Supporting Information

Green and efficient one-pot three-component synthesis of novel drug-like furo[2,3-*d*]pyrimidines as potential active site inhibitors and putative allosteric hotspots modulators of both SARS-CoV-2 M^{Pro} and PL^{Pro}

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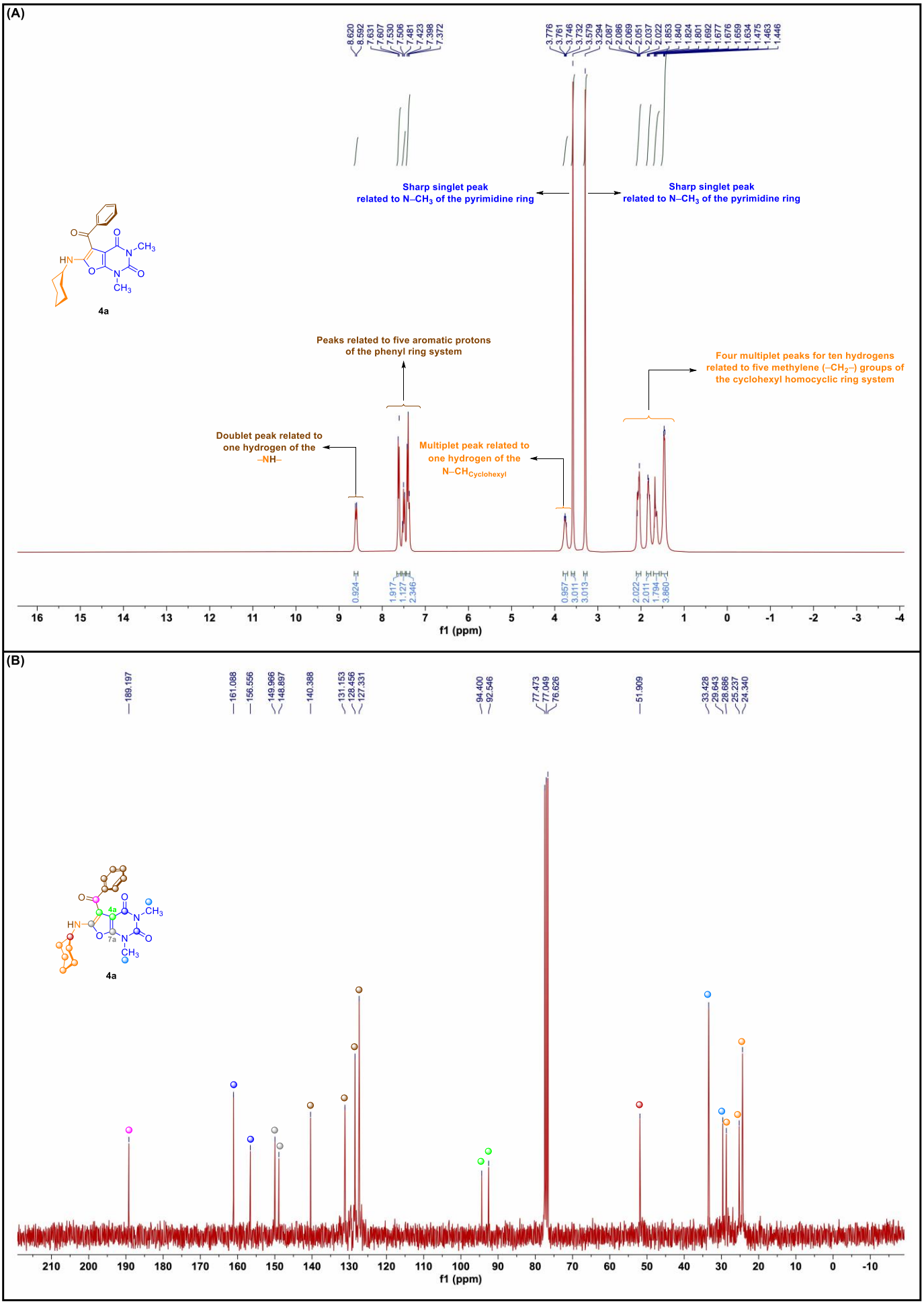


Figure S1. Characterized ^{1}H NMR (**A**) and $^{13}C\{^{1}H\}$ NMR (**B**) spectra of **4a**, respectively.

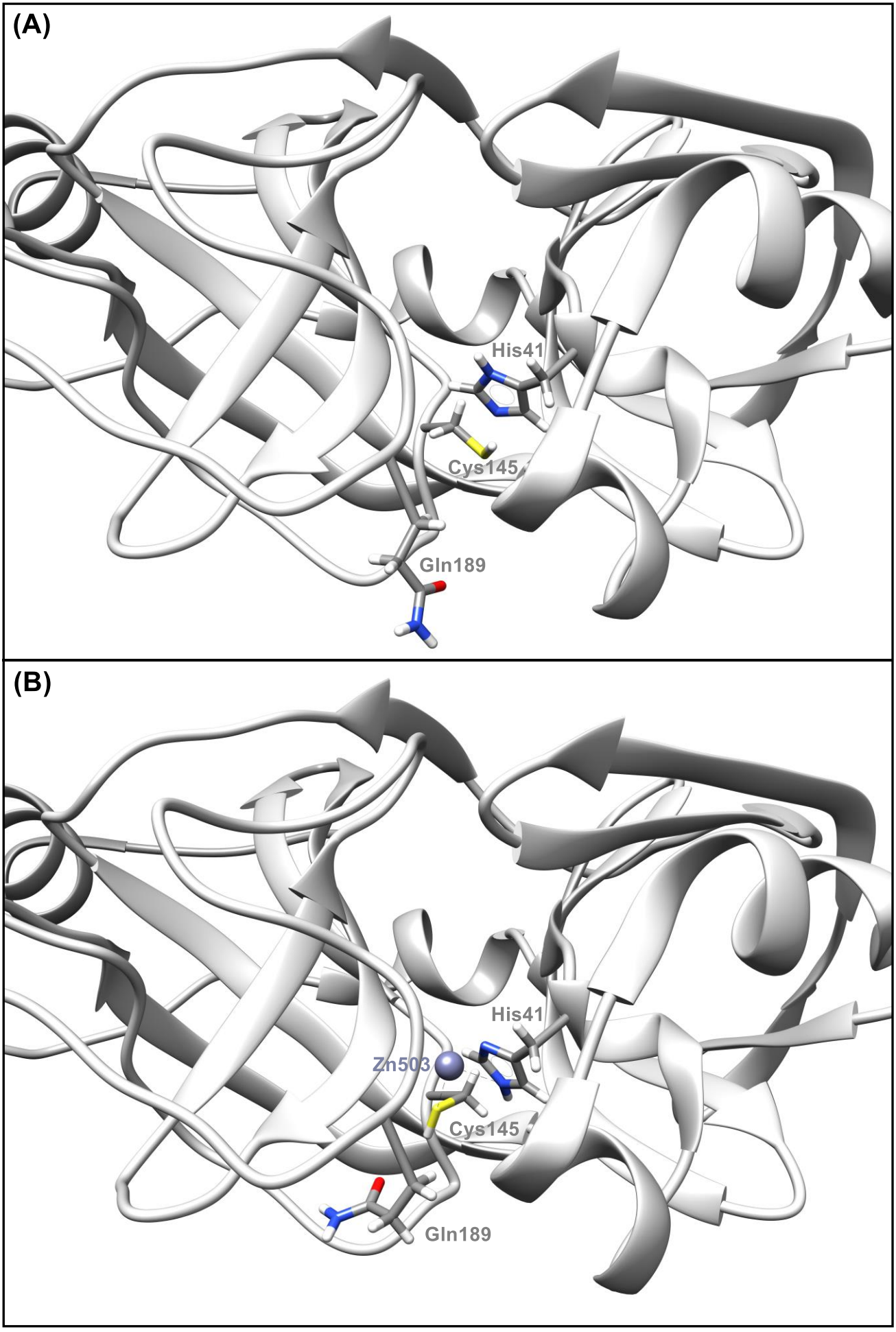


Figure S2. Views of the metal-free (**A**) and Zn^{II}-containing (**B**) SARS-CoV-2 M^{Pro} active site, respectively.

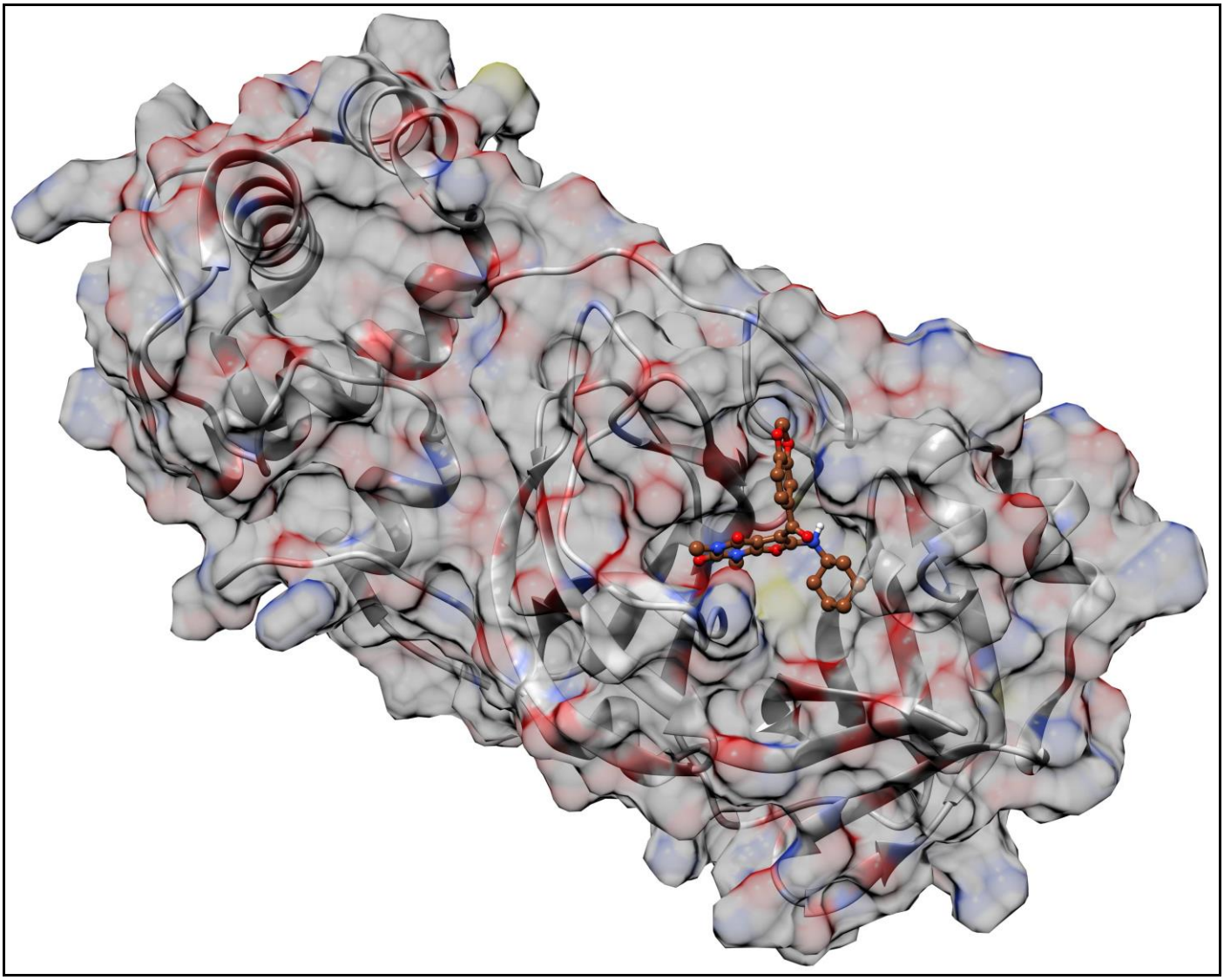


Figure S3. General perspective of the predicted position of **4g** in the metal-free active site of the SARS-CoV-2 M^{Pro} (PDB ID: 7AEH).

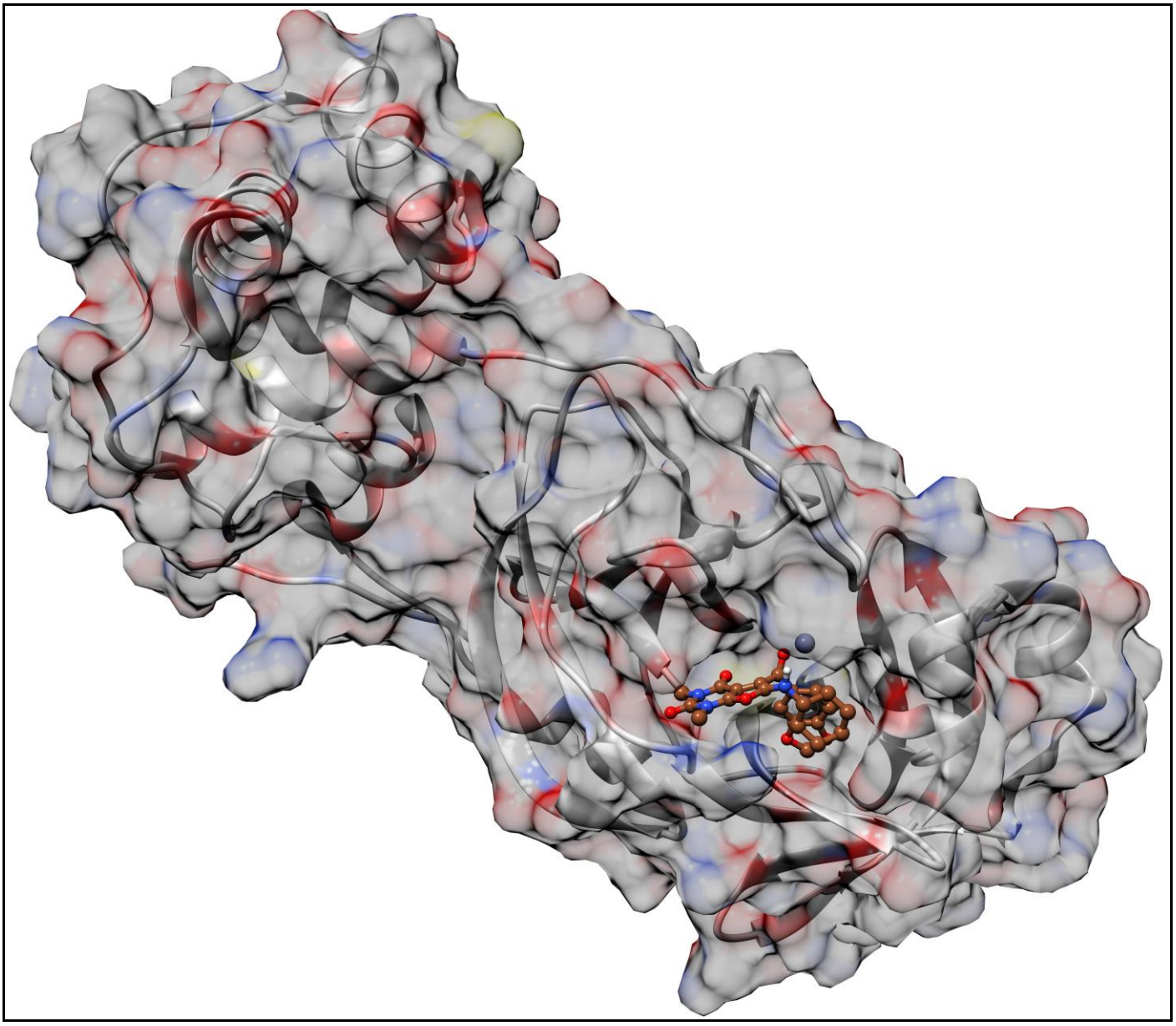


Figure S4. General perspective of the predicted position of **4g** in the Zn^{II}-containing active site of the SARS-CoV-2 M^{Pro} (PDB ID: 7MHK).

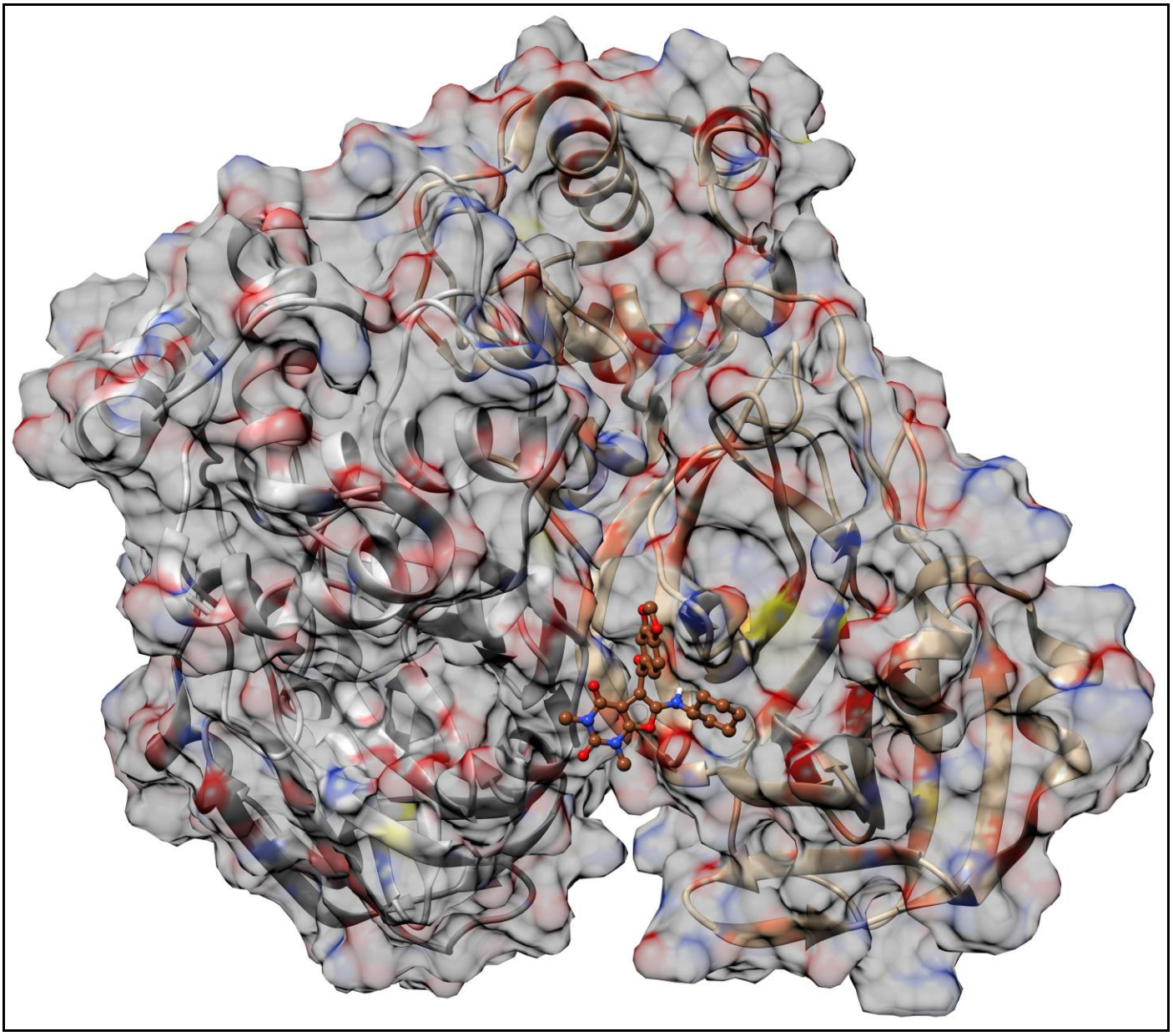


Figure S5. General perspective of the predicted position of **4g** in the allosteric site I (dimerization site) of the SARS-CoV-2 M^{Pro} (PDB ID: 7VLP).

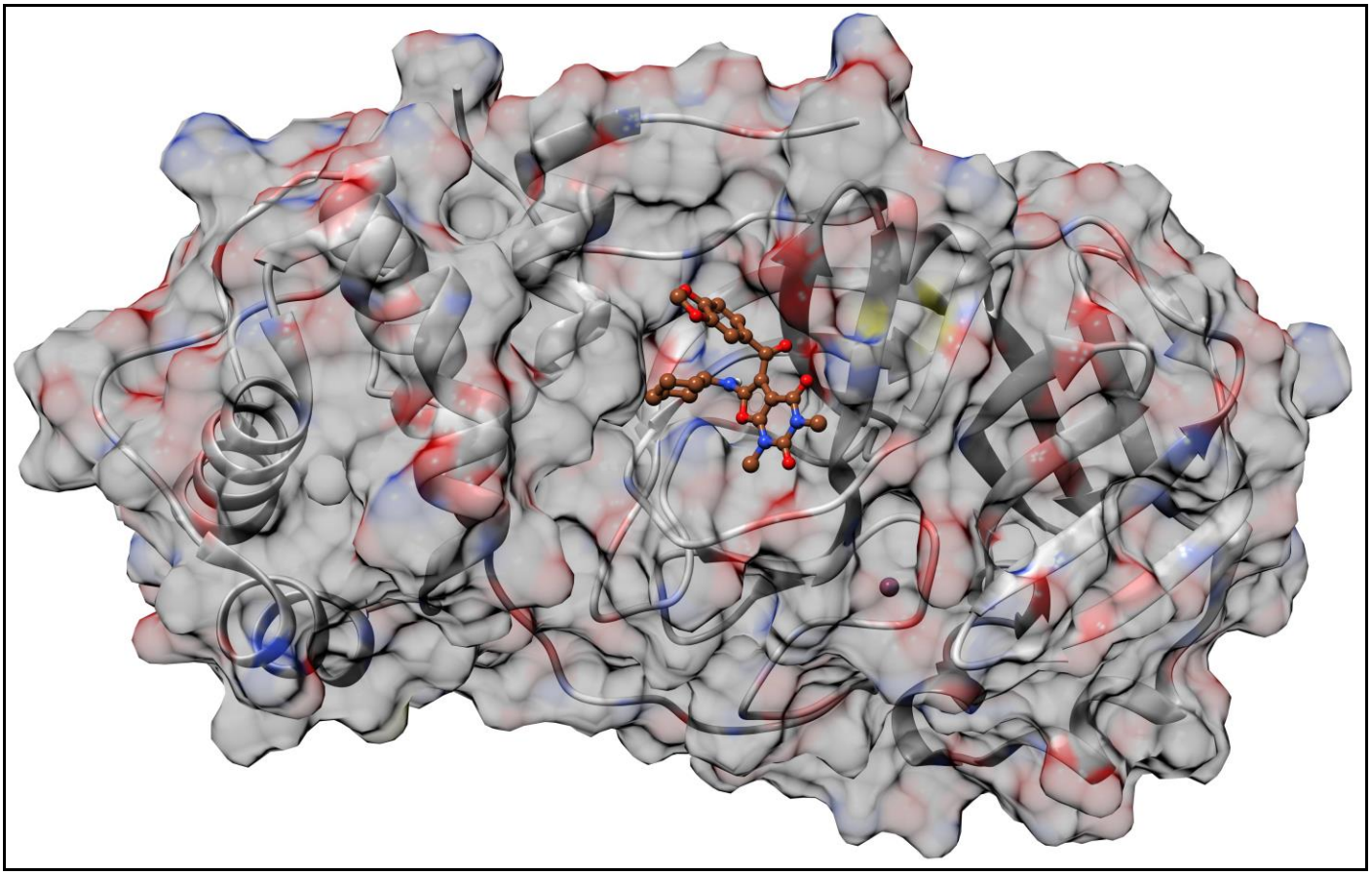


Figure S6. General perspective of the predicted position of **4g** in the allosteric site II (cryptic site) of the SARS-CoV-2 M^{Pro} (PDB ID: 7MHK).

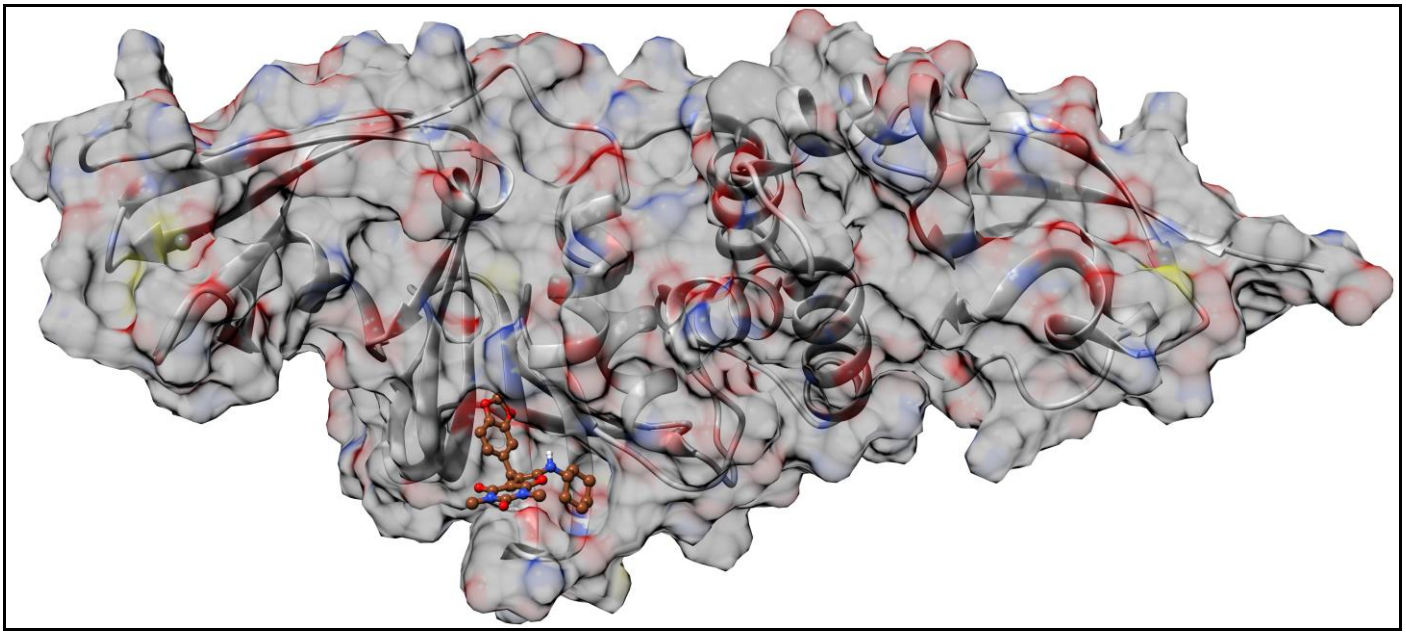


Figure S7. General perspective of the predicted position of **4g** in the active site of the SARS-CoV-2 PL^{Pro} (PDB ID: 6WX4).

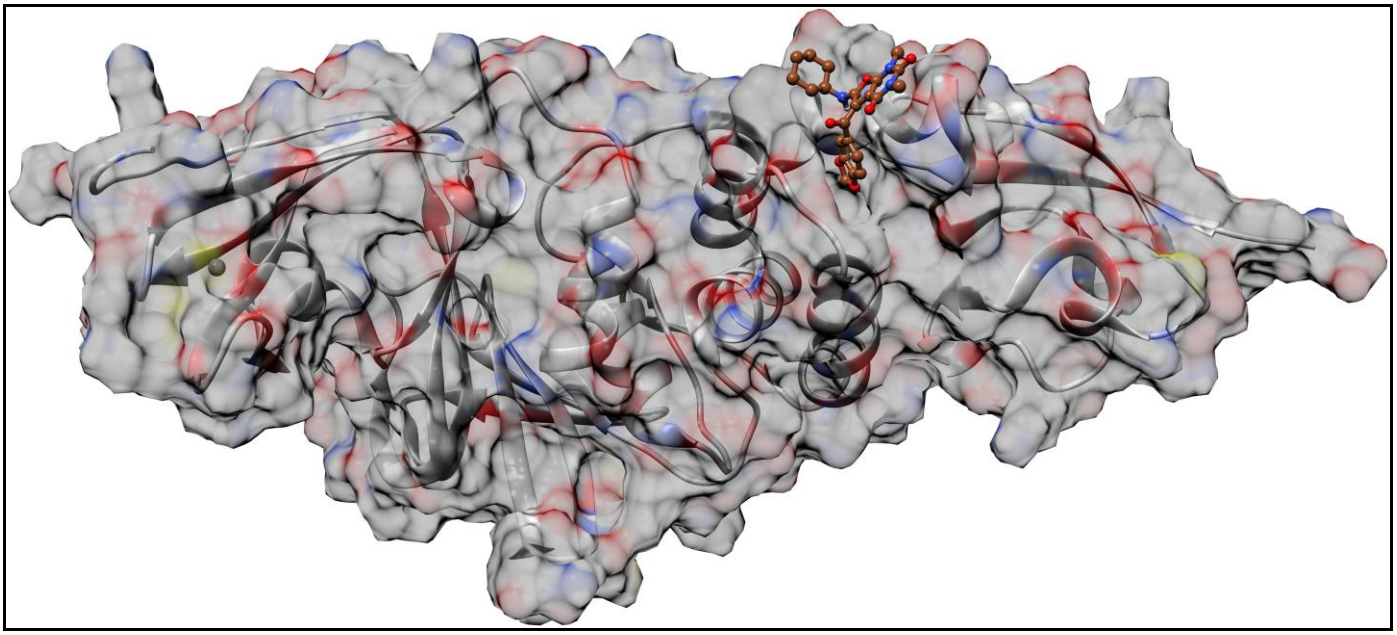


Figure S8. General perspective of the predicted position of **4g** in the allosteric site of the SARS-CoV-2 PL^{Pro} (PDB ID: 6WX4).

Table S1. Molecular docking results related to between **4a**–**n** and SARS-CoV-2 M^{Pro} metal-free active site (PDB ID: 7AEH).

Entry	Compound	Binding energy (−Kcal/mol)	Interaction	
			Conventional hydrogen bond (number / distance)	**Other interactions**
1	4a	−7.4	Thr25 (1 / 2.884 Å) His41 (1 / 3.079 Å) Ser46 (1 / 3.494 Å) Gly143 (1 / 2.017 Å) His164 (1 / 2.758 Å)	His41 (Carbon hydrogen bond; π–π Stacked; π–Alkyl) Cys44 (Carbon hydrogen bond; Alkyl) Met49 (Alkyl; π–Sulfur) Asn142 (Carbon hydrogen bond) Cys145 (π–Alkyl) Met165 (Alkyl)
2	4b	−7.7	Thr25 (1 / 2.906 Å) His41 (1 / 3.108 Å) Ser46 (1 / 3.483 Å) Gly143 (1 / 1.956 Å) His164 (1 / 2.786 Å)	His41 (π–π Stacked) Cys44 (Carbon hydrogen bond; Alkyl) Met49 (Alkyl; π–Sulfur) Asn142 (Carbon hydrogen bond) Cys145 (π–Alkyl) Met165 (Alkyl)
3	4c	−7.7	Thr25 (1 / 2.912 Å) His41 (1 / 3.104 Å) Gly143 (1 / 1.949 Å) His164 (1 / 2.782 Å)	His41 (π–π Stacked) Cys44 (Carbon hydrogen bond; Alkyl) Met49 (Alkyl; π–Sulfur) Asn142 (Carbon hydrogen bond) Cys145 (π–Alkyl) Met165 (Alkyl)
4	4d	−7.7	Thr25 (1 / 2.902 Å) His41 (1 / 2.966 Å) Ser46 (1 / 3.493 Å) Gly143 (1 / 1.929 Å) His164 (1 / 2.817 Å)	His41 (π–π Stacked) Cys44 (Carbon hydrogen bond; Alkyl) Met49 (Alkyl; π–Sulfur) Cys145 (π–Alkyl) Met165 (Alkyl)
5	4e	−7.4	His41 (1 / 3.160 Å) Gly143 (2 / 2.123 Å and 2.713 Å) Cys145 (1 / 3.309 Å) His164 (1 /2.654 Å)	His41 (π–π Stacked) Cys44 (Carbon hydrogen bond) Met49 (Alkyl) Asn142 (Carbon hydrogen bond) Cys145 (π–Sulfur) Met165 (Alkyl)
6	4f	−7.9	Gly143 (1 / 2.156 Å) Ser144 (4 / 2.297 Å, 2.437 Å, 2.478 Å, and 2.689 Å) Cys145 (1 / 2.341 Å) His163 (1 / 2.144 Å) Gln189 (1 / 3.020 Å)	His41 (π–Alkyl) Met49 (Alkyl) Cys145 (π–Alkyl) His163 (π–Alkyl) Met165 (Carbon hydrogen bond) Gln166 (Carbon hydrogen bond) His172 (π–Alkyl)
7	4g	−8.5	Ser144 (1 / 2.625 Å) His163 (1 / 2.415 Å)	His41 (π–Alkyl) Met49 (Alkyl) Cys145 (Alkyl; π–Alkyl) His163 (π–Alkyl) His164 (Carbon hydrogen bond) Pro168 (π–Alkyl) Gln189 (Carbon hydrogen bond; π–σ) Thr190 (Carbon hydrogen bond)
8	4h	−6.9	Gly143 (1 / 2.286 Å) Cys145 (1 / 3.259 Å) Gln189 (1 / 2.952 Å)	His41 (Carbon hydrogen bond; π–Alkyl) Met49 (Alkyl) Asn142 (Carbon hydrogen bond) Cys145 (π–Alkyl) Met165 (Alkyl)

Table S1. Continued.

Entry	Compound	Binding energy (−Kcal/mol)	Interaction	
			Conventional hydrogen bond (number / distance)	**Other interactions**
9	4i	−7.2	Ser144 (1 / 2.504 Å) His163 (1 / 2.340 Å)	Met49 (Alkyl) Cys145 (Alkyl) His163 (π–Alkyl) His164 (Carbon hydrogen bond) Pro168 (Alkyl)
10	4j	−7.2	Ser144 (1 / 2.490 Å) His163 (1 / 2.377 Å)	Met49 (Alkyl) Cys145 (Alkyl) His163 (π–Alkyl) His164 (Carbon hydrogen bond) Pro168 (Alkyl)
11	4k	−7.2	Gly143 (1 / 2.193 Å) Ser144 (1 / 3.251 Å) His163 (1 / 2.221 Å) Gln189 (1 / 3.045 Å)	His41 (Carbon hydrogen bond; π–Alkyl) Met49 (Alkyl) Leu141 (Amide–π stacked) Asn142 (Carbon hydrogen bond) Cys145 (Alkyl; π–Alkyl) His163 (Halogen {F}) Met165 (Alkyl) Glu166 (Halogen {F})
12	4l	−7.2	Ser144 (1 / 2.342 Å) His163 (1 / 2.293 Å) Glu166 (1 / 3.044 Å)	Met49 (Alkyl) Cys145 (Alkyl) His163 (π–Alkyl) His164 (Carbon hydrogen bond) Glu166 (Carbon hydrogen bond; π–Donor hydrogen bond) Pro168 (Alkyl; π–Alkyl)
13	4m	−7.3	Gly143 (1 / 2.730 Å) Ser144 (2 / 2.889 Å and 3.371 Å) His163 (2 / 2.349 Å and 3.027 Å) Glu166 (1 / 2.146 Å) Gln189 (1 / 2.779 Å)	His41 (Carbon hydrogen bond; π–σ) Met49 (Alkyl) Asn142 (Carbon hydrogen bond) Cys145 (Alkyl; π–Alkyl) His163 (π–Alkyl) His164 (Carbon hydrogen bond) Met165 (Alkyl)
14	4n	−7.5	Ser144 (1 / 2.547 Å) His163 (1 / 2.329 Å)	Met49 (Alkyl) Cys145 (Alkyl) His163 (π–Alkyl) His164 (Carbon hydrogen bond) Gln189 (π–σ) Thr190 (Carbon hydrogen bond)

Table S2. Molecular docking results between **4a**–**n** and SARS-CoV-2 M^{Pro} Zn^{II}-containing active site (PDB ID: 7MHK).

Entry	Compound	Binding energy (−Kcal/mol)	Interaction	
			Conventional hydrogen bond (number / distance)	**Other interactions**
1	4a	−7.2	His41 (1 / 3.369 Å) Gln189 (1 / 2.192 Å)	Thr26 (Carbon hydrogen bond) Ser46 (Carbon hydrogen bond) Met49 (*π*–Alkyl) Cys145 (*π*–Alkyl; *π*–Sulfur) Met165 (Carbon hydrogen bond) Zn503 (Metal–acceptor)
2	4b	−7.2	His41 (1 / 3.433 Å) Gly143 (1 / 2.709 Å) Cys145 (2 / 2.401 Å and 3.239 Å) Glu166 (3 / 2.757 Å, 2.880 Å, and 3.253 Å)	Leu27 (Alkyl) His41 (Carbon hydrogen bond; *π*–Alkyl) Met49 (Alkyl) Leu141 (Amide–*π* stacked; Alkyl) Asn142 (Carbon hydrogen bond) Cys145 (Alkyl; *π*–Alkyl) Met165 (Carbon hydrogen bond) Glu166 (*π*–Anion) Zn503 (*π*–Cation)
3	4c	−7.2	Gly143 (1 / 2.659 Å) Cys145 (2 / 2.404 Å, 3.150 Å, and 3.186 Å) His163 (1 / 3.309 Å) Glu166 (3 / 2.794 Å, 2.904 Å, and 3.327 Å) Gln189 (1 / 3.332 Å)	Thr26 (Carbon hydrogen bond) Leu27 (Alkyl) His41 (Carbon hydrogen bond; *π*–Alkyl) Met49 (Alkyl) Leu141 (Amide–*π* stacked) Asn142 (Carbon hydrogen bond) Cys145 (Alkyl; *π*–Alkyl) Met165 (Carbon hydrogen bond) Glu166 (*π*–Anion) Zn503 (*π*–Cation)
4	4d	−7.1	His41 (1 / 2.821 Å) Ser144 (1 / 3.409 Å) Cys145 (1 / 3.372 Å) Gln189 (1 / 2.355 Å)	Thr26 (Carbon hydrogen bond) Leu27 (Alkyl) His41 (*π*–Alkyl) Ser46 (Carbon hydrogen bond) Met49 (*π*–Alkyl) Phe140 (Halogen {F}) Leu141 (Halogen {F}) Cys145 (*π*–Alkyl; *π*–Sulfur) Met165 (Carbon hydrogen bond) Zn503 (Metal–acceptor)
5	4e	−7.6	His41 (1 / 3.353 Å) Cys145 (1 / 3.458 Å)	Thr26 (Carbon hydrogen bond) Leu27 (Alkyl) Ser46 (Carbon hydrogen bond) Met49 (Alkyl; *π*–Alkyl) Glu166 (*π*–Donor hydrogen bond) Zn503 (Metal–acceptor)
6	4f	−7.4	Leu141 (1 / 3.063 Å) Gly143 (2 / 2.332 Å and 3.122 Å) Ser144 (4 / 2.491 Å, 2.645 Å, 2.780 Å, and 3.305 Å) Cys145 (3 / 2.470 Å, 2.830 Å, and 3.128 Å) His163 (1 / 2.479 Å)	Met49 (Alkyl) Phe140 (Carbon hydrogen bond) Cys145 (*π*–Sulfur) His163 (*π*–Alkyl) Glu166 (Carbon hydrogen bond) Zn503 (Metal–acceptor)
7	4g	−7.7	His41 (1 / 3.165 Å) Cys145 (1 / 3.099 Å) Glu166 (1 / 2.809 Å) Gln189 (2 / 2.532 Å and 2.890 Å)	Met49 (Alkyl; *π*–Alkyl) Phe140 (Carbon hydrogen bond) Leu141 (Carbon hydrogen bond) Cys145 (*π*–Alkyl) His163 (*π*–Alkyl) Met165 (Carbon hydrogen bond) Zn503 (*π*–Cation)

Table S2. Continued.

Entry	Compound	Binding energy (−Kcal/mol)	Interaction	
			Conventional hydrogen bond (number / distance)	**Other interactions**
8	4h	−6.5	Cys145 (1 / 3.044 Å)	Thr26 (Carbon hydrogen bond) Ser46 (Carbon hydrogen bond) Met49 (*π*–Alkyl) Asn142 (Carbon hydrogen bond) Cys145 (Alkyl; *π*–Alkyl)
9	4i	−6.6	Thr24 (1 / 2.113 Å) Thr25 (1 / 3.115 Å) Thr26 (1 / 2.023 Å) Gly143 (1 / 3.007 Å)	Thr26 (Carbon hydrogen bond) His41 (*π*–Alkyl) Thr45 (Carbon hydrogen bond) Met49 (Alkyl) Asn142 (Amide–*π* stacked) Gly143 (Carbon hydrogen bond) Cys145 (Alkyl)
10	4j	−6.6	Thr24 (1 / 2.056 Å) Thr25 (1 / 3.124 Å) Thr26 (1 / 1.986 Å) Gly143 (1 / 3.061 Å)	Thr25 (Carbon hydrogen bond) Thr26 (Carbon hydrogen bond) His41 (*π*–Alkyl) Thr45 (Carbon hydrogen bond) Met49 (Alkyl) Asn142 (Amide–*π* stacked) Gly143 (Carbon hydrogen bond) Cys145 (Alkyl)
11	4k	−6.8	Cys145 (1 / 3.064 Å) His164 (1 / 3.389 Å)	Thr26 (Carbon hydrogen bond) Ser46 (Carbon hydrogen bond) Met49 (*π*–Alkyl) Asn142 (Carbon hydrogen bond) Cys145 (Alkyl; *π*–Alkyl)
12	4l	−6.7	His41 (1 / 3.194 Å) Gly143 (1 / 3.479 Å) Cys145 (1 / 2.810 Å) Glu166 (1 / 3.097 Å) Gln189 (2 / 2.180 Å and 3.210 Å)	Leu27 (Alkyl) His41 (*π*–Alkyl) Met49 (*π*–Alkyl) Phe140 (Carbon hydrogen bond) Leu141 (Carbon hydrogen bond) Cys145 (Alkyl; *π*–Alkyl; *π*–Sulfur) His163 (*π*–Alkyl) Met165 (Carbon hydrogen bond) Zn503 (*π*–Cation; Metal–acceptor)
13	4m	−7.2	Phe140 (1 / 2.267 Å) Leu141 (1 / 2.965 Å) Asn142 (3 / 2.303 Å, 3.205 Å, and 3.390 Å) Ser144 (1 / 2.764 Å) His163 (1 / 2.470 Å)	Leu27 (Alkyl) His41 (*π*–Alkyl) Ser46 (Carbon hydrogen bond) Asn142 (*π*–Donor hydrogen bond) Cys145 (*π*–Alkyl)
14	4n	−7.4	Thr25 (1 / 2.687 Å) His41 (1 / 2.363 Å) Ser46 (1 / 2.952 Å) Cys145 (2 / 3.079 Å and 3.391 Å)	His41 (*π*–Alkyl) Thr45 (Carbon hydrogen bond; Amide–*π* stacked) Ser46 (van der Waals) Met49 (*π*–Alkyl) Leu141 (Carbon hydrogen bond) Cys145 (Alkyl; *π*–Alkyl)

Table S3. Molecular docking results between **4a**–**n** and SARS-CoV-2 M^{Pro} allosteric site I (PDB ID: 7VLP).

Entry	Compound	Binding energy (−Kcal/mol)	Interaction	
			Conventional hydrogen bond (number / distance)	**Other interactions**
1	4a	−6.1	Gly302A (2 / 2.095 Å and 2.912 Å) Asn142B (1 / 2.392 Å)	Gly302A (Carbon hydrogen bond) Asn142B (*π*–Donor hydrogen bond; *π*–*σ*)
2	4b	−6	Gly302A (2 / 2.113 Å and 2.957 Å) Asn142B (2 / 2.629 Å and 2.848 Å)	Gly302A (Carbon hydrogen bond) Asn142B (*π*–*σ*)
3	4c	−6.1	Gly302A (2 / 2.112 Å and 2.939 Å) Asn142B (2 / 2.615 Å and 2.705 Å)	Gly302A (Carbon hydrogen bond) Asn142B (*π*–*σ*)
4	4d	−6.1	Gly302A (2 / 2.102 Å and 2.941 Å) Asn142B (2 / 2.552 Å and 2.614 Å)	Gly302A (Carbon hydrogen bond) Asn142B (*π*–*σ*)
5	4e	−6	Gly302A (2 / 2.098 Å and 2.912 Å) Asn142B (2 / 2.412 Å, 3.225 Å, and 3.442 Å)	Gly302A (Carbon hydrogen bond) Asn141B (Alkyl; *π*–Alkyl) Asn142B (*π*–*σ*)
6	4f	−6.3	Gly302A (2 / 2.193 Å and 2.893 Å) Asn142B (2 / 2.294 Å, 2.336 Å, 2.763 Å, and 3.319 Å)	Gly302A (Carbon hydrogen bond) Asn141B (Alkyl) Asn142B (*π*–*σ*)
7	4g	−6.4	Gly302A (2 / 2.065 Å and 2.922 Å) Asn142B (2 / 2.179 Å, 2.398 Å, and 3.379 Å)	Gly302A (Carbon hydrogen bond) Asn142B (*π*–*σ*)
8	4h	−5.3	Tyr154A (2 / 2.032 Å and 3.112 Å)	Val297A (Alkyl) Arg298A (*π*–Alkyl) Val303A (*π*–*σ*; *π*–Alkyl)
9	4i	−5.8	Gly302A (2 / 2.022 Å and 3.166 Å) Val303A (1 / 2.994 Å) Thr304A (2 / 2.198 Å and 2.820 Å) Ser121B (1 / 3.252 Å)	Val303A (Alkyl) Tyr118B (*π*–Alkyl) Leu141B (Alkyl)
10	4j	−5.8	Gly302A (2 / 2.042 Å and 3.141 Å) Val303A (1 / 3.055 Å) Thr304A (2 / 2.252 Å and 2.730 Å) Ser121B (1 / 3.269 Å)	Val303A (Alkyl) Thr304A (Carbon hydrogen bond) Tyr118B (*π*–Alkyl) Leu141B (Alkyl)
11	4k	−5.6	Tyr154A (2 / 2.108 Å and 3.127 Å)	Val297A (Alkyl) Arg298A (*π*–Alkyl) Val303A (*π*–*σ*; *π*–Alkyl)
12	4l	−5.6	Tyr154A (2 / 1.993 Å and 3.087 Å)	Val297A (Alkyl) Arg298A (*π*–Alkyl) Val303A (Alkyl; *π*–*σ*; *π*–Alkyl)
13	4m	−5.5	Tyr154A (2 / 2.022 Å and 3.116 Å)	Asp153A (Carbon hydrogen bond) Val297A (Alkyl) Arg298A (*π*–Alkyl) Gly302A (Carbon hydrogen bond) Val303A (Alkyl; *π*–*σ*; *π*–Alkyl)
14	4n	−5.9	Tyr154A (2 / 1.974 Å and 3.080 Å)	Ile152A (Carbon hydrogen bond) Val297A (Alkyl) Arg298A (*π*–Alkyl) Gly302A (Carbon hydrogen bond) Val303A (Alkyl; *π*–*σ*; *π*–Alkyl)

Table S4. Molecular docking results between **4a**–**n** and SARS-CoV-2 M^{Pro} allosteric site II (PDB ID: 7MHK).

Entry	Compound	Binding energy (−Kcal/mol)	Interaction	
			Conventional hydrogen bond (number / distance)	**Other interactions**
1	4a	−7.8	Gly109 (1 / 2.425 Å) Gln110 (1 / 2.918 Å) His246 (2 / 2.956 Å and 3.197 Å)	Ile200 (Alkyl) Val202 (Alkyl; π–Alkyl) Asn203 (Carbon hydrogen bond) His246 (π–π T-Shaped; π–Alkyl) Ile249 (Alkyl; π–Alkyl) Pro293 (Alkyl)
2	4b	−7.5	His246 (3 / 3.253 Å, 3.280 Å, and 3.349 Å)	Pro108 (Alkyl; π–Alkyl) Ile200 (Alkyl) Val202 (Alkyl) Pro293 (Alkyl) Phe294 (π–Alkyl)
3	4c	−7.5	Gln107 (1 / 3.066 Å) Gln110 (1 / 3.450 Å) His246 (3 / 3.223 Å, 3.266 Å, and 3.329 Å)	Pro108 (Alkyl; π–Alkyl) Ile200 (Alkyl) Val202 (Alkyl) Pro293 (Alkyl)
4	4d	−7.8	Gly109 (1 / 2.570 Å) His246 (2 / 3.021 Å and 3.130 Å)	Ile200 (Alkyl) Val202 (Alkyl; π–Alkyl) Asn203 (Carbon hydrogen bond) His246 (π–π T-Shaped; π–Alkyl) Ile249 (Alkyl; π–Alkyl) Pro293 (Alkyl)
5	4e	−7.7	His246 (2 / 2.487 Å and 3.389 Å)	Pro108 (Alkyl; π–Alkyl) Pro132 (Alkyl) Ile200 (Alkyl) Val202 (Alkyl; π–Alkyl) His246 (π–π T-Shaped) Ile249 (Alkyl; π–Alkyl) Pro293 (Alkyl) Phe294 (π–Alkyl)
6	4f	−7.9	Gln110 (2 / 2.598 Å and 3.292 Å) Tyr111 (1 / 2.018 Å) Asn151 (1 / 2.792 Å) Arg298 (2 / 2.640 Å and 2.719 Å)	Val104 (Alkyl) Ile106 (Alkyl) Gln110 (π–Donor hydrogen bond) Ile152 (Carbon hydrogen bond) Asp153 (Carbon hydrogen bond) Arg298 (π–Donor hydrogen bond; π–Cation; Alkyl; π–Alkyl) Val303 (Alkyl) Phe305 (π–Alkyl)
7	4g	−8.1	Lys102 (2 / 2.317 Å and 3.117 Å) Gln110 (3 / 2.380 Å, 3.343 Å, and 3.460 Å) Asn151 (4 / 2.397 Å, 2.623 Å, 3.382 Å, and 3.445 Å) Ser158 (1 / 2.895 Å) Arg298 (2/ 2.157 Å and 2.486 Å)	Lys102 (Alkyl) Val104 (Alkyl; π–Alkyl) Gln110 (Carbon hydrogen bond) Ser158 (Carbon hydrogen bond)
8	4h	−7	Gln110 (1 / 3.222 Å) His246 (3 / 2.530 Å, 3.170 Å, and 3.292 Å)	Gly109 (Carbon hydrogen bond) Val202 (π–Alkyl) His246 (π–Donor hydrogen bond; π–π T-Shaped; π–Alkyl) Ile249 (π–Alkyl) Pro293 (π–Alkyl)
9	4i	−7	Asn151 (1 / 3.490 Å) Asp153 (1 / 2.722 Å) Arg298 (3 / 1.868 Å, 2.321 Å, and 2.692 Å)	Phe294 (π–π T-Shaped; π–Alkyl) Val303 (Alkyl)
10	4j	−7.3	Gln110 (3 / 2.792 Å, 2.860 Å, and 3.108 Å) Asn151 (1 / 2.320 Å) Ile152 (1 / 3.091 Å) Arg298 (2 / 3.285 Å and 3.409 Å)	Val104 (Alkyl; π–Alkyl) Ile106 (Alkyl) Gln110 (π–Donor hydrogen bond) Asp153 (Carbon hydrogen bond) Phe294 (π–Alkyl)

Table S4. Continued.

Entry	Compound	Binding Energy (−Kcal/mol)	Interaction	
			Conventional hydrogen bond (number / distance)	**Other interactions**
11	4k	−7.5	Gln110 (1 / 2.811 Å) Asn151 (1 / 2.358 Å) Ile152 (1 / 3.191 Å) Arg298 (2 / 3.297 Å and 3.389 Å)	Val104 (Alkyl; π–Alkyl) Ile106 (Alkyl) Gln110 (π–Donor hydrogen bond) Asp153 (Carbon hydrogen bond) Ser158 (Carbon hydrogen bond) Arg298 (π–Cation)
12	4l	−6.7	Gln110 (3 / 2.561 Å, 2.711 Å, and 2.770 Å) Asn151 (4 / 2.141 Å, 2.879 Å, 3.322 Å, and 3.478 Å) Arg298 (1 / 3.363 Å)	Lys102 (Alkyl) Val104 (Alkyl; π–Alkyl) Asp153 (Carbon hydrogen bond) Ser158 (Carbon hydrogen bond) Arg298 (π–Cation) Val303 (Alkyl)
13	4m	−6.6	Gln110 (1 / 2.171 Å) Thr111 (4 / 2.262 Å, 2.902 Å, 3.322 Å, and 3.421 Å) Asn151 (1 / 3.222 Å) Arg298 (3 / 2.311 Å, 2.538 Å, and 2.871 Å)	Asp153 (Carbon hydrogen bond) Phe294 (π–Alkyl) Arg298 (π–Donor hydrogen bond; Alkyl; π–Alkyl) Val303 (Alkyl)
14	4n	−7.1	Gln110 (1 / 2.317 Å) Thr111 (1 / 3.177 Å) Asn151 (1 / 3.466 Å) Asp153 (1 / 2.528 Å) Arg298 (5 / 2.459 Å, 2.791 Å, 3.325 Å, 3.350 Å, and 3.379 Å)	Thr111 (Carbon hydrogen bond) Asp153 (π–Anion)

Table S5. Molecular docking results between **4a**–**n** and SARS-CoV-2 PL^{Pro} active site (PDB ID: 6WX4).

Entry	Compound	Binding energy (−Kcal/mol)	Interaction	
			Conventional hydrogen bond (number / distance)	**Other interactions**
1	4a	−7.5	Asp164 (1 / 3.384 Å) Tyr273 (1 / 2.651 Å)	Leu162 (Alkyl; π–σ) Gly163 (Carbon hydrogen bond) Pro248 (Alkyl) Tyr264 (π–π T-Shaped; π–Alkyl) Tyr268 (π–Alkyl)
2	4b	−7.5	Tyr268 (1 / 2.592 Å) Tyr273 (1 / 3.311 Å)	Leu162 (Carbon hydrogen bond; Alkyl) Glu167 (Carbon hydrogen bond; π–Anion) Pro248 (Alkyl) Tyr264 (π–π Stacked; π–Alkyl) Tyr273 (π–Alkyl)
3	4c	−7.8	Tyr268 (1 / 2.447 Å) Tyr273 (1 / 3.240 Å)	Leu162 (Alkyl) Glu167 (Carbon hydrogen bond; π–Anion) Pro248 (Alkyl) Tyr264 (π–π Stacked; π–Alkyl) Tyr273 (π–Alkyl)
4	4d	−8.1	Tyr268 (1 / 2.442 Å) Tyr273 (1 / 3.425 Å)	Leu162 (Alkyl) Asp164 (π–Anion) Pro248 (Carbon hydrogen bond) Tyr264 (π–π Stacked; π–Alkyl)
5	4e	−7.9	Gly163 (1 / 3.227 Å) Asp164 (1 / 3.379 Å) Tyr273 (1 / 2.078 Å)	Cys111 (Alkyl) Leu162 (Alkyl) Gly163 (Carbon hydrogen bond) Asp164 (π–Anion) Pro248 (Carbon hydrogen bond; Alkyl) Tyr264 (π–π Stacked; π–σ) Tyr273 (π–Alkyl) Thr301 (Carbon hydrogen bond)
6	4f	−7.8	Asp164 (1 / 3.158 Å) Gly271 (3 / 1.784 Å, 1.894 Å, and 3.043 Å) Tyr273 (1 / 1.826 Å)	Cys111 (Alkyl) Tyr112 (π–Alkyl) Leu162 (Alkyl; π–Alkyl) Gly163 (Carbon hydrogen bond) Asp164 (Carbon hydrogen bond; π–Anion) Pro248 (Alkyl) Tyr264 (π–Alkyl) Tyr273 (π–Alkyl) Thr301 (Carbon hydrogen bond)
7	4g	−8.4	Arg166 (1 / 3.027 Å) Tyr273 (1 / 2.977 Å) Thr301 (1 / 3.376 Å)	Leu162 (Alkyl) Asp164 (π–Anion) Arg166 (Carbon hydrogen bond; π–Alkyl) Met208 ((π–Sulfur) Ala246 (Amide–π stacked) Pro247 (van der Waals) Tyr264 (π–Alkyl) Tyr268 (Carbon hydrogen bond; π–π T-Shaped; π–Alkyl) Asp302 (Carbon hydrogen bond)
8	4h	−7.4	Asp164 (1 / 3.124 Å) Tyr273 (1 / 1.904 Å)	Leu162 (π–Alkyl) Gly163 (Carbon hydrogen bond) Asp164 (π–Anion) Pro248 (Carbon hydrogen bond; Alkyl) Tyr264 (π–σ) Tyr273 (π–Alkyl) Thr301 (Carbon hydrogen bond)

Table S5. Continued.

Entry	Compound	Binding Energy (−Kcal/mol)	Interaction	
			Conventional hydrogen bond (number / distance)	**Other interactions**
9	4i	−7	Lys157 (1 / 2.847 Å) Tyr264 (1 / 2.769 Å) Tyr268 (1 / 2.270 Å) Thr301 (1 / 3.435 Å)	Leu162 (Alkyl) Asp164 (π–Anion) Pro248 (Alkyl) Tyr264 (π–σ) Tyr273 (π–Alkyl) Thr301 (Carbon hydrogen bond)
10	4j	−7	Lys157 (1 / 2.682 Å) Tyr264 (1 / 2.902 Å) Tyr268 (1 / 2.200 Å) Thr301 (1 / 3.474 Å)	Leu162 (Alkyl) Asp164 (π–Anion) Pro248 (Alkyl) Tyr264 (π–σ) Tyr273 (π–Alkyl)
11	4k	−7.7	Asp164 (1 / 3.170 Å) Gly271 (1 / 2.263 Å) Tyr273 (1 / 1.949 Å)	Leu162 (π–Alkyl) Gly163 (Carbon hydrogen bond) Asp164 (π–Anion) Pro248 (Carbon hydrogen bond; Alkyl) Tyr264 (π–π T-Shaped; π–σ) Gln269 (Halogen {F}) Cys270 (Carbon hydrogen bond; Halogen {F}) Gly271 (Halogen {F}) Tyr273 (π–Alkyl) Thr301 (Carbon hydrogen bond)
12	4l	−7.5	Gly163 (1 / 3.299 Å) Asp164 (1 / 3.218 Å) Tyr273 (1 / 1.857 Å)	Cys111 (Alkyl) Leu162 (Alkyl; π–Alkyl) Gly163 (Carbon hydrogen bond) Asp164 (π–Anion) Pro248 (Carbon hydrogen bond; Alkyl) Tyr264 (π–π T-Shaped; π–σ; π–Alkyl) Tyr273 (π–Alkyl) Thr301 (Carbon hydrogen bond)
13	4m	−7.6	Asp164 (1 / 3.108 Å) Tyr264 (1 / 3.399 Å) Cys270 (1 / 2.456 Å) Gly271 (2 / 2.023 Å and 2.596 Å) Tyr273 (1 / 1.823 Å)	Cys111 (Alkyl) Leu162 (Alkyl; π–Alkyl) Gly163 (Carbon hydrogen bond) Asp164 (Carbon hydrogen bond; π–Anion) Pro248 (Alkyl) Tyr264 (π–π T-Shaped; π–Alkyl) Tyr273 (π–Alkyl) Thr301 (Carbon hydrogen bond)
14	4n	−7.5	Lys157 (2 / 2.355 Å and 2.981 Å) Tyr264 (1 / 2.855 Å) Gln269 (1 / 3.043 Å)	Leu162 (Alkyl) Asp164 (π–Anion) Pro248 (Alkyl) Tyr264 (π–σ) Tyr273 (π–Alkyl)

Table S6. Molecular docking results between **4a**–**n** and SARS-CoV-2 PL^{Pro} allosteric site (PDB ID: 6WX4).

Entry	Compound	Binding energy (−Kcal/mol)	Interaction	
			Conventional hydrogen bond (number / distance)	**Other interactions**
1	4a	−6.5		Pro59 (Alkyl) Arg65 (Carbon hydrogen bond; π–Alkyl) Ala68 (Alkyl) Phe69 (π–σ) Thr74 (Carbon hydrogen bond) Pro77 (Carbon hydrogen bond; Alkyl)
2	4b	−7.3	Arg65 (2 / 2.376 Å and 3.368 Å)	Pro59 (Alkyl) Arg65 (Alkyl; π–Alkyl) Val66 (Alkyl; π–Alkyl) Phe69 (π–Alkyl)
3	4c	−7.2		Pro59 (Alkyl) Asp62 (π–Anion) Arg65 (Carbon hydrogen bond; Alkyl; π–Alkyl) Val66 (Carbon hydrogen bond) Ala68 (Alkyl) Phe69 (π–π Stacked; π–Alkyl)
4	4d	−7.2	Arg65 (1 / 2.373 Å) Val66 (1 / 3.353 Å)	Asp62 (π–Anion) Arg65 (π–Alkyl) Val66 (Alkyl) Phe69 (π–σ)
5	4e	−7.4	Arg65 (1 / 3.473 Å)	Pro59 (Alkyl) Asp62 (π–Anion) Arg65 (Carbon hydrogen bond; Alkyl; π–Alkyl) Val66 (Carbon hydrogen bond) Ala68 (Alkyl) Phe69 (π–π Stacked; π–Alkyl)
6	4f	−6.8	Pro59 (1 / 2.815 Å) Arg65 (1 / 2.691 Å)	Pro59 (Alkyl) Asp62 (π–Anion) Arg65 (Carbon hydrogen bond; π–Alkyl) Ala68 (Alkyl) Phe69 (π–σ) Thr74 (Carbon hydrogen bond) Thr75 (Carbon hydrogen bond) Pro77 (Carbon hydrogen bond)
7	4g	−7.8	Arg65 (1 / 2.355 Å) Val66 (1 / 3.164 Å)	Pro59 (π–Alkyl) Asp62 (π–Anion) Arg65 (π–Alkyl) Val66 (Alkyl) Ala68 (π–Alkyl) Phe69 (π–σ)
8	4h	−5.9	Arg65 (3 / 2.646 Å, 3.067 Å, and 3.144 Å) Phe69 (1 / 3.179 Å)	Pro59 (Alkyl; π–Alkyl) Arg65 (Alkyl; π–Alkyl; Unfavorable acceptor-acceptor) Ala68 (Alkyl) Thr74 (Carbon hydrogen bond) Pro77 (Carbon hydrogen bond; π–Alkyl)
9	4i	−5.8	Arg65 (1 / 3.289 Å)	Pro59 (Alkyl) Arg65 (Carbon hydrogen bond; Alkyl; π–Alkyl) Val66 (Alkyl) Ala68 (Alkyl) Pro77 (Alkyl)
10	4j	−6.3	Arg65 (1 / 2.569 Å) Thr75 (2 / 2.255 Å and 3.235 Å)	Pro59 (Alkyl; π–Alkyl) Arg65 (Carbon hydrogen bond; π–Alkyl) Ala68 (Alkyl; π–Alkyl)

Table S6. Continued.

Entry	Compound	Binding energy (−Kcal/mol)	Interaction	
			Conventional hydrogen bond (number / distance)	**Other interactions**
11	4k	−6.6	Arg65 (1 / 2.522 Å) Thr75 (2 / 2.316 Å and 3.289 Å)	Pro59 (π–Alkyl) Arg65 (Carbon hydrogen bond; π–Alkyl) Ala68 (π–Alkyl) Thr74 (Halogen {F}) Pro77 (Alkyl)
12	4l	−6	Arg65 (3 / 2.621 Å, 3.145 Å, and 3.163 Å) Thr75 (1 / 3.405 Å)	Pro59 (Alkyl; π–Alkyl) Arg65 (Alkyl; π–Alkyl; Unfavorable acceptor–acceptor) Ala68 (Alkyl) Thr74 (Carbon hydrogen bond) Pro77 (Carbon hydrogen bond; Alkyl; π–Alkyl)
13	4m	−6.5	Arg65 (3 / 2.132 Å, 2.208 Å, and 3.191 Å) Phe69 (1 / 3.273 Å) Thr74 (1 / 3.408 Å) Thr75 (3 / 2.135 Å, 3.304 Å, and 3.314 Å)	Pro59 (π–Alkyl) Arg65 (Carbon hydrogen bond; Alkyl; π–Alkyl) Thr75 (Unfavorable donor–donor) Pro77 (Alkyl; π–Alkyl)
14	4n	−6.7	Arg65 (3 / 2.107 Å, 2.325 Å, and 2.907 Å) Thr75 (1 / 2.433 Å)	Pro59 (π–Alkyl) Asn60 (Carbon hydrogen bond) Arg65 (Carbon hydrogen bond; π–σ; π–Alkyl) Ala68 (π–Alkyl) Pro77 (Carbon hydrogen bond; Alkyl; π–Alkyl)

Table S7. Physicochemical properties and lipophilicity of **4a**–**n**.

Entry	Compound	Chemical formula	Molecular weight (MW) (g/mol)	Number of heavy atoms	Number of aromatic heavy atoms	Fraction Csp3	Number of rotatable bonds	Number of hydrogen bond acceptors	Number of hydrogen bond donors	Molar refractivity (MR)	Topological polar surface area (TPSA) (Å^2)	Log $P_{o/w}$ (iLOGP)	Log $P_{o/w}$ (XLOGP3)	Log $P_{o/w}$ (WLOGP)	Log $P_{o/w}$ (MLOGP)	Log $P_{o/w}$ (SILICOS-IT)	Consensus Log $P_{o/w}$
1	4a	$C_{21}H_{23}N_3O_4$	381.43	28	15	0.38	4	4	1	108.36	86.24	3.37	4.23	2.62	2.38	2.79	3.08
2	4b	$C_{21}H_{22}BrN_3O_4$	460.32	29	15	0.38	4	4	1	116.06	86.24	3.65	4.92	3.38	2.97	3.47	3.68
3	4c	$C_{21}H_{22}ClN_3O_4$	415.87	29	15	0.38	4	4	1	113.37	86.24	3.54	4.86	3.27	2.86	3.43	3.59
4	4d	$C_{21}H_{22}FN_3O_4$	399.42	29	15	0.38	4	5	1	108.32	86.24	3.41	4.33	3.17	2.76	3.21	3.38
5	4e	$C_{21}H_{22}BrN_3O_4$	460.32	29	15	0.38	4	4	1	116.06	86.24	3.46	4.92	3.38	2.97	3.47	3.64
6	4f	$C_{22}H_{25}N_3O_6$	427.45	31	15	0.41	5	6	2	116.87	115.70	3.34	3.85	2.33	1.70	2.38	2.72
7	4g	$C_{22}H_{23}N_3O_6$	425.43	31	15	0.41	4	6	1	114.42	104.70	3.47	4.04	2.34	1.97	2.64	2.89
8	4h	$C_{19}H_{21}N_3O_4$	355.39	26	15	0.32	4	4	1	100.90	86.24	3.17	3.40	2.08	1.93	2.46	2.61
9	4i	$C_{19}H_{20}BrN_3O_4$	434.28	27	15	0.32	4	4	1	108.60	86.24	3.58	4.10	2.84	2.53	3.15	3.24
10	4j	$C_{19}H_{20}ClN_3O_4$	389.83	27	15	0.32	4	4	1	105.91	86.24	3.50	4.03	2.73	2.42	3.11	3.16
11	4k	$C_{19}H_{20}FN_3O_4$	373.38	27	15	0.32	4	5	1	100.86	86.24	3.30	3.50	2.64	2.31	2.90	2.93
12	4l	$C_{19}H_{20}BrN_3O_4$	434.28	27	15	0.32	4	4	1	108.60	86.24	3.38	4.10	2.84	2.53	3.15	3.20
13	4m	$C_{20}H_{23}N_3O_6$	401.41	29	15	0.35	5	6	2	109.41	115.70	3.17	3.02	1.79	1.26	2.08	2.27
14	4n	$C_{20}H_{21}N_3O_6$	399.40	29	15	0.35	4	6	1	106.96	104.70	3.43	3.22	1.81	1.53	2.35	2.47

Table S8. Water solubility of **4a**–**n**.

Entry	Compound	Log *S* (ESOL) / Solubility (mg/ml) / Class	Log *S* (Ali) / Solubility (mg/ml) / Class	Log *S* (SILICOS-IT) / Solubility (mg/ml) / Class
1	4a	−5.00 / 3.80e−03 / Moderately soluble	−5.75 / 6.76e−04 / Moderately soluble	−5.37 / 1.62e−03 / Moderately soluble
2	4b	−5.91 / 5.63e−04 / Moderately soluble	−6.47 / 1.57e−04 / Poorly soluble	−6.15 / 3.25e−04 / Poorly soluble
3	4c	−5.60 / 1.05e−04 / Moderately soluble	−6.41 / 1.63e−04 / Poorly soluble	−5.96 / 4.58e−04 / Moderately soluble
4	4d	−5.16 / 2.74e−03 / Moderately soluble	−5.86 / 5.57e−04 / Moderately soluble	−5.64 / 9.23e−04 / Moderately soluble
5	4e	−5.91 / 5.63e−04 / Moderately soluble	−6.47 / 1.57e−04 / Poorly soluble	−6.15 / 3.25e−04 / Poorly soluble
6	4f	−4.94 / 4.87e−03 / Moderately soluble	−5.98 / 4.52e−04 / Moderately soluble	−4.88 / 5.57e−03 / Moderately soluble
7	4g	−5.12 / 3.25e−03 / Moderately soluble	−5.94 / 4.86e−04 / Moderately soluble	−5.09 / 3.49e−03 / Moderately soluble
8	4h	−4.35 / 1.59e−02 / Moderately soluble	−4.89 / 4.57e−03 / Moderately soluble	−5.17 / 2.43e−03 / Moderately soluble
9	4i	−5.26 / 2.37e−03 / Moderately soluble	−5.62 / 1.05e−03 / Moderately soluble	−5.95 / 4.86e−04 / Moderately soluble
10	4j	−4.94 / 4.45e−03 / Moderately soluble	−5.54 / 1.11e−03 / Moderately soluble	−5.75 / 6.85e−04 / Moderately soluble
11	4k	−4.51 / 1.16e−02 / Moderately soluble	−4.99 / 3.78e−03 / Moderately soluble	−5.43 / 1.38e−03 / Moderately soluble
12	4l	−5.26 / 2.37e−03 / Moderately soluble	−5.62 / 1.05e−03 / Moderately soluble	−5.95 / 4.86e−04 / Moderately soluble
13	4m	−4.28 / 2.09e−02 / Moderately soluble	−5.11 / 3.08e−03 / Moderately soluble	−4.68 / 8.35e−03 / Moderately soluble
14	4n	−4.46 / 1.37e−02 / Moderately soluble	−5.09 / 3.24e−03 / Moderately soluble	−4.88 / 5.22e−03 / Moderately soluble

Solubility class: Log *S* Class = Insoluble < −10 < Poorly < −6 < Moderately < −4 < Soluble < −2 < Very < 0 < Highly.

Table S9. Pharmacokinetics of **4a**–**n**.

Entry	Compound	Gastrointestinal (GI) absorption	BBB permeant	P-glycoprotein (P-gp) substrate	Cytochrome P450 1A2 (CYP1A2) inhibitor	Cytochrome P450 2C19 (CYP2C19) inhibitor	Cytochrome P450 C9 (CYP2C9) inhibitor	Cytochrome P450 2D6 (CYP2D6) inhibitor	Cytochrome P450 3A4 (CYP3A4) inhibitor	Log K_p (skin permeation) (cm/s)
1	4a	High	No	No	No	Yes	Yes	No	Yes	−5.62
2	4b	High	No	No	No	Yes	Yes	No	Yes	−5.61
3	4c	High	No	No	No	Yes	Yes	No	Yes	−5.39
4	4d	High	No	No	No	Yes	Yes	No	No	−5.66
5	4e	High	No	No	No	Yes	Yes	No	Yes	−5.61
6	4f	High	No	No	No	No	Yes	No	No	−6.17
7	4g	High	No	No	No	Yes	Yes	No	Yes	−6.03
8	4h	High	No	No	No	No	Yes	No	No	−6.05
9	4i	High	No	No	No	Yes	Yes	No	Yes	−6.04
10	4j	High	No	No	No	Yes	Yes	No	Yes	−5.82
11	4k	High	No	No	No	No	Yes	No	No	−6.09
12	4l	High	No	No	No	Yes	Yes	No	Yes	−6.04
13	4m	High	No	No	No	No	Yes	No	No	−6.60
14	4n	High	No	No	No	Yes	Yes	No	Yes	−6.45

Table S10. Drug-likeness and medicinal chemistry of **4a**–**n**.

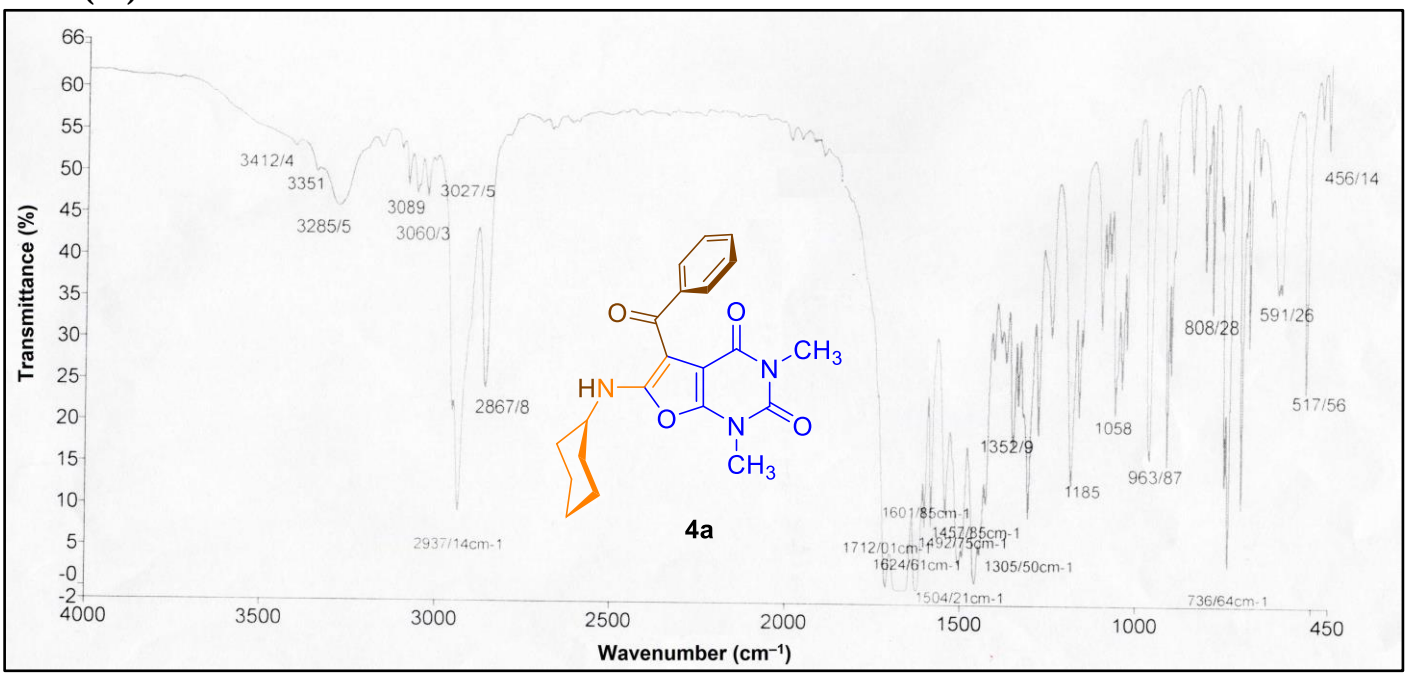
Entry	Compound	Lipinski (Pfizer) filter	Ghose (Amgen) filter	Veber (GSK) filter	Egan (Pharmacia) filter	Muegge (Bayer) filter	Abbot bioavailability score	Pan assay interference structures (PAINS) alert	Brenk alert	Lead-likeness	Synthetic accessibility score
1	4a	Yes (violation = 0)	Yes	Yes	Yes	Yes	0.55	0	0	No (violation = 2)[A]	3.79
2	4b	Yes (violation = 0)	Yes	Yes	Yes	Yes	0.55	0	0	No (violation = 2)[A]	3.79
3	4c	Yes (violation = 0)	Yes	Yes	Yes	Yes	0.55	0	0	No (violation = 2)[A]	3.79
4	4d	Yes (violation = 0)	Yes	Yes	Yes	Yes	0.55	0	0	No (violation = 2)[A]	3.79
5	4e	Yes (violation = 0)	Yes	Yes	Yes	Yes	0.55	0	0	No (violation = 2)[A]	3.82
6	4f	Yes (violation = 0)	Yes	Yes	Yes	Yes	0.55	0	0	No (violation = 2)[A]	3.94
7	4g	Yes (violation = 0)	Yes	Yes	Yes	Yes	0.55	0	0	No (violation = 2)[A]	3.92
8	4h	Yes (violation = 0)	Yes	Yes	Yes	Yes	0.55	0	0	No (violation = 1)[B]	3.64
9	4i	Yes (violation = 0)	Yes	Yes	Yes	Yes	0.55	0	0	No (violation = 2)[A]	3.64
10	4j	Yes (violation = 0)	Yes	Yes	Yes	Yes	0.55	0	0	No (violation = 2)[A]	3.62
11	4k	Yes (violation = 0)	Yes	Yes	Yes	Yes	0.55	0	0	No (violation = 1)[B]	3.62
12	4l	Yes (violation = 0)	Yes	Yes	Yes	Yes	0.55	0	0	No (violation = 2)[A]	3.68
13	4m	Yes (violation = 0)	Yes	Yes	Yes	Yes	0.55	0	0	No (violation = 1)[B]	3.78
14	4n	Yes (violation = 0)	Yes	Yes	Yes	Yes	0.55	0	0	No (violation = 1)[B]	3.77

Lipinski (Pfizer) filter: MW ≤ 500; MLOGP ≤ 4.15; Number of nitrogen (N) or oxygen (O) ≤ 10; Number of NH or OH ≤ 5.
Ghose filter: 160 ≤ MW ≤ 480; −0.4 ≤ WLOGP ≤ 5.6; 40 ≤ MR ≤ 130; 20 ≤ Atoms ≤ 70.
Veber (GSK) filter: Number of rotatable bonds ≤ 10; TPSA ≤ 140 $Å^2$.
Egan (Pharmacia) filter: WLOGP ≤ 5.88; TPSA ≤ 131.6 $Å^2$.
Muegge (Bayer) filter: 200 ≤ MW ≤ 600; −2 ≤ XLOGP ≤ 4.15; TPSA ≤ 150 $Å^2$; Number of rings ≤ 7; Number of carbon atoms > 4; Number of heteroatoms > 1; Number of rotatable bonds ≤ 15; Number of H-bond acceptors ≤ 10; Number of H-bond donors ≤ 5.
Lead-likeness: 250 ≤ MW ≤ 350; XLOGP ≤ 3.5; Number of rotatable bonds ≤ 7.
Synthetic accessibility score: From 1 (very easy) to 10 (very difficult).
A: Violations related to MW > 350 and XLOGP3 > 3.5.
B: Violation related to MW > 350.

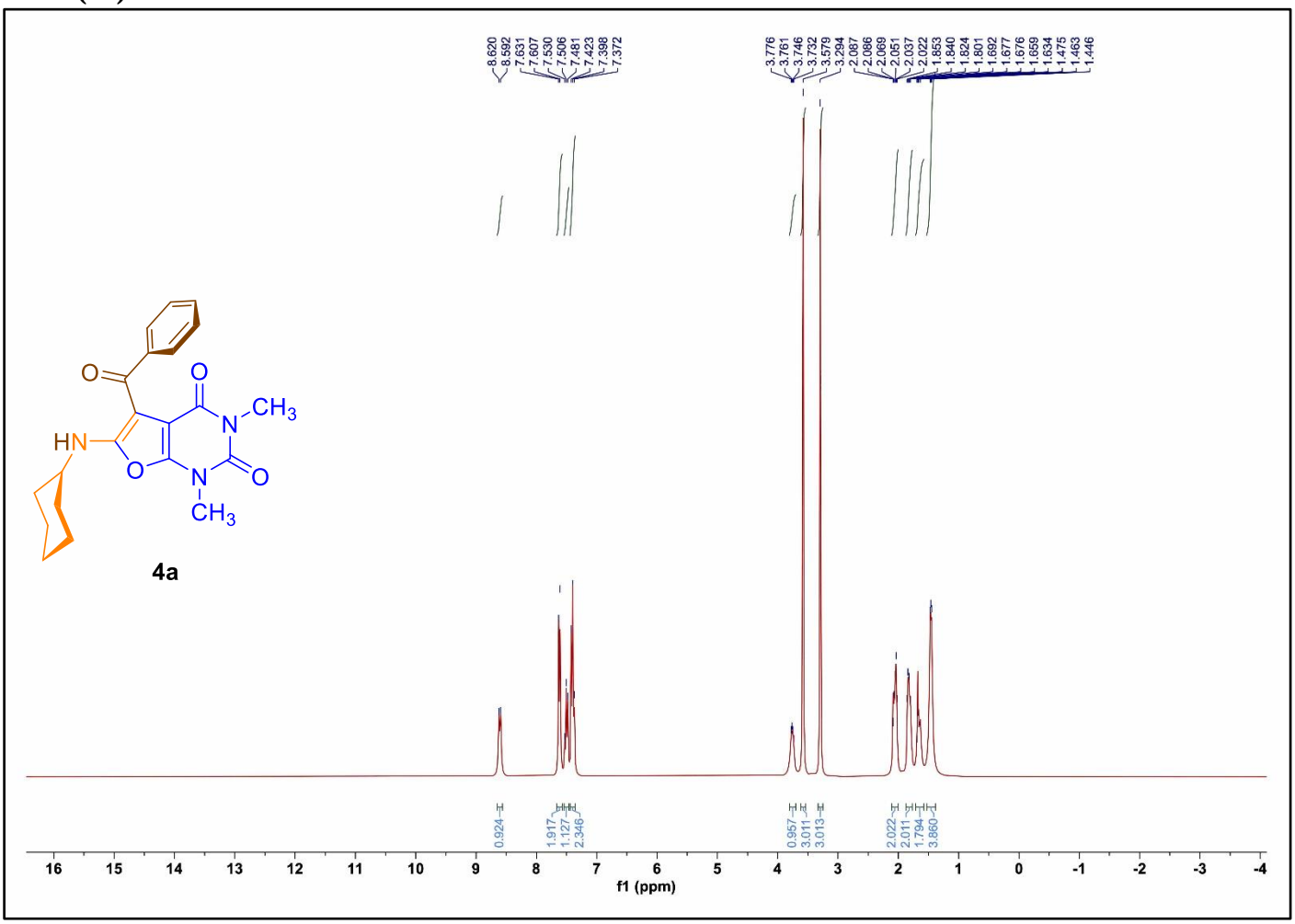
Table S11. Toxicity of **4a**–**n**.

Entry	Compound	Ames toxicity	Maximum tolerated dose (human) (log mg/kg/day)	Human Ether-à-go-go-Related Gene I (*h*ERG I) inhibitor	Human Ether-à-go-go-Related Gene II (*h*ERG II) inhibitor	Oral rat acute toxicity (LD_{50}) (mol/kg)	Oral rat chronic toxicity (LOAEL) (log mg/kg body weight/day)	Hepatotoxicity	Skin sensitization	*Tetrahymena pyriformis* toxicity (log μg/L)	Minnow toxicity (log mM)
1	4a	No	−0.264	No	No	2.489	1.408	Yes	No	0.528	2.606
2	4b	No	−0.177	No	No	2.602	1.573	Yes	No	0.512	1.968
3	4c	No	−0.173	No	No	2.595	1.6	Yes	No	0.514	2.114
4	4d	No	−0.04	No	No	2.622	1.303	Yes	No	0.426	2.597
5	4e	No	−0.261	No	No	2.621	1.572	Yes	No	0.502	1.895
6	4f	No	−0.468	No	No	2.673	1.148	Yes	No	0.343	2.557
7	4g	No	−0.099	No	No	2.793	1.306	Yes	No	0.313	2.628
8	4h	No	+0.241	No	No	2.37	1.427	Yes	No	0.782	1.371
9	4i	No	+0.289	No	No	2.523	1.358	Yes	No	0.759	0.751
10	4j	No	+0.293	No	No	2.513	1.369	Yes	No	0.762	0.897
11	4k	No	+0.408	No	Yes	2.531	1.256	Yes	No	0.602	1.003
12	4l	No	+0.222	No	No	2.532	1.354	Yes	No	0.746	0.68
13	4m	No	−0.092	No	Yes	2.47	1.251	Yes	No	0.405	1.787
14	4n	No	+0.308	No	Yes	2.692	1.166	Yes	No	0.371	0.641

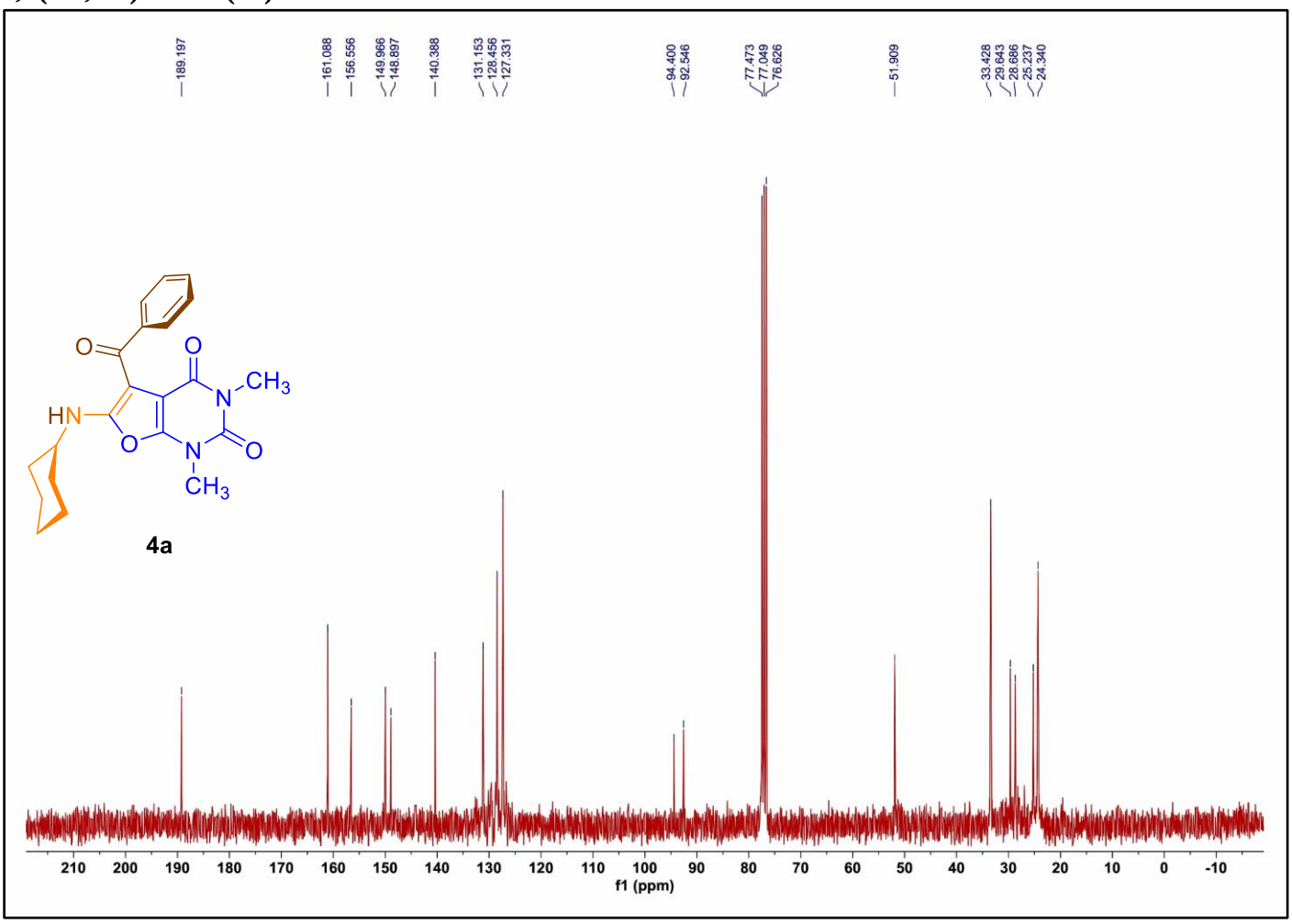
FT-IR Spectrum of 5-benzoyl-6-(cyclohexylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4a)



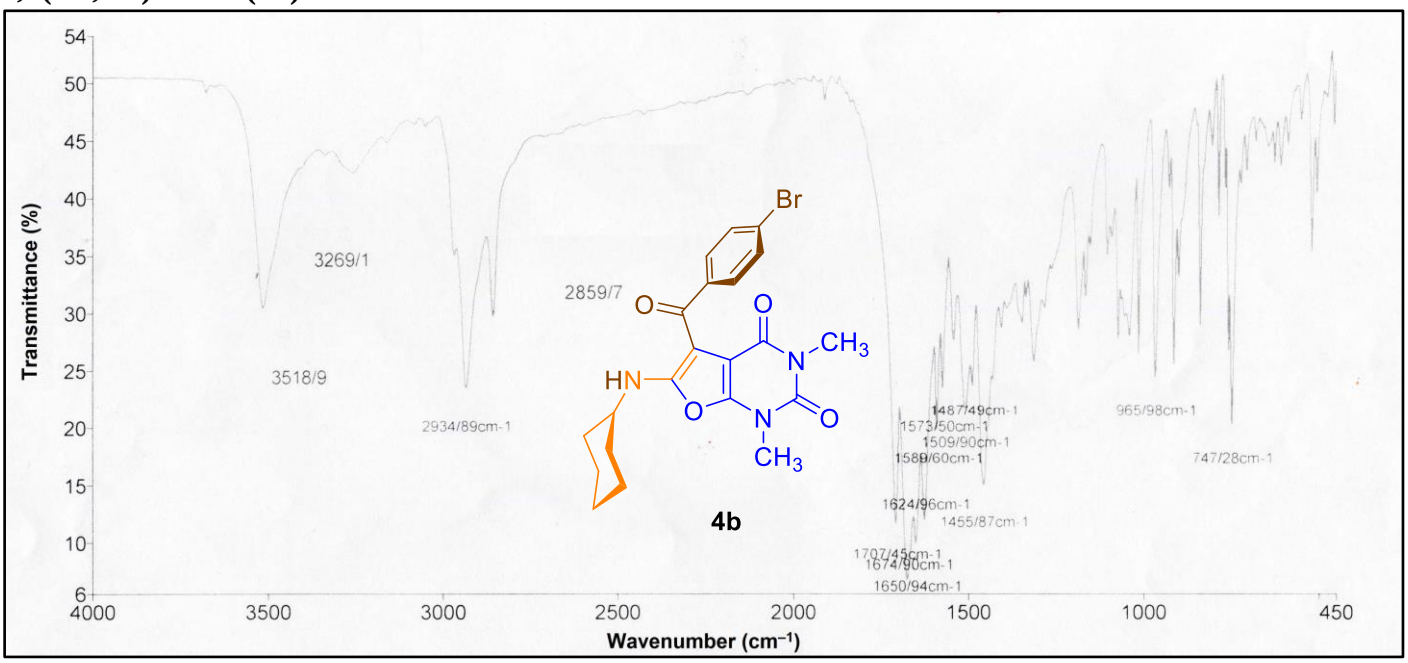
^{1}H NMR Spectrum of 5-benzoyl-6-(cyclohexylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4a)



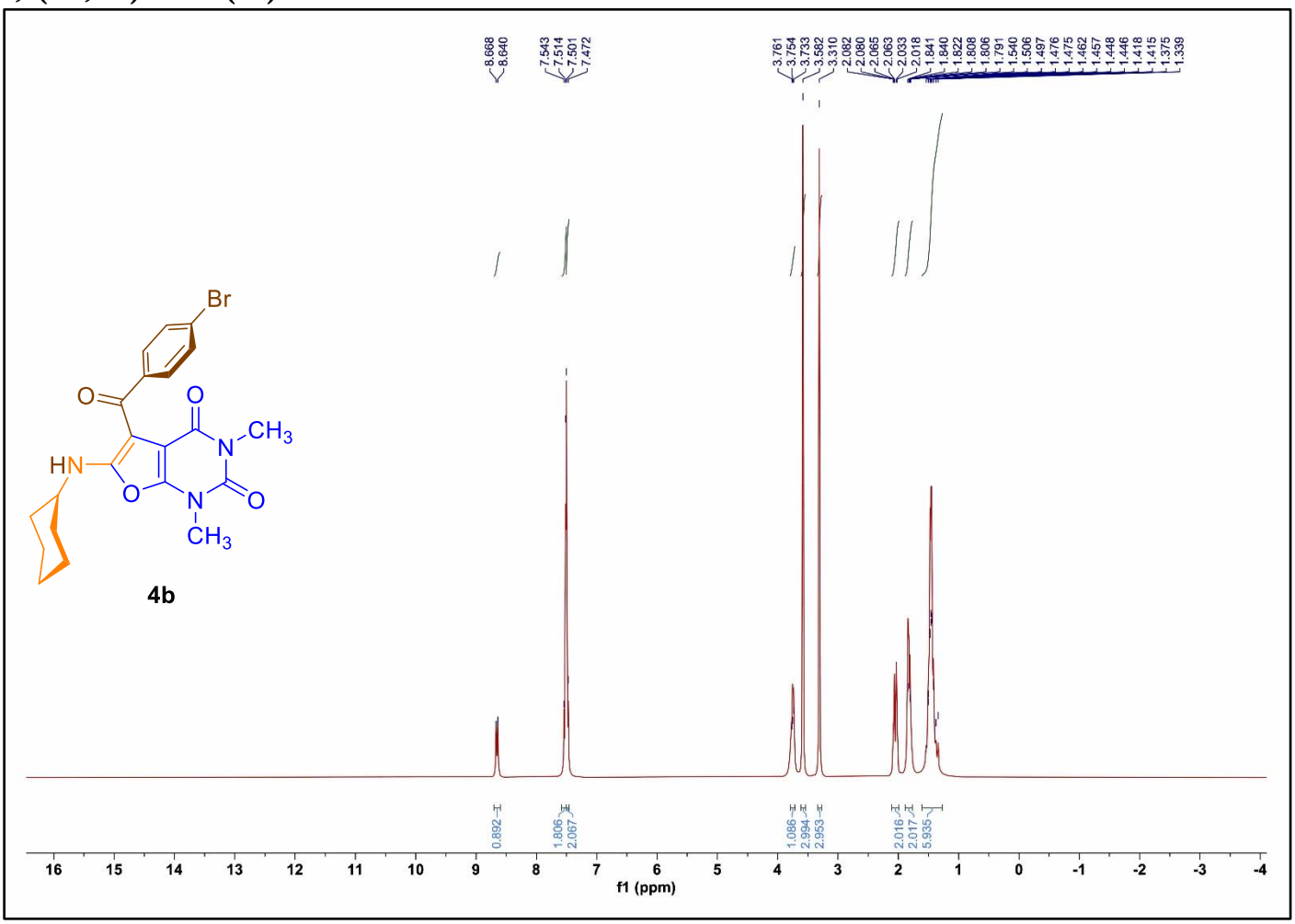
$^{13}C\{^{1}H\}$ NMR Spectrum of 5-benzoyl-6-(cyclohexylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4a)



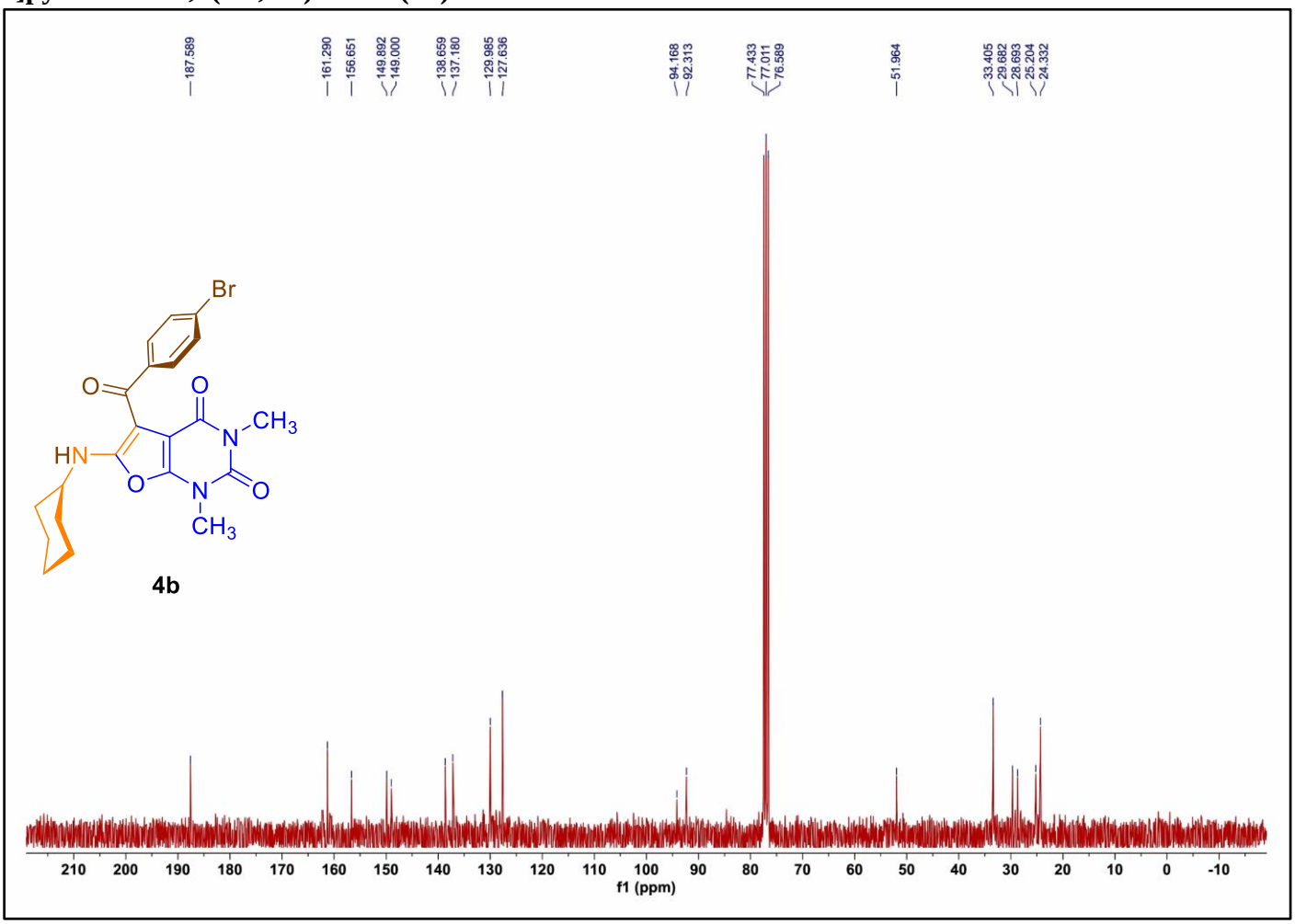
FT-IR Spectrum of 5-(4-bromobenzoyl)-6-(cyclohexylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4b)



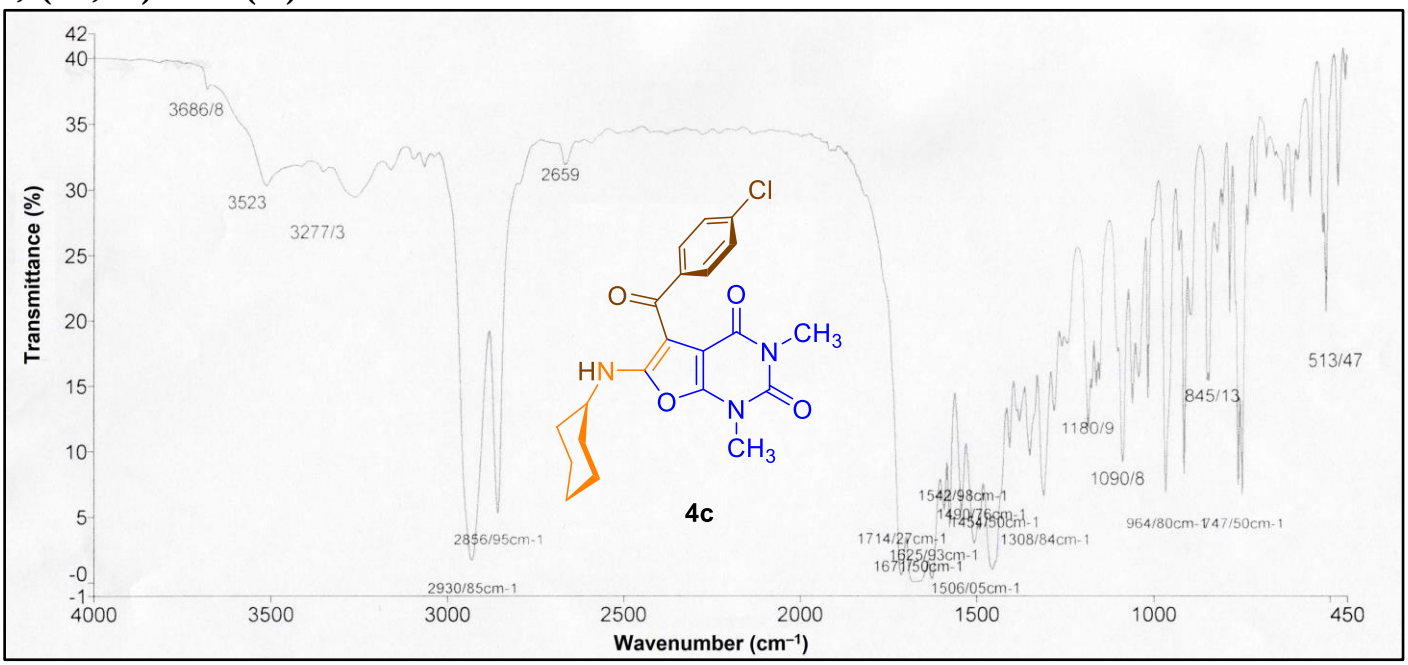
^{1}H NMR Spectrum of 5-(4-bromobenzoyl)-6-(cyclohexylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4b)



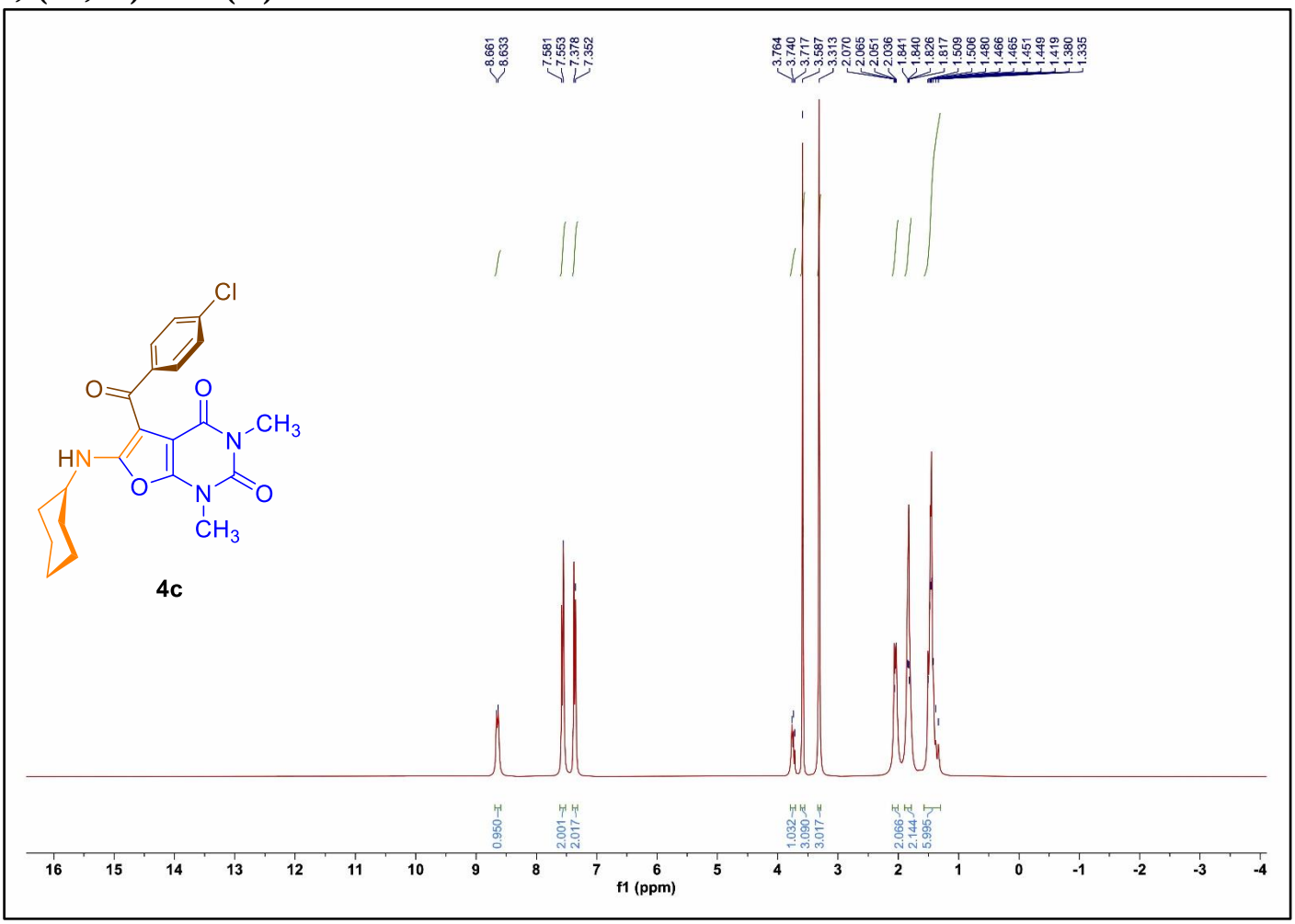
$^{13}C\{^{1}H\}$ NMR Spectrum of 5-(4-bromobenzoyl)-6-(cyclohexylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4b)



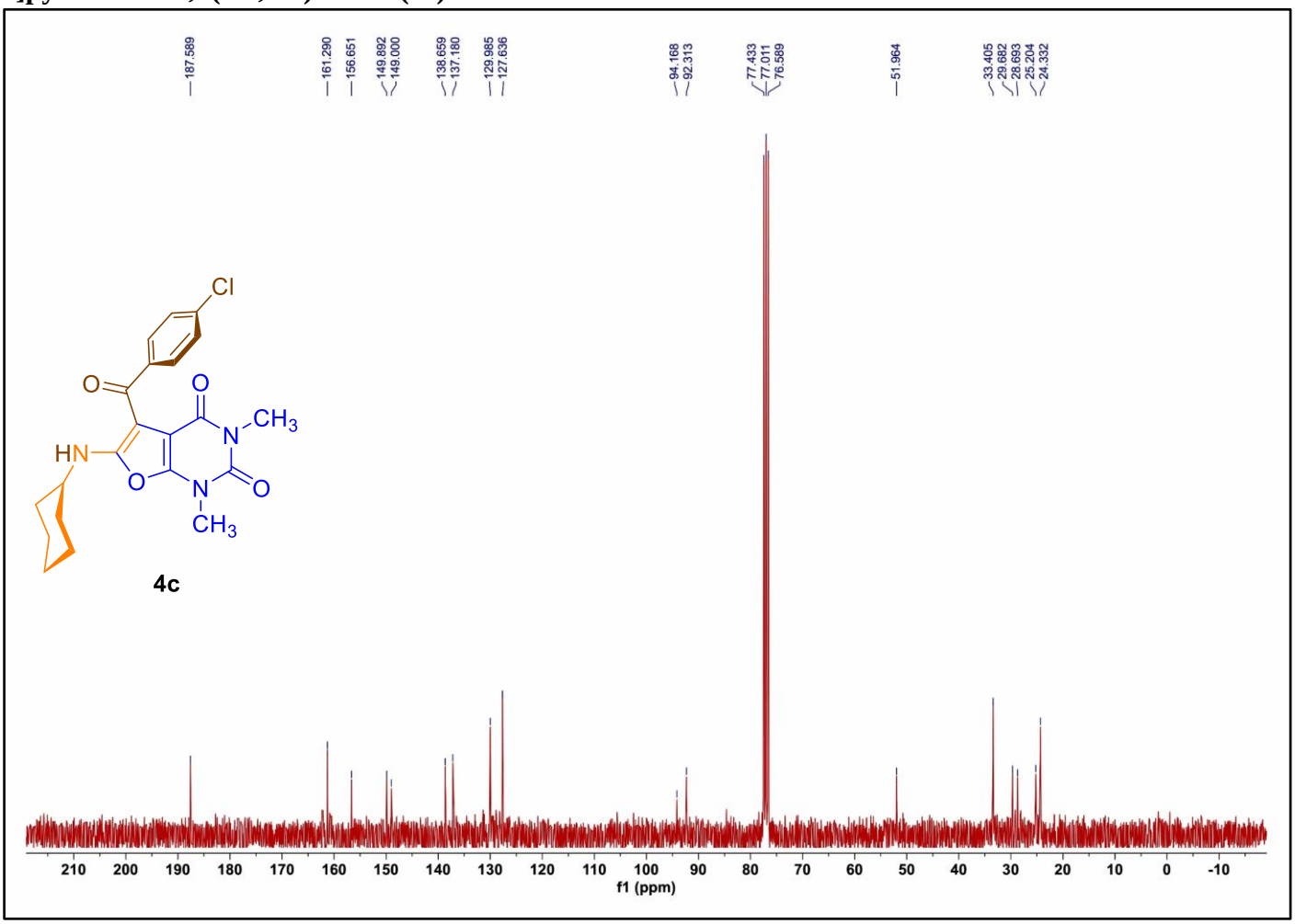
FT-IR Spectrum of 5-(4-chlorobenzoyl)-6-(cyclohexylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4c)



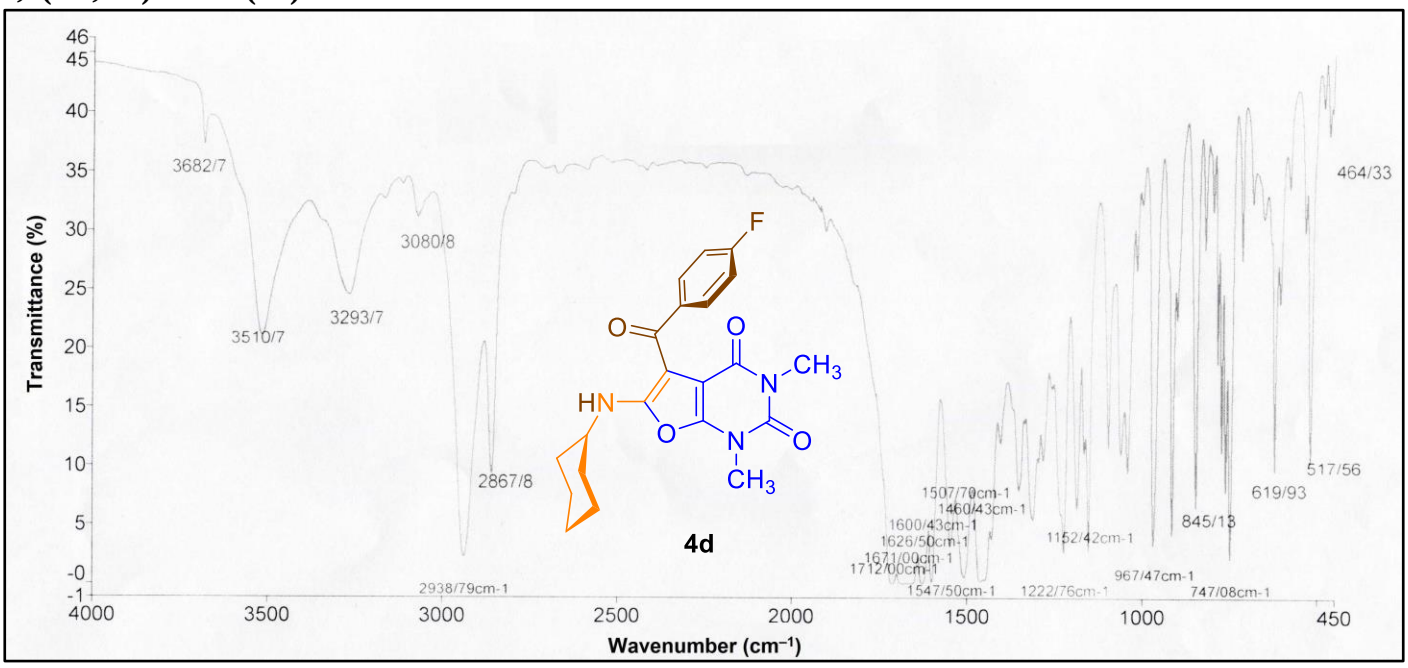
^{1}H NMR Spectrum of 5-(4-chlorobenzoyl)-6-(cyclohexylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4c)



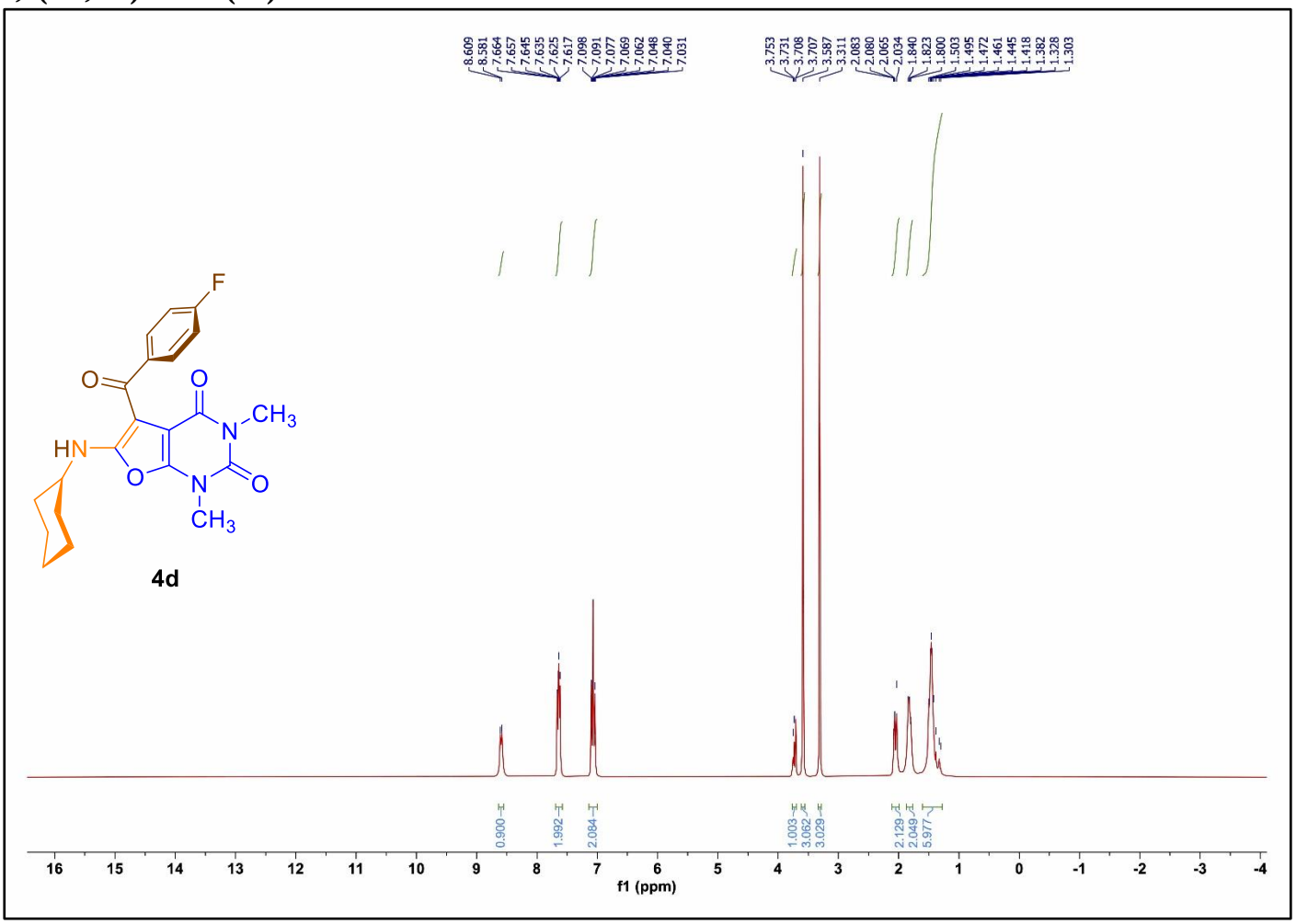
$^{13}C\{^{1}H\}$ NMR Spectrum of 5-(4-chlorobenzoyl)-6-(cyclohexylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4c)



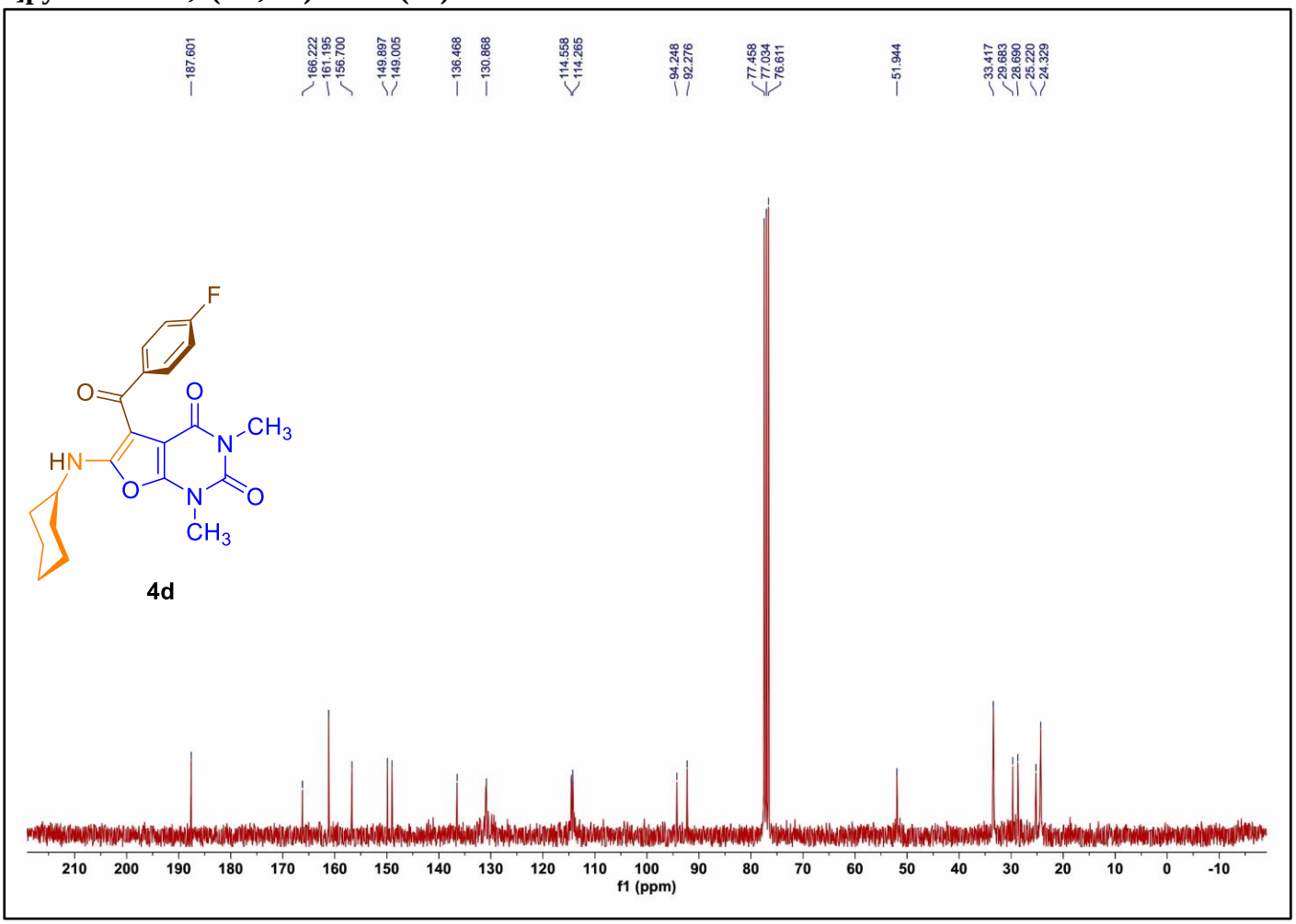
FT-IR Spectrum of 5-(4-fluorobenzoyl)-6-(cyclohexylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4d)



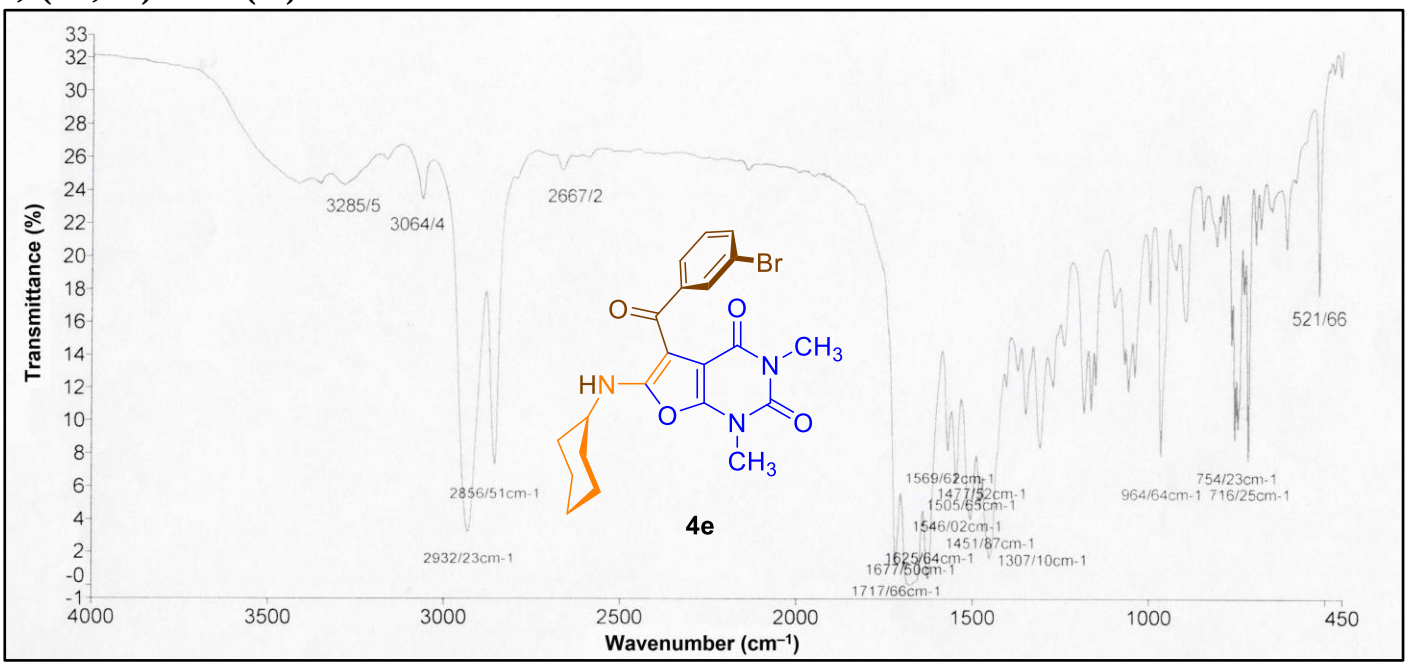
^{1}H NMR Spectrum of 5-(4-fluorobenzoyl)-6-(cyclohexylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4d)



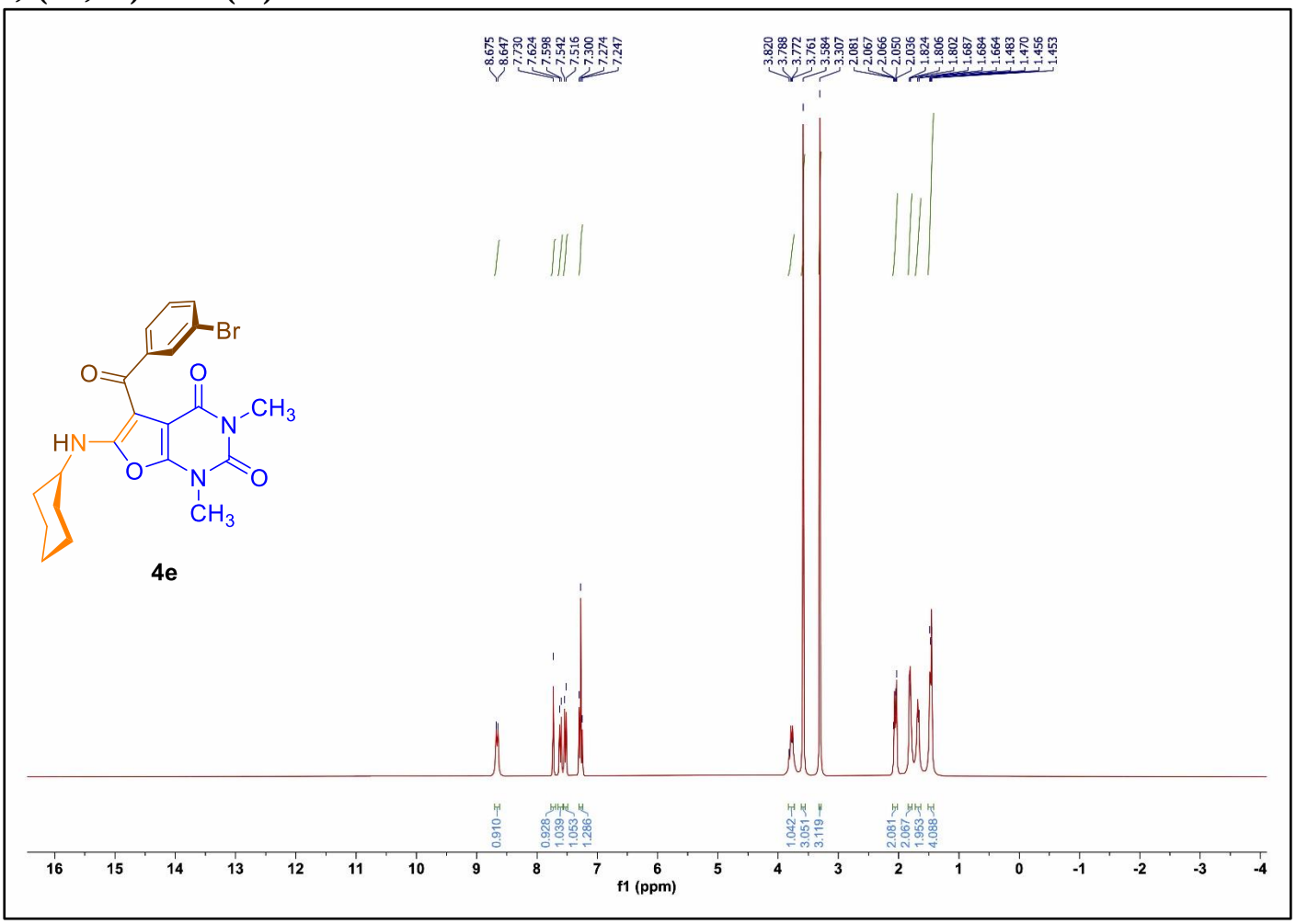
$^{13}C\{^{1}H\}$ NMR Spectrum of 5-(4-fluorobenzoyl)-6-(cyclohexylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4d)



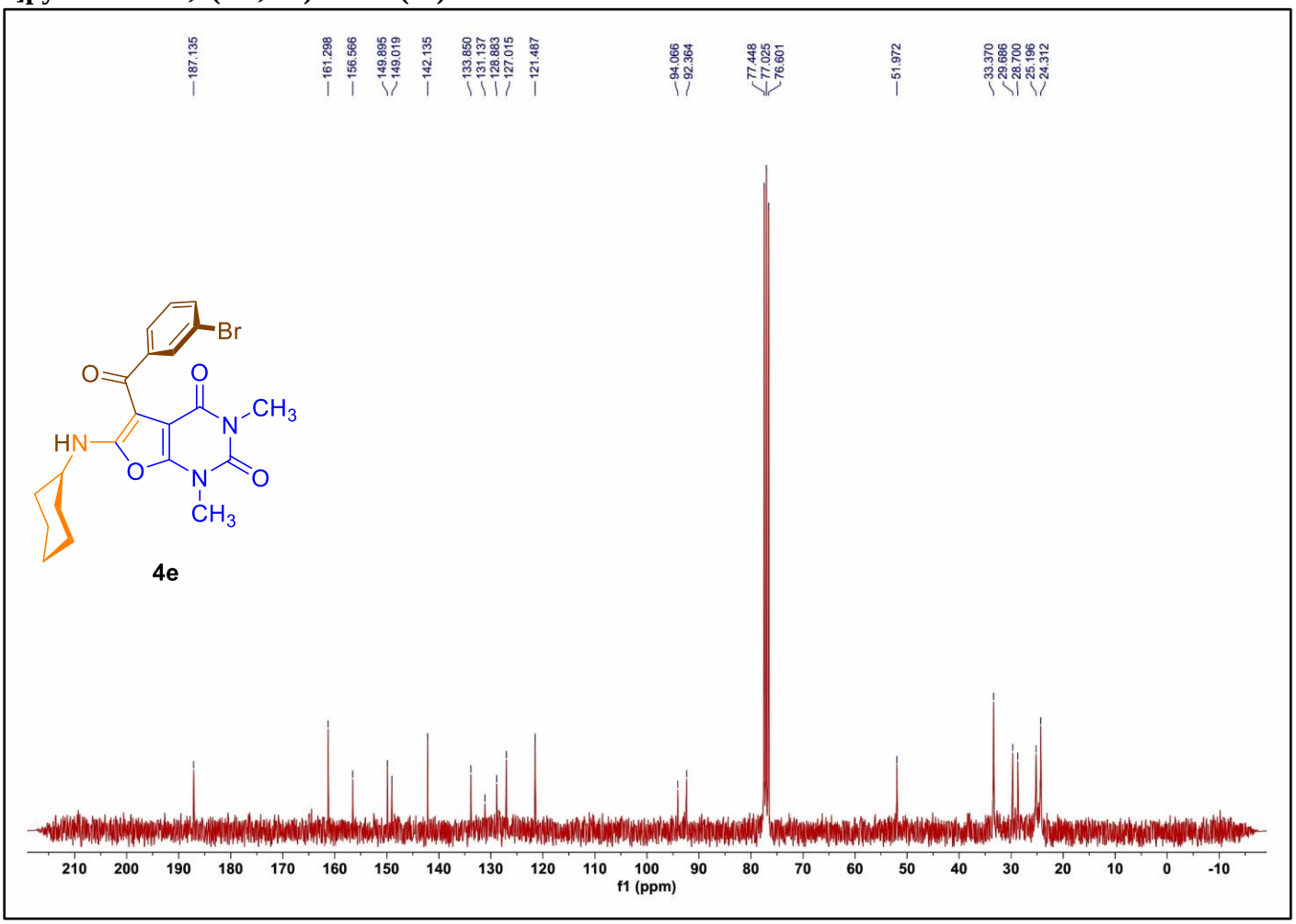
FT-IR Spectrum of 5-(3-bromobenzoyl)-6-(cyclohexylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4e)



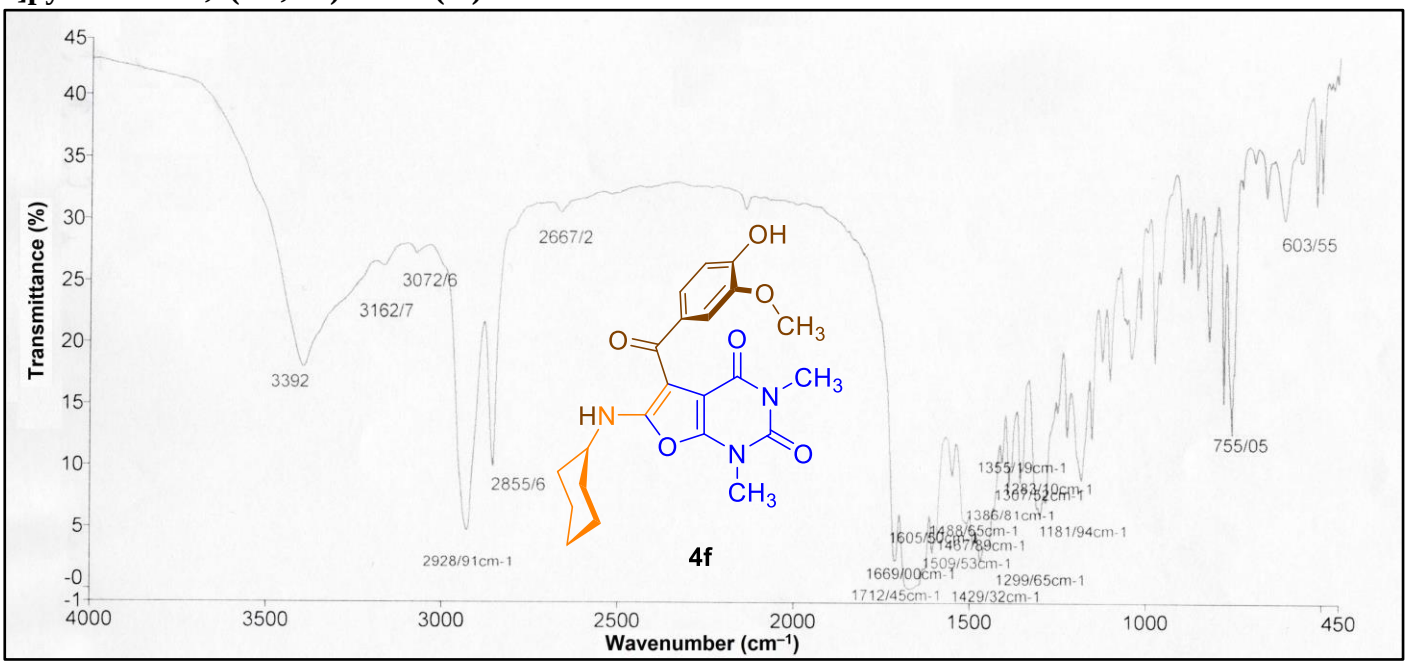
^{1}H NMR Spectrum of 5-(3-bromobenzoyl)-6-(cyclohexylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4e)



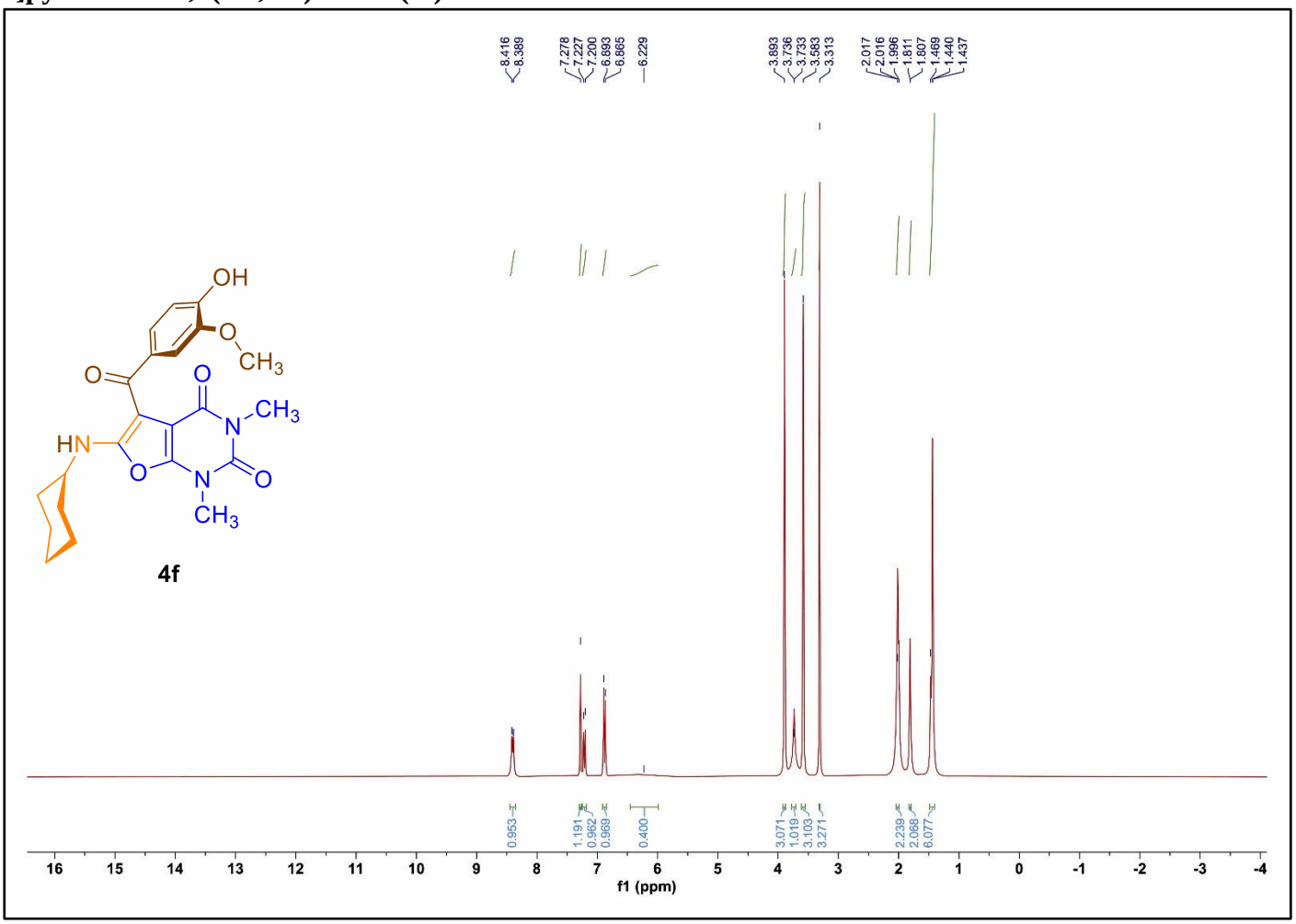
$^{13}C\{^{1}H\}$ NMR Spectrum of 5-(3-bromobenzoyl)-6-(cyclohexylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4e)



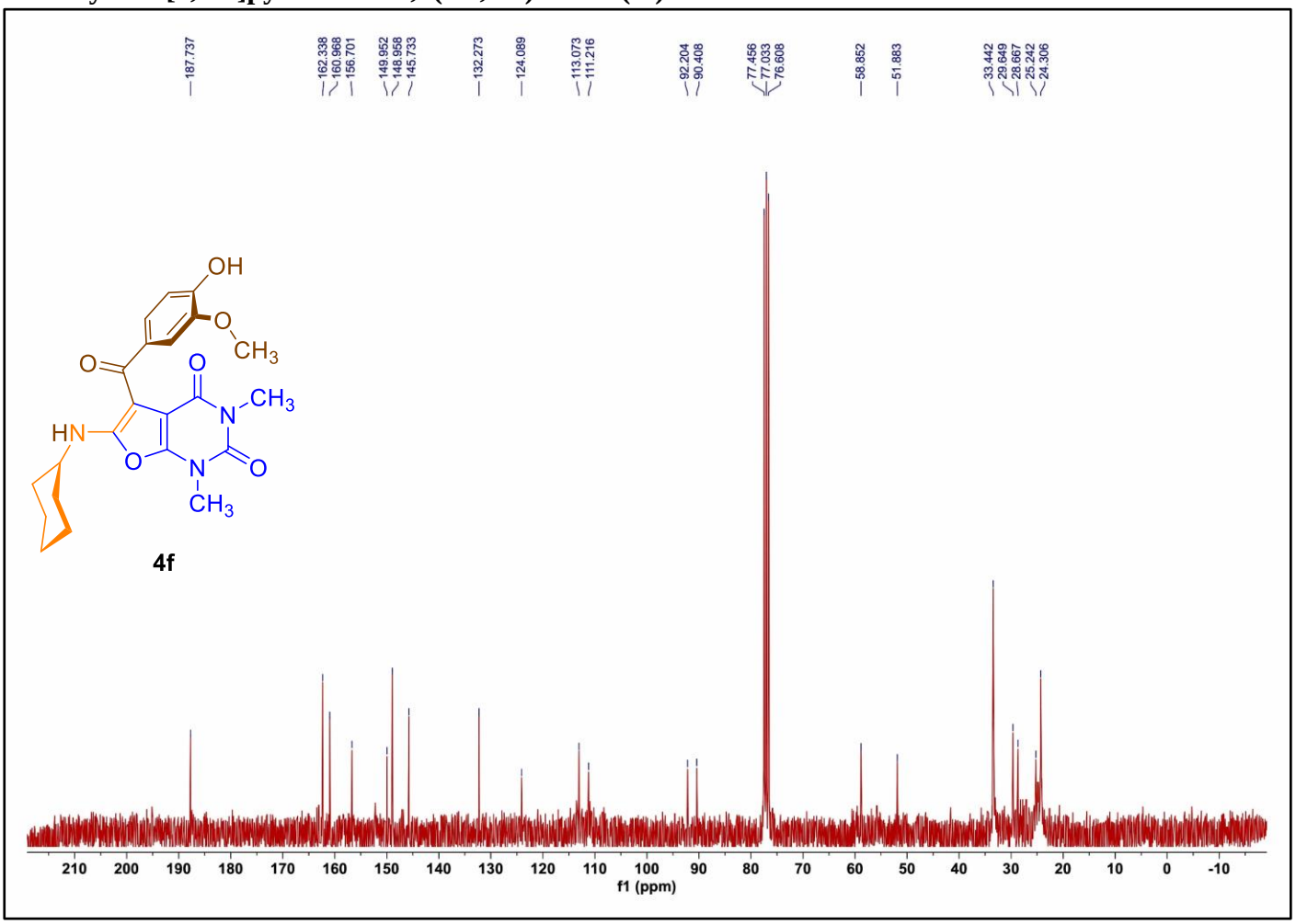
FT-IR Spectrum of 5-(4-hydroxy-3-methoxybenzoyl)-6-(cyclohexylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4f)



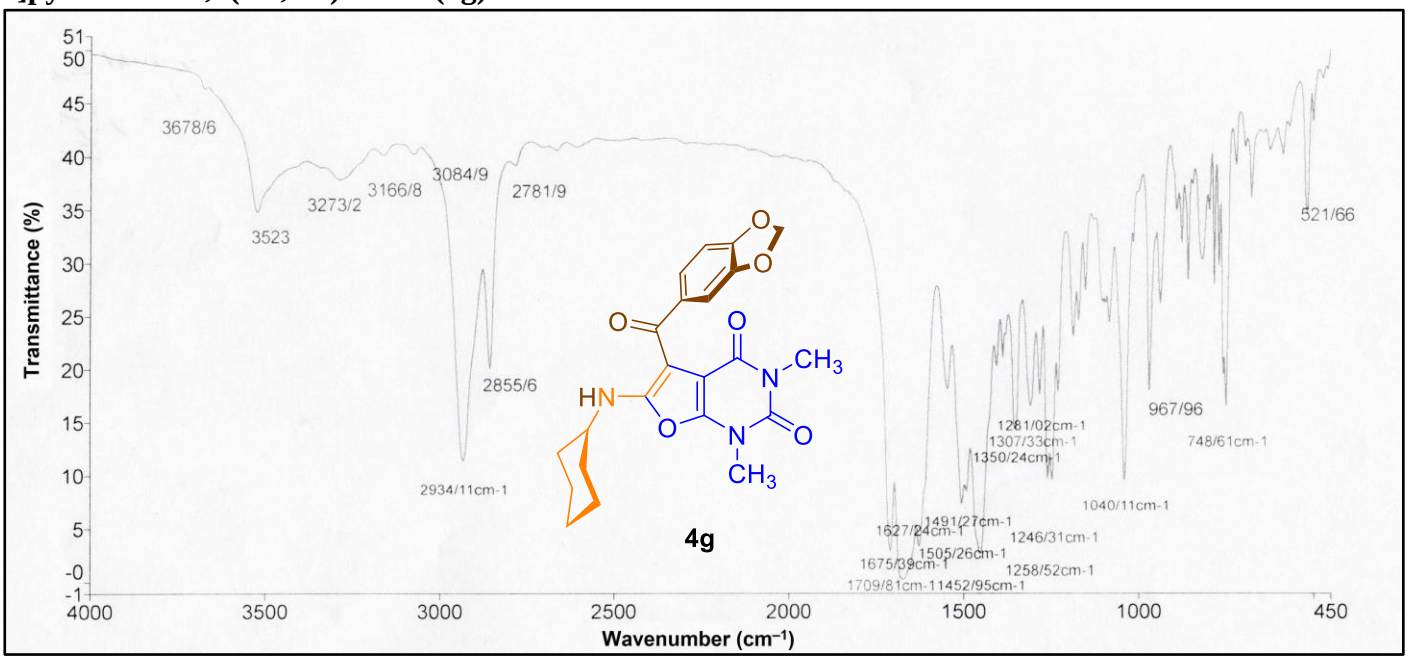
^{1}H NMR Spectrum of 5-(4-hydroxy-3-methoxybenzoyl)-6-(cyclohexylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4f)



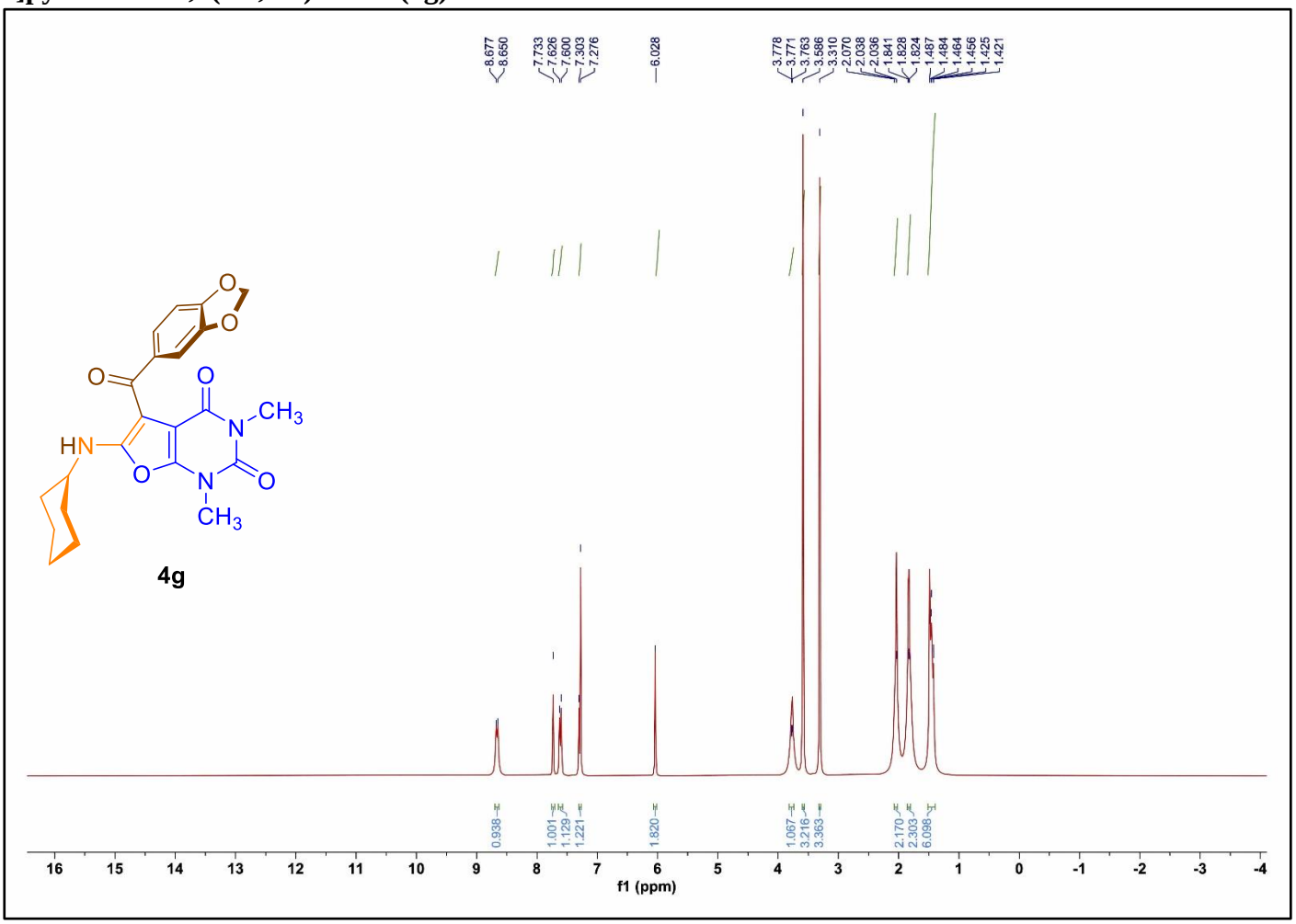
$^{13}C\{^{1}H\}$ NMR Spectrum of 5-(4-hydroxy-3-methoxybenzoyl)-6-(cyclohexylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4f)



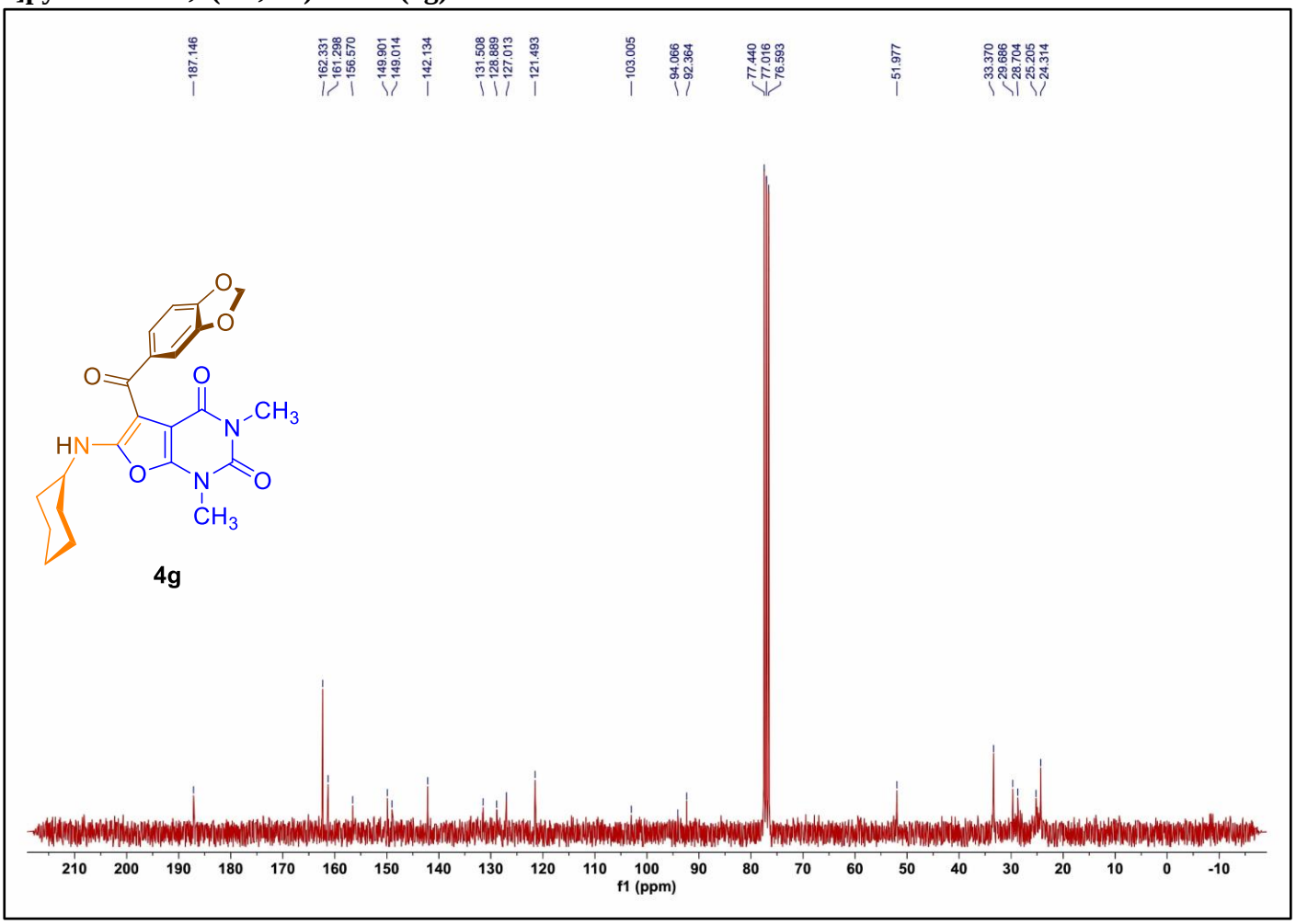
FT-IR Spectrum of 5-(3,4-methylendioxybenzoyl)-6-(cyclohexylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4g)



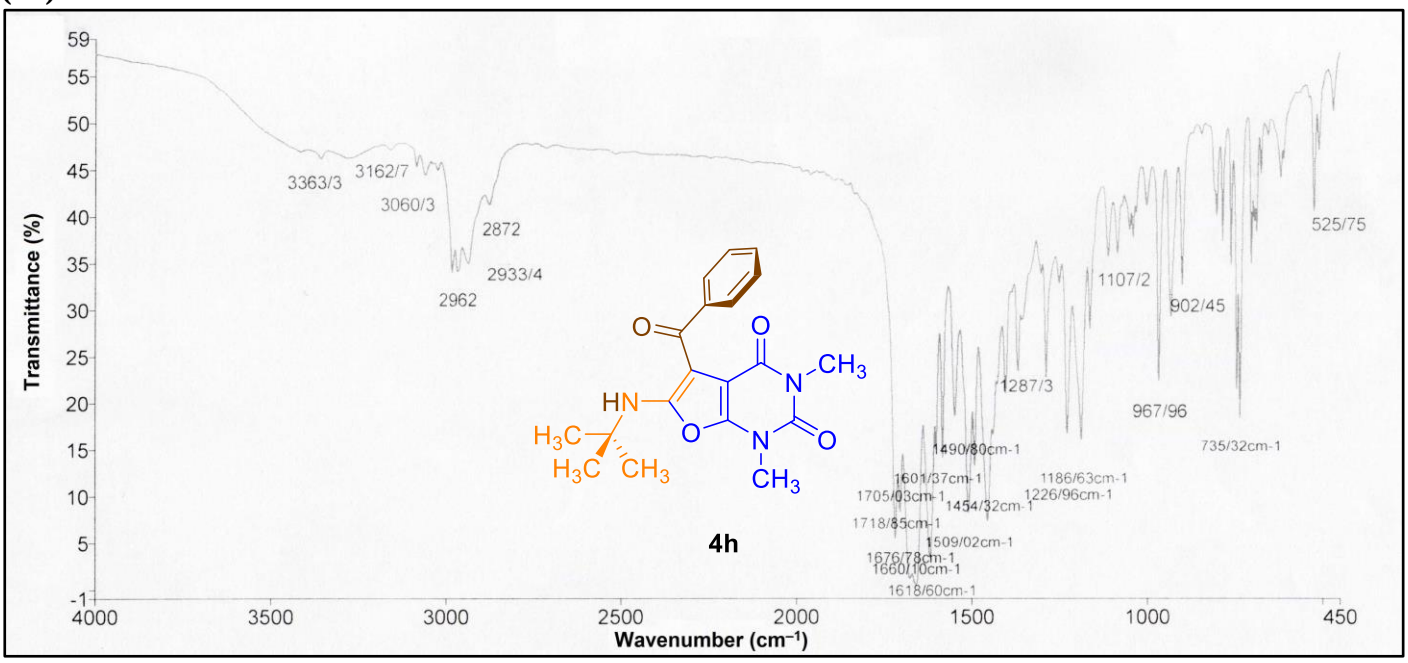
^{1}H NMR Spectrum of 5-(3,4-methylendioxybenzoyl)-6-(cyclohexylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4g)



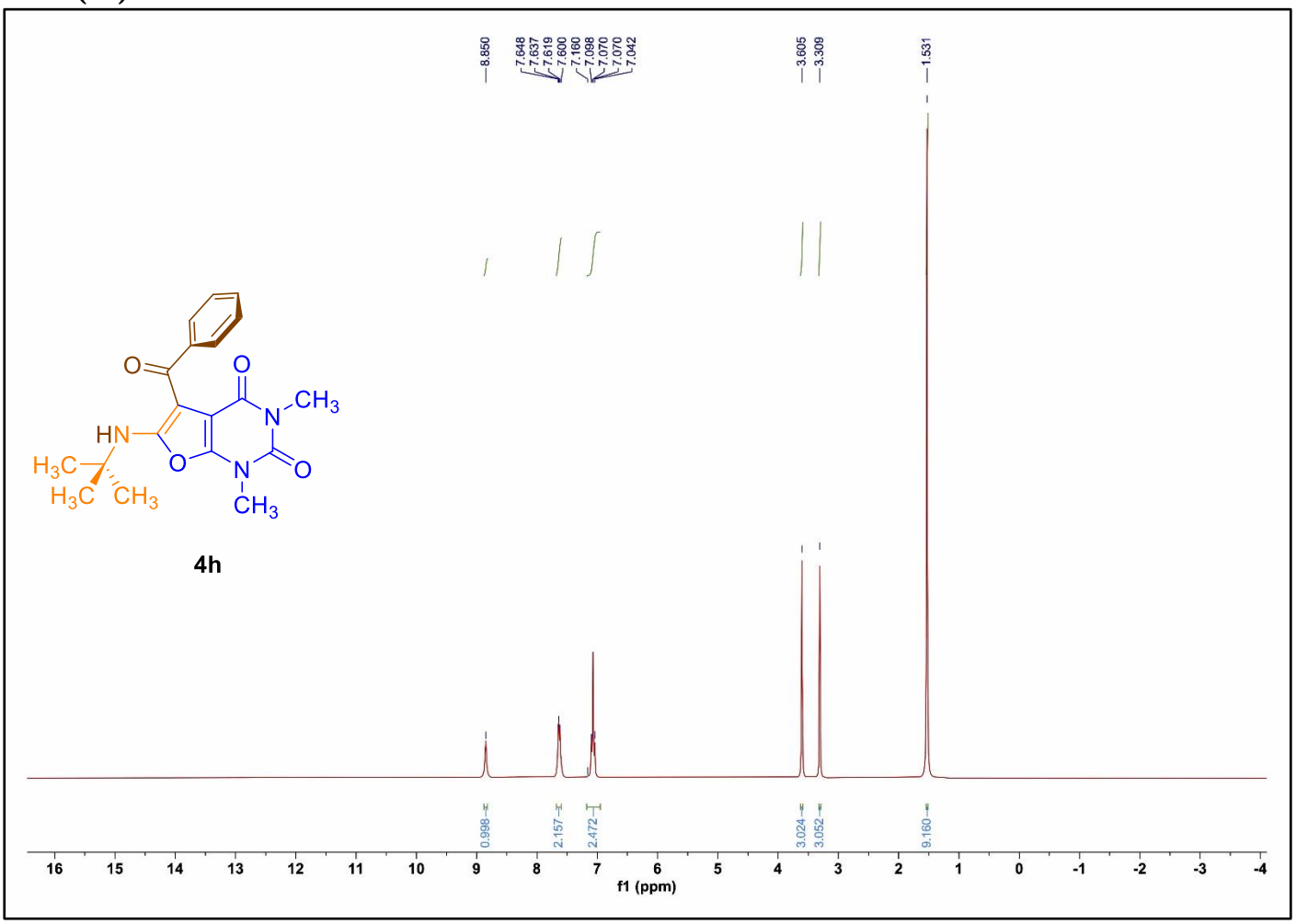
$^{13}C\{^{1}H\}$ NMR Spectrum of 5-(3,4-methylendioxybenzoyl)-6-(cyclohexylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4g)



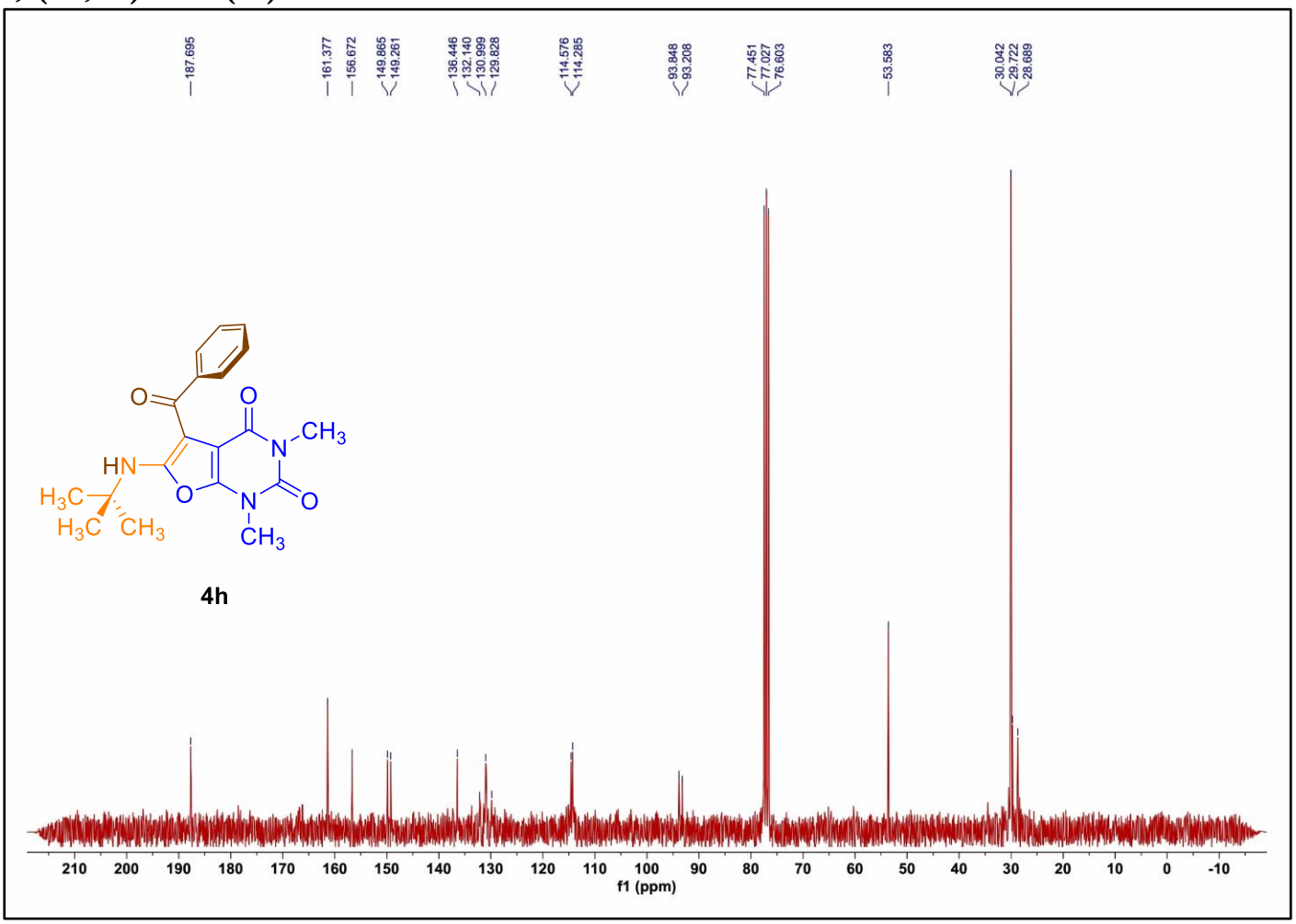
FT-IR Spectrum of 5-benzoyl-6-(*tert*-butylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4h)



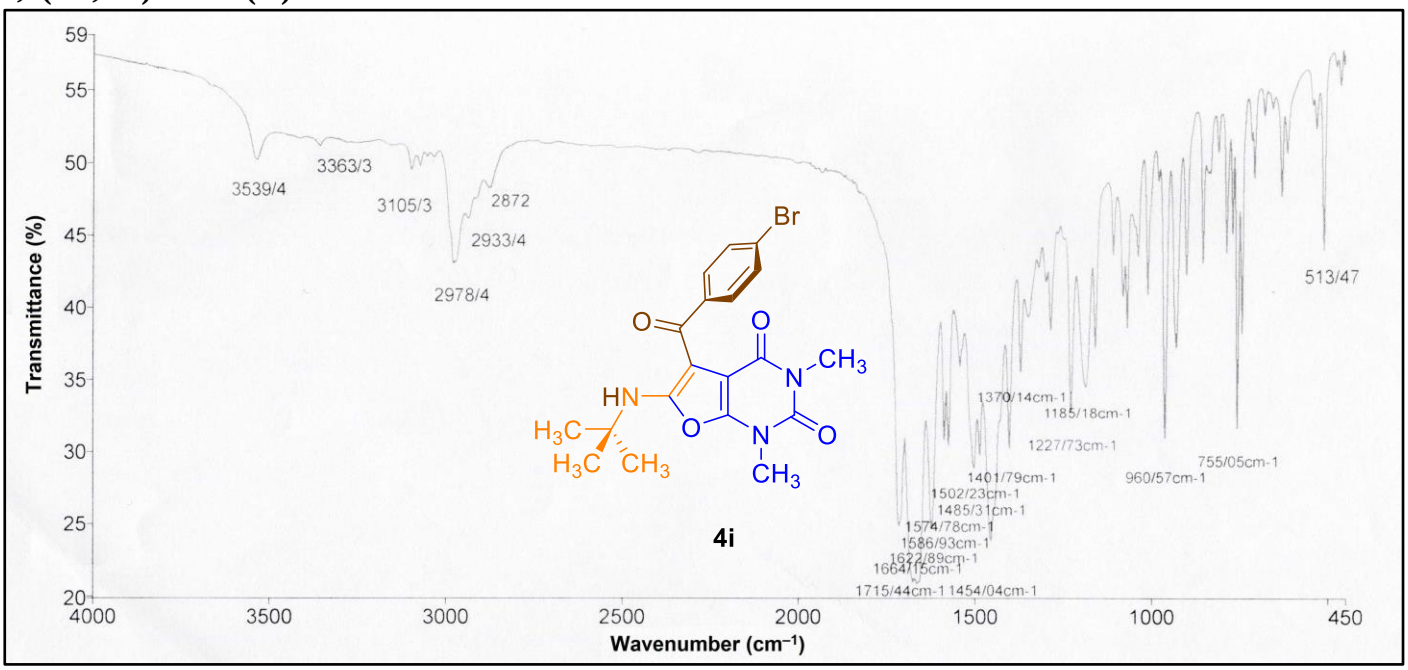
^{1}H NMR Spectrum of 5-benzoyl-6-(*tert*-butylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4h)



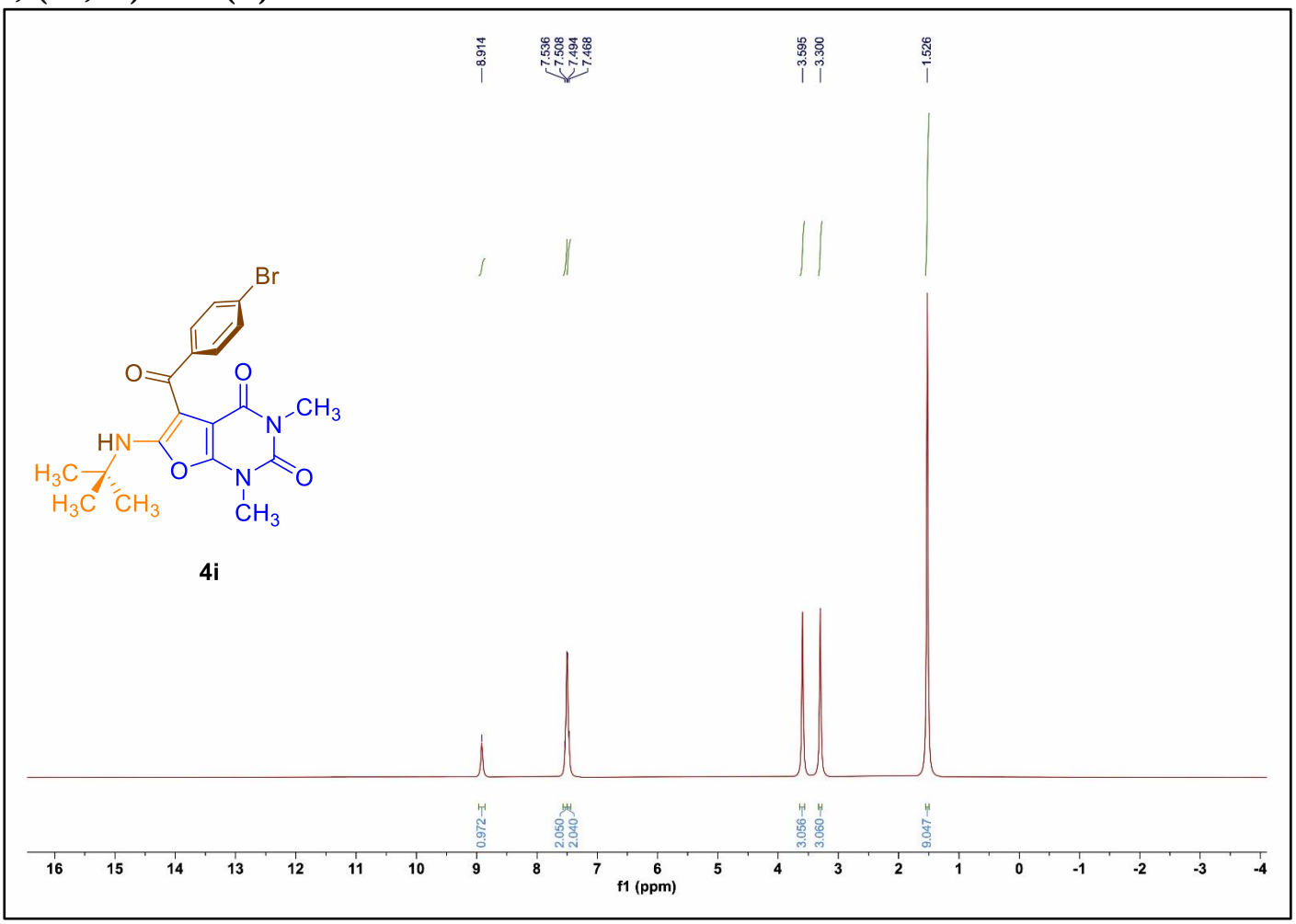
$^{13}C\{^{1}H\}$ NMR Spectrum of 5-benzoyl-6-(*tert*-butylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4h)



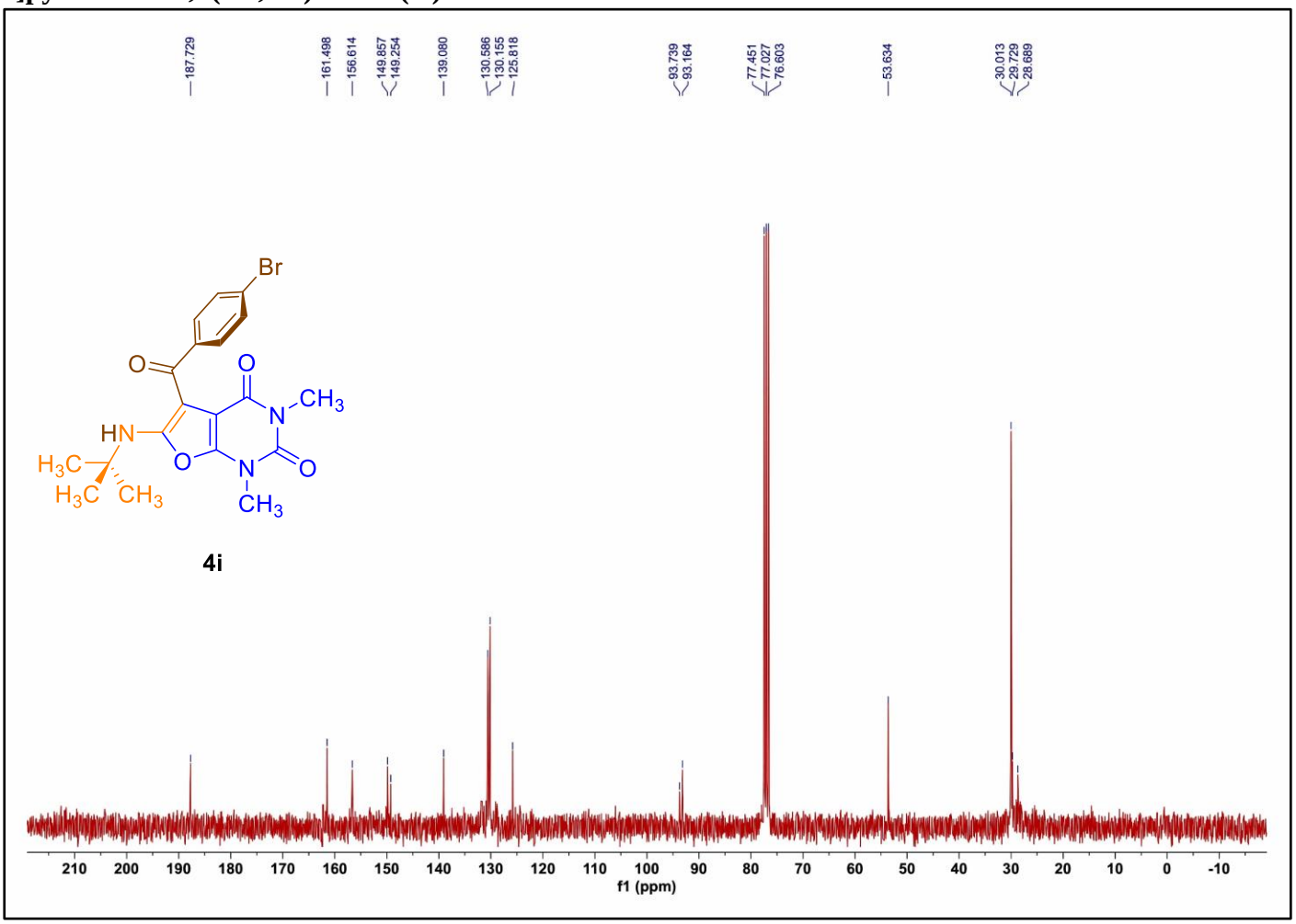
FT-IR Spectrum of 5-(4-bromobenzoyl)-6-(*tert*-butylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4i)



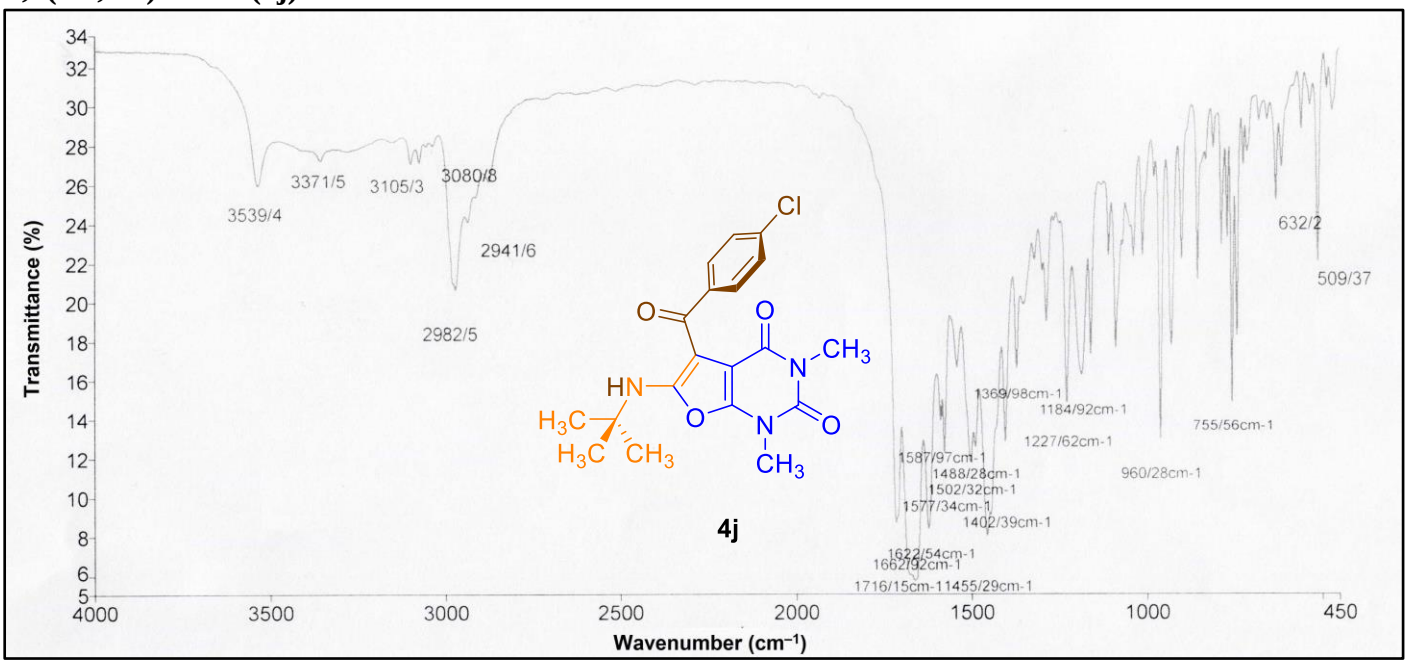
^{1}H NMR Spectrum of 5-(4-bromobenzoyl)-6-(*tert*-butylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4i)



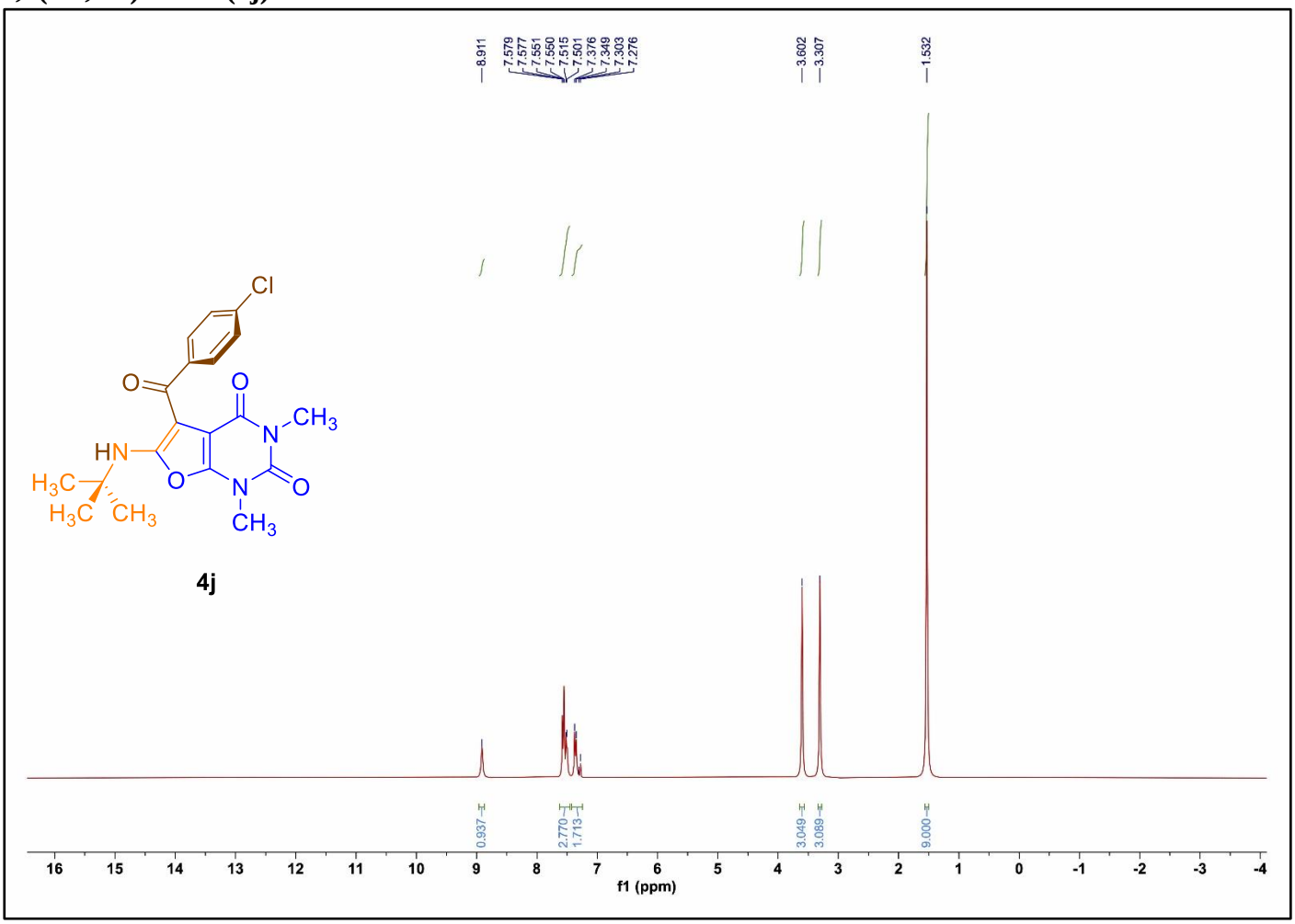
$^{13}C\{^{1}H\}$ NMR Spectrum of 5-(4-bromobenzoyl)-6-(*tert*-butylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4i)



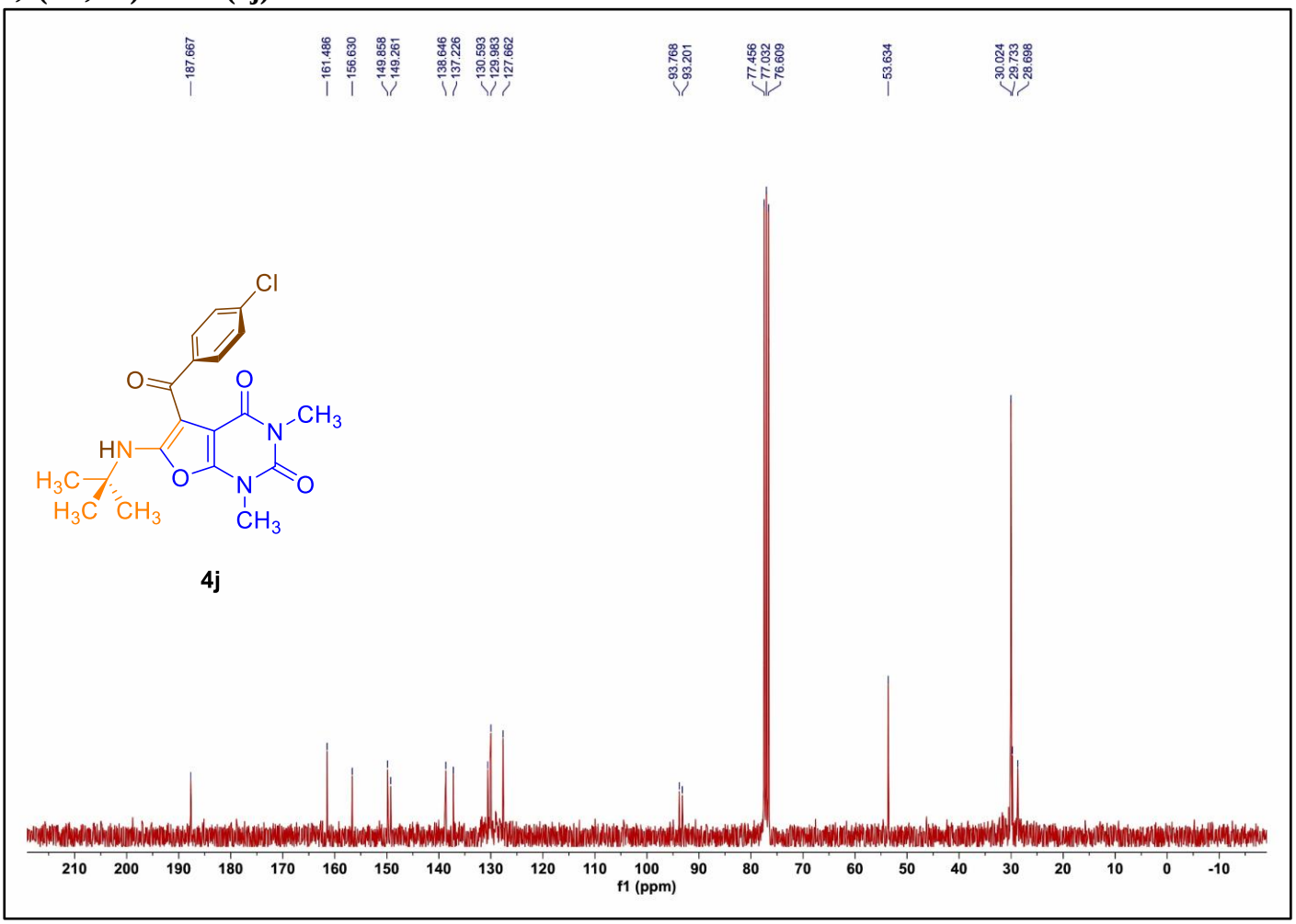
FT-IR Spectrum of 5-(4-chlorobenzoyl)-6-(*tert*-butylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4j)



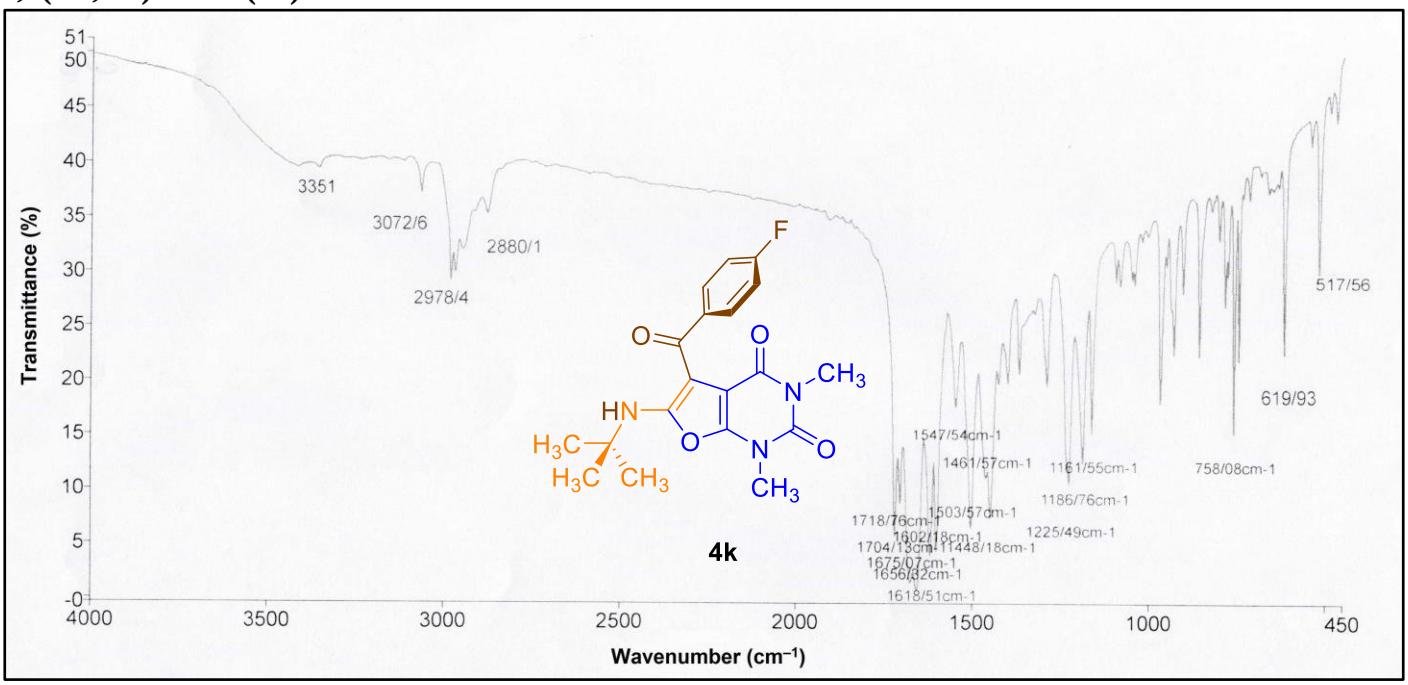
^{1}H NMR Spectrum of 5-(4-chlorobenzoyl)-6-(*tert*-butylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4j)



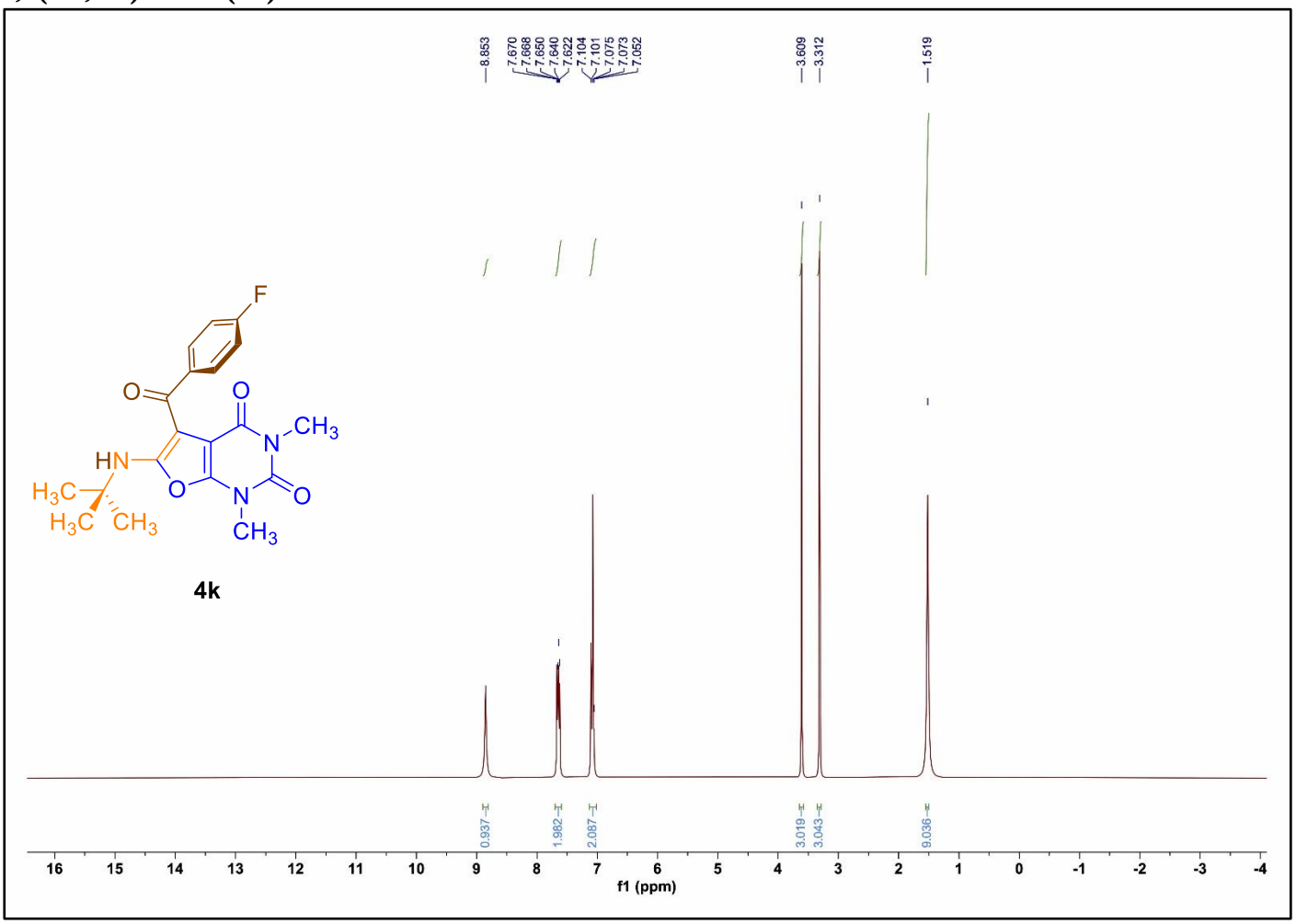
$^{13}C\{^{1}H\}$ NMR Spectrum of 5-(4-chlorobenzoyl)-6-(*tert*-butylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4j)



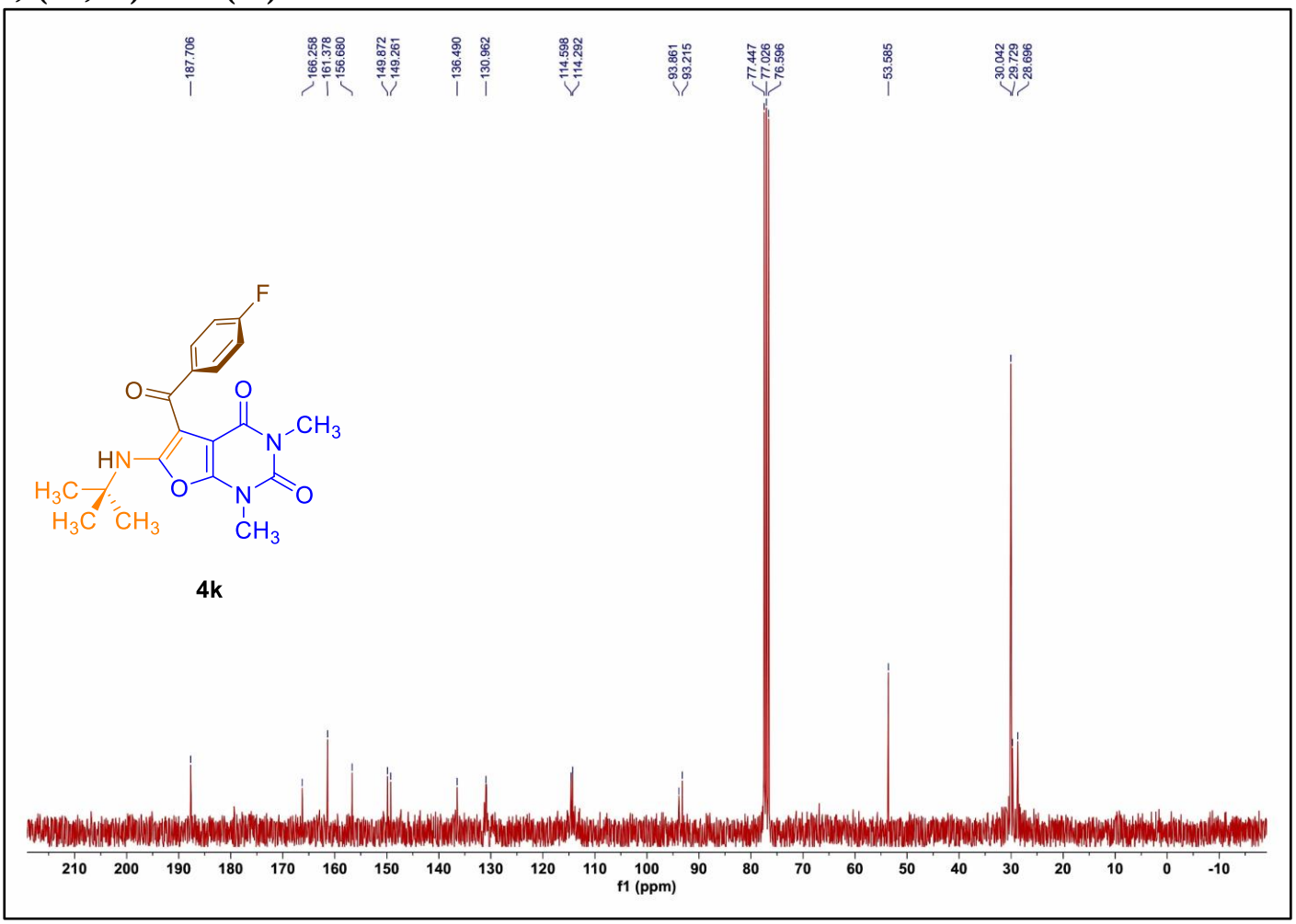
FT-IR Spectrum of 5-(4-fluorobenzoyl)-6-(*tert*-butylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4k)



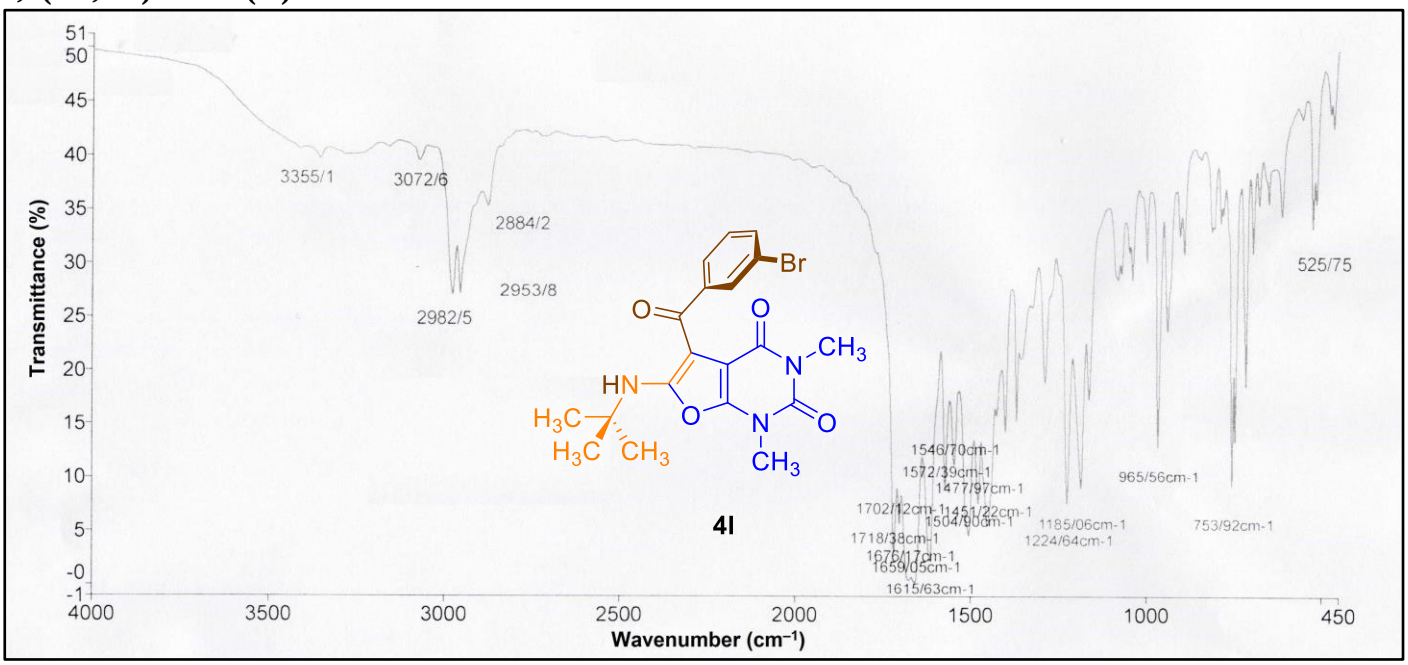
^{1}H NMR Spectrum of 5-(4-fluorobenzoyl)-6-(*tert*-butylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4k)



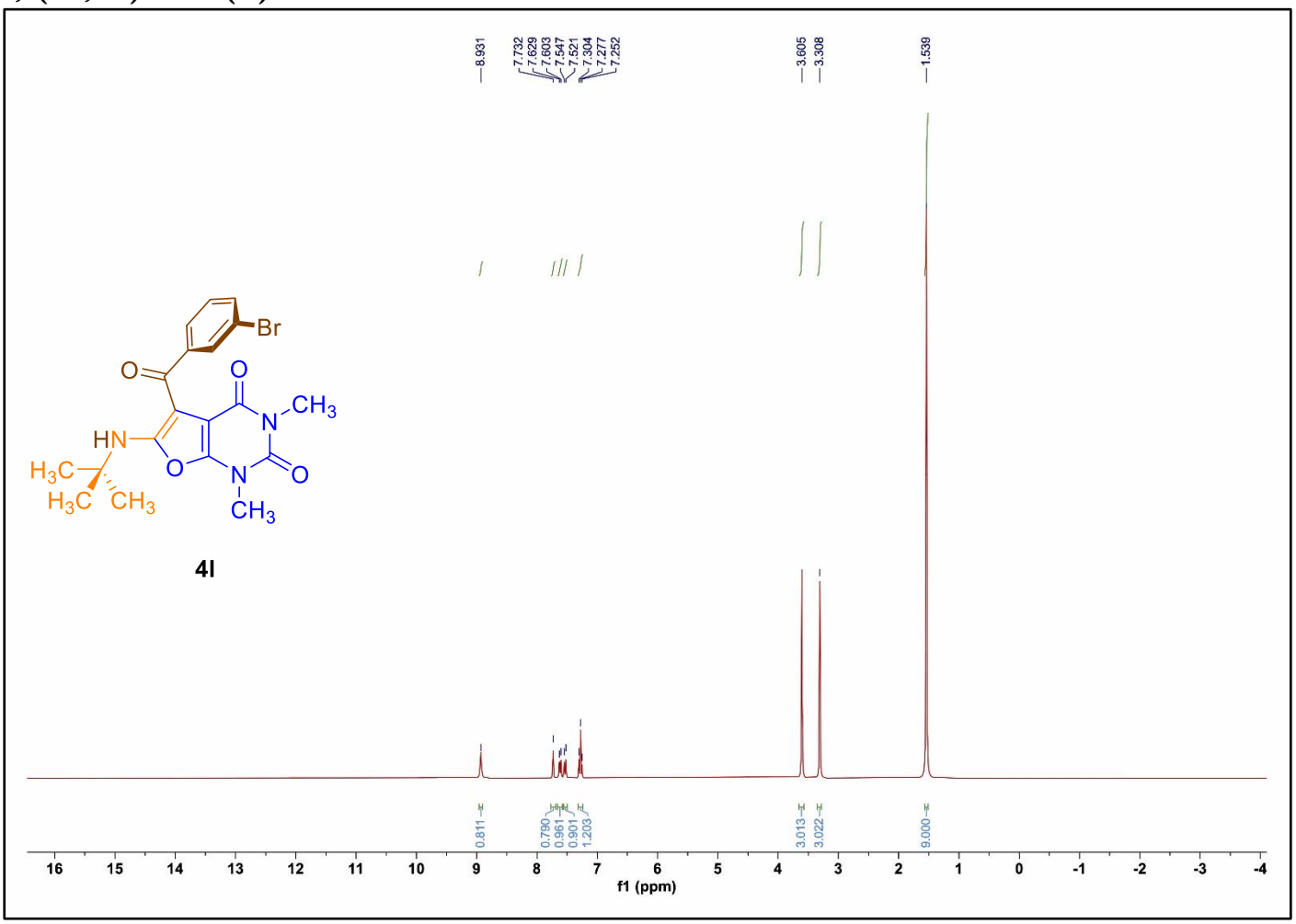
$^{13}C\{^{1}H\}$ NMR Spectrum of 5-(4-fluorobenzoyl)-6-(*tert*-butylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4k)



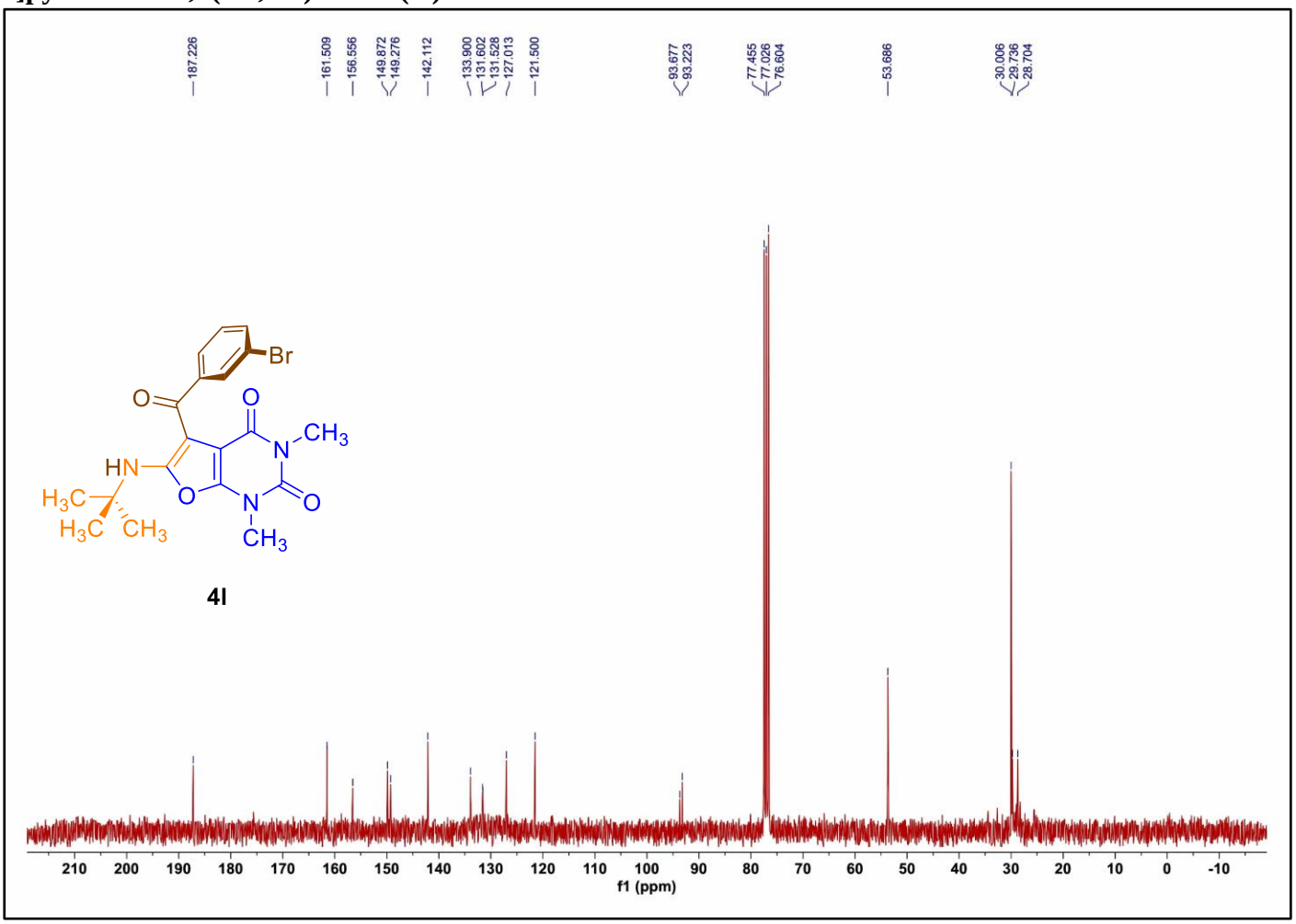
FT-IR Spectrum of 5-(3-bromobenzoyl)-6-(*tert*-butylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4l)



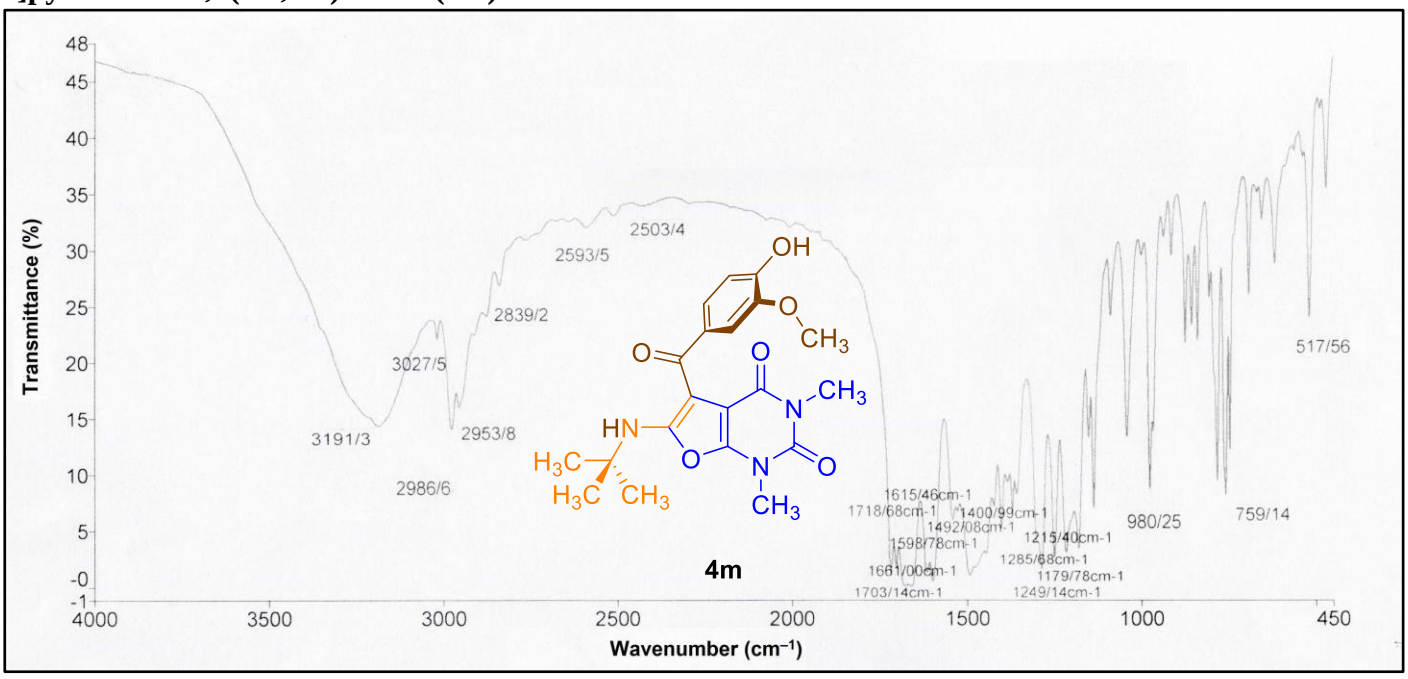
^{1}H NMR Spectrum of 5-(3-bromobenzoyl)-6-(*tert*-butylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4l)



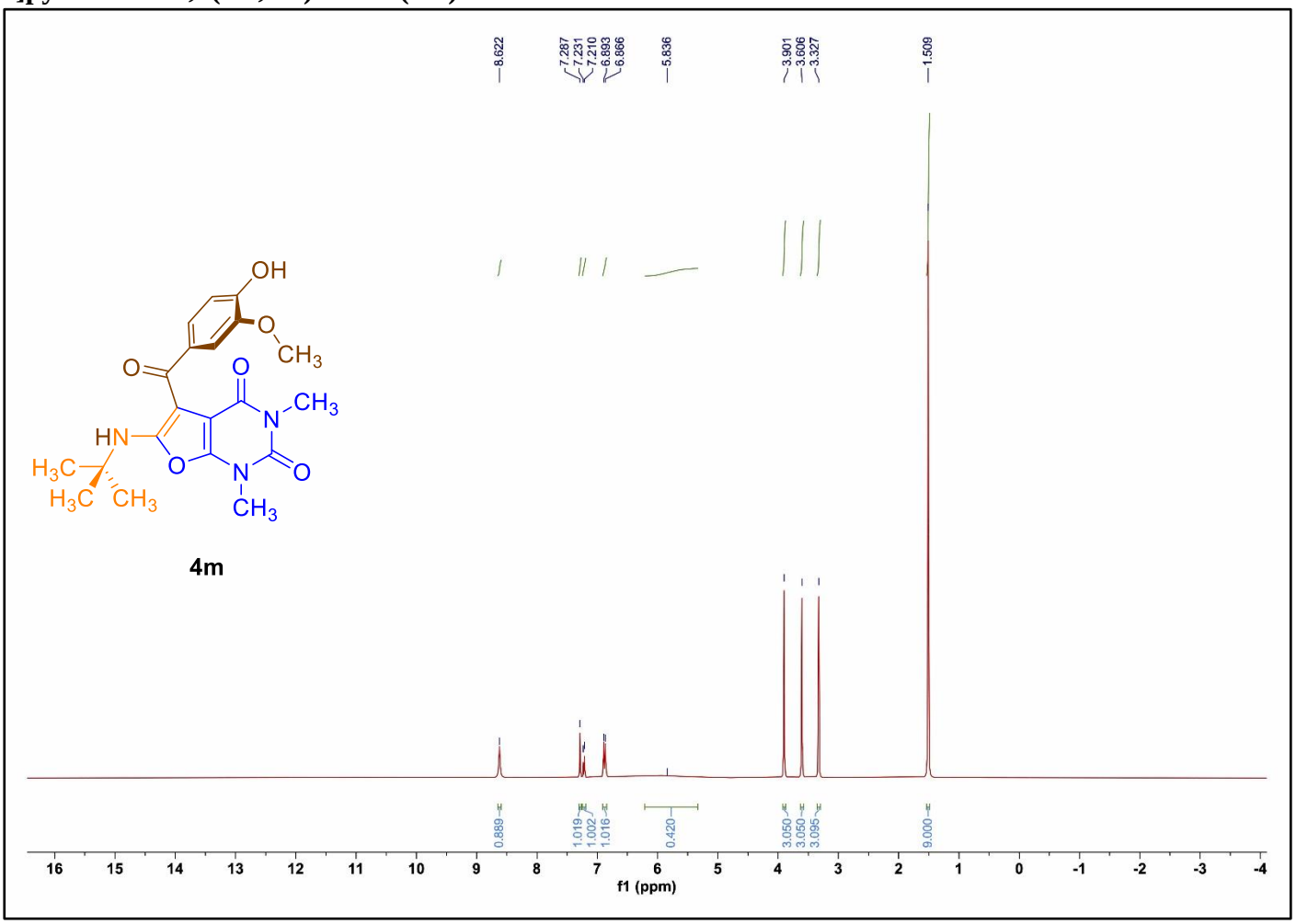
$^{13}C\{^{1}H\}$ NMR Spectrum of 5-(3-bromobenzoyl)-6-(*tert*-butylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4l)



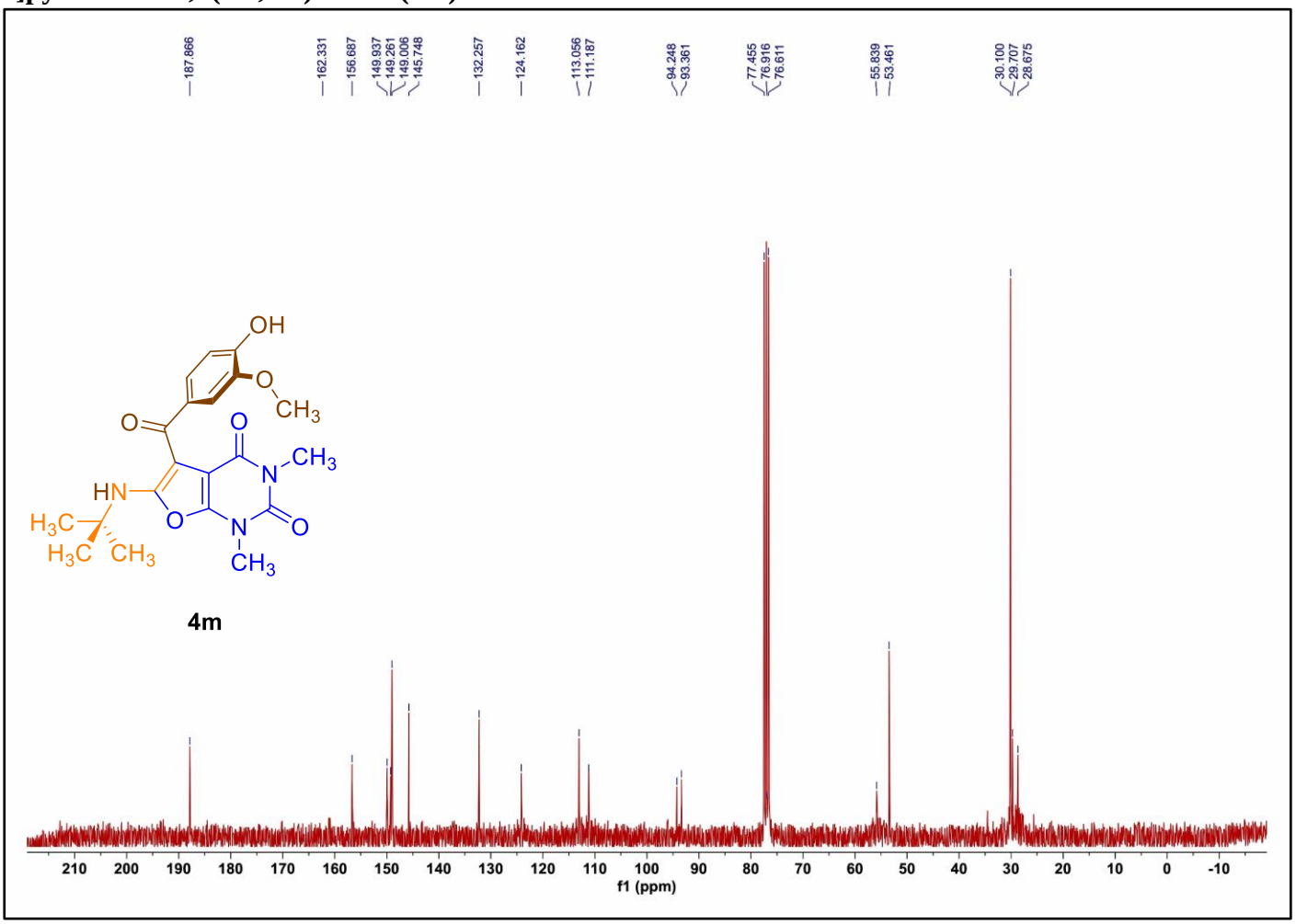
FT-IR Spectrum of 5-(4-hydroxy-3-methoxybenzoyl)-6-(*tert*-butylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4m)



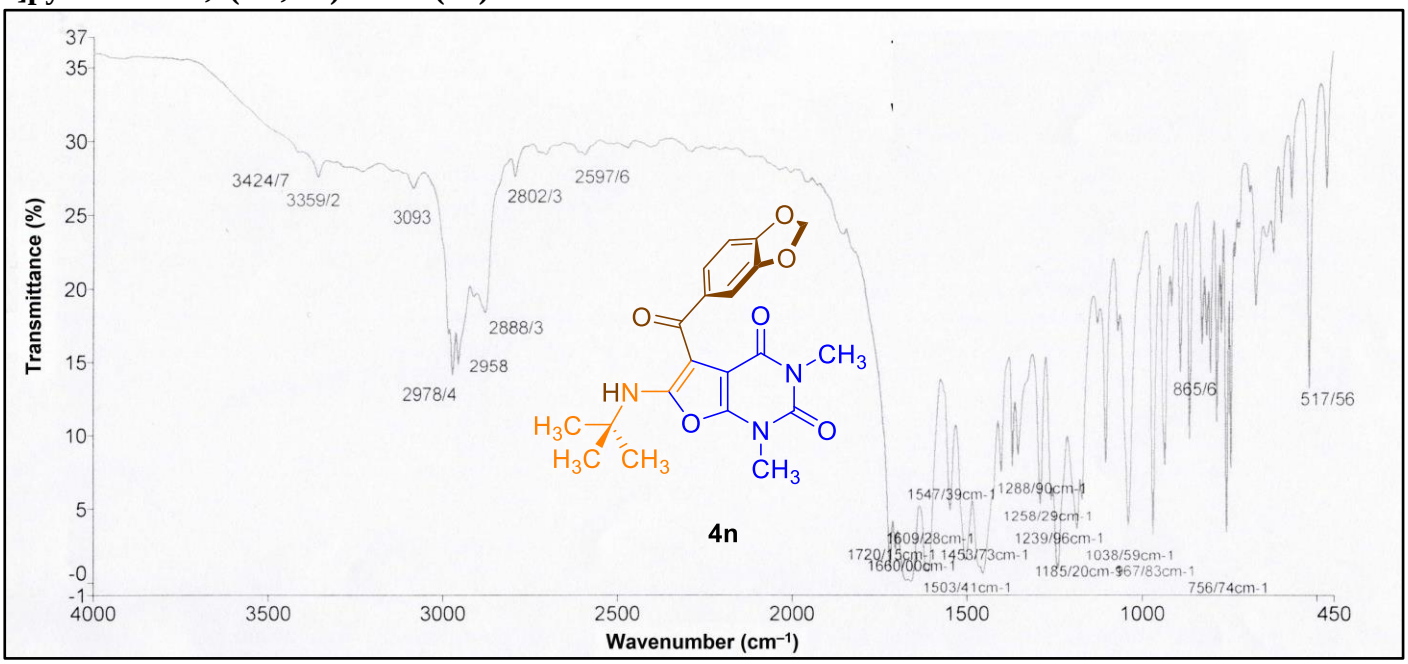
^{1}H NMR Spectrum of 5-(4-hydroxy-3-methoxybenzoyl)-6-(*tert*-butylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4m)



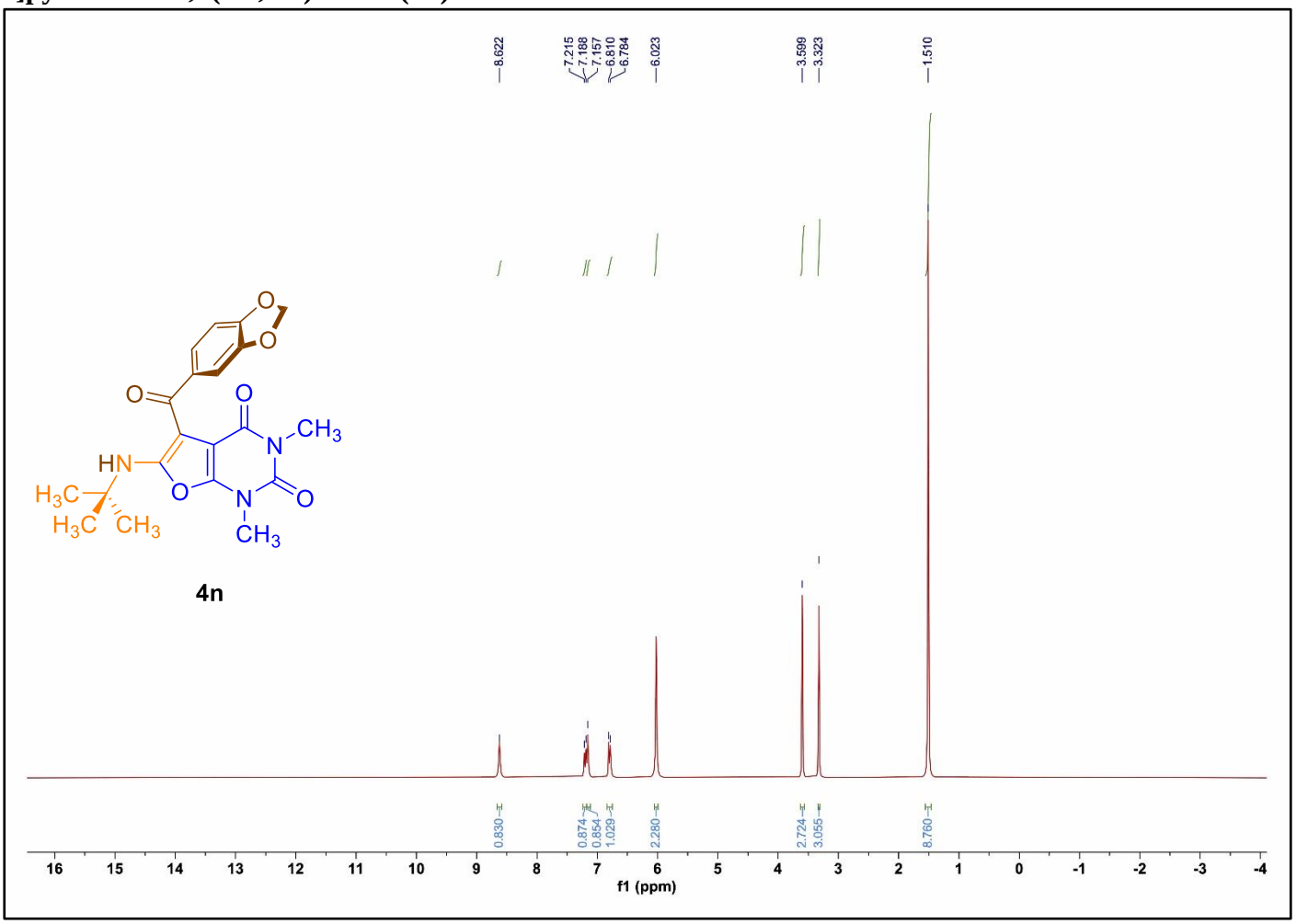
$^{13}C\{^{1}H\}$ NMR Spectrum of 5-(4-hydroxy-3-methoxybenzoyl)-6-(*tert*-butylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4m)



FT-IR Spectrum of 5-(3,4-methylendioxybenzoyl)-6-(*tert*-butylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4n)



^{1}H NMR Spectrum of 5-(3,4-methylendioxybenzoyl)-6-(*tert*-butylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4n)



$^{13}C\{^{1}H\}$ NMR Spectrum of 5-(3,4-methylendioxybenzoyl)-6-(*tert*-butylamino)-1,3-dimethylfuro[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4n)