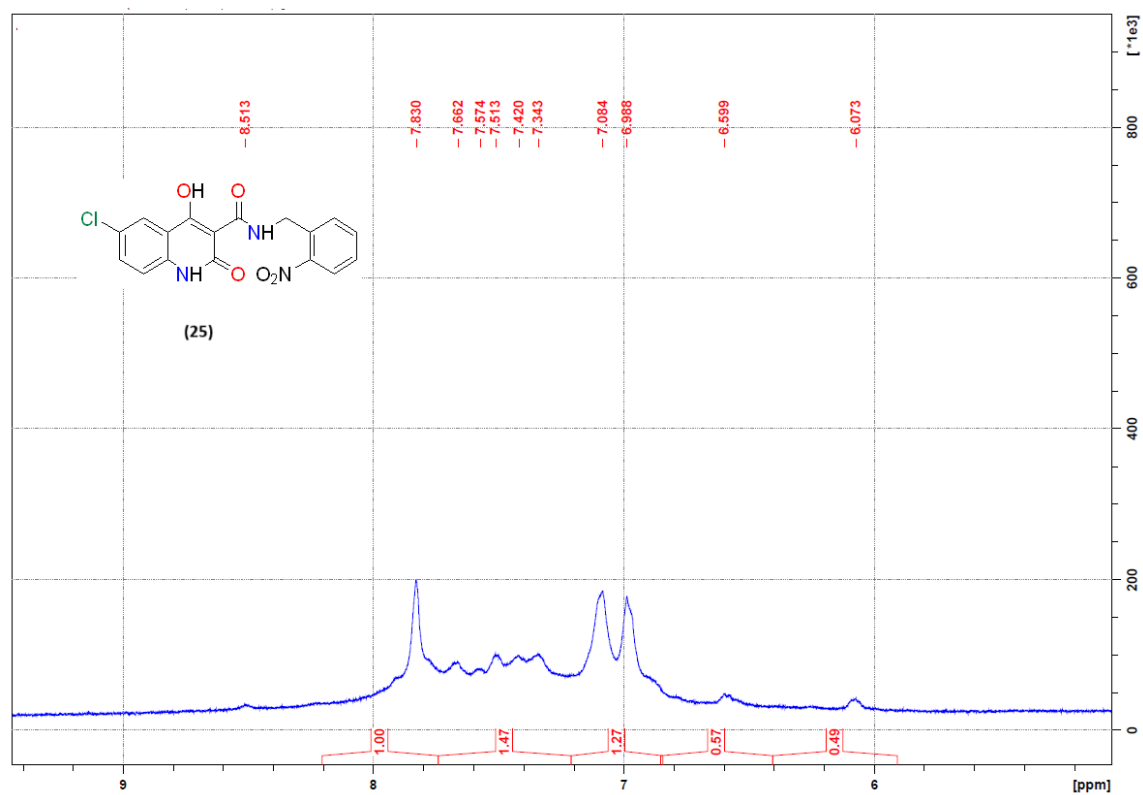
¹³C-NMR(DMSO-*d*₆+NaOD) spectrum of *N*-(3-bromobenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**24**).



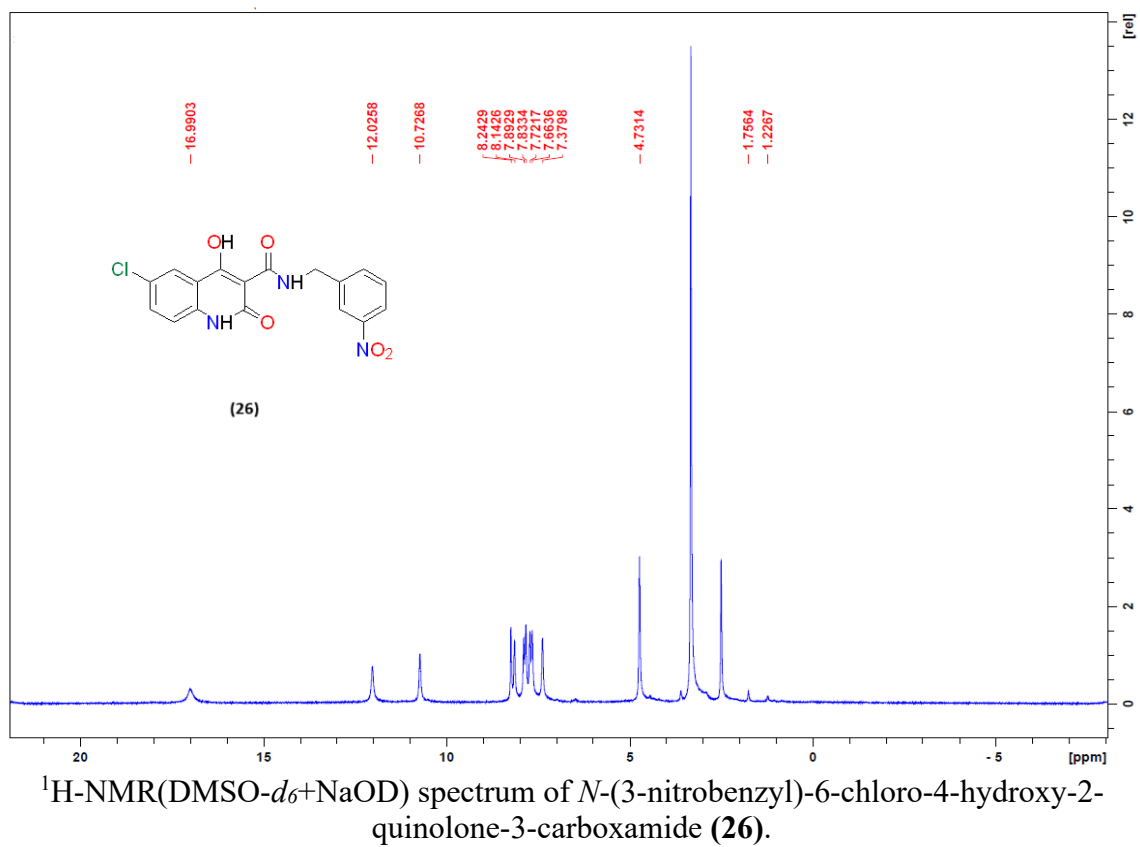
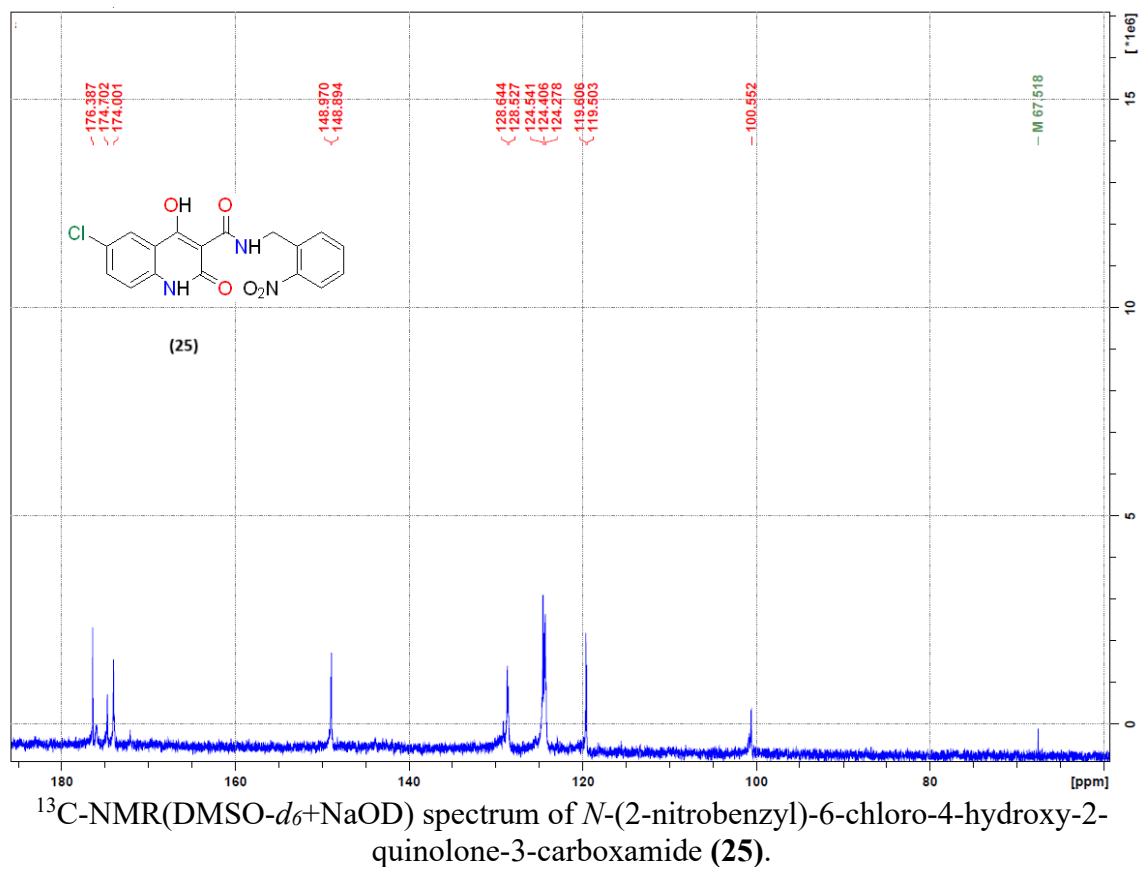
^{13}C -DEPT-135-NMR (DMSO- d_6 +NaOD) spectrum of *N*-(3-bromobenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**24**).

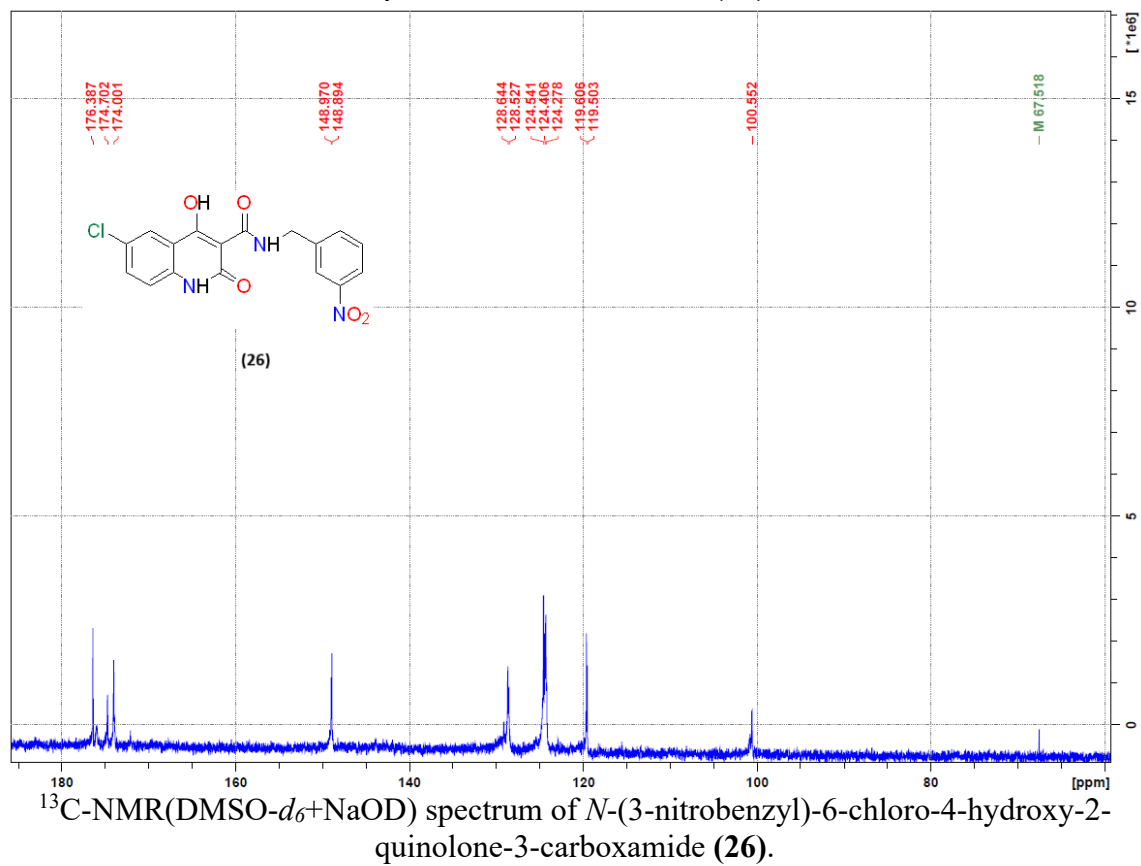
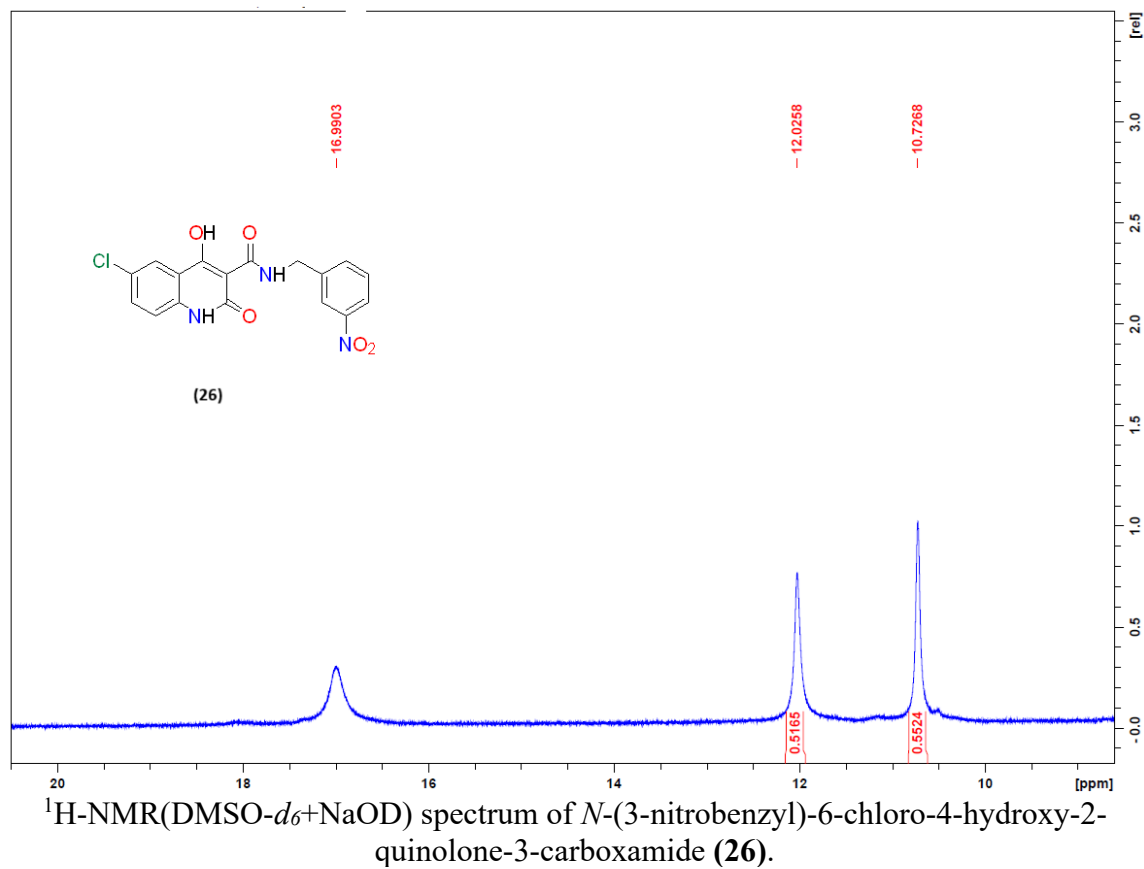


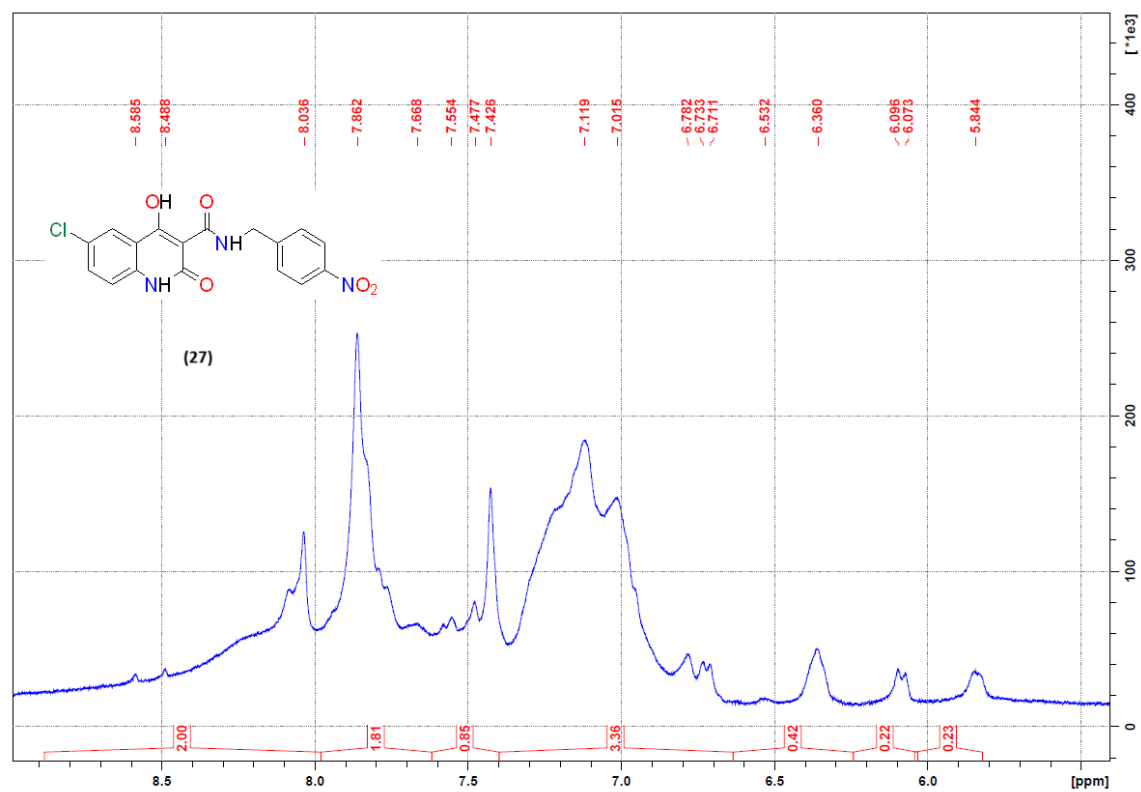
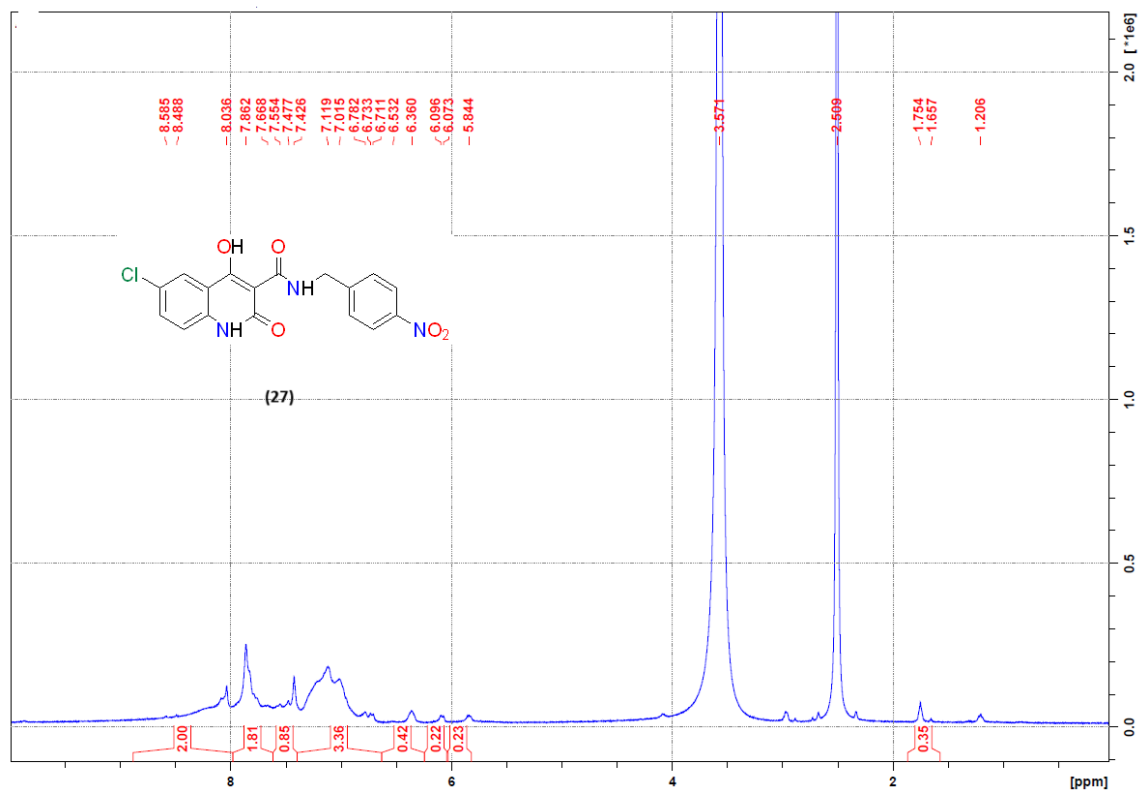
^1H -NMR($\text{DMSO-}d_6 + \text{NaOD}$) spectrum of *N*-(2-nitrobenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**25**).



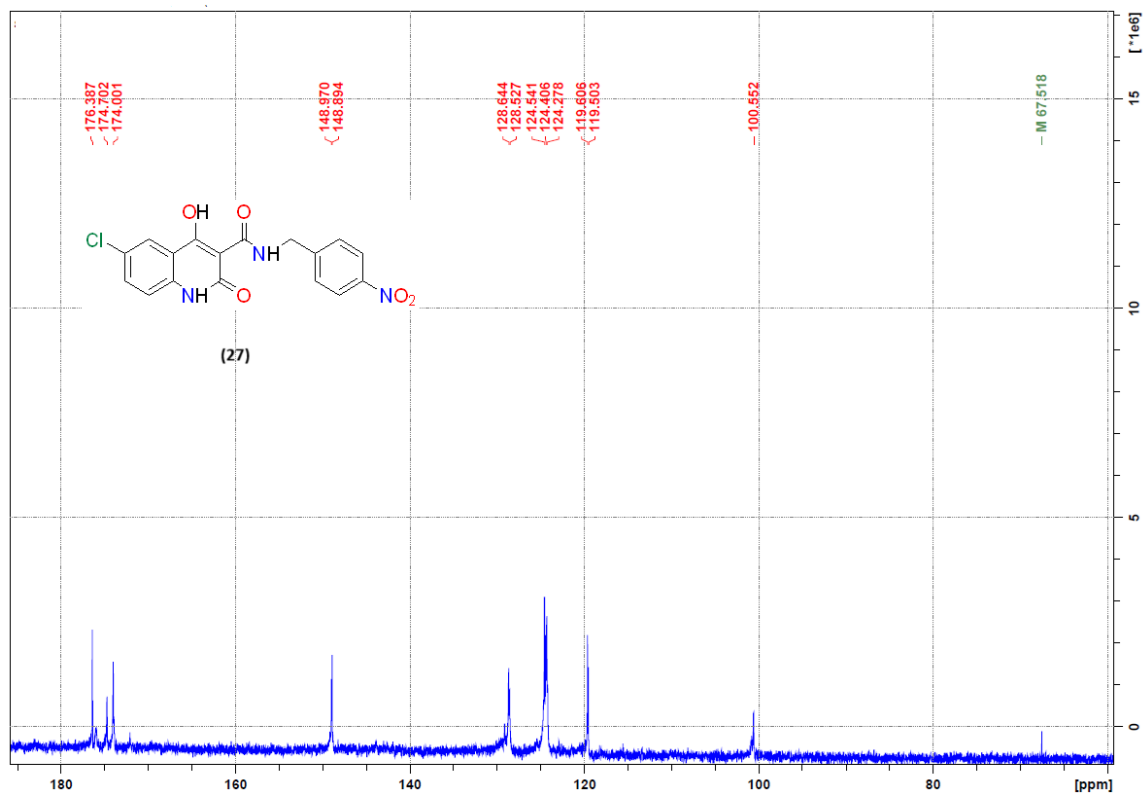
^1H -NMR($\text{DMSO-}d_6 + \text{NaOD}$) spectrum of *N*-(2-nitrobenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**25**).







^1H -NMR($\text{DMSO-}d_6$ +NaOD) spectrum of *N*-(4-nitrobenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**27**).



^{13}C -NMR($\text{DMSO-}d_6$ +NaOD) spectrum of *N*-(4-nitrobenzyl)-6-chloro-4-hydroxy-2-quinolone-3-carboxamide (**27**).