Synthesis and Anticancer Activity of New 2-methylquinoline with Pyridine, Thiazole and Pyrazole Derivatives

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Abstract

This work presents a novel class of 2-methylquinoline derivatives that combine pyridine, thiazole, pyrazole ring systems. The precursor 1-(2-methylquinolin-3-yl) ethanone (1) is combined with aldehydes, malononitrile and ethyl cyanoacetate in a one-pot synthesis to produce 2-amino-6-(2-methylquinolin-3-yl)-4-phenylpyridine hybrids 2 and 3. Synthetic approaches to the (E)-1-(1-(2-methylquinolin-3-yl) ethylidene) hybrids 5, 6, to treat 1 with thiosemicarbazide and 1-chloropropan-2-one and to get 7, 8, the compound 1 is treated with bromine and thiourea. Then by using 2-chloroacetyl chloride and ammonium thiocyanate compounds 9, 10 were prepared.

Furthermore compound 11 is formed when dimethoxy-N,N-dimethylmethanamine and xylene are treated with compound 1. The 2-methyl-3-(1H-pyrazol-3-yl) quinoline motif 12 was prepared by reacting 1 with dimethylamine and then treating the mixture with hydrazine. When examined in vitro on A549 and MCF-7 cancer cell lines, the anti-cancer effects were comparable to those of doxorubicin.

Keywords: Quinoline, Pyridine, Malononitrile, Thiosemicarbazide, Anti-cancer activity.

Introduction

The nitrogen-containing heterocycle quinoline is much desired for its synthetic potential and unique pharmacological effects in the fields of chemical and medicinal sciences[1]. Derivatives of this moiety with diverse pharmacological properties have been made possible by functionalizing it at various points of interest[2]. The quinoline nucleus is present in a variety of organic substances (Cinchona alkaloids) and pharmaceutically active drugs that exhibit a wide array of biological activities[3]. There are a number of medicinal uses for quinoline including its anti-inflammatory, anticonvulsant, cardiotonic, anticancer, antifungal, antibacterial and analgesic properties[4-10]. The pyridine skeleton is a fundamental component of several natural products including alkaloids, vitamins and coenzymes. It is an essential part of the family of heterocyclic compounds[11-13]. Pyrazole and its derivatives exhibit almost every medicinal property including anticancer[16-17], anti-inflammatory[26], antifungal and antibacterial effects[19]. A novel class of hybrids between quinoline and pyridine, thiazole, pyrazole is designed, synthesized and characterized physicochemically in this study[20-25].

Material and Methods

General procedure for the synthesis of 4-aryl-6-(6,8-dichloro-2-methylimidazo[1,2-a]pyridin-3-yl)nicotinonitriles 2, 3 and 4: The compound 1-(2-methylquinolin-3-yl) ethanone 1a and 1-(furo[2,3-b]pyridin-5-yl)ethanone 1b derivative (0.48 g, 2 mmol), substituted benzaldehyde (2 mmol) and ammonium acetate (1.23 g, 16 mmol) were combined in 20 mL of pure ethanol. Then, either malononitrile or ethyl cyanoacetate (2 mmol) was added to the mixture. The combination underwent reflux for a duration of 6 hours followed by a cooling period, during which the product precipitated and was then separated. The solid was obtained by filtering the mixture and then purifying it by recrystallization from ethanol to get the corresponding compounds 2, 3 and 4 respectively.

2-amino-6-(2-methylquinolin-3-yl)-4-phenylpyridine-3-carbonitrile (2): Yellowish brown solid, yield 71%, MP 221–223°C, IR (KBr): 3219 (NH_2), 2123 (CN) cm^{-1}. ^1H NMR (DMSO-d_6) δ ppm: 2.86 (s, 3H-CH_3), 6.87 (s, 2H-NH_2) 7.39 (m, 5H-ArH), 7.80 (m, 4H, ArH), 7.85 (s, 1H, Pyridine-H), 8.59 (s, 1H, Quinoline-H). ^{13}C NMR (DMSO-d_6) δ ppm: 24.06, 94.25, 115.71, 118.29, 124.23, 127.64, 128.18, 128.47, 130.50, 130.96, 134.65, 138.12, 149.22, 154.71, 156.10, 162.22. MS m/z: 336.14. Anal. Calcd: $C_{22}H_{16}N_4$; C, 78.55; H, 4.79; N, 16.66%. Found: C, 78.57; H, 4.83; N, 16.69%.

1,2-dihydro-6-(2-methylquinolin-3-yl)-2-oxo-4-phenylpyridine-3-carbonitrile (3): Yellowish brown solid, yield: 65%, MP 234–235°C, IR (KBr): 2216 (CN), 1611 (C=O) cm^{-1}. ^1H NMR (DMSO-d_6) δ ppm: 2.80 (s, 3H-CH_3), 6.84 (s, 1H, Pyridine-H), 7.51 (m, 5H-ArH), 7.64 (m, 3H-ArH), 7.86 (m, 2H-ArH), 8.03 (s, 1H, Quinoline-H). ^{13}C NMR (DMSO-d_6) δ ppm: 23.55, 110.63, 114.13, 116.63, 124.10, 128.49, 129.06, 130.07, 131.26, 133.17, 136.43, 146.47, 150.07, 157.92, 160.15, 160.90. MS m/z: 337.14. Anal. Calcd: $C_{22}H_{15}N_3O$; C, 78.32; H, 4.48; N, 12.46%. Found: C, 78.37; H, 4.52; N, 12.49%.

6-(furo[2,3-b]pyridin-5-yl)-1,2-dihydro-2-oxo-4-phenylpyridine-3-carbonitrile (4): Yellowish brown solid, yield: 66%, MP 235–237°C, IR (KBr): 2220 (CN), 1615 (C=O) cm^{-1}. ^1H NMR (DMSO-d_6) δ ppm: 6.46 (s, 1H, Pyridine-H), 6.88 (s, 1H, Furon-H), 7.39 (m, 3H-ArH), 7.57 (m, 4H-ArH),

7.97 (s, 1H-NH), 8.00 (s, 1H, Pyridine-H). ^{13}C NMR (DMSO-d_6) δ ppm:23.50, 11.63, 11.45, 116.70, 118.37, 128.34, 129.36, 132.96, 136.43, 147.03, 147.63, 157.92, 158.67, 159.51, 160.90. MS m/z: 313.09. Anal. Calcd: $C_{19}H_{11}N_3O_2$; C, 72.84; H, 3.54; N, 13.41%. Found: C, 72.86; H, 3.56; N, 13.46%.

Synthesis of (E)-1-(1-(2-methylquinolin-3-yl)ethylidene) thiosemicarbazide (5): A mixture of equimolar amounts of 1-(2-methylquinolin-3-yl)ethanone 1a (1.21 g, 5 mmol) and thiosemicarbazide (0.45 g, 5 mmol) in absolute ethanol (15 mL) containing 1mL acetic acid was refluxed for 4h. The solid that separated after storing the reaction mixture overnight, was collected by filtration and dried. Yellow solid, yield 70%, MP 201–203ºC, IR (KBr): 3307, 3203 (NH and NH_2),1622 (C=N), 1296 cm^{-1} (C=S). ^{1}H NMR (DMSO-d_6) δ ppm: 2.66 (s, 3H-CH_3), 2.93 (s, 3H-CH_3) 6.82 (s, 2H-NH_2), 7.56 (m, 4H-ArH), 7.97 (s, 1H, Quinoline-H), 10.34 (s, 1H-NH). ^{13}C NMR (DMSO-d_6) δ ppm: 14.78, 23.55, 124.10, 127.97, 128.29, 128.82, 131.25, 133.24, 150.63, 151.69, 157.52, 181.20. MS m/z: 258.09. Anal. Calcd: $C_{13}H_{14}N_4S$; C, 60.44; H, 5.46; N, 21.69%. Found: C, 60.46; H, 5.48; N, 21.72%.

Synthesis of (E)-1-(1-(2-methylquinolin-3-yl)ethylidene)-2-(4-methylthiazol-2-yl)hydrazine (6): It was mixed with 0.5 mL of trimethylamine, 20 mL of dioxane and 1-chloropropan-2-one (2 mmol) to make a solution of thiosemicarbazone 5 (0.63 g, 2 mmol). After that, the mixture was refluxed and stirred for 4h before being let to cool. After diluting with 20 mL of cold water, a solid byproduct was obtained, which was then dried and filtered. Lastly, thiazole derivatives 6 were obtained by recrystallizing the crude product from an ethanol/dioxane combination (1:1). Yellow solid, yield 72%, MP 226–229ºC, IR (KBr): 3309 (NH), 1625 (C=N) cm^{-1}. ^{1}H NMR (DMSO-d_6) δ ppm: 2.44 (s, 3H-CH_3), 2.62 (s, 3H-CH_3), 2.81 (s, 3H-CH_3), 6.04 (s, 1H, Thiazole-1H), 7.64 (m, 3H-ArH), 8.30 (s, 1H, Quinoline-H), 8.87 (s, 1H-NH). ^{13}C NMR (DMSO-d_6) δ ppm: 14.78, 15.64, 23.55, 105.37, 124.10, 127.97, 128.29, 128.82, 13125, 133.24, 145.47, 151.69, 154.80, 157.52, 159.50. MS m/z: 296.11. Anal. Calcd: $C_{16}H_{16}N_4S$; C, 64.84; H, 5.44; N, 18.90%. Found: C, 64.86; H, 5.49; N, 18.95%.

Synthesis of 2-bromo-1-(2-methylquinolin-3-yl)ethanone (7): 1-(2-methylquinolin-3-yl)ethanone derivative (2.43 g, 10 mmol) was diluted in 30 mL of glacial acetic acid in a 250 mL round-bottom flask. After stirring the mixture for 10 minutes at 60-70°C, glacial acetic acid (5 mL) and bromine (1.6 mL, 10 mmol) were added drop wise. For 30 minutes, the stirring was maintained at a temperature of 60-70ºC. The reaction was maintained at room temperature for three hours before being stored overnight at 20-25°C. In order to get the bromoacetyl derivative 7, the solid that separated after being diluted with ice-cold water, was recovered and recrystallized from ethanol. White Solid, yield 69%, MP 220–223ºC, IR (KBr): 1659 (C=O), 1629 (C=N) cm^{-1}. ^{1}H NMR (DMSO-d_6) δ ppm: 2.62 (s, 3H-CH_3), 4.23 (s, 2H-CH_2), 7.56 (m, 4H-ArH), 8.01 (s, 1H, Quinoline-H) ^{13}C NMR (DMSO-d_6) δ ppm: 23.55, 34.84, 124.10, 126.64, 127.97, 128.29, 129.13, 131.26, 134.09, 151.66, 161.02, 191.86. MS m/z: 262.99. Anal. Calcd: $C_{12}H_{10}BrNO$; C, 54.57; H, 3.82; N, 15.30%. Found: C, 54.58; H, 3.85; N, 15.35%.

Synthesis of 4-(2-methylquinolin-3-yl)thiazol-2-amine (8): The compound 2-bromoacetyl derivative 7 (1.60 g, 5 mmol) was combined with thiourea (0.38 g, 5 mmol) and diluted in 20 mL of dry acetone. The combination underwent reflux for a duration of 2h and then cooled down to the ambient temperature. Subsequently, it was transferred into ice-cold water and alkalized by adding a saturated sodium bicarbonate solution. The yellow solid obtained was recovered using suction filtering and then purified by recrystallization from ethanol to get the desired aminothiazole derivative 8. White Solid, yield 69%, MP 232–235ºC, IR (KBr): 1626 (C=N) cm^{-1}. ^{1}H NMR (DMSO-d_6) δ ppm: 2.81 (s, 3H-CH_3), 6.65 (s, 1H, Thiazole-H), 7.37 (m, 3H-ArH), 7.96 (s, 3H-ArH), 8.35 (s, 1H, Quinoline-H) ^{13}C NMR (DMSO-d_6) δ ppm: 23.59, 118.56, 124.10, 127.97, 128.29, 129.85, 131.26, 132.54, 151.72, 157.71, 158.23, 166.45. MS m/z: 241.07. Anal. Calcd: $C_{13}H_{11}N_3S$; C, 64.70; H, 4.59; N, 17.41%. Found: C, 64.72; H, 4.62; N, 17.45%.

Synthesis of 2-chloro-N-(4-(2-methylquinolin-3-yl) thiazol-2-yl)acetamide (9): The aminothiazole derivative 8, anhydrous sodium carbonate (0.70 g, 5 mmol) and 30 mL of dry acetone were added to a 250 mL conical flask. After the solution had been agitated at room temperature for ten minutes, 0.56 mL (7 mmol) of chloroacetyl chloride was gently added. The solution was diluted with 30 mL of ice-cold water after being stirred for an extra four hours. We recrystallized the white solid that precipitated from the ethanol solution. White Solid, yield 72%, MP 235–236ºC, IR (KBr): 1632 (C=N) cm^{-1}. ^{1}H NMR (DMSO-d_6) δ ppm: 3.08 (s, 3H-CH_3), 4.46 (s, 2H-CH_2), 6.29 (s, 1H, NH), 7.32 (s, 1H, Thiazole-H), 7.35 (s, 4H-ArH), 8.32 (s, 1H, Quinoline-H) ^{13}C NMR (DMSO-d_6) δ ppm: 23.56, 41.99, 121.17, 124.10, 127.97, 128.29, 129.85, 131.86, 132.54, 151.72, 156.24, 157.71, 169.25, 171.55. MS m/z: 317.79. Anal. Calcd: $C_{15}H_{12}ClN_3OS$; C, 56.69; H, 3.81; N, 13.22%. Found: C, 56.72; H, 3.84; N, 13.25%.

Synthesis of (Z)-2-(4-(2-methylquinolin-3-yl)thiazol-2-ylimino)thiazolidin-4-one (10): An ethanol solution containing 0.75 g of chloroacetamide derivative 9 (2 mmol) was added to a 50 mL round-bottom flask. It was heated under reflux for 4 hours after adding 0.23 g or 3 mmol, of ammonium thiocyanate and then allowed to cool. The (Z)-2-(4-(2-methylquinolin-3-yl)thiazol-2-ylimino)thiazolidin-4-one 10 was produced by collecting and drying the crystals that separated. White Solid, yield 75%, MP 237–239ºC, IR (KBr): 3307 (NH), 1660 (C=O), 1632 (C=N) cm^{-1}. ^{1}H NMR (DMSO-d_6) δ ppm: 3.11 (s, 3H-CH_3), 4.15 (s, 2H-CH_2), 7.29 (s, 1H, Thiazole-H), 7.29 (s, 1H, NH), 7.38 (m, 4H-ArH), 8.29 (s, 1H, Quinoline-H) ^{13}C NMR (DMSO-d_6) δ ppm: 23.56, 34.34, 123.80, 124.10, 127.97, 128.29, 129.85,

131.26, 132.54, 151.72, 157.68, 160.56, 171.44, 180.18. MS m/z: 340.05. Anal. Calcd: $C_{16}H_{12}N_4OS_2$; C, 56.45; H, 3.55; N, 16.46%. Found: C, 56.49; H, 3.56; N, 16.49%.

Synthesis of (E)-3-(dimethylamino)-1-(2-methylquinolin-3-yl)prop-2-en-1-one (11): A solution containing 1.09 g of 1-(2-methylquinolin-3-yl)ethanone 1 and 0.53 mL of DMF/DMA was heated under reflux for 5 hours in 25 mL of xylene. The concentration of the compounds was 4.5 mmol. The solvent was extracted using reduced-pressure distillation and the remaining solid was ground with 3.5 mL of cold ethanol. To get the corresponding (E)-3-(dimethylamino)-1-(2-methylquinolin-3-yl)prop-2-en-1-one derivative 11, the solid that was obtained after tritration, was heated in 30 mL of ethanol and then recrystallized. White Solid, yield 77%, MP 235–237°C, IR (KBr): 1665 (C=O), 1635 (C=N) cm^{-1}. ^1H NMR (DMSO-d_6) δ ppm: 2.69 (s, 3H-CH_3), 2.87 (s, 6H-CH_3), 5.73 (d, *J*=4.0 MHz, 2H-CH), 7.49 (m, 2H-ArH), 8.29 (s, 1H, Quinoline-H), 8.30 (m, 2H-ArH). ^{13}C NMR (DMSO-d_6) δ ppm: 23.55, 41.17, 93.59, 124.10, 127.97, 128.29, 128.58. 131.25, 133.25, 133.59, 152.37, 158.25, 160.11, 188.08. MS m/z: 240.13. Anal. Calcd: $C_{15}H_{16}N_2O$; C, 74.97; H, 6.71; N, 11.66%. Found: C, 74.99; H, 6.75; N, 11.69%.

Synthesis of 2-methyl-3-(1H-pyrazol-3-yl)quinoline (12). Hydrazine hydrate (0.15%, 3 mmol) was added to a solution of enaminone compound 11 (0.59 g, 2 mmol) in 20 mL of ethanol and the mixture was reflux-heated for 5h. The 2-methyl-3-(1H-pyrazol-3-yl)quinoline hybrid 13 was produced by filtering and drying the crystals that formed during cooling. White Solid, yield 75%, MP 225–227°C, IR (KBr): 3317 (NH), 1625 (C=N) cm^{-1}. ^1H NMR (DMSO-d_6) δ ppm: 2.95 (s, 3H-CH_3), 7.06 (m, 2H, Pyrazole-H), 7.38 (m, 2H-ArH), 7.54 (m, 2H-ArH), 8.27 (s, 1H, Quinoline-H), 10.37 (s, 1H-NH). ^{13}C NMR (DMSO-d_6) δ ppm: 23.55, 41.93, 124.10, 126.53, 127.97, 128.29, 129.65, 131.16, 132.64, 146.23, 153.76, 158.25. MS m/z: 209.10. Anal. Calcd: $C_{13}H_{11}N_3$; C, 74.62; H, 5.30; N, 20.08%. Found: C, 74.65; H, 5.35; N, 20.10%

Results and Discussion

The melting points were ascertained using an unaltered Gallenkamp electric device. An FTIR spectrometer from Thermo Scientific, the Nicolet iS10, was used to capture the KBr infrared spectra. The spectrometer from JEOL was used to record the 1H NMR (500 MHz) and 13C NMR (125 MHz) spectra in DMSO (D_6). At 70 eV, the mass spectra have been measured using a Quadrupole GC-MS (DSQII) instrument. Using a Perkin Elmer 2400 analyzer, we calculated the amounts of carbon, hydrogen, nitrogen.

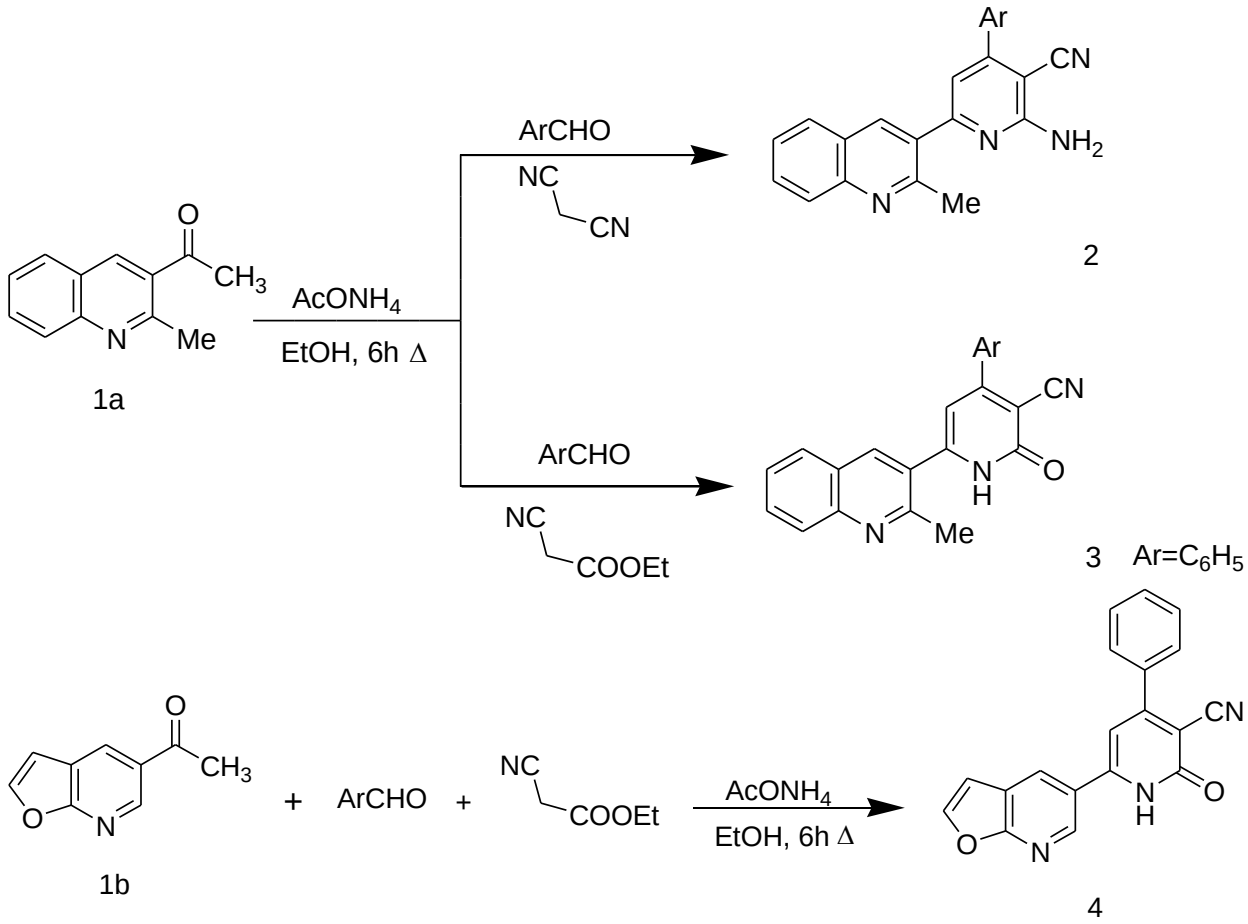
The work began by taking the compound 1-(2-methylquinolin-3-yl)ethanone, 1-(furo[2,3-b]pyridin-5-yl) ethanone (1a-b) available commercially. The one-pot reaction with active nitriles and different aromatic aldehydes demonstrated that the acetyl group of (1) was reactive. The compound 2-amino-6-(2-methylquinolin-3-yl)-4-phenylpyridine-3-carbonitrile (2) and 1,2-dihydro-6-(2-methylquinolin-3-yl)-2-oxo-4-phenylpyridine-3-carbonitrile (3) and 6-(furo[2,3-b]pyridin-5-yl)-1,2-dihydro-2-oxo-4-phenylpyridine-3-carbonitrile (4) were produced by the three-component reaction of ketone 1 by substituted benzaldehyde and malononitrile or ethyl cyanoacetate in boiling ethanol and ammonium acetate respectively (Scheme 1).

Analysis of IR, ^1H, ^{13}C and mass spectra allowed for the establishment of structures for compounds 2, 3 and 4. The processes that lead to the production of pyridine ring systems in products 2, 3 and 4 are detailed involving an initial formation of imine from methyl ketone and ammonium acetate[18]. The condensation reaction of 3-acetylimidazo[1,2-a]pyridine derivative 1 with thiosemicarbazide has been achieved in the presence of ethanol and drops of acetic acid. The condensation product has been analyzed and identified as the expected thiosemicarbazone (5). Thiosemicarbazone (5) underwent a reaction in dioxane containing triethylamine with 1-chloropropan-2-one to produce (E)-1-(1-(2-methylquinolin-3-yl)ethylidene)-2-(4-methylthiazol-2-yl)hydrazine (6) accordingly (Scheme 2).

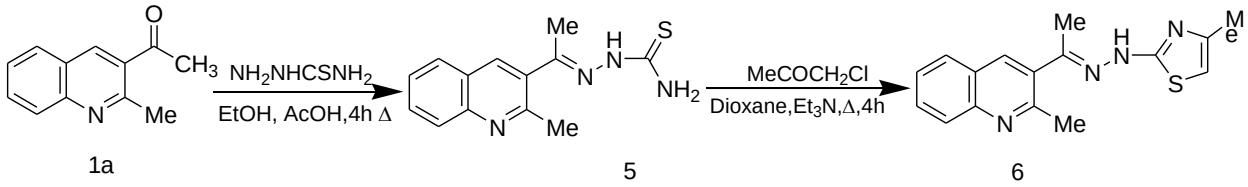
The appropriate 2-bromo-1-(2-methylquinolin-3-yl) ethanone (7) was produced by treating (1) with bromine in acetic acid, this compound then interacted with thiourea (Hantzsch reaction) to yield the equivalent 4-(2-methylquinolin-3-yl)thiazol-2-amine (8) (Scheme 3). To produce the chloroacetamide derivative (9), the organic substances (8) underwent chloroacetylation at the amino function of the thiazole moiety. This was accomplished by stirring chloroacetyl chloride with dry acetone and potassium carbonate. By analyzing its spectra, the structure of compound (9) was determined. The existence of N-H and carbonyl (C=O) functional groups was announced by absorptions at 3218 and 1680 cm^{-1} in the infrared spectra of compound (9).

Two distinct singlet signals at δ 3.08 and 4.46 ppm, corresponding to the protons of the methyl and methylene groups, were detectable in the ^1H NMR spectra. A singlet signal at δ 7.32 ppm was detected for the proton of thiazole-C5. The NH group proton was detected as a singlet at 6.29 ppm. The (Z)-2-(4-(2-methylquinolin-3-yl)thiazol-2-ylimino)thiazolidin-4-one (10) was produced by refluxing equimolar quantities of 2-chloro-N-(4-(2-methylquinolin-3-yl)thiazol-2-yl)acetamide (9) with ammonium thiocyanate in boiling ethanol.

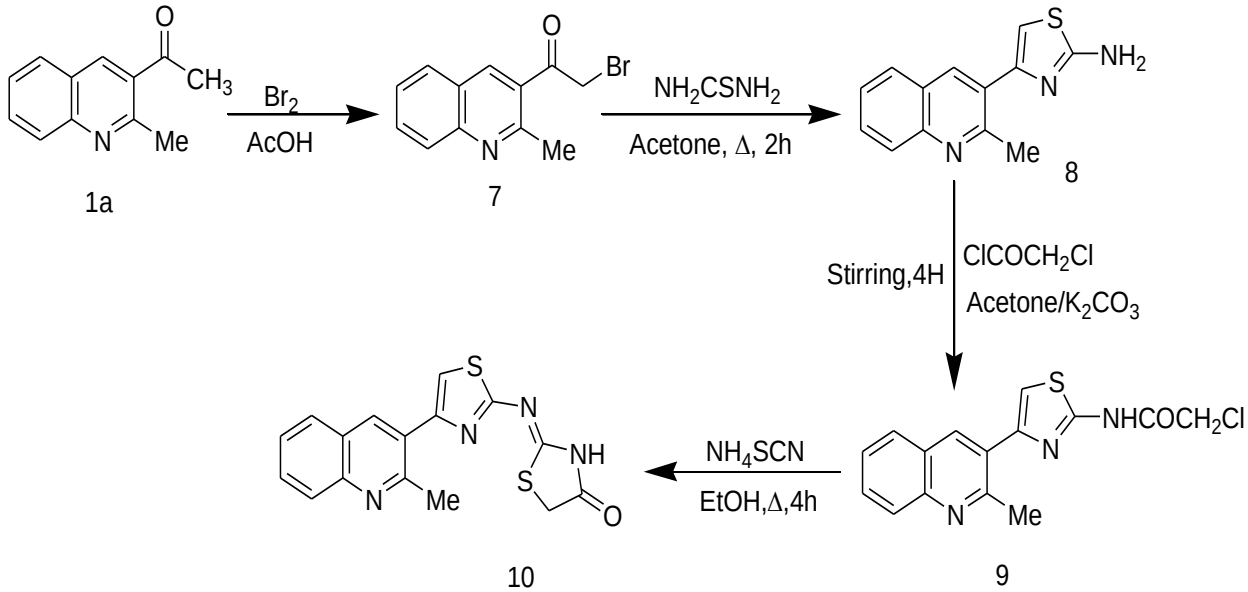
The conforming enaminone compound (11) shown in scheme 4 was produced by boiling compound (1) in xylene and condensing it with the dimethoxy-N,N-dimethylmethanamine reagent, according to its acetyl group. The 2-methyl-3-(1H-pyrazol-3-yl)quinoline (12) was prepared by heating enaminone compound (11) with hydrazine hydrate in ethyl alcohol (Scheme 4).



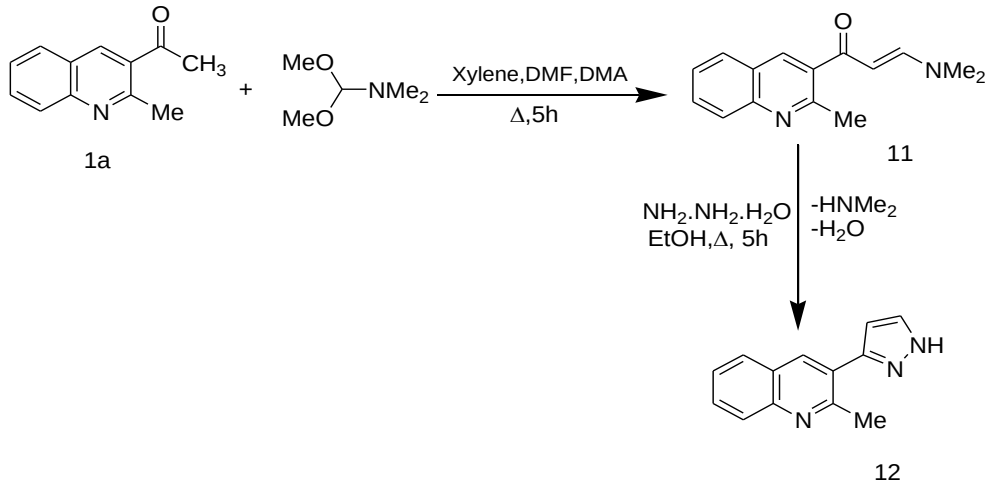
Scheme 1: Synthesis of (2-methylquinolin-3-yl)-2-oxo-4-phenylpyridine-3-carbonitrile hybrids.



Scheme 2: Synthesis of (E)-1-(1-(2-methylquinolin-3-yl)ethylidene) hydrazine derivatives 5 and 6.



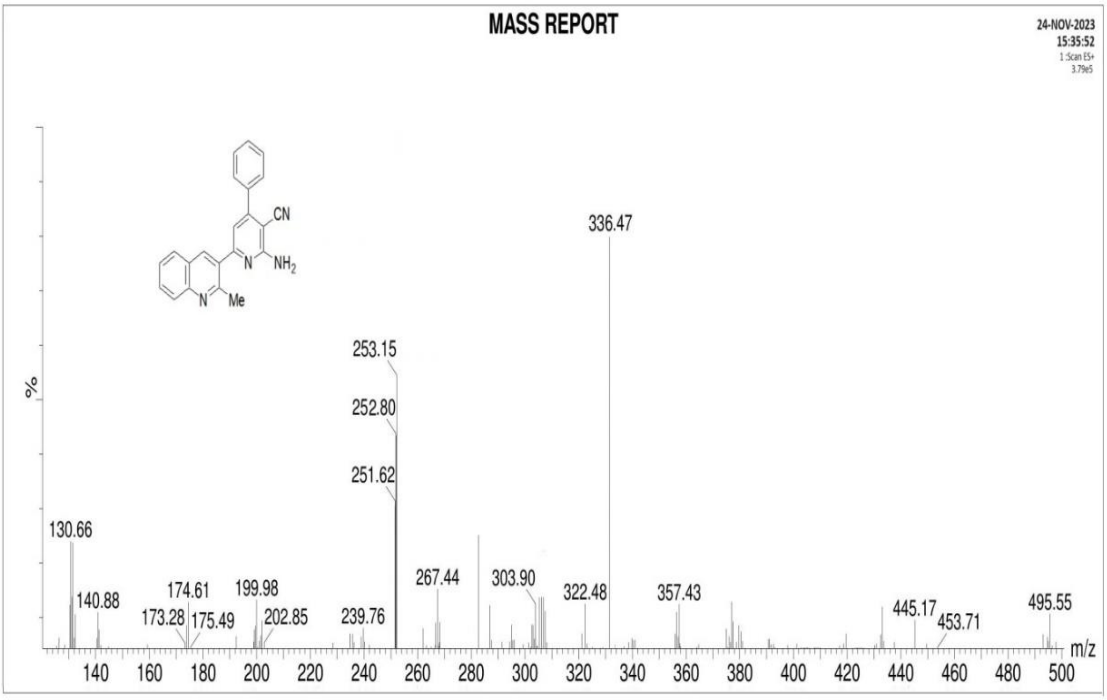
Scheme 3: Synthesis of (Z)-2-(4-(2-methylquinolin-3-yl)thiazol-2-ylimino)thiazolidin-4-one 7–10.



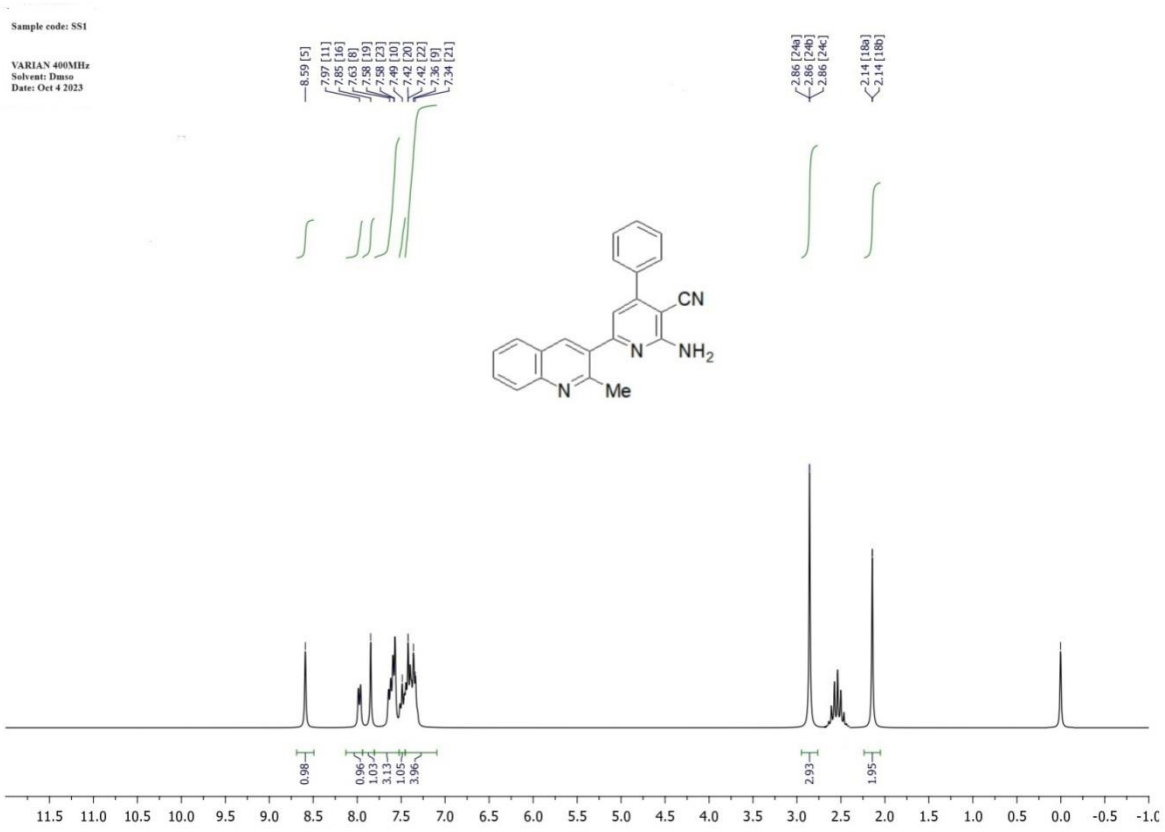
Scheme 4: 2-methyl-3-(1H-pyrazol-3-yl)quinoline (12) was prepared by heating enaminone compound (11) with hydrazine hydrate in ethyl alcohol

Table 1
***In vitro* cytotoxicity of targets (2-12) with IC_{50} in Mm.**

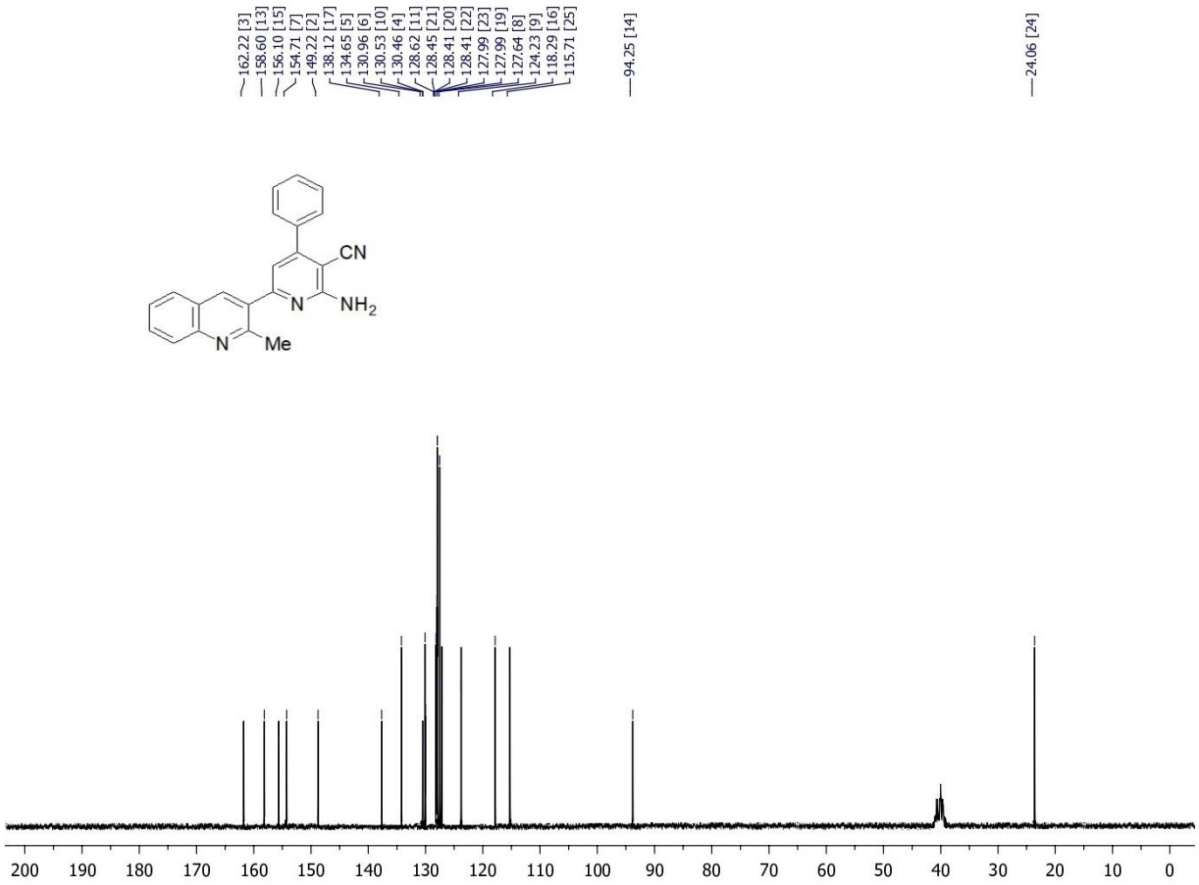
Compound	[b]MCF-7	[c]A549
2	46.1	50.9
3	40.1	60.4
4	27	33.1
5	23.9	25.8
6	30.7	39.3
7	12.2	16.2
8	40.1	50.4
9	15	21.3
10	33.8	39.2
11	12	10.5
12	40.5	40.4
Doxorubicin	2.9	5.5



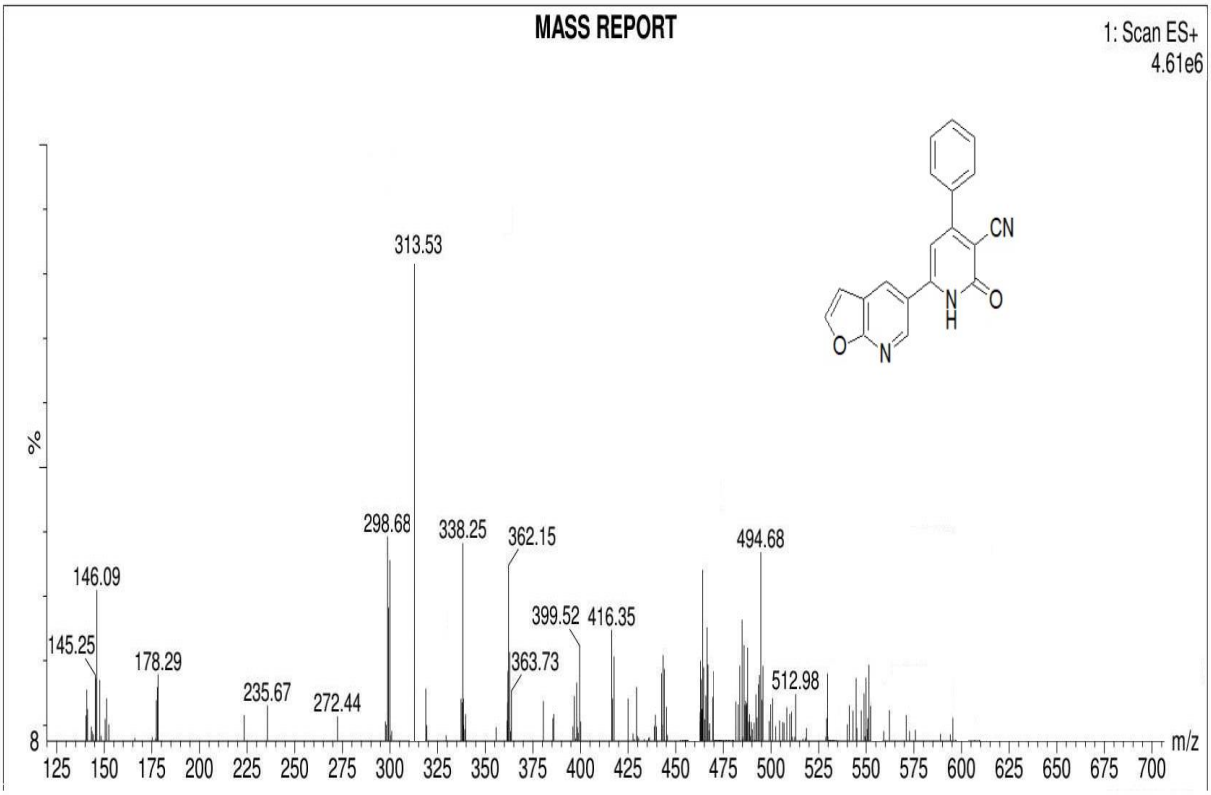
Suppl. Figure 1: Mass spectra of compound 2.



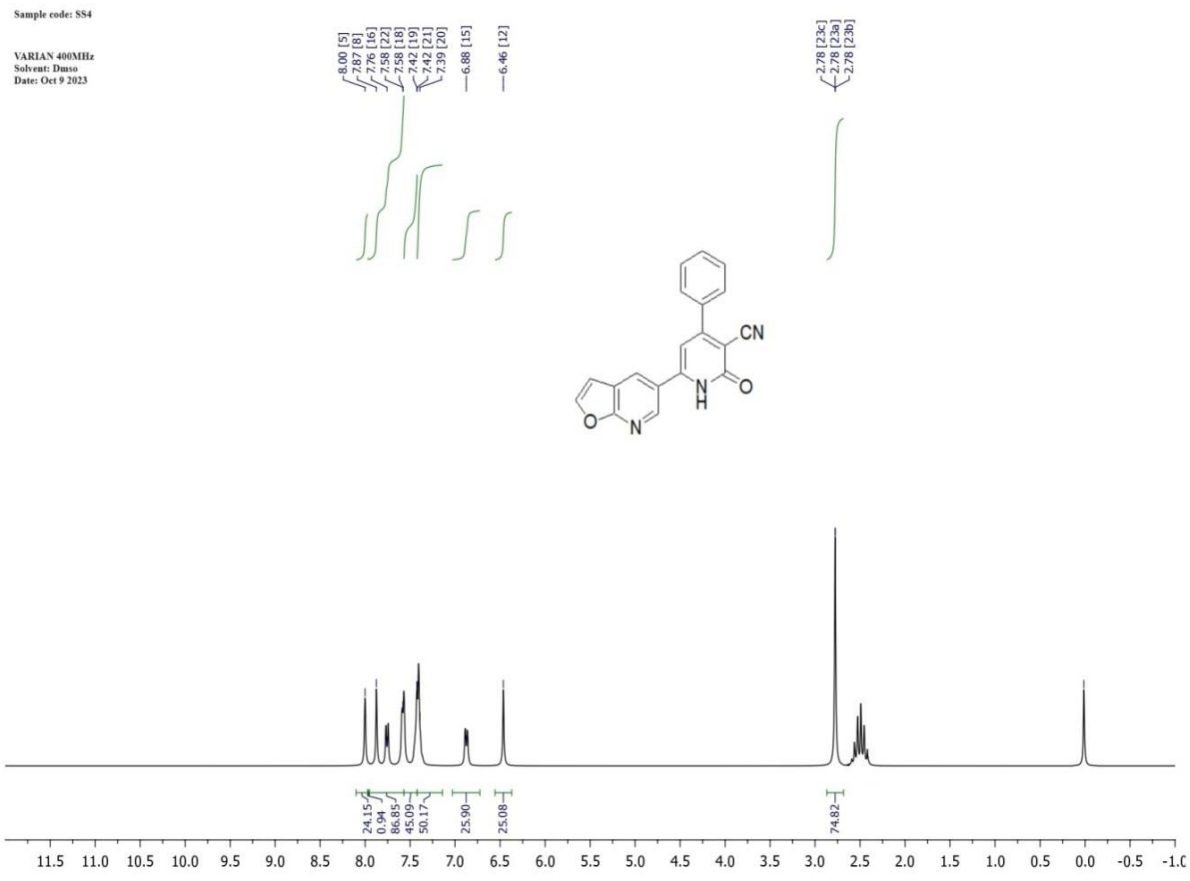
Suppl. Figure 2: ^{1}H NMR spectra of compound 2.



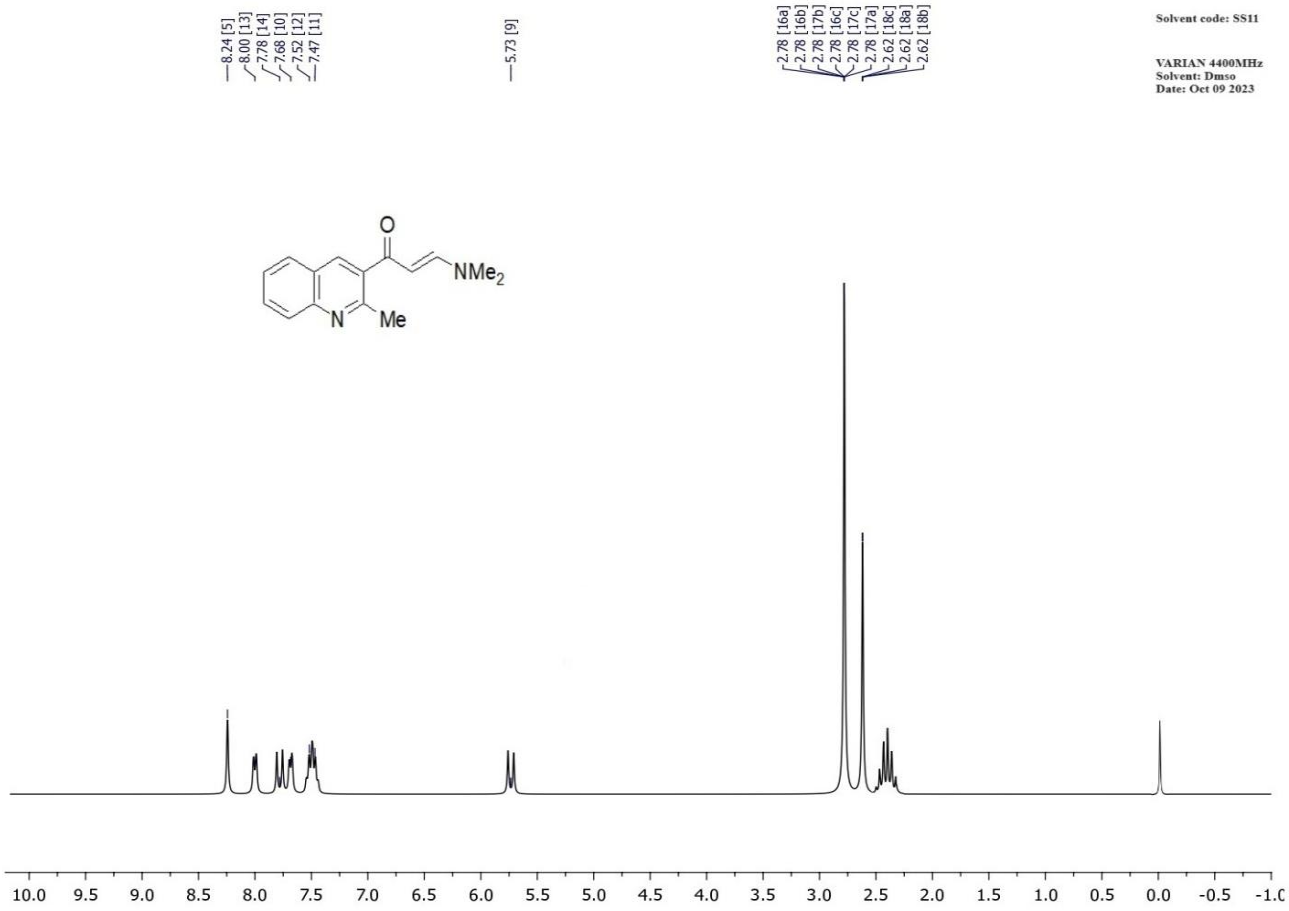
Suppl. Figure 3: ^{13}C NMR spectra of compound 2



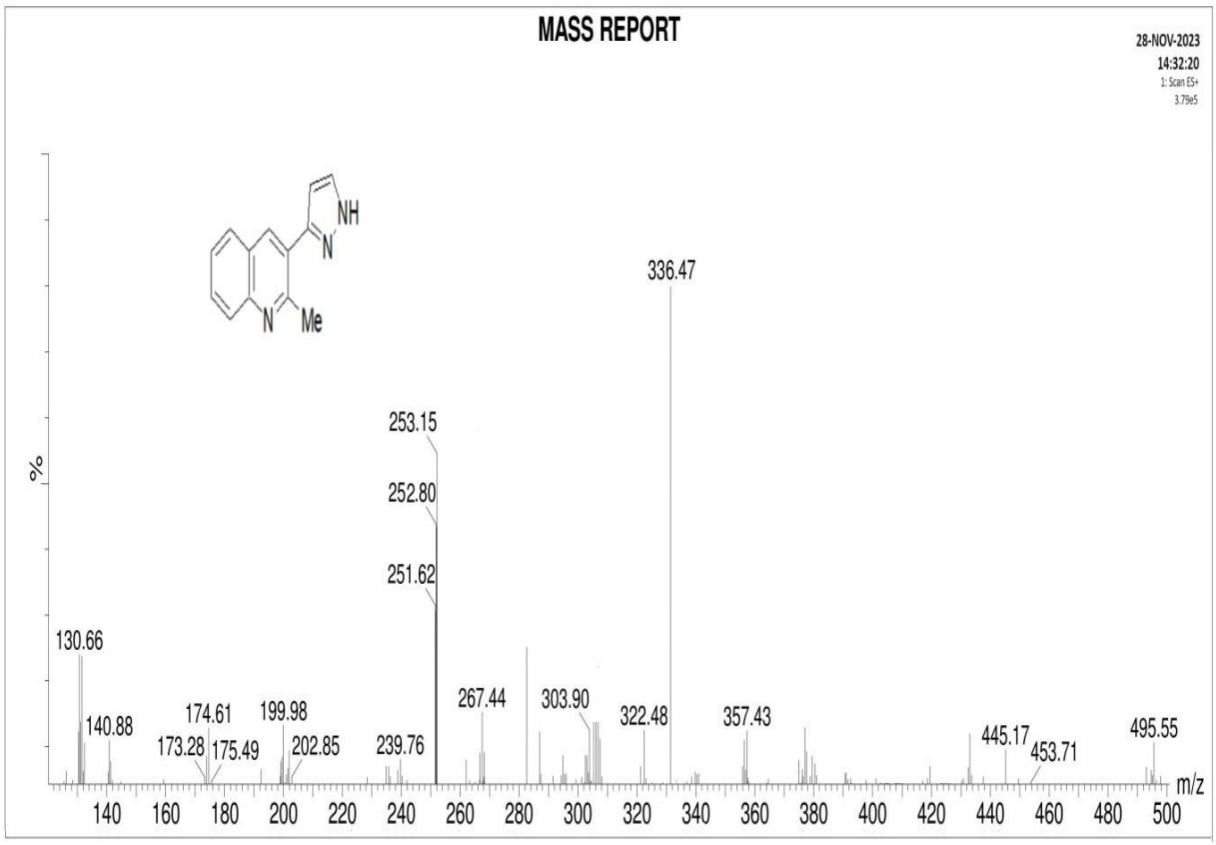
Suppl. Figure 4: Mass spectra of compound 4



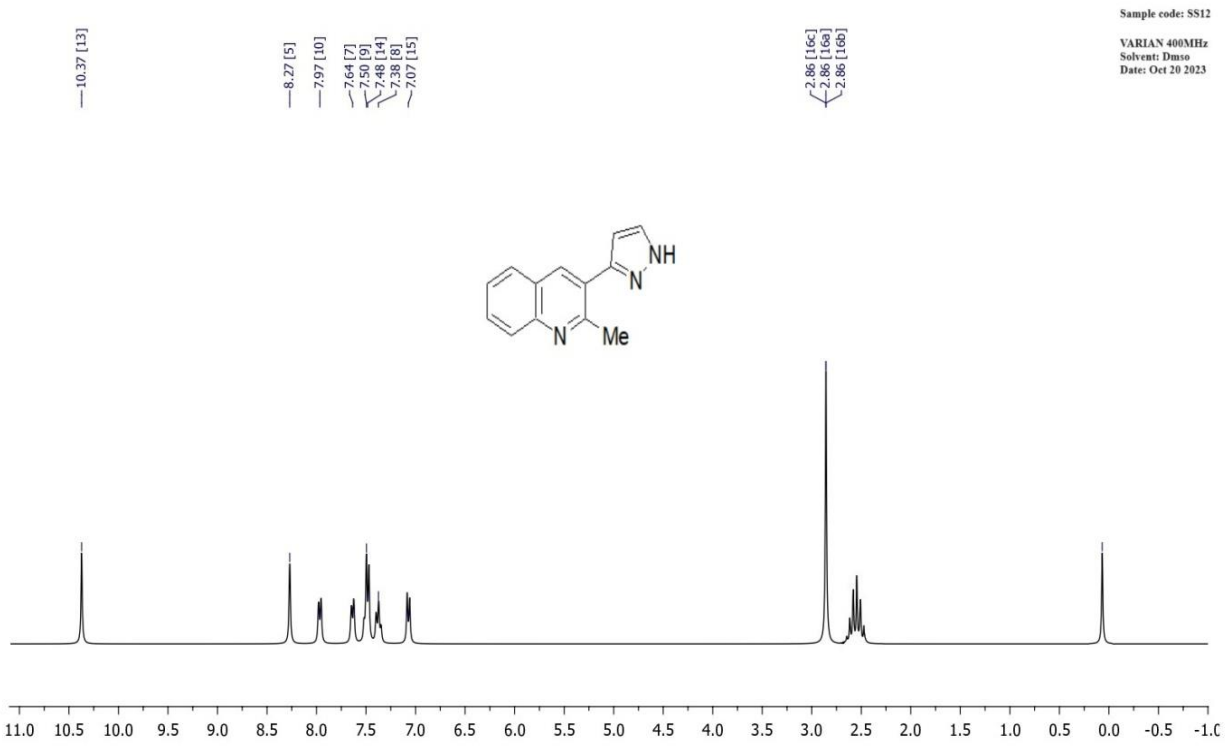
Suppl. Figure 5: ^{1}H NMR spectra of compound 4.



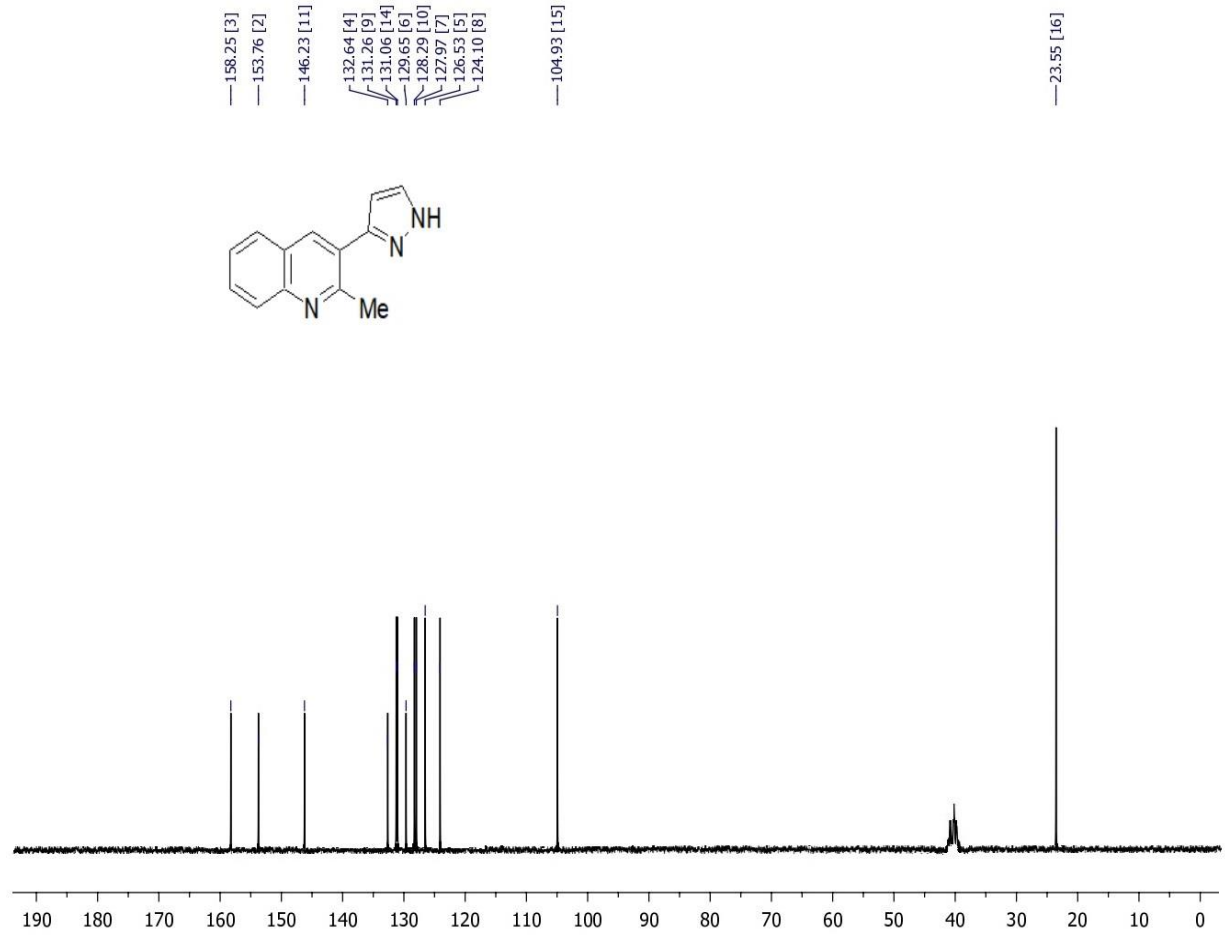
Suppl. Figure 6: ^{1}H NMR spectra of compound 11.



Suppl. Figure 7: Mass spectra of compound 12.



Suppl. Figure 8: ^{1}H NMR spectra of compound 12



Suppl. Figure 9: ^{13}C NMR spectra of compound 12.

Anti-cancer activity: Compounds 2-12 were tested for their cytotoxicity *in vitro* utilizing A-549 and MCF-7 cancer cell lines. The MTT assay was used to assess cell viability after exposure to the test substances. The cells were incubated at a temperature of 37°C with a mixture of 5% CO_2 and 95% air. They were supplied with a favorable environment including 10% FBS and 1X Penicillin/Streptomycin. The cell densities for MCF-7 and A-549 were 2x104 cells/well in a 96-well plate. After the cells were cultured in full medium for one day, they were transferred to decreased serum media. As a control, we used DMSO. The cells were treated with different dosages of test substances for 48 hours before being exposed to MTT (2.5 mg/mL) and incubated in a CO_2 incubator for 4 hours. The formazan crystals were dissolved by adding 100 µL of DMSO after the media had been removed from each well. As a direct correlation between cell number and optical density, the samples were mixed well before being analyzed using an Elisa plate reader set at 570 nm wavelength. We methodically performed each experiment three times to ensure accuracy and data was reported as the ratio of cytotoxicity to viability. Doxorubicin was used as a reference drug against which IC_{50} values derived from cytotoxicity were evaluated in %. Among these compounds, 2, 3, 6, 8, 10 and 12 showed stronger anti-cancer properties than doxorubicin.

Conclusion

The purpose of this research was to develop and test new heterocycles based on 1-(2-methylquinolin-3-yl)ethanone for their anticancer activity. We were able to accomplish our goal by creating three different sets of hybrid structures, each of which used 1-(2-methylquinolin-3-yl)ethanone core with either pyridine, thiazole, or pyrazole fragments. The findings clearly show that molecules with superior anticancer activity were produced by combining a thiazole ring with 1-(2-methylquinolin-3-yl)ethanone core, rather than with pyridine or pyrazole. *In vitro* cytotoxicity testing was performed on compounds 2–12 using A-549 and MCF-7 cancer cell lines and showed promising activity.

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