Supplementary Material

3a-(4-Chlorophenyl)-1-methyl-3a,4-dihydroimidazo[1,5-*a*]quinazolin-5(3*H*)-one: Synthesis and In Silico Evaluation as a Ligand in the μ-Opioid Receptor

Contents

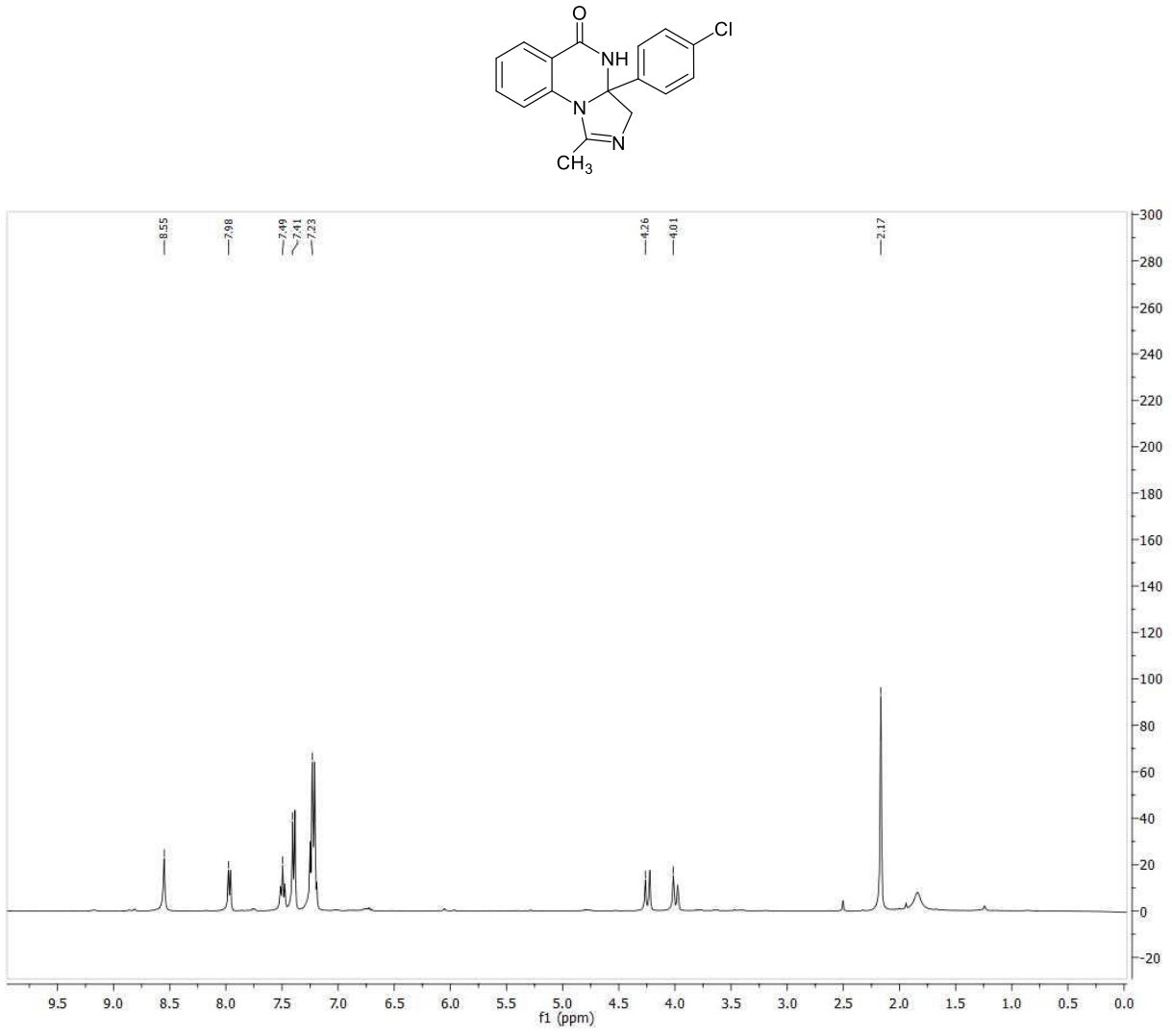

Figure S1. [1]HNMR spectrum of the title compound recorded in $CDCl_3$ at 400MHz.

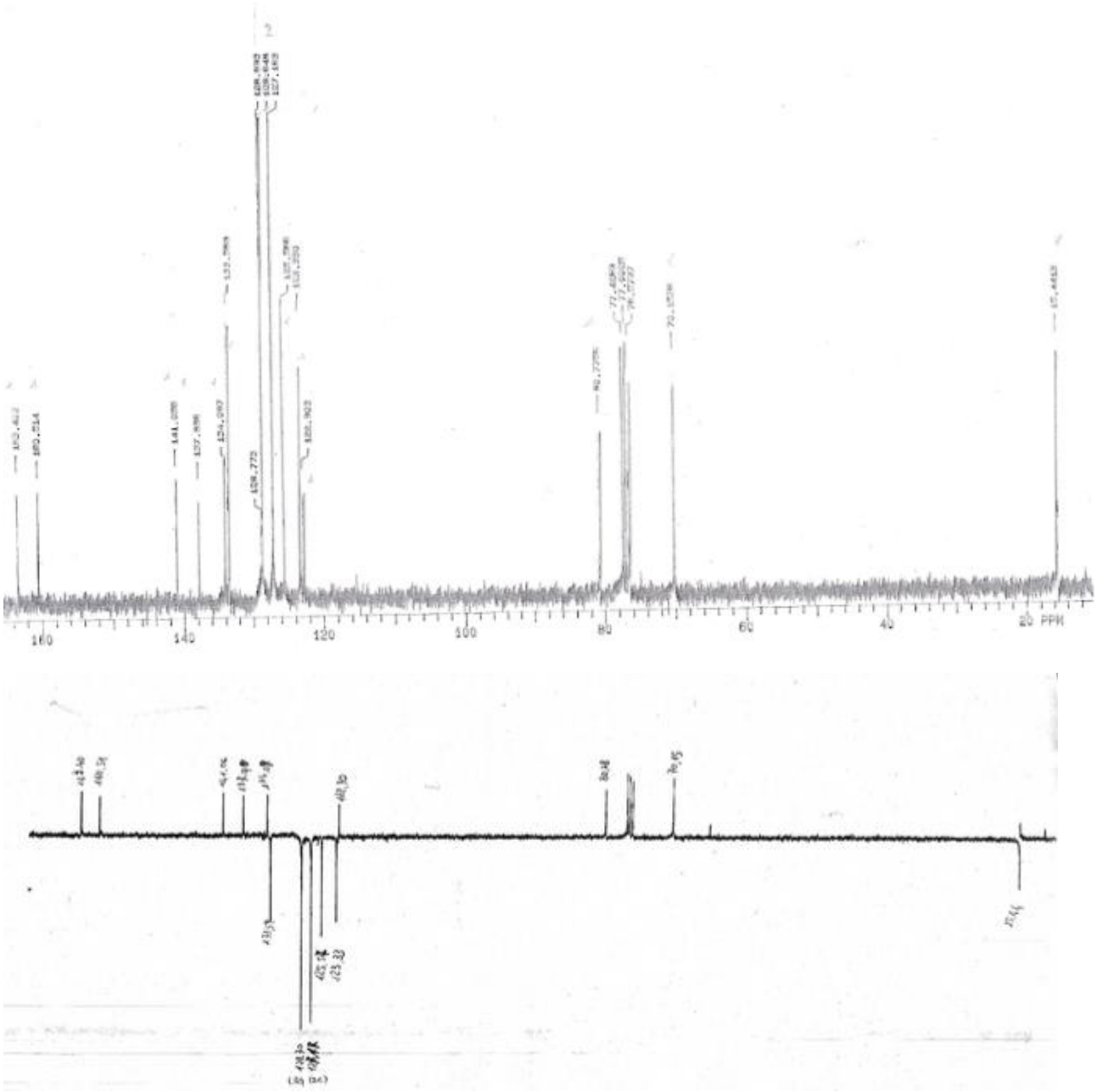

Figure S2. ^{13}CNMR and APT spectra of the title compound recorded in $CDCl_3$ at 75.43 MHz.

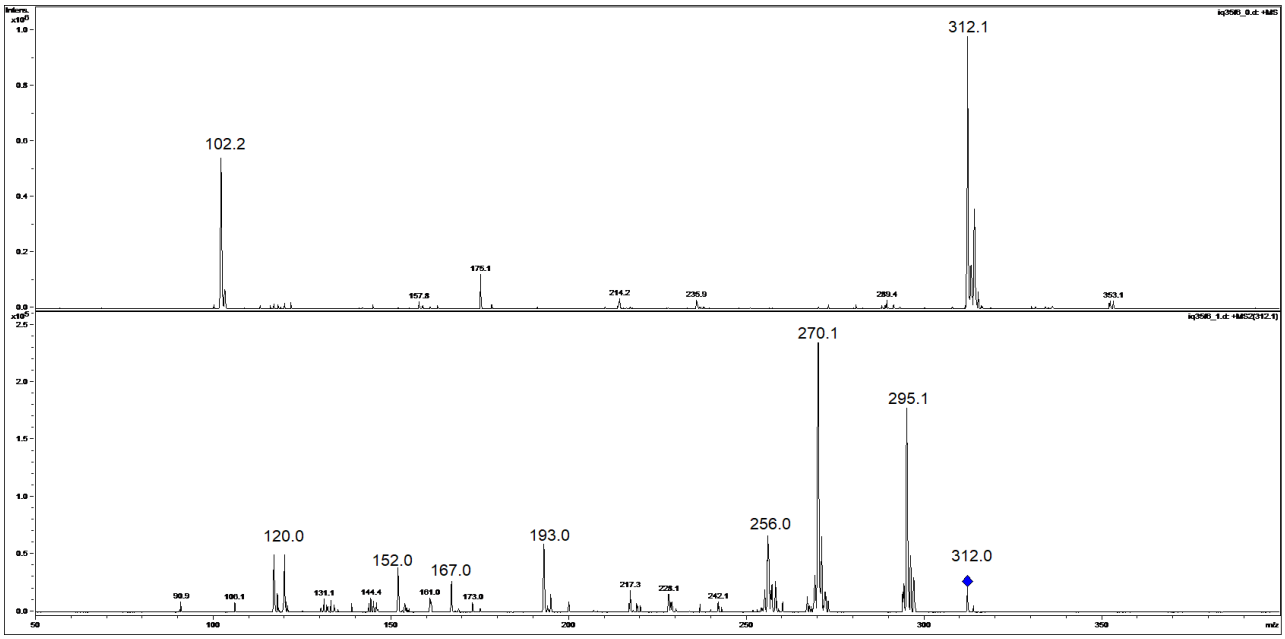

Figure S3. ESI(+)-MS spectrum of title compound and data from MS/MS fragmentation experiment on the $[M+H]^+$ ion at *m*/z 312.

Table S1. Energy values and interactions with μ-opioid receptor obtained by docking calculation using the Autodock Vina tool of title compound enantiomers (*S*)-**5** and (*R*)-**5** and the known opioids BU72, morphine and fentanyl, each of them considered in both neutral and protonated forms.

Compound	Energy (kcal/mol)	H-bond	π interactions	VdW interactions	Charge-charge interactions
BU72	-12.1	-	Val300, His297	Ile144, Ile296, Ile322	Asp147
BU72 protonated	-12.6	His54	Ile144, His297, Val300, Trp318,	Ile322, Ile296	Asp147
Morphine	-8.8	Tyr326	Tyr148, Met151 His297	Ile296, Val300, Ile322	-
Morphine protonated	-8.9	Asp147 Tyr326	Tyr148, Met151, His297	Ile296, Ile322	His297
Fentanyl	-8.8	-	Val143, Ile144, Met151, Cys217, Ile296, His297, Ile322, Tyr326	Ile296, Val300	-
Fentanyl protonated	-8.9	-	Val143, Ile144, Val236, Ile296 Trp293, Val300, Tyr326,	Ile322	Asp147, His54
(*R*)-5	-9.1	Tyr148	His54, Ile296, His297, Val300, Trp318	Lys233, Val236, Val300	-
(*R*)-5 protonated	-9.0	-	Asp147, Ser55, Trp293, Ile296, Ile322, Tyr326	Ile296, Ile322	Asp147
(*S*)-5	-9.0	-	Tyr148, Val236, Ile296, Ile322, Val300, Tyr326,	Lys233, Val236, Val300, Ile322	-
(*S*)-5 protonated	-9.1	His54	Tyr148, Met151, Ile236, Ile296, Val300, Ile322, Tyr326	Lys233, Val236, Val300, Ile322	Asp147

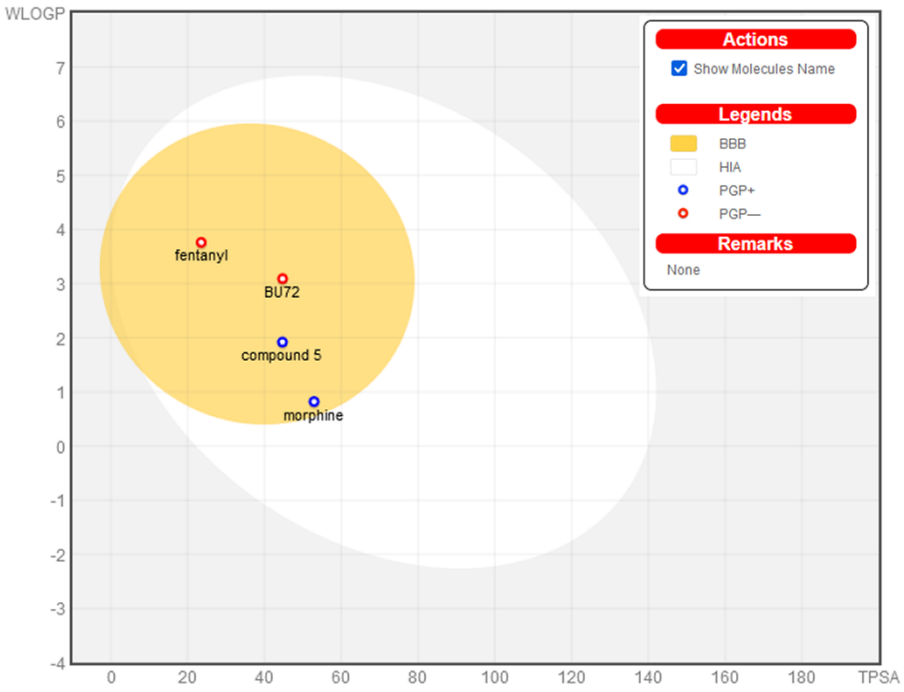

Figure S4. WLOGP-*versus*-TPSA in Brain Or IntestinaL EstimateD permeation method (BOILED)-Egg visualization for title compound **5**, morphine, fentanyl and BU72 evaluated by using Swiss-ADME software. Blue dots for P-glycoprotein (P-gp) substrates (PGP+) and red dots for P-gp non-substrate (PGP−). Swiss ADME. Available online: http://www.swissadme.ch/ (accessed on 4 March 2023).