Base-Promoted Transition-Metal-Free Synthesis of Quinazolinones with Antioxidant Activity

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1. General considerations

Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded at 500 and 400 MHz in dimethyl sulphoxide (DMSO, 2.50 ppm). ^{1}H coupling constants (J) are reported in Hertz (Hz), with multiplicities specified as follows: s (singlet), d (doublet), t (triplet), and m (multiplet).

2. Experimental section

2.1 Materials

All solvents were utilized without any prior purification. K_2CO_3, 2-aminobenzamide, and benzoyl chlorides, along with various bases, were obtained from esteemed suppliers such as Sigma-Aldrich and Avra Chemical Company and employed directly without additional purification. Unless specified otherwise, all reactions were conducted in accurately oven-dried glassware, utilizing magnetic stirring and heating via a silicone oil bath under aerobic conditions. The progress of reactions was monitored using thin-layer chromatography (TLC) on 0.25 mm Merck TLC silica gel plates, with ultraviolet (UV) light serving as the visualizing agent. For the purification of reaction products, column chromatography was executed using silica gel (60–120 mesh, Merck) with hexane and ethyl acetate as eluents. The process of concentrating the solutions involved the removal of volatile solvents using a rotary evaporator attached to a dry diaphragm pump (10–15 mm Hg), followed by further reduction to a constant weight using an oil pump (300 mTorr), a technique referred to as concentration in *vacuo*.

2.2 Methods

2.2.1 General procedure for the synthesis of 2-phenyl quinazoline-4(3*H*)-ones

In a sealed tube, 2-amino benzamide (1.0 equiv.), benzoyl chloride (1.5 equiv.), K_2CO_3 (2.5 equiv.), and PEG-200 (2.0 mL) were taken and stirred at 130 ^{o}C for the required time. The progress of the reaction was monitored through TLC. After completion of the reaction, the mixture was cooled to room temperature and diluted with 20 mL of water. The aqueous phase was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with 15 mL of water, dried over anhydrous sodium sulfate, filtered, and concentrated in a vacuum, and the products were purified by column chromatography using *n*-hexane and ethyl acetate as eluents to afford the corresponding products in good to excellent yields. ^{1}H NMR

spectra of all the isolated products were recorded and compared to the standard samples for confirmation.

2.2.2 In-vitro antioxidant activity (DPPH assay)

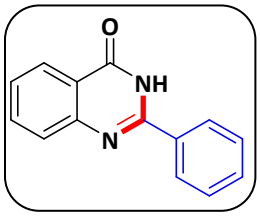
The scavenging activity of 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical against synthesized materials was measured using 96-well plates as reported by Lee et al.[1] A 0.34 mM DPPH solution was prepared by dissolving DPPH in methanol. In brief, 100µL of DPPH solution was combined with 100µL of the samples at different concentrations varying between 5 and 100 µg/mL. Ascorbic acid served as the reference standard compound. The above mixture was incubated for 30 min in the dark at room temperature. At 517 nm wavelengths, the decreased intensity of the reaction mixture was evaluated after the incubation period. A lower absorbance value indicates a better free-radical scavenging activity of the gels. Using the following formula, the DPPH radical scavenging activity for the sample was determined.

$$\textit{Scavenging activity (\%)} = A_{control} - A_{sample} / A_{control} \times 100$$

Where $A_{control}$ and A_{sample} refer to the absorbance of the control and sample.

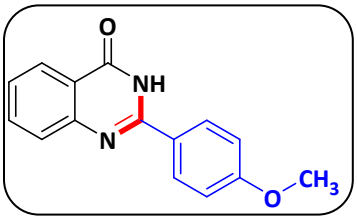
3. Spectroscopic data of newly obtained products

2-phenylquinazolin-4(3*H*)-one (3a)[2]



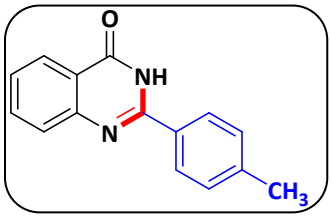
Purified by column chromatography (15% ethyl acetate in hexane), white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.54 (s, 1H), 8.20-8.16 (m, 3H), 7.85 (t, *J* = 7.75 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.61-7.52 (m, 4H).

2-(4-methoxyphenyl) quinazolin-4(3*H*)-one (3b)[2]



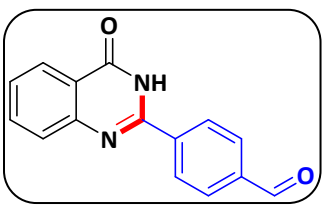
Purified by column chromatography (20% ethyl acetate in hexane), white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.42 (s, 1H), 8.17 (dd, *J* = 30.7, 8.25 Hz, 3H), 7.81 (t, *J* = 7.5 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.48 (t, *J* = 7.25 Hz, 1H), 7.09 (d, *J* = 8.0 Hz, 2H), 3.85 (s, 3H).

2-(p-tolyl) quinazolin-4(3*H*)-one (3c)[2]



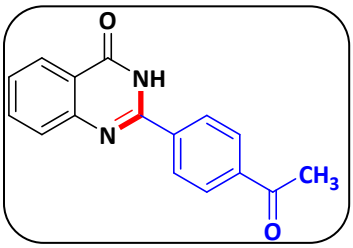
Purified by column chromatography (15% ethyl acetate in hexane), white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.48 (s, 1H), 8.15 (d, *J* = 8.0 Hz, 1H), 8.10 (d, *J* = 7.0 Hz, 2H), 7.83 (t, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.36 (d, *J* = 7.5 Hz, 2H), 2.40 (s, 3H).

4-(4-Oxo-3,4-dihydroquinazolin-2-yl) benzaldehyde (3d)[9]



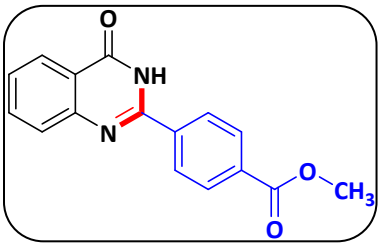
Purified by column chromatography (17% ethyl acetate in hexane), white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.72 (s, 1H), 10.11 (s, 1H), 8.36 (d, *J* = 8.0 Hz, 2H), 8.17 (d, *J* = 8.0 Hz, 1H), 8.06 (d, *J* = 8.0 Hz, 2H), 7.86 (t, *J* = 7.5 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H).

2-(4-Acetylphenyl) quinazolin-4(3*H*)-one (3e)[9]



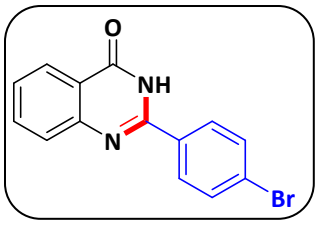
Purified by column chromatography (28% ethyl acetate in hexane), white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.71 (s, 1H), 8.32 (d, *J* = 7.5 Hz, 2H), 8.18 (d, *J* = 7.5 Hz, 1H), 8.10 (d, *J* = 7.5 Hz, 2H), 7.87 (t, *J* = 7.5 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.56 (t, *J* = 7.25 Hz, 1H), 2.65 (s, 3H).

Methyl 4-(4-oxo-3,4-dihydroquinazolin-2-yl) benzoate (3f)[9]



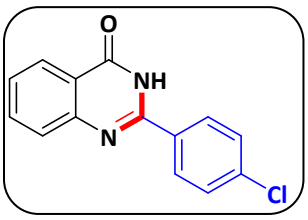
Purified by column chromatography (20% ethyl acetate in hexane), white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.72 (s, 1H), 8.32 (d, *J* = 7.5 Hz, 1H), 8.20 (d, *J* = 8.0 Hz, 1H), 8.12 (d, *J* = 7.0 Hz, 2H), 7.85 (d, *J* = 8.5 Hz, 2H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.58 (t, *J* = 7.75 Hz, 1H), 3.91 (s, 3H).

2-(4-bromophenyl) quinazolin-4(3*H*)-one (3g)[2]



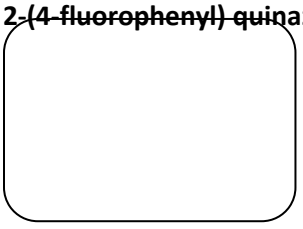
Purified by column chromatography (16% ethyl acetate in hexane), white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.58 (s, 1H), 8.12-8.07 (m, 3H), 7.81 (t, *J* = 7.6 Hz, 1H), 7.71 (t, *J* = 8.4 Hz, 3H), 7.50 (t, *J* = 7.4 Hz, 1H).

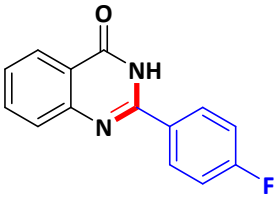
2-(4-chlorophenyl) quinazolin-4(3*H*)-one (3h)[4]



Purified by column chromatography (16% ethyl acetate in hexane), white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.62 (s, 1H), 8.20 (d, *J* = 8.0 Hz, 2H), 8.16 (d, *J* = 8.0 Hz, 1H), 7.85 (t, *J* = 7.5 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 2H), 7.54 (t, *J* = 7.5 Hz, 1H).

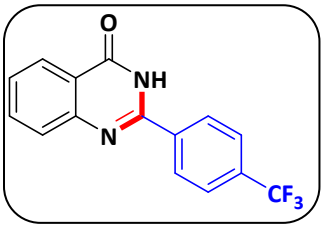
2-(4-fluorophenyl) quinazolin-4(3*H*)-one (3i)[2]





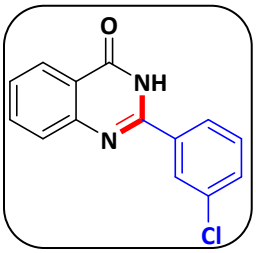
Purified by column chromatography (15% ethyl acetate in hexane), white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.59 (s, 1H), 8.26 (t, *J* = 6.5 Hz, 2H), 8.16 (d, *J* = 8.0 Hz, 1H), 7.85 (t, *J* = 7.5 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.53 (t, *J* = 7.25 Hz, 1H), 7.40 (t, *J* = 8.25 Hz, 2H).

2-(4-(trifluoromethyl) phenyl) quinazolin-4(3*H*)-one (3j)[5]



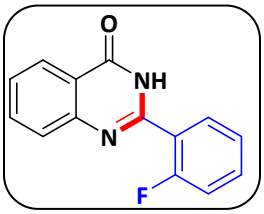
Purified by column chromatography (17% ethyl acetate in hexane), white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.75 (s, 1H), 8.38 (d, *J* = 8.0 Hz, 2H), 8.18 (d, *J* = 8.0 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 2H), 7.88 (t, *J* = 7.5 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.57 (dd, *J* = 7.25, 1H).

2-(3-chlorophenyl) quinazolin-4(3*H*)-one (3k)[3]



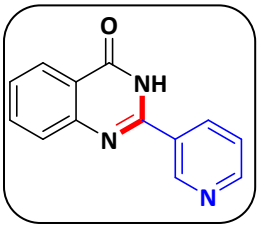
Purified by column chromatography (15% ethyl acetate in hexane), white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.65 (s, 1H), 8.18-8.15 (m, 1H), 7.79 (t, *J* = 8.4 Hz, 1H), 7.69-7.64 (m, 2H), 7.58-7.49 (m, 3H), 7.45 (t, *J* = 7.2 Hz, 1H).

2-(2-fluorophenyl) quinazolin-4(3*H*)-one (3l)[7]



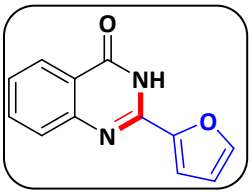
Purified by column chromatography (14% ethyl acetate in hexane), white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.59 (s, 1H), 8.18 (d, *J* = 7.5 Hz, 1H), 7.86 (t, *J* = 7.5 Hz, 1H), 7.79 (t, *J* = 7.25 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.63 (dd, *J* = 13.25, 7.25 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.39 (dd, *J* = 18.25, 9.25 Hz, 2H).

2-(pyridin-3-yl) quinazolin-4(3*H*)-one (3m)[2]



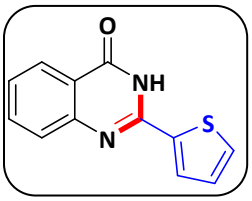
Purified by column chromatography (50% ethyl acetate in hexane), white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.75 (s, 1H), 9.30 (s, 1H), 8.76 (d, *J* = 4.0 Hz, 1H), 8.50 (d, *J* = 7.5 Hz, 1H), 8.18 (d, *J* = 8.0 Hz, 1H), 7.87 (t, *J* = 7.5 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.61-7.54 (m, 2H).

2-(furan-2-yl) quinazolin-4(3*H*)-one (3n)[8]



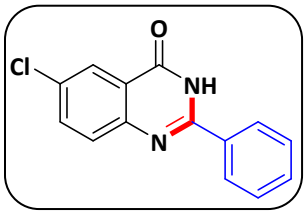
Purified by column chromatography (23% ethyl acetate in hexane), white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.58 (s, 1H), 8.18 (d, *J* = 7.5 Hz, 1H), 8.06 (s, 1H), 7.88 (t, *J* = 8.0 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.69 (s, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 6.81 (s,1H).

2-(thiophen-2-yl) quinazolin-4(3*H*)-one (3o)[5]



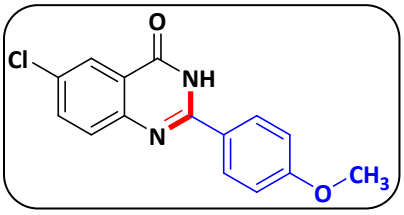
Purified by column chromatography (15% ethyl acetate in hexane), yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.63 (s, 1H), 8.19 (s, 1H), 8.08 (d, *J* = 7.6 Hz, 1H), 7.84-7.74 (m, 2H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.45 (t, *J* = 7.2 Hz, 1H), 7.2 (s, 1H).

6-chloro-2-phenylquinazolin-4(3*H*)-one (3p)[3]



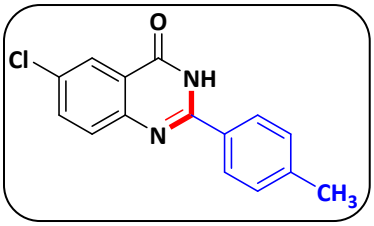
Purified by column chromatography (17% ethyl acetate in hexane), white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.77 (s, 1H), 8.23 (d, *J* = 7.5 Hz, 2H), 8.15 (s, 1H), 7.92 (d, *J* = 8.5 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.67 (t, *J* = 6.75 Hz, 1H), 7.62 (t, *J* = 7.25 Hz, 2H).

6-chloro-2-(4-methoxyphenyl) quinazolin-4(3*H*)-one (3q)[2]



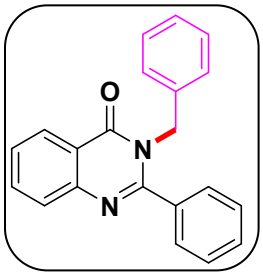
Purified by column chromatography (25% ethyl acetate in hexane), white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.58 (s, 1H), 8.19 (d, *J* = 8.5 Hz, 2H), 8.06 (s, 1H), 7.84 (d, *J* = 8.5 Hz, 1H), 7.77 (d, *J* = 8.5 Hz, 1H), 7.10 (d, *J* = 8.5 Hz, 2H), 3.86 (s, 3H).

6-chloro-2-(4-methylphenyl) quinazolin-4(3*H*)-one (3r)[10]



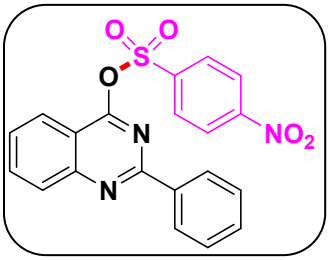
Purified by column chromatography (21% ethyl acetate in hexane), white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.59 (s, 1H), 8.07-8.03 (m, 3H), 7.81 (d, *J* = 8.8 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.32 (d, *J* = 8.4 Hz, 2H), 2.35 (s, 3H).

3-benzyl-2-phenylquinazolin-4(3*H*)-one (4a)[6]



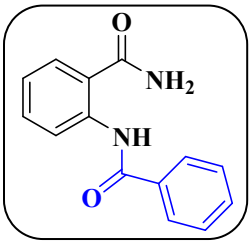
Purified by column chromatography (20% ethyl acetate in hexane), yellow solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.56 (d, *J* = 4.0 Hz, 2H), 8.20 (d, *J* = 8.0 Hz, 1H), 8.00-7.95 (m, 2H), 7.67-7.63 (m, 3H), 7.57 (d, *J* = 3.5 Hz, 3H), 7.44 (t, *J* = 7.5 Hz, 2H), 7.37 (t, *J* = 7.25 Hz, 1H), 5.82 (s, 2H).

2-phenylquinazolin-4-yl 4-nitrobenzenesulfonate (5a)[11]



Purified by column chromatography (40% ethyl acetate in hexane), yellow solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.21-8.15 (m, 5H), 7.88 (t, *J* = 7.75 Hz, 1H), 7.84 (d, *J* = 9.0 Hz, 1H), 7.65-7.57 (m, 4H).

N-(2-carbamoylphenyl) benzamide (IM1)[12]



Purified by column chromatography (22% ethyl acetate in hexane), white solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.98 (s, 1H), 8.71 (d, *J* = 8.5 Hz, 1H), 8.44 (s, 1H), 7.96-7.86 (m, 4H), 7.71-7.54 (m, 4H), 7.18 (t, *J* = 7.5 Hz, 1H).

4. Computational details

DFT analysis

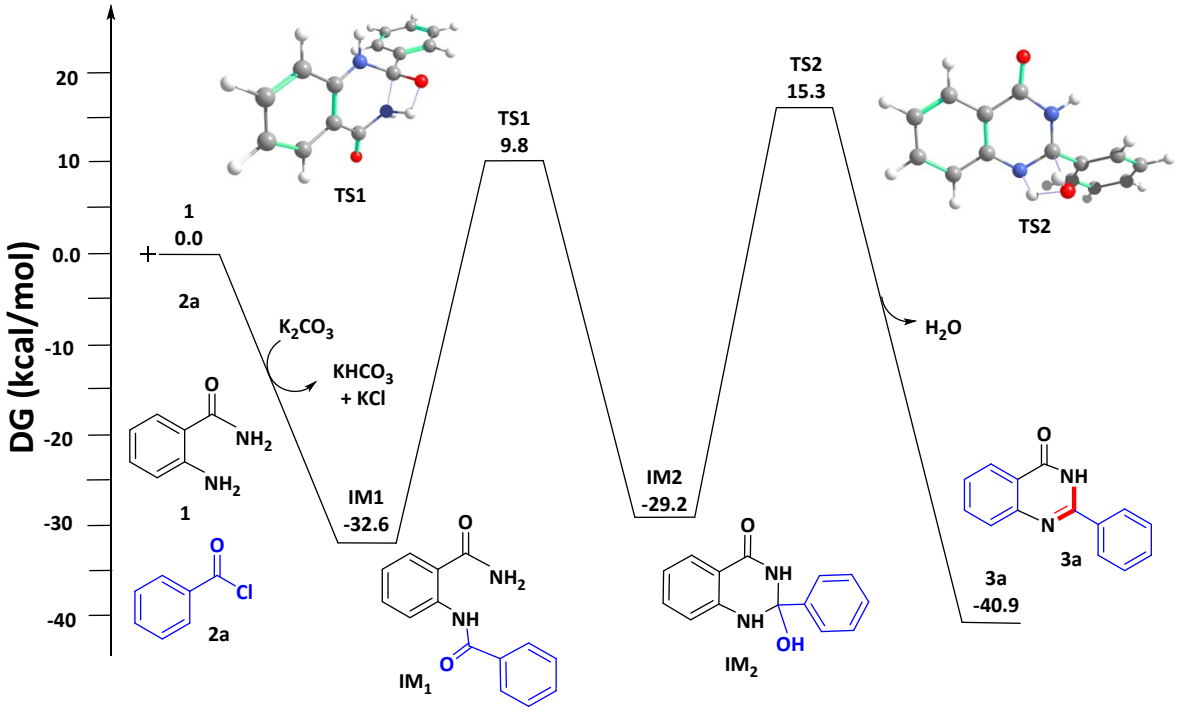


Fig. S1 Gibbs free energy profile. Free energy values are the M062x(SMD)/def2-TZVP//BP86/def2-SVP level of theory.

To gain deeper insights into the mechanism, we performed quantum mechanical calculations using DFT. The BP86 method was employed, with the def2-SVP basis set for the optimization using the Gaussian 16

suite. For the calculations, we considered **1** and **2a** as model substrates. The reaction begins with the addition of **1** with **2a** in the presence of K_2CO_3, giving intermediate complex **IM1**, via the abstraction of chloride from **2a** and the deprotonation of **1** and liberating KCl and $KHCO_3$. This step formation of **IM1** is highly exergonic by -32.6 kcal/mol. Next, nucleophilic attack of the primary amide N to the carbonyl carbon of the secondary amide and intramolecular proton transfer leads to the formation of **IM2** *via* the four-membered cyclic transition state **TS1** with the highest energy barrier of 42.4 kcal/mol. Finally, the elimination of water through another intramolecular proton transfer through the cyclic transition state **TS2**, with a transition state energy barrier of 44.5 kcal/mol, to afford the desired product **3a** and complete the reaction mechanism.

All calculations were performed employing a DFT method implemented in the Gaussian 16 suite of programs.[13] For geometry optimization and frequency analysis, we adopted the BP86 functional.[14] During geometry optimization, we used the split-valence plus single polarization basis set def2-SVP[15] for non-metals. The geometries were optimized without any symmetry constraints. For each transition state, in addition to analyzing the character of the normal mode associated with the imaginary frequency, intrinsic reaction coordinate (IRC) analysis[16] was performed to confirm that it connects the correct reactant and product on the potential energy surface. To refine the computed energy, single-point calculations were performed using the hybrid-meta-GGA M06-2X functional[17,18] with the def2-TZVP[15] basis set. Solvation energies were evaluated implicitly by a self-consistent reaction field (SCRF) approach for all the intermediates and transition states, in PEG-200 solvent using the SMD continuum solvation model.[19] The free energies (ΔG), calculated at the M06-2X(SMD)/def2-TZVP//BP86/def2-SVP level, are reported throughout the article unless otherwise mentioned. The ΔG value is obtained by augmenting the in-solvent electronic energy (ΔE), calculated at M06-2X(SMD)/def2-TZVP, with the corresponding free energy corrections calculated at BP86/def2-SVP in the gas phase.

Table S1**.** Cartesian coordinates (Å) of the optimized structures of all intermediates and transition states at BP86/def2-SVP level of theory. E_e^S represents the absolute electronic energy in Hartree at the M06-2X/def2-TZVP level of theory in PEG-200 solvent.

1

E_e^S= -456.3176876

C	-4.543985000	-3.628021000	2.474950000
C	-5.782230000	-3.625135000	3.155969000
C	-3.337478000	-3.773885000	3.229902000
C	-5.867890000	-3.813191000	4.539425000
C	-3.438420000	-3.962859000	4.632639000
C	-4.680534000	-3.991097000	5.275879000
H	-6.681726000	-3.473335000	2.539250000
H	-6.846651000	-3.819740000	5.042838000
H	-2.511990000	-4.077443000	5.220326000
H	-4.719664000	-4.140619000	6.366984000
C	-4.623028000	-3.458105000	0.977609000
O	-5.616875000	-2.993152000	0.420170000
N	-3.506439000	-3.850683000	0.247358000
H	-3.660508000	-3.889813000	-0.764194000
H	-2.875711000	-4.554771000	0.645506000
N	-2.073627000	-3.773595000	2.628904000
H	-1.295506000	-3.656994000	3.282870000
H	-1.983886000	-3.171872000	1.803012000

2a

E_e^S= -805.1812265

C	1.056466000	1.205156000	-9.543242000
C	-0.177424000	1.233601000	-8.847276000
C	2.268269000	1.187839000	-8.817771000
C	-0.193478000	1.244514000	-7.446762000
C	2.244772000	1.198817000	-7.415156000
C	1.017385000	1.227111000	-6.728460000
H	-1.111713000	1.246731000	-9.428532000
H	3.221064000	1.165913000	-9.365866000
H	-1.154687000	1.266764000	-6.909752000
H	3.191827000	1.185125000	-6.853529000
H	1.003599000	1.235638000	-5.626903000
C	0.980990000	1.195286000	-11.031585000
O	-0.023760000	1.208469000	-11.689441000
Cl	2.607305000	1.159350000	-11.878005000

K_2CO_3
E_e^S= -1463.811401

O	-0.940006000	-1.132150000	0.000351000
O	-0.939022000	1.133006000	-0.000466000
O	1.035445000	-0.000308000	-0.002107000
C	-0.328177000	0.000099000	-0.000600000
K	1.072861000	-2.475246000	0.001682000
K	1.073137000	2.474464000	0.001585000

$KHCO_3$
E_e^S= -864.438629

O	-0.643503000	-1.194899000	0.024323000
O	-0.992858000	1.023429000	-0.002700000
O	1.130792000	0.207454000	0.016094000
C	-0.141186000	0.091598000	0.011887000
K	0.860069000	2.698428000	-0.012922000
H	0.158769000	-1.756283000	0.033705000

KCl
E_e^S= -1060.222716

K	2.853372000	-8.309799000	-3.861778000
Cl	2.853372000	-8.309799000	-6.525371000

IM1
E_e^S= -800.7045118

H	4.771554000	17.366661000	-1.087199000
C	5.024397000	17.668145000	-0.059063000
C	5.418409000	18.975481000	0.249127000
C	5.748201000	19.302540000	1.576615000
C	5.692803000	18.319953000	2.573944000
C	5.271566000	17.004507000	2.273488000
C	4.920498000	16.668534000	0.934050000
C	4.427791000	15.319266000	0.425853000
N	4.014174000	14.407086000	1.364128000
N	5.263750000	16.015432000	3.306406000
H	5.476969000	19.737155000	-0.543862000
H	6.075362000	20.321733000	1.836609000
H	5.994885000	18.561743000	3.603805000
H	3.923025000	14.660846000	2.350364000
O	4.388694000	15.074404000	-0.780601000
H	5.873162000	15.203267000	3.140172000
C	5.038950000	16.185724000	4.682051000
O	5.604045000	15.447444000	5.486816000
C	4.029521000	17.212523000	5.123055000
C	4.136766000	17.692473000	6.447476000
C	2.941242000	17.628252000	4.322931000
C	3.193013000	18.598670000	6.952480000
C	1.987210000	18.520837000	4.837460000
C	2.116116000	19.015105000	6.147952000
H	4.970520000	17.330064000	7.068141000
H	2.826330000	17.242262000	3.298798000
H	3.291235000	18.976494000	7.982518000
H	1.135949000	18.830900000	4.211064000
H	1.370021000	19.721204000	6.546120000
H	3.588364000	13.546914000	1.013753000

TS1
E_e^S= -800.6267707

H	4.375770000	17.729232000	-1.110195000
C	4.724225000	17.940408000	-0.087395000
C	4.979105000	19.240719000	0.343508000
C	5.433561000	19.446908000	1.668411000
C	5.624524000	18.374139000	2.539450000
C	5.369245000	17.039100000	2.118774000
C	4.899603000	16.832058000	0.779862000
C	4.662474000	15.485506000	0.250565000
N	4.587768000	14.448970000	1.279778000
N	5.655576000	15.976011000	2.945365000
H	4.828842000	20.095230000	-0.333172000
H	5.637211000	20.469419000	2.025264000
H	5.978612000	18.550640000	3.568052000
H	3.574920000	14.443264000	1.908984000
O	4.476514000	15.173006000	-0.917770000
H	5.980778000	16.210697000	3.887308000
C	4.934012000	14.691142000	2.905715000
O	3.676084000	14.674255000	3.304835000
C	5.847497000	13.569720000	3.402877000
C	5.265906000	12.544961000	4.175317000
C	7.228484000	13.527079000	3.112908000
C	6.055020000	11.485360000	4.652402000
C	8.015851000	12.465243000	3.588524000
C	7.430050000	11.443071000	4.358716000
H	4.188892000	12.622447000	4.391914000
H	7.683645000	14.332665000	2.514340000
H	5.596466000	10.689613000	5.261125000
H	9.093017000	12.434467000	3.358806000
H	8.049499000	10.612055000	4.732549000
H	4.831514000	13.519723000	0.897331000

IM2
E_e^S= -800.7033229

H	4.156789000	16.698264000	-1.285716000
C	4.413655000	17.323434000	-0.416301000
C	4.207295000	18.707742000	-0.411187000
C	4.574101000	19.453492000	0.729580000
C	5.132658000	18.828427000	1.851496000
C	5.334360000	17.427096000	1.854913000
C	4.972521000	16.674648000	0.702778000
C	5.238780000	15.213265000	0.659347000
N	5.795498000	14.707338000	1.837136000
C	5.706073000	15.361768000	3.132234000
N	5.922859000	16.777740000	2.934500000
H	3.767901000	19.210867000	-1.285948000
H	4.417503000	20.544172000	0.746703000
H	5.412262000	19.420744000	2.738025000
H	5.967670000	13.697626000	1.831350000
C	6.784182000	14.798214000	4.079539000
C	6.486492000	14.553588000	5.434484000

C	8.094755000	14.571847000	3.607232000
C	7.482697000	14.074287000	6.304456000
C	9.086880000	14.090328000	4.476072000
C	8.782773000	13.839146000	5.827137000
H	5.465703000	14.744480000	5.798532000
H	8.330463000	14.779873000	2.551934000
H	7.238847000	13.884022000	7.361837000
H	10.105917000	13.912500000	4.097171000
H	9.562230000	13.461375000	6.507824000
O	5.052911000	14.492101000	-0.320406000
O	4.394023000	15.224413000	3.706458000
H	4.187533000	14.268860000	3.751642000
H	6.003145000	17.309030000	3.803820000

TS2

E_e^S= -800.6264101

C	-11.797500000	12.882202000	-2.527067000
O	-13.503389000	12.081523000	-1.886584000
C	-11.422514000	13.409111000	-1.175064000
C	-10.333702000	12.836290000	-0.488673000
C	-12.112514000	14.499982000	-0.601714000
C	-9.930460000	13.357665000	0.753108000
C	-11.702858000	15.021071000	0.633237000
C	-10.608238000	14.452757000	1.313249000
H	-9.809233000	11.982992000	-0.944511000
H	-13.004354000	14.908804000	-1.103132000
H	-9.077731000	12.904844000	1.283341000
H	-12.251467000	15.865745000	1.079001000
H	-10.291324000	14.861224000	2.285910000
N	-11.455873000	11.573130000	-2.851496000
H	-12.430226000	11.233984000	-2.266939000
C	-11.390791000	11.199474000	-4.190291000
C	-11.565256000	12.139241000	-5.250708000
C	-11.164595000	9.837725000	-4.523044000
C	-11.483553000	11.722608000	-6.599281000
C	-11.098969000	9.442028000	-5.860948000
C	-11.251397000	10.381342000	-6.909544000
H	-11.032682000	9.110656000	-3.707073000
H	-11.617084000	12.486345000	-7.381130000
H	-10.919456000	8.381473000	-6.100445000
H	-11.190151000	10.054295000	-7.958752000
C	-11.840079000	13.549964000	-4.931205000
O	-11.999428000	14.469888000	-5.726007000
N	-11.878194000	13.811698000	-3.534486000
H	-14.088229000	12.083837000	-2.675319000
H	-11.976224000	14.802321000	-3.286069000

H_2O

E_e^S= -76.4332672

O	-3.554848000	17.747721000	-15.491348000
H	-3.554848000	18.506514000	-14.878006000
H	-3.554848000	16.988929000	-14.878006000

3a

E_e^S= -724.2685464

H	5.028089000	16.734073000	-1.232297000
C	5.028089000	17.245440000	-0.257114000
C	5.028089000	18.638908000	-0.153145000
C	5.028089000	19.250896000	1.123478000
C	5.028089000	18.476352000	2.285863000
C	5.028089000	17.058936000	2.204509000
C	5.028089000	16.449728000	0.910184000
C	5.028089000	14.977370000	0.801778000
N	5.028089000	14.352808000	2.070743000
C	5.028089000	15.021718000	3.283341000
N	5.028089000	16.322144000	3.384978000
H	5.028089000	19.261557000	-1.061493000
H	5.028089000	20.350029000	1.201494000
H	5.028089000	18.932174000	3.287523000
H	5.028089000	13.326762000	2.059023000
C	5.028089000	14.153648000	4.508240000
C	3.808812000	13.740938000	5.086958000
C	6.247366000	13.740939000	5.086958000
C	3.811097000	12.926943000	6.232218000
C	6.245080000	12.926943000	6.232218000
C	5.028089000	12.518084000	6.805392000
H	2.856207000	14.069767000	4.642096000
H	7.199970000	14.069767000	4.642096000
H	2.855465000	12.613189000	6.681310000
H	7.200712000	12.613189000	6.681310000
H	5.028089000	11.880799000	7.703864000
O	5.028089000	14.311360000	-0.22961100

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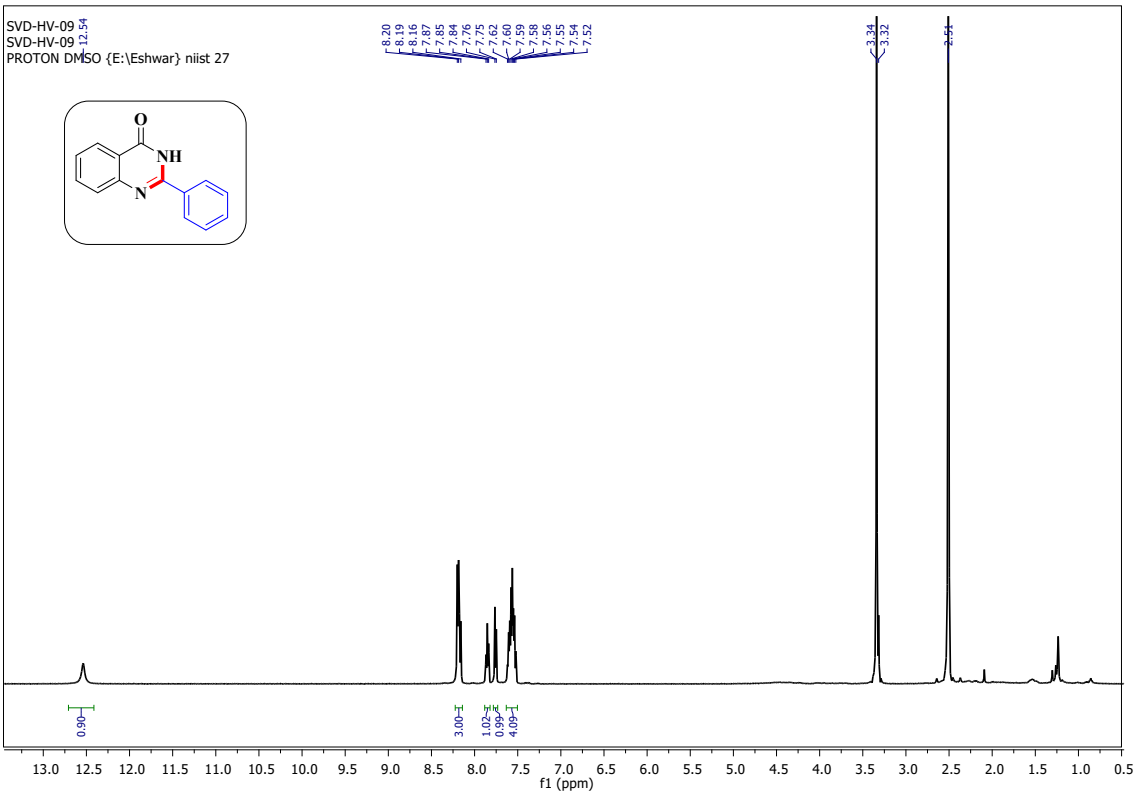
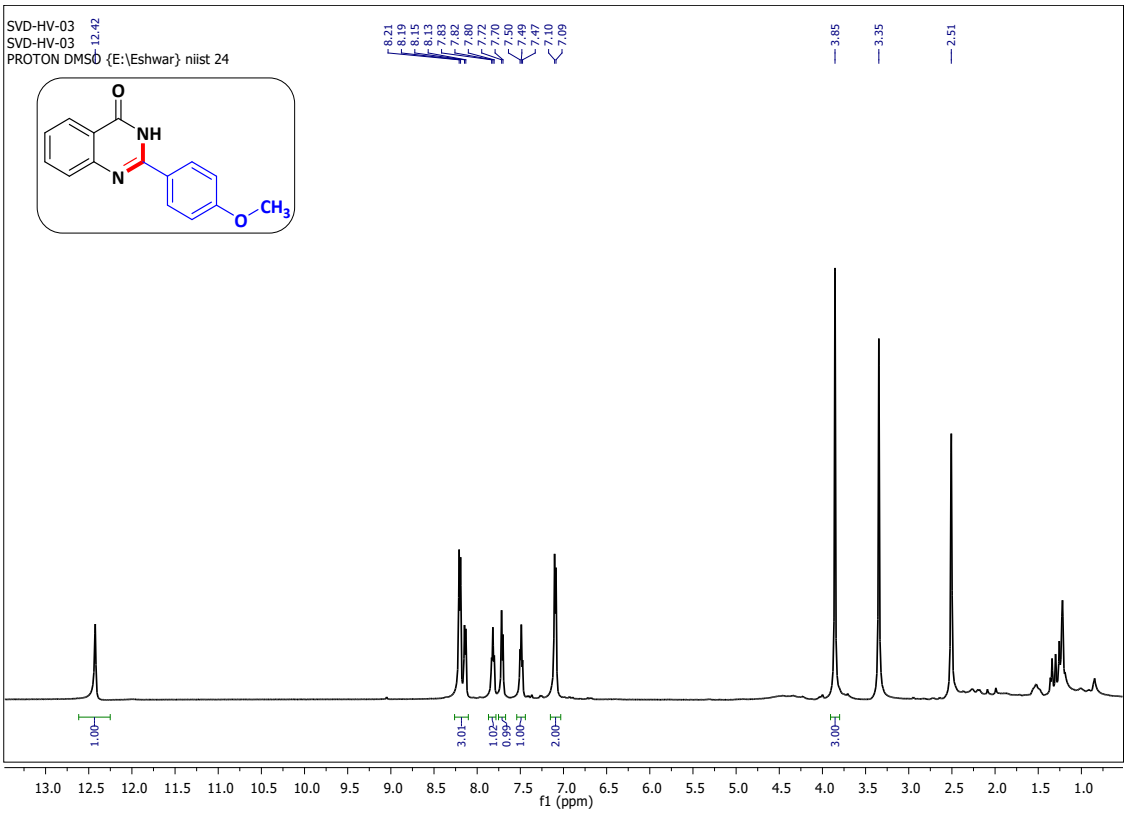
Appendix I: **Spectral copies of ^{1}H NMR of compounds obtained in this study**

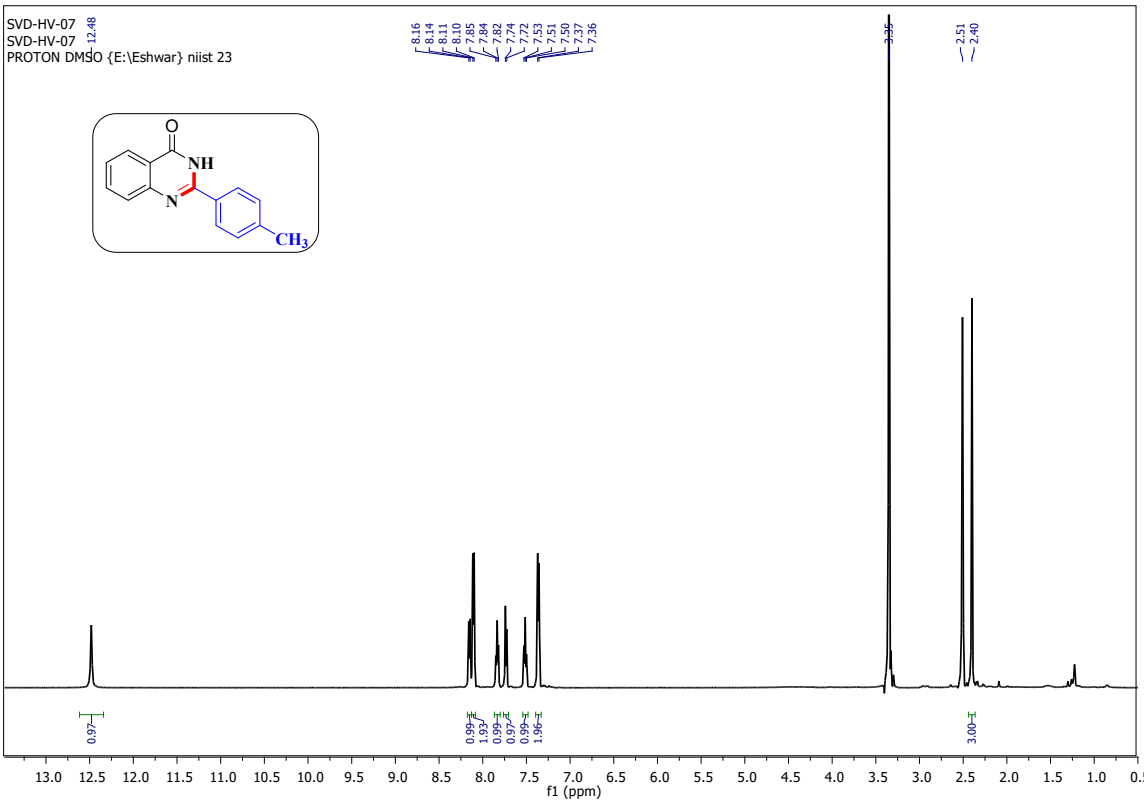
2-phenylquinazolin-4(3*H*)-one (3a)



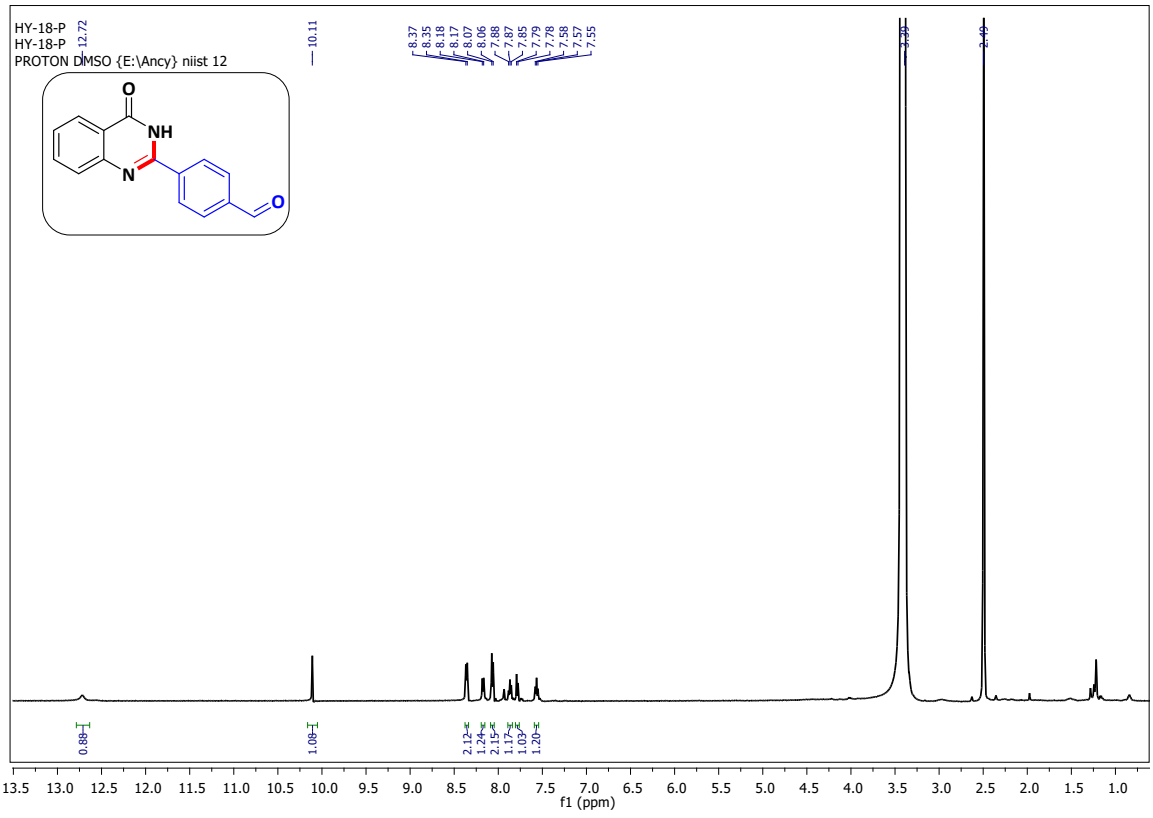
2-(4-methoxyphenyl) quinazolin-4(3*H*)-one (3b)



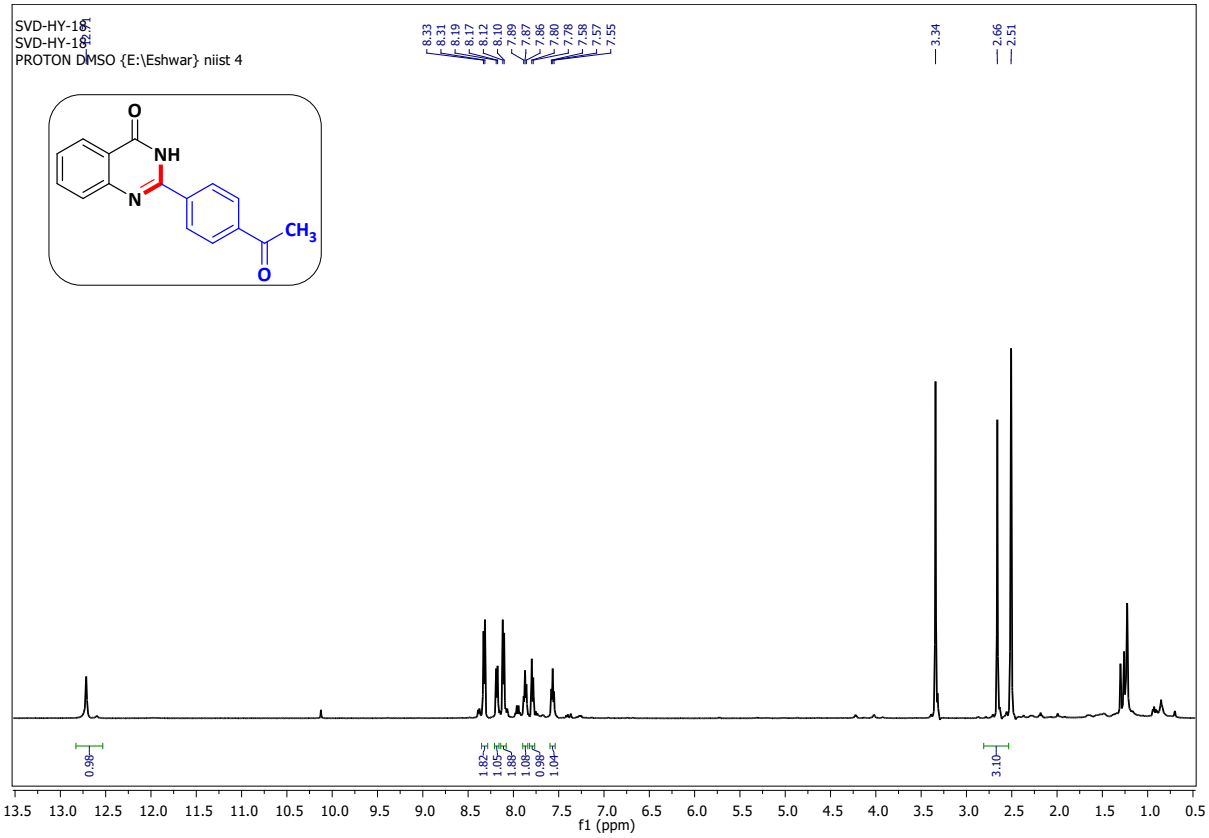
2-(p-tolyl) quinazolin-4(3*H*)-one (3c)



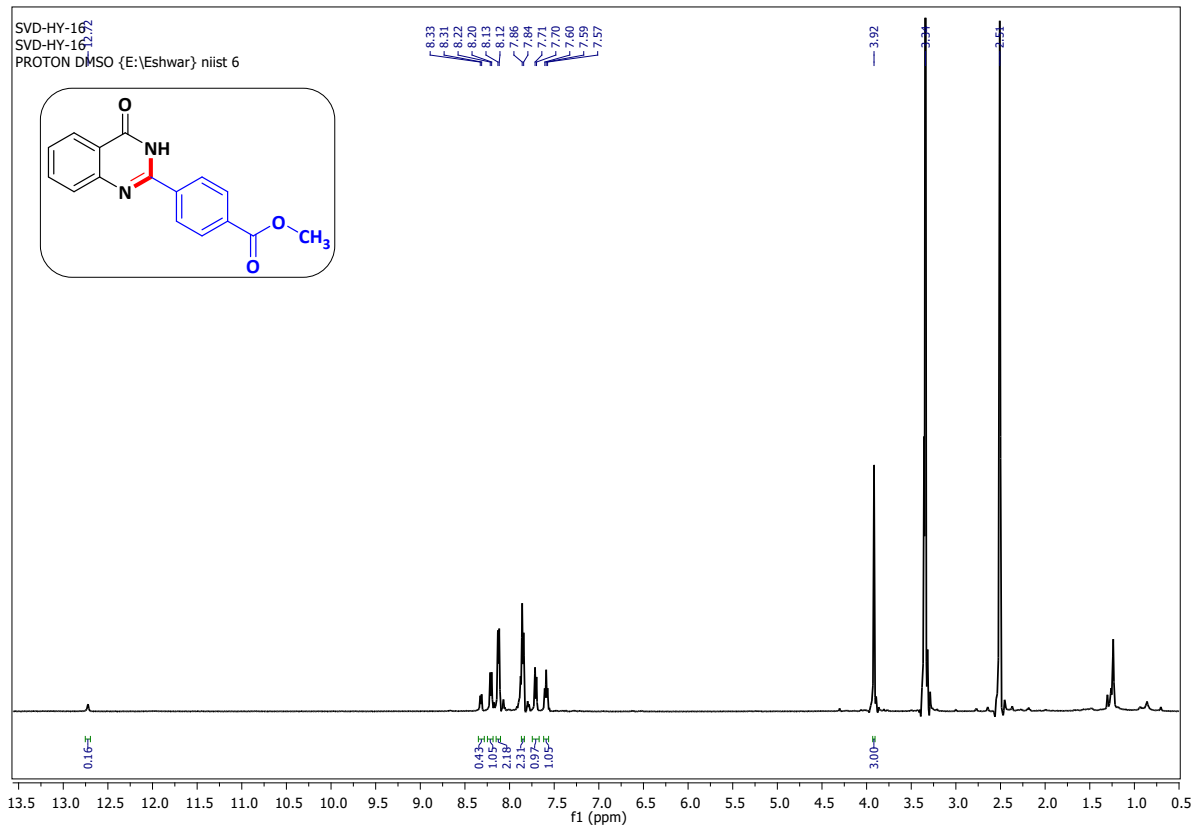
4-(4-Oxo-3,4-dihydroquinazolin-2-yl) benzaldehyde (3d)



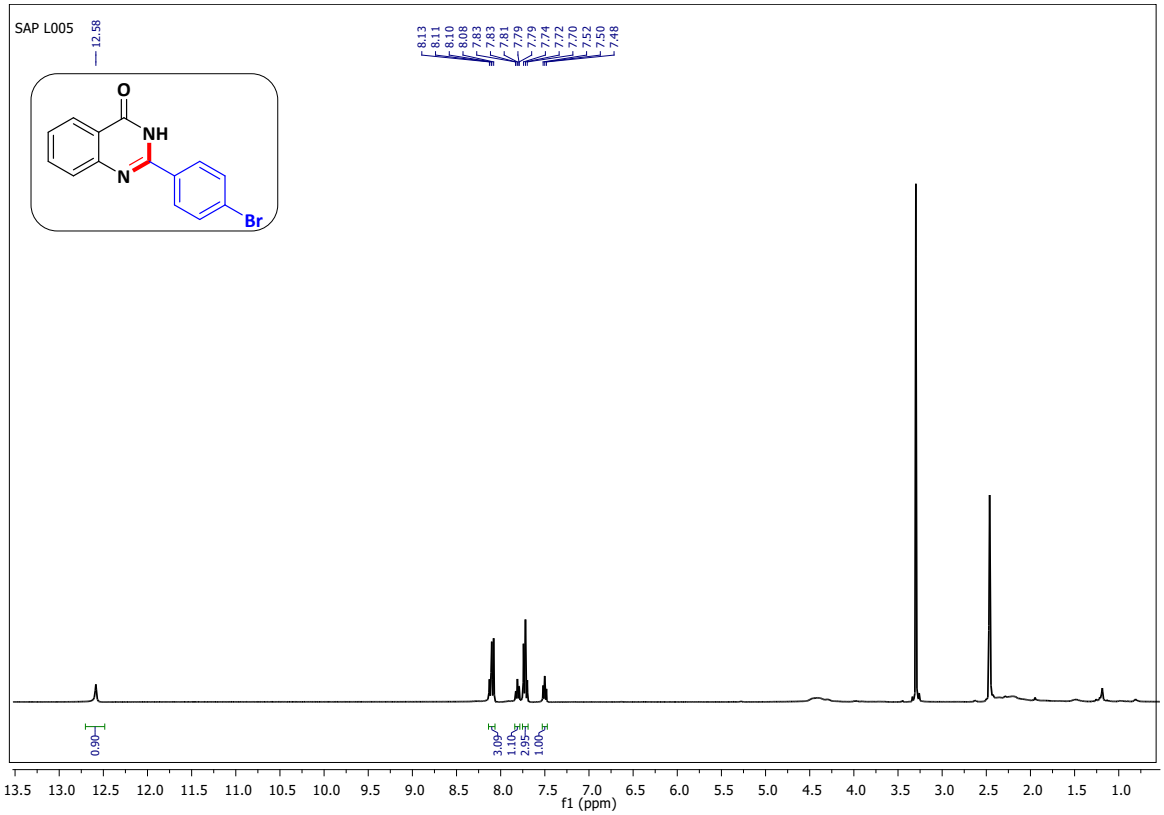
2-(4-Acetylphenyl) quinazolin-4(3*H*)-one (3e)



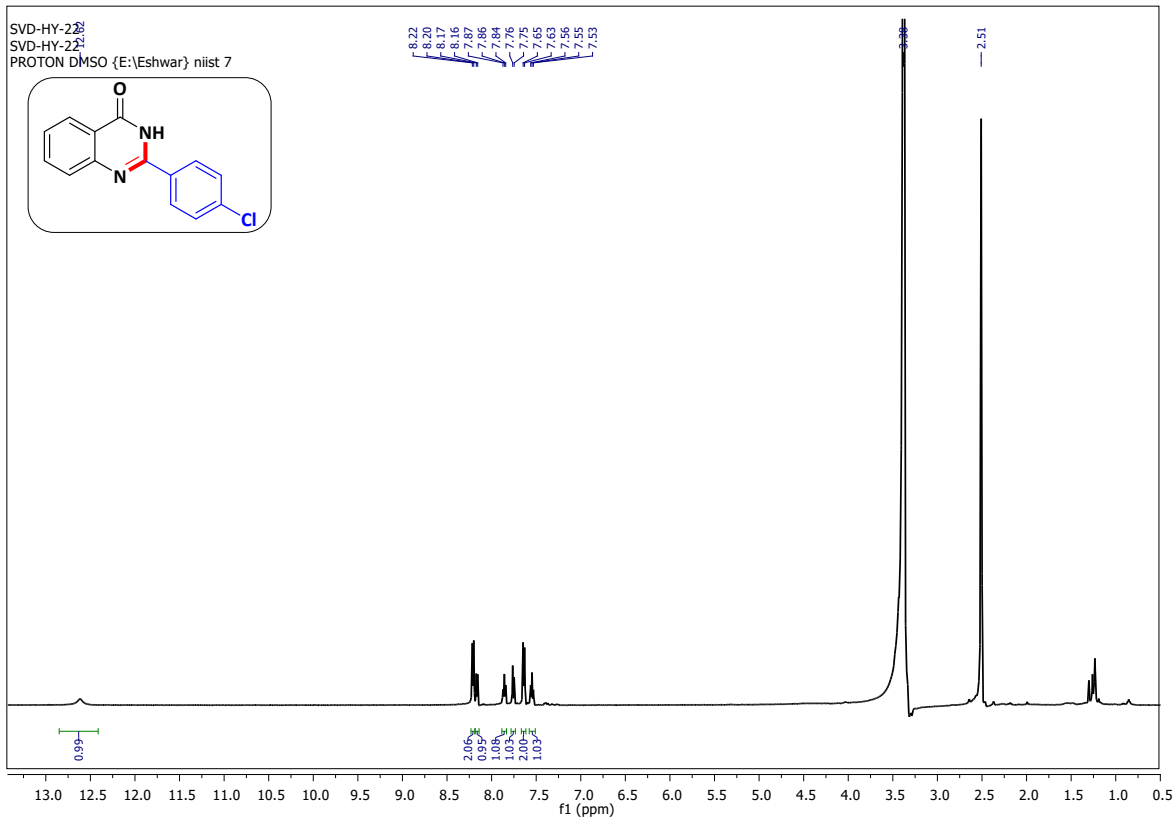
Methyl 4-(4-oxo-3,4-dihydroquinazolin-2-yl) benzoate (3f)



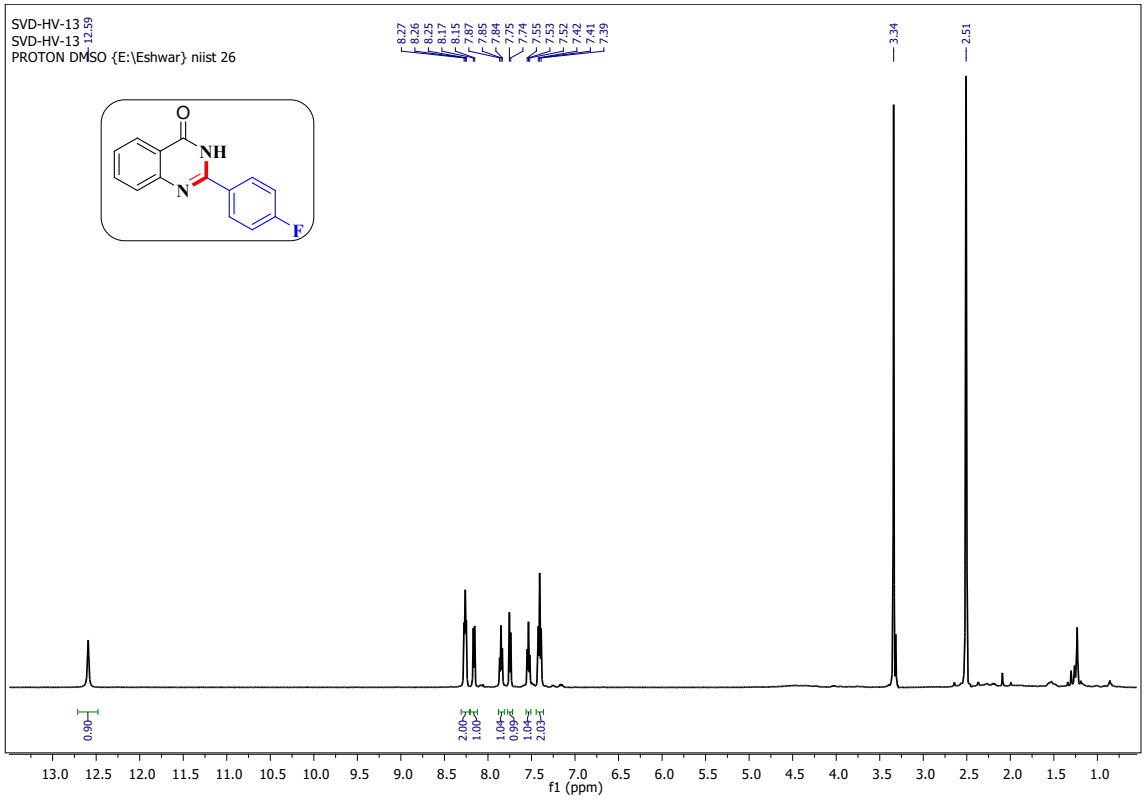
2-(4-bromophenyl) quinazolin-4(3*H*)-one (3g)



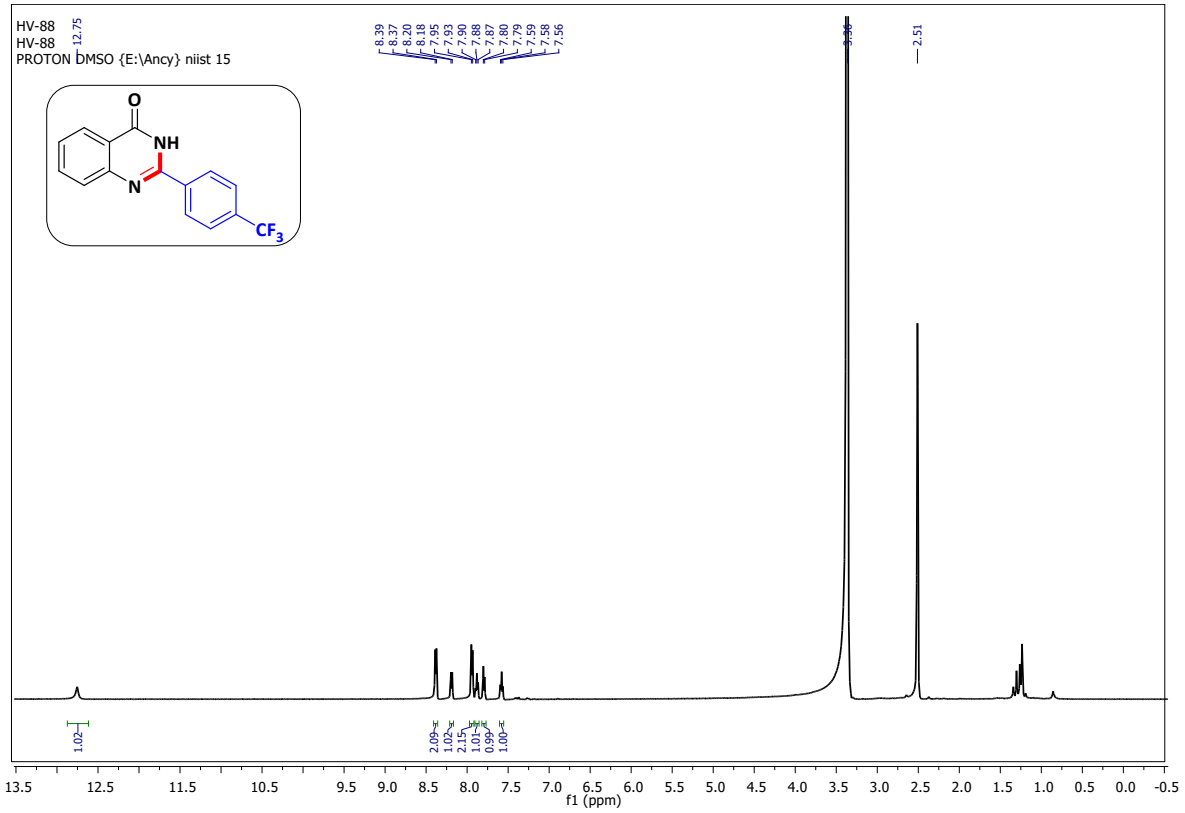
2-(4-Chlorophenyl) quinazolin-4(3*H*)-one (3h)



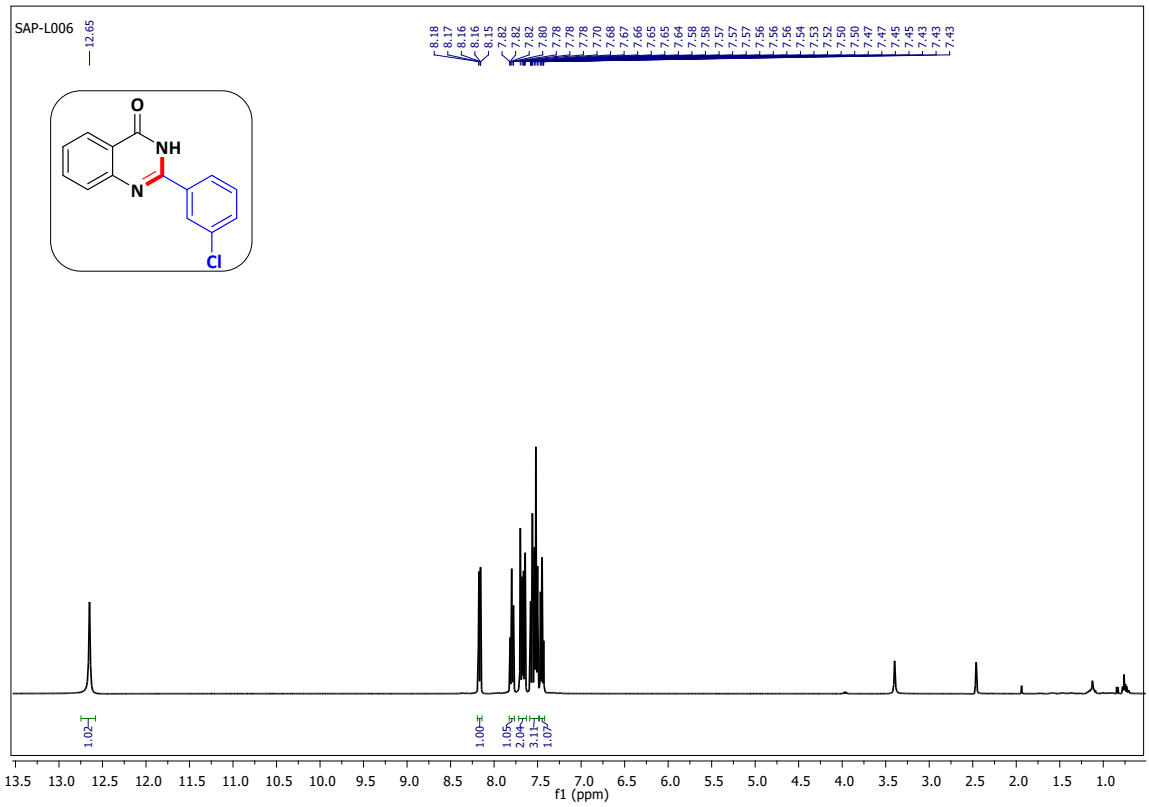
2-(4-fluorophenyl) quinazolin-4(3*H*)-one (3i)



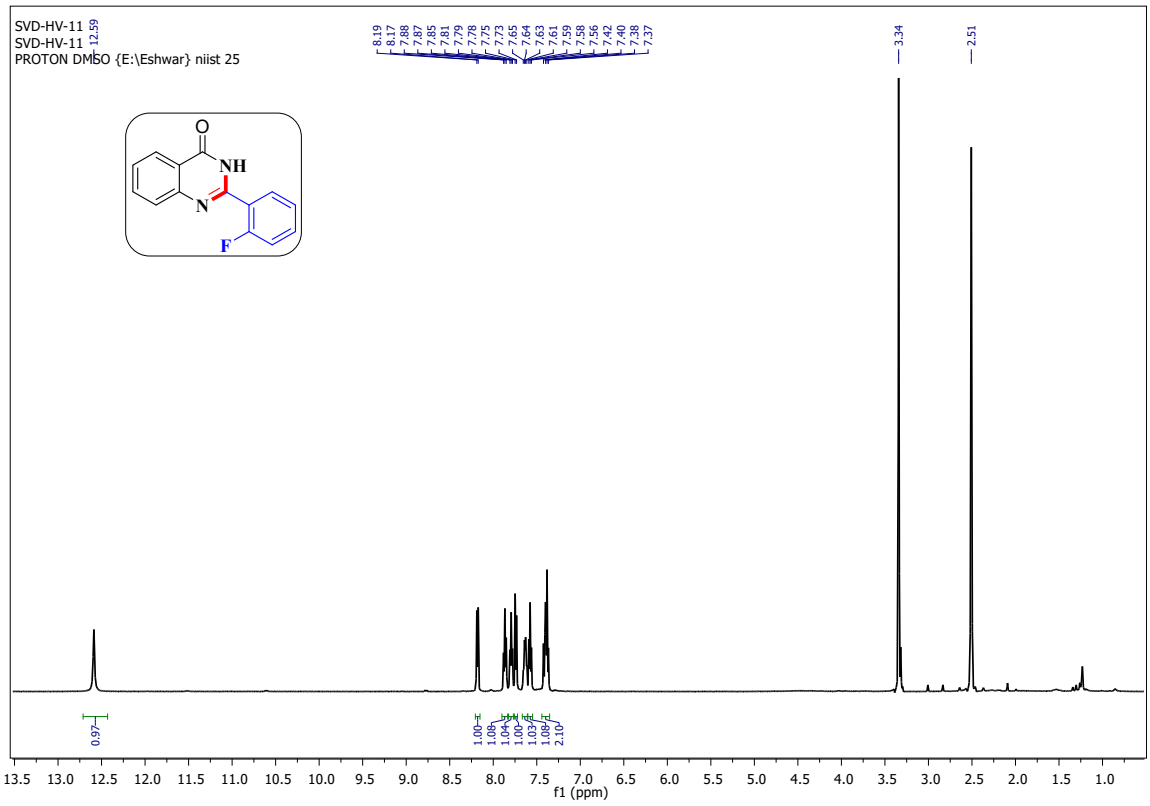
2-(4-(trifluoromethyl) phenyl) quinazolin-4(3*H*)-one (3j)



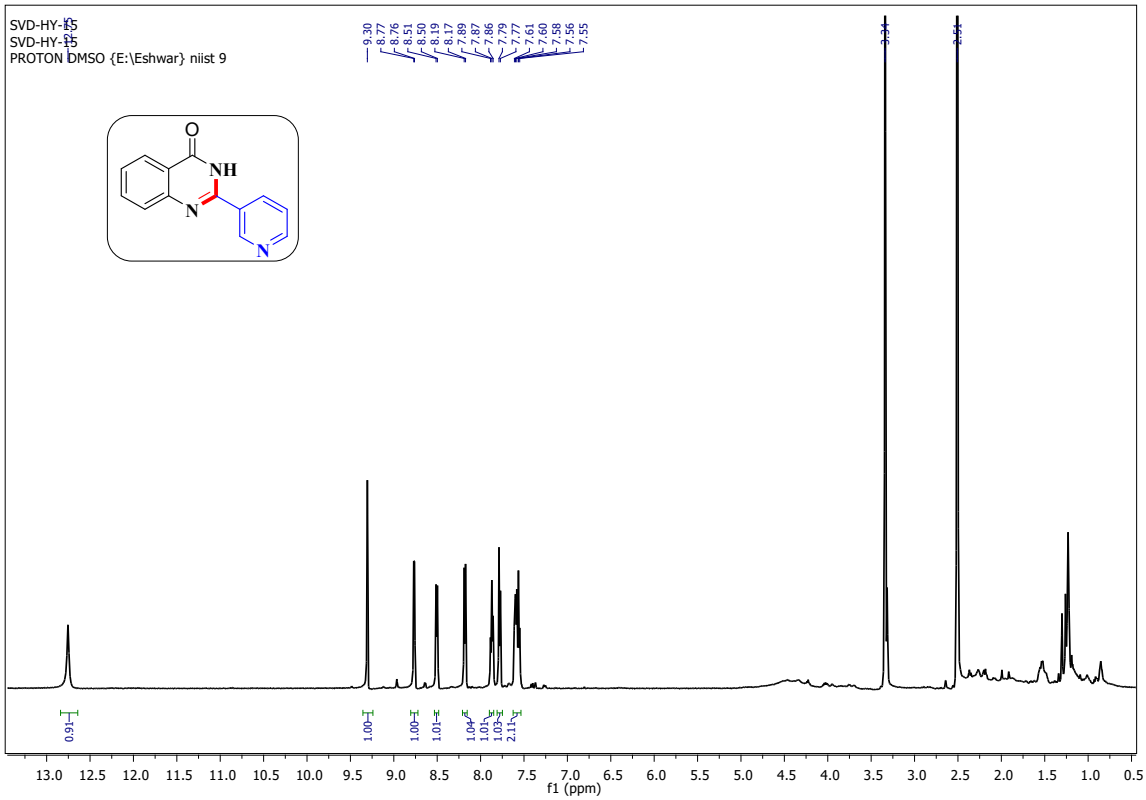
2-(3-Chlorophenyl) quinazolin-4(3*H*)-one (3k)



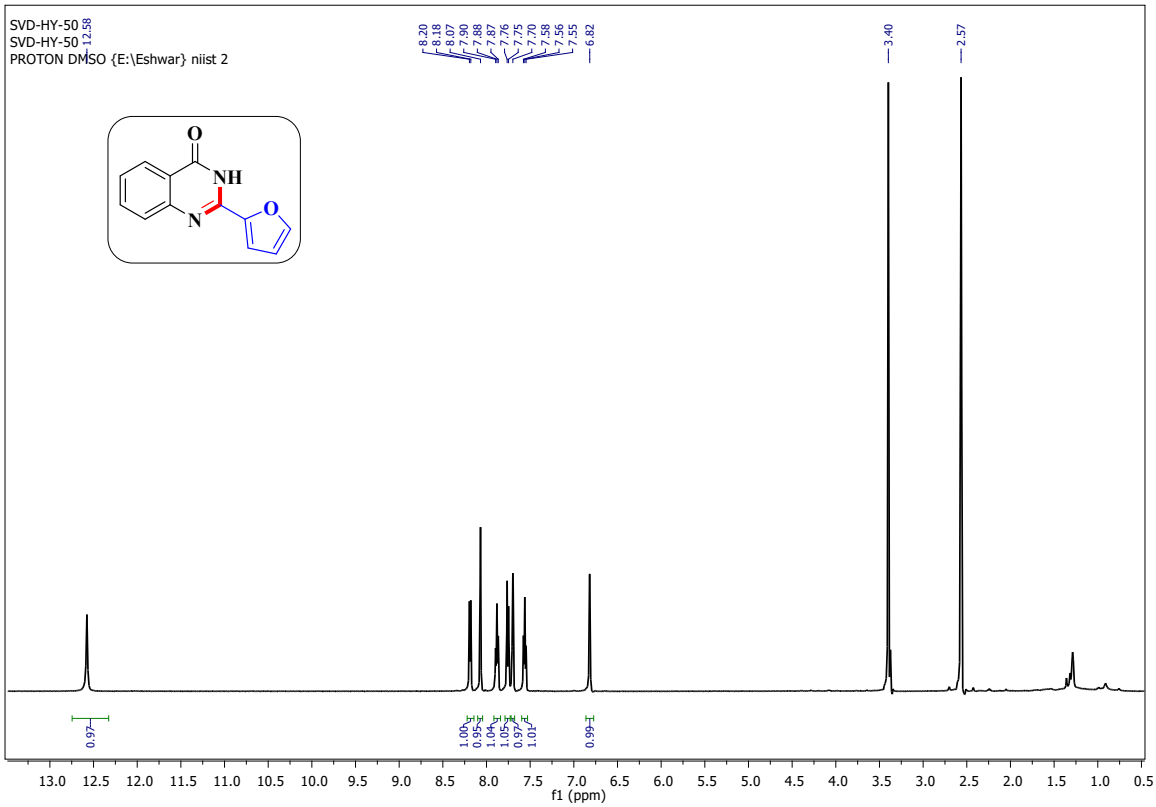
2-(2-fluorophenyl) quinazolin-4(3*H*)-one (3l)



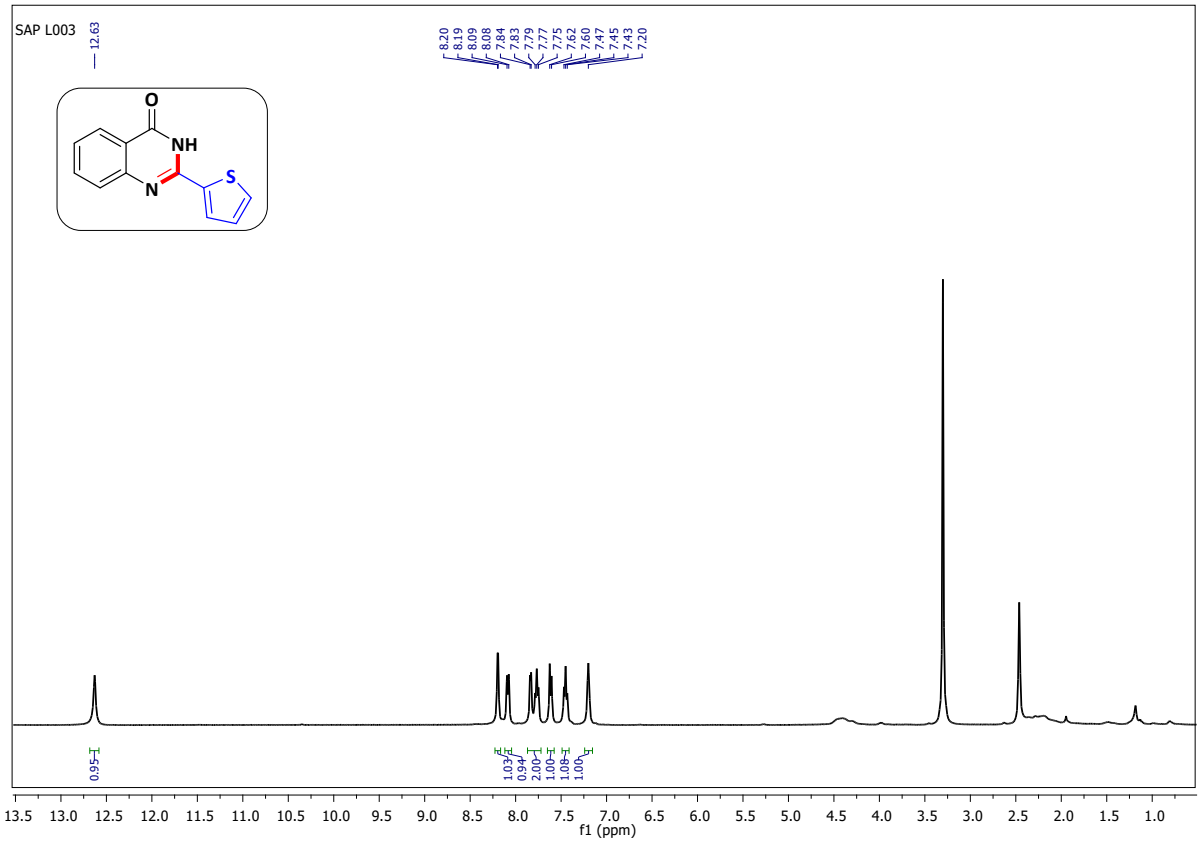
2-(pyridin-3-yl) quinazolin-4(3*H*)-one (3m)



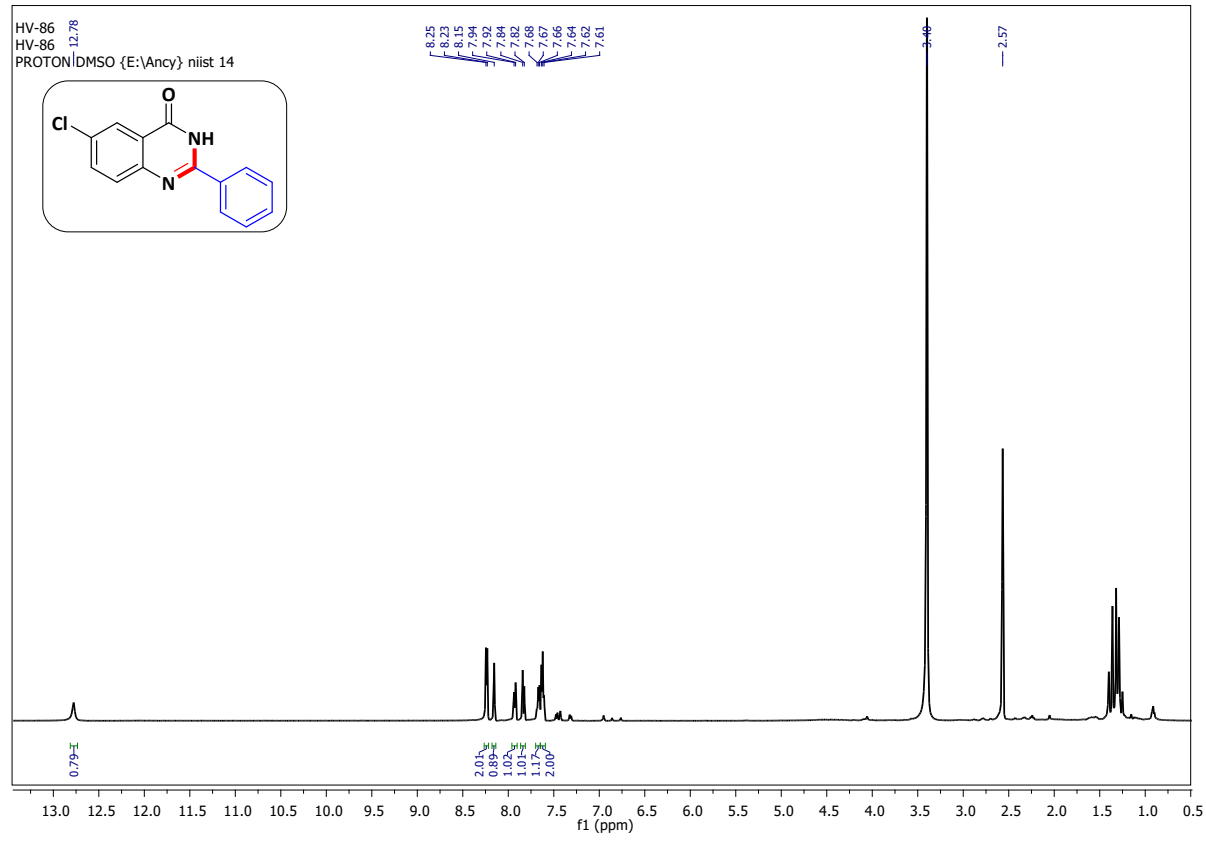
2-(furan-2-yl) quinazolin-4(3*H*)-one (3n)



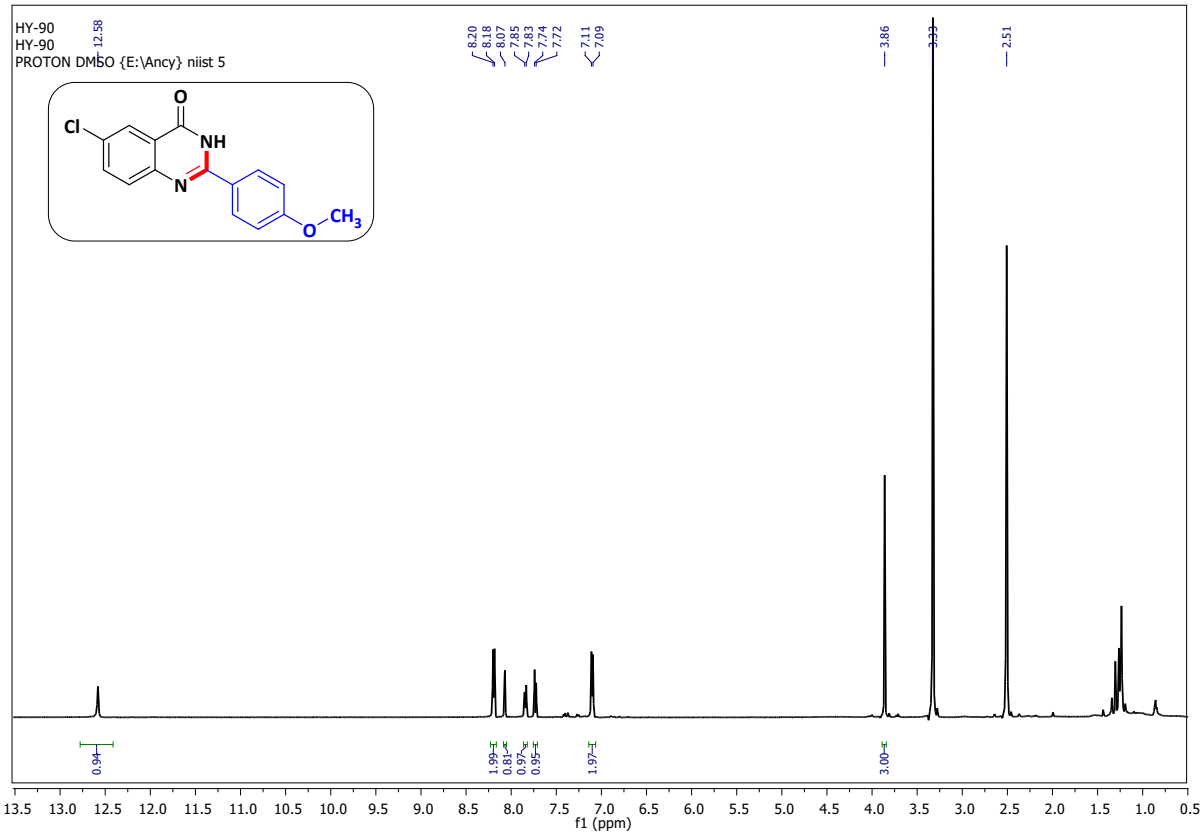
2-(thiophen-2-yl) quinazolin-4(3*H*)-one (3o)



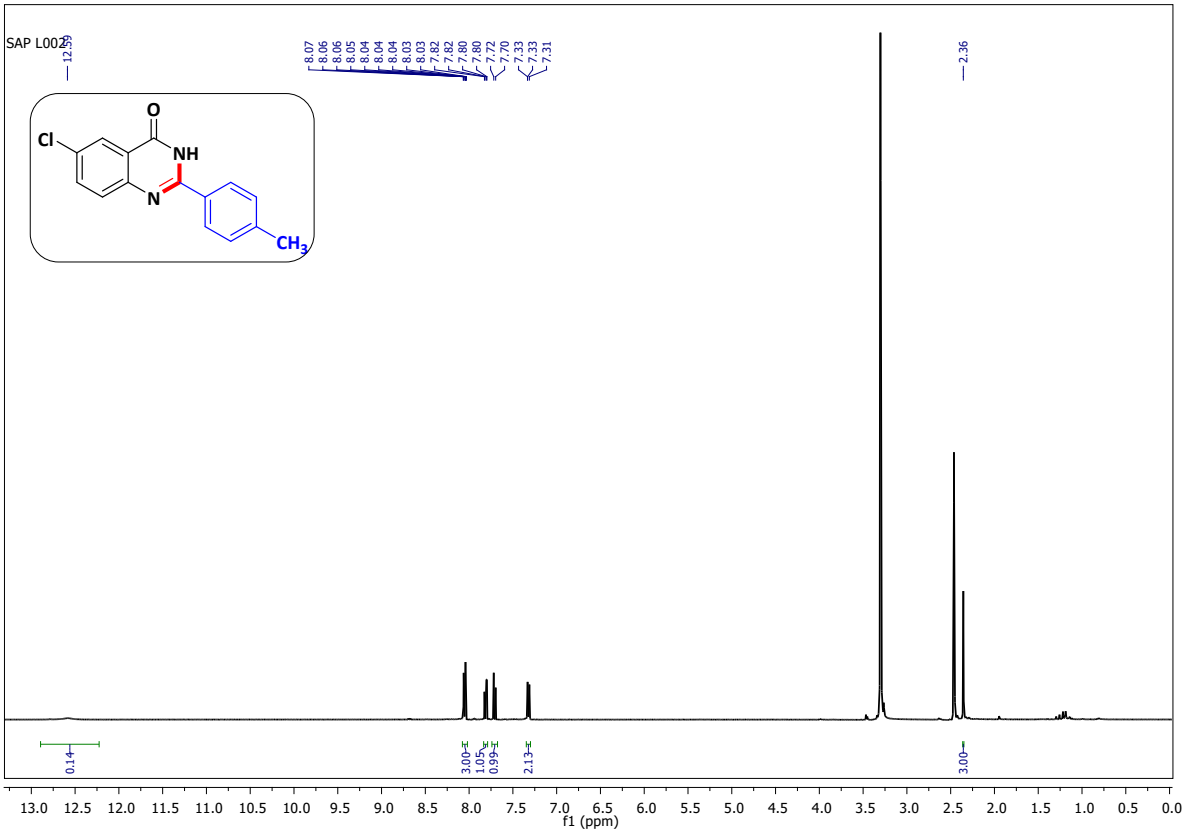
6-chloro-2-phenylquinazolin-4(3*H*)-one (3p)



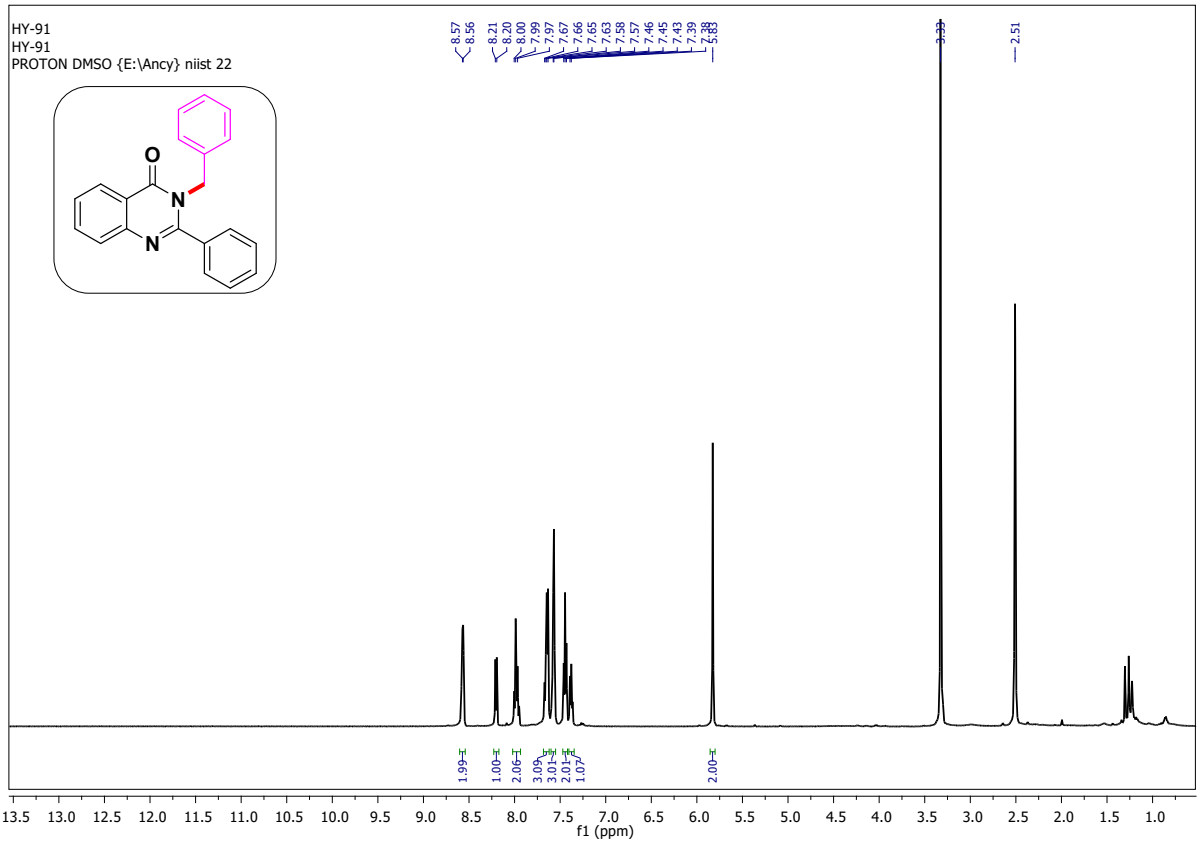
6-chloro-2-(4-methoxyphenyl) quinazolin-4(3*H*)-one (3q)



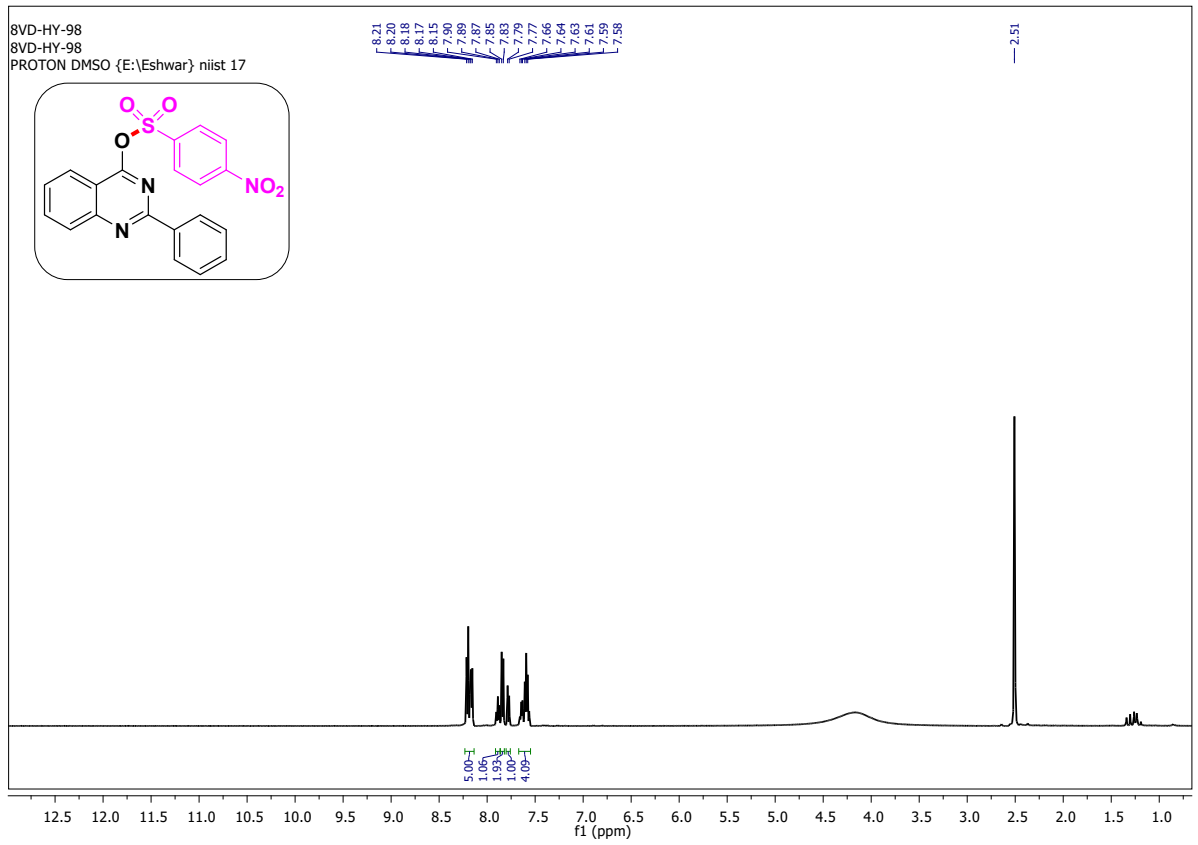
6-chloro-2-(4-methylphenyl) quinazolin-4(3*H*)-one (3r)



3-benzyl-2-phenylquinazolin-4(3*H*)-one (4a)



2-phenylquinazolin-4-yl 4-nitrobenzenesulfonate (5a)



N-(2-carbamoylphenyl) benzamide (IM1)