

Synthesis of 2-(1-((1-(methylsulfonyl)-1H-indol-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile

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Abstract

Benzimidazole derivatives are important class of organic compounds and show wide range of biological activity. Hence the researchers are paying more attention towards synthesis of these compounds. A series of Benzimidazole (**5**) was synthesized. The newly synthesized Benzimidazole derivatives (**5**) were characterized by ¹H NMR, ¹³C NMR, Mass, and IR spectral data. Benzimidazole (**1**) reacts with 2-chloroquinoline-3-carbonitrile (**2**) to offers 2-(1H-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile (**3**) which on reaction with propargylbromide produces 2-(1-(prop-2-ynyl)-1H-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile (**4**). Compound **4** is cyclised with 1-iodo-2-(methylsulfonyl)benzene to form 2-(1-((1-(methylsulfonyl)-1H-indol-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile (**5**).

INTRODUCTION

A heterocyclic compound is one which possesses a cyclic structure with at least two different kinds of hetero atoms in the ring. Nitrogen, oxygen, and sulphur are the most common heteroatoms. Heterocyclic compounds are very widely distributed in nature and are essential to life in various ways.

Nitrogen containing heterocycles are one of the most extensively synthesized and screened compounds as they show diverse pharmacological activities.

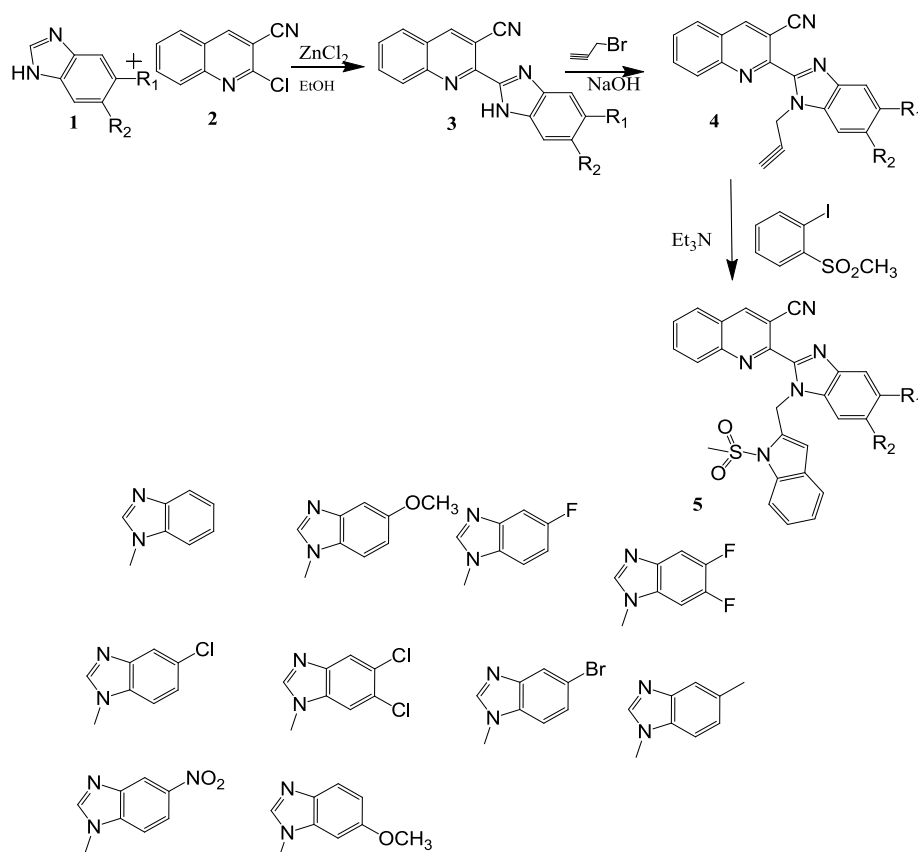
A few new classes of antimicrobials have been developed since the late 1980s [1–3], and much research has focused only on the chemical modification of existing drugs to improve their potency and/or ability to overcome antibiotic resistance mechanisms.

Even if this approach does not improve antimicrobial activity directly, it may lead to derivatives that can usefully inhibit virulence mechanisms [4]

Compounds having benzimidazole as a structural motif have been widely used in medicinal chemistry and drug development, and researchers are actively seeking new uses and applications of this heterocycle [5]. Benzimidazole-containing compounds have numerous medical and biological activities, such as antitumor [6] antibacterial [7,8].

Quinoline and their derivatives are important constituents of pharmacologically active synthetic compounds. The quinoline nucleus also occurs in the structure of numerous naturally occurring alkaloids which have been associated with a broad spectrum of biological activities [9]. The fusion of quinoline to the tetrazole ring is known to increase the biological activity [10]. The tetrazole group, which is considered as a carboxylic group pharmacore, possesses a wide range of biological activities. Several substituted tetrazoles have been shown to possess anti-inflammatory [11, 12], antimalarial [13], anticancer [14], antifungal [15, 16], anticonvulsant [17, 18], antibacterial [19, 20], vasorelaxing [21, 22], antiviral [23] and CNS dispersant activities [24].

SCHEME

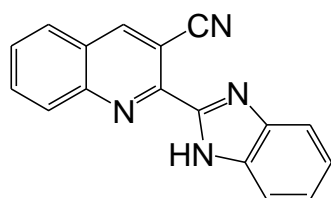


EXPERIMENTAL SECTION

Chemicals and solvents were reagent grade and used without further purification. The ^1H NMR was recorded in the indicated solvent on a Varian 400 MHz spectrometer with TMS as internal standard. All chemical shifts (δ) were reported in ppm from internal TMS. Mass spectra were measured on a Jeol JMS D-300 spectrometer. The homogeneity of the compounds was checked using pre-coated TLC plates (E.Merk Kieselgel 60 F₂₅₄).

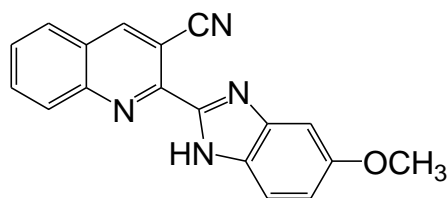
2-(1H-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile (3)

A mixture of 2-chloroquinoline-3-carbonitrile (0.01 mmole), and benzimidazole (0.01 mmole) and anhydrous ZnCl_2 (0.012 mmole) in Ethanol (10 mL) was refluxed for 7hr under a nitrogen atmosphere. After completion of the reaction, (monitored by TLC) the mixture was poured into ice-cold water (15 mL), stirred for 10 min and then extracted from ethylacetate.



^1H NMR(DMSO-d₆, 400MHz): δ 11.63(brs, 1H), 8.90(s,1H), 8.79(d, 1H), 8.21(d,1H), 8.00-7.83(m, 2H), 7.80-7.72(m, 2H), 7.50-7.58(m, 2H); ^{13}C NMR(DMSO-d₆, 100MHz): 149.5, 139.2, 132.5, 130.2, 128.0, 126.2, 125.3, 121.6, 118.6, 114.3, 110.3, 107.9, 103.8;

MS: m/z 271 [M+H] Yield: 76%.

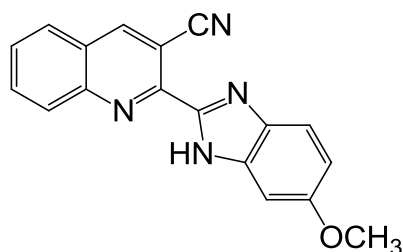


2-(5-methoxy-1H-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile

^1H NMR(DMSO-d₆, 400MHz): δ 11.60(brs, 1H), 8.92(s,1H), 8.77(d, 1H), 8.19(d,1H), 7.99-7.84(m, 2H), 7.82-7.73(m, 2H), 7.57(s, 1H), 3.82(s, 3H); ^{13}C NMR(DMSO-d₆,

100MHz): 149.3, 139.3, 132.4, 130.3, 128.1, 126.3, 125.2, 121.3, 117.4, 115.2, 112.5, 110.2, 107.8, 103.5, 56.2;

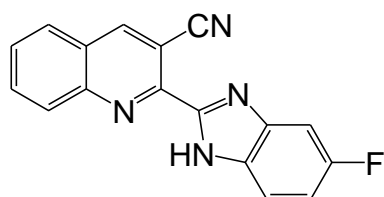
MS: m/z 301 [M+H], Yield: 78%.



2-(6-methoxy-1H-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile

$^1\text{H NMR}$ (DMSO- d_6 , 400MHz): δ 11.61(brs, 1H), 8.93(s,1H), 8.77(d, 1H), 8.19(d,1H), 7.99-7.83(m, 2H), 7.82-7.72(m, 2H), 7.57(s, 1H), 3.82(s, 3H); $^{13}\text{C NMR}$ (DMSO- d_6 , 100MHz): 149.3, 139.3, 132.4, 130.3, 128.1, 126.3, 125.2, 121.2, 117.4, 115.2, 112.5, 110.2, 107.8, 103.4, 56.1;

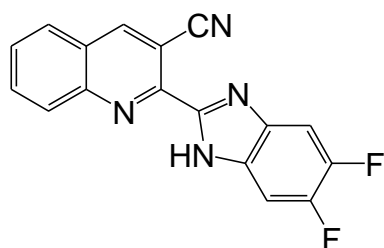
MS: m/z 301 [M+H] Yield: 80%.



2-(5-fluoro-1H-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile

$^1\text{H NMR}$ (DMSO- d_6 , 400MHz): δ 11.61(brs, 1H), 8.89(s,1H), 8.78(d, 1H), 8.23(m,1H), 8.00(m, 1H), 7.80-7.72(m, 2H), 7.51-7.58(m, 2H); $^{13}\text{C NMR}$ (DMSO- d_6 , 100MHz): 149.5, 139.2, 132.5, 130.2, 128.0, 126.2, 125.3, 121.6, 121.3, 118.6, 114.3, 110.3, 107.9, 107.5, 103.1;

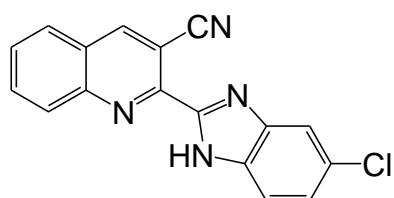
MS: m/z 289 [M+H] Yield: 82%.



2-(5,6-difluoro-1H-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile

$^1\text{H NMR}$ (DMSO- d_6 , 400MHz): δ 11.65(brs, 1H), 8.87(s,1H), 8.79(d, 1H), 8.22(m,1H), 8.03(m, 1H), 7.82-7.72(m, 2H), 7.51-7.56(m, 1H); $^{13}\text{C NMR}$ (DMSO- d_6 , 100MHz): 149.2, 139.1, 132.3, 130.2, 128.2, 126.2, 125.2, 121.5, 121.2, 118.5, 114.5, 110.2, 107.8, 107.8, 103.8;

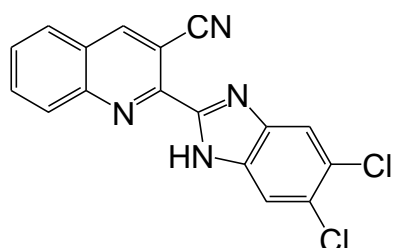
MS: m/z 307 [M+H] Yield: 68%.



2-(5-chloro-1H-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile

$^1\text{H NMR}$ (DMSO- d_6 , 400MHz): δ 11.61(brs, 1H), 8.89(s,1H), 8.78(d, 1H), 8.23(m,1H), 8.00(m, 1H), 7.80-7.72(m, 2H), 7.51-7.58(m, 2H); $^{13}\text{C NMR}$ (DMSO- d_6 , 100MHz): 149.5, 139.2, 132.5, 130.2, 128.0, 126.2, 125.3, 121.3, 118.2, 114.1, 110.2, 107.3, 103.2;

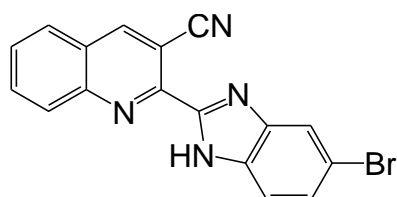
MS: m/z 306 [M+H] Yield: 77%.



2-(5,6-dichloro-1H-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile

$^1\text{H NMR}$ (DMSO- d_6 , 400MHz): δ 11.64(brs, 1H), 8.91(s,1H), 8.79(d, 1H), 8.21(m, 1H), 8.01(m, 1H), 7.80-7.70(m, 1H), 7.51-7.55(m, 2H); $^{13}\text{C NMR}$ (DMSO- d_6 , 100MHz): 149.5, 139.2, 132.3, 130.2, 128.0, 126.2, 125.3, 121.3, 118.2, 114.1, 110.2, 107.3, 103.6;

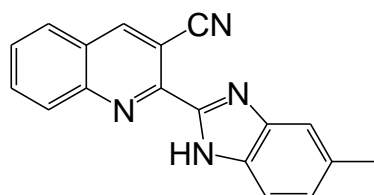
MS: m/z 271 [M+H] Yield: 80%.



2-(5-bromo-1H-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile

$^1\text{H NMR}$ (DMSO- d_6 , 400MHz): δ 11.62(brs, 1H), 8.88(s,1H), 8.79(d, 1H), 8.22(m,1H), 8.01(m, 1H), 7.83-7.72(m, 2H), 7.51-7.58(m, 2H); $^{13}\text{C NMR}$ (DMSO- d_6 , 100MHz): 149.6, 139.4, 132.3, 130.2, 128.2, 126.2, 125.2, 121.2, 118.4, 114.5, 110.2, 107.2, 103.4;

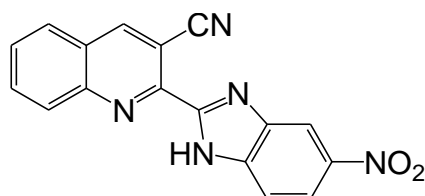
MS: m/z 305 [M+H] Yield: 80%.



2-(5-methyl-1H-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile

$^1\text{H NMR}$ (DMSO- d_6 , 400MHz): δ 11.58(brs, 1H), 8.74(s,1H), 8.70(d, 1H), 8.20(m,1H), 8.08(m, 1H), 7.80-7.73(m, 2H), 7.51-7.57(m, 2H), 2.36(s, 3H); $^{13}\text{C NMR}$ (DMSO- d_6 , 100MHz): 149.8, 140.2, 132.8, 131.2, 129.1, 127.1, 124.3, 121.4, 118.2, 114.4, 111.2, 107.2, 104.2, 21.4;

MS: m/z 285 [M+H] Yield: 81%.



2-(5-nitro-1H-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile

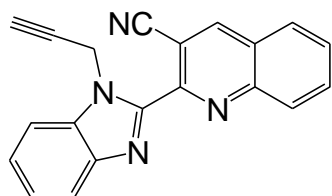
$^1\text{H NMR}$ (DMSO- d_6 , 400MHz): δ 11.52(brs, 1H), 8.95(s,1H), 8.84(d, 1H), 8.18(m,1H), 8.00(m, 1H), 7.84-7.80(m, 2H), 7.51-7.56(m, 2H); $^{13}\text{C NMR}$ (DMSO- d_6 ,

100MHz): 149.6, 135.9, 132.3, 130.2, 128.2, 126.4, 125.2, 121.2, 118.4, 114.2, 110.5, 107.1, 103.1;

MS: m/z 316 [M+H] Yield: 74%.

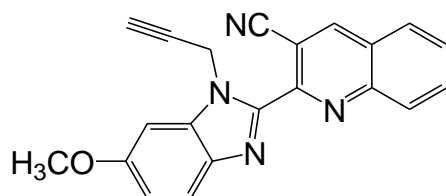
2-(1-(prop-2-ynyl)-1H-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile (4)

To a mixture of 2-(1H-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile (0.01 mmole), propargyl bromide (0.015 mmole) and 50 mol% tetrabutylammonium bromide in 10 mL of toluene was added 10 mL of 50% NaOH drop wise at room temperature. The reaction mixture was then stirred at room temperature for 7 h. After completion of the reaction, (monitored by TLC) the reaction mixture was diluted with water and extracted from ethylacetate.



$^1\text{H NMR}$ (DMSO- d_6 , 400MHz): δ 8.93(s,1H), 8.78(d, 1H), 8.20(d,1H), 8.02(d, 1H), 7.92(m, 1H), 7.78-7.98(m, 2H), 7.59(d, 1H), 7.51(d, 1H), 5.39(s, 2H), 2.63(s, 1H); $^{13}\text{C NMR}$ (DMSO- d_6 , 100MHz): 149.8, 142.8, 141.6, 132.5, 128.1, 127.2, 125.9, 121.9, 116.3, 113.1, 111.3, 107.8, 103.7, 78.1, 76.2, 35.8;

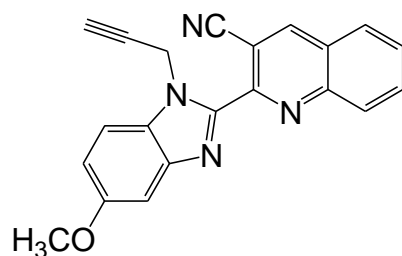
MS: m/z 309 [M+H] Yield: 72%.



2-(6-methoxy-1-(prop-2-ynyl)-1H-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile

$^1\text{H NMR}$ (DMSO- d_6 , 400MHz): δ 8.91(s,1H), 8.78(d, 1H), 8.20(d,1H), 8.02(d, 1H), 7.92(m, 1H), 7.78-7.97(m, 2H), 7.59(d, 1H), 5.38(s, 2H), 3.90(s, 3H), 2.62(s, 1H); $^{13}\text{C NMR}$ (DMSO- d_6 , 100MHz): 149.7, 142.8, 141.6, 132.5, 128.1, 127.2, 125.9, 121.8, 115.1, 114.5, 112.3, 103.7, 78.1, 76.3, 56.6, 35.7;

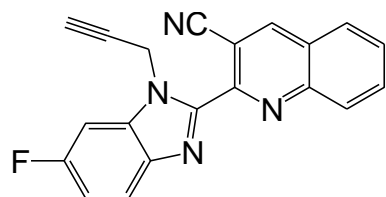
MS: m/z 339 [M+H] Yield: 78%.



2-(5-methoxy-1-(prop-2-ynyl)-1H-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile

$^1\text{H NMR}$ (DMSO- d_6 , 400MHz): δ 8.89(s,1H), 8.78(d, 1H), 8.20(d,1H), 8.01(d, 1H), 7.92(m, 1H), 7.78-7.98(m, 2H), 7.59(d, 1H), 5.36(s, 2H), 3.91(s, 3H), 2.61(s, 1H); $^{13}\text{C NMR}$ (DMSO- d_6 , 100MHz): 149.7, 142.8, 141.6, 132.5, 128.1, 127.2, 125.9, 121.8, 115.1, 114.5, 112.3, 103.7, 78.1, 76.3, 56.6, 35.7;

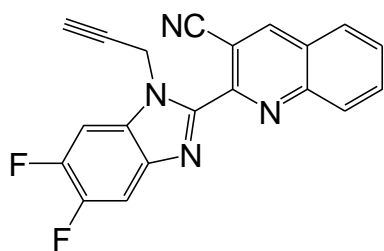
MS: m/z 339 [M+H] Yield: 74%.



2-(6-fluoro-1-(prop-2-ynyl)-1H-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile

$^1\text{H NMR}$ (DMSO- d_6 , 400MHz): δ 8.90(s, 1H), 8.79(m, 1H), 8.19(d, 1H), 8.03(m, 1H), 7.92(m, 1H), 7.78-7.65(m, 2H), 7.60(m, 1H), 5.38(s, 2H), 2.61(s, 1H); $^{13}\text{C NMR}$ (DMSO- d_6 , 100MHz): 149.6, 142.8, 141.6, 132.5, 128.1, 127.2, 125.9, 121.8, 121.3, 115.1, 114.5, 112.3, 110.6, 103.7, 78.1, 76.3, 35.7;

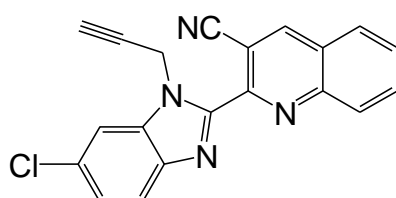
MS: m/z 327 [M+H] Yield: 82%.



2-(5,6-difluoro-1-(prop-2-ynyl)-1H-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile

$^1\text{H NMR}$ (DMSO- d_6 , 400MHz): δ 8.90(s, 1H), 8.78(d, 1H), 8.18(d, 1H), 8.03(m, 1H), 7.92(m, 1H), 7.78-7.97(m, 1H), 7.59(m, 1H), 5.39(s, 2H), 2.61(s, 1H); $^{13}\text{C NMR}$ (DMSO- d_6 , 100MHz): 149.8, 142.7, 141.7, 132.5, 128.2, 127.2, 125.9, 121.8, 121.5, 115.3, 114.5, 112.3, 110.8, 103.7, 78.1, 76.3, 35.6;

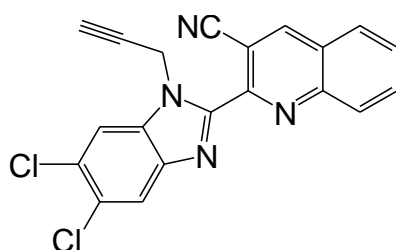
MS: m/z 345 [M+H] Yield: 70%.



2-(6-chloro-1-(prop-2-ynyl)-1H-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile

$^1\text{H NMR}$ (DMSO- d_6 , 400MHz): δ 8.89(s, 1H), 8.80(d, 1H), 8.19(d, 1H), 8.01(d, 1H), 7.91(m, 1H), 7.78-7.98(m, 2H), 7.59(d, 1H), 5.37(s, 2H), 2.60(s, 1H); $^{13}\text{C NMR}$ (DMSO- d_6 , 100MHz): 149.6, 142.9, 141.6, 132.3, 128.1, 127.2, 125.8, 121.8, 115.1, 114.5, 112.3, 103.7, 78.1, 76.3, 35.8;

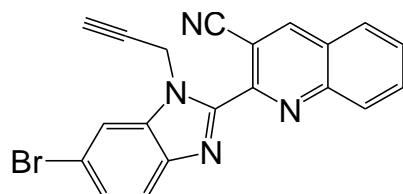
MS: m/z 344 [M+H] Yield: 76%.



2-(5,6-dichloro-1-(prop-2-ynyl)-1H-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile $^1\text{H NMR}$ (DMSO- d_6 , 400MHz): δ 8.89(s, 1H), 8.79(d, 1H), 8.21(d, 1H), 8.01(d, 1H), 7.92(m, 1H), 7.78-7.98(m, 1H), 7.59(m, 1H), 5.38(s, 2H), 2.61(s, 1H); ^{13}C

NMR(DMSO-d₆, 100MHz): 149.8, 142.8, 141.6, 132.4, 128.1, 127.2, 125.8, 121.8, 115.1, 114.5, 112.3, 103.8, 78.1, 76.3, 35.8;

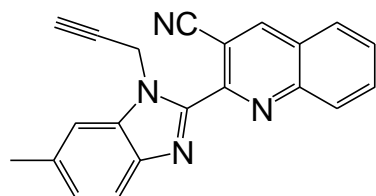
MS: *m/z* 378 [M+H] Yield: 74%.



2-(6-bromo-1-(prop-2-ynyl)-1H-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile

¹H NMR(DMSO-d₆, 400MHz): δ 8.81(s, 1H), 8.80(d, 1H), 8.20(d, 1H), 8.02(d, 1H), 7.92(m, 1H), 7.78-7.98(m, 2H), 7.58(d, 1H), 5.36(s, 2H), 2.60(s, 1H); **¹³C NMR**(DMSO-d₆, 100MHz): 148.9, 142.3, 141.9, 132.5, 128.8, 127.8, 125.5, 121.8, 115.1, 114.5, 112.4, 103.7, 78.1, 76.3, 35.5;

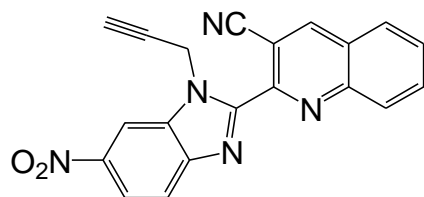
MS: *m/z* 388 [M+H] Yield: 80%.



2-(6-methyl-1-(prop-2-ynyl)-1H-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile

¹H NMR(DMSO-d₆, 400MHz): δ 8.81(s, 1H), 8.79(d, 1H), 8.21(d, 1H), 8.01(d, 1H), 7.90(m, 1H), 7.78-7.98(m, 2H), 7.58(d, 1H), 5.38(s, 2H), 2.61(s, 1H), 2.31(s, 3H); **¹³C NMR**(DMSO-d₆, 100MHz): 149.9, 142.8, 141.9, 132.5, 128.1, 126.9, 125.9, 121.6, 115.1, 114.5, 112.3, 103.7, 78.1, 76.3, 35.9, 22.8;

MS: *m/z* 323 [M+H] Yield: 78%.



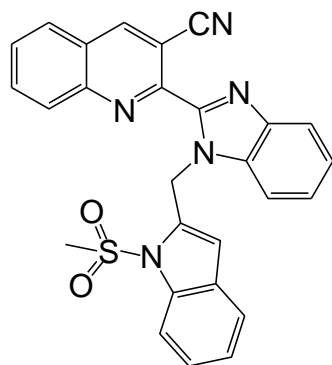
2-(6-nitro-1-(prop-2-ynyl)-1H-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile

¹H NMR(DMSO-d₆, 400MHz): δ 8.91(s, 1H), 8.80(d, 1H), 8.17(d, 1H), 8.02(d, 1H), 8.17-9.2(m, 1H), 7.78-7.98(m, 2H), 7.58(d, 1H), 5.36(s, 2H), 2.60(s, 1H); ¹³C NMR(DMSO-d₆, 100MHz): 148.9, 142.3, 141.9, 132.5, 128.8, 127.8, 125.5, 121.8, 115.1, 114.5, 112.4, 103.4, 78.1, 76.1, 35.2;

MS: *m/z* 354 [M+H] Yield: 80%.

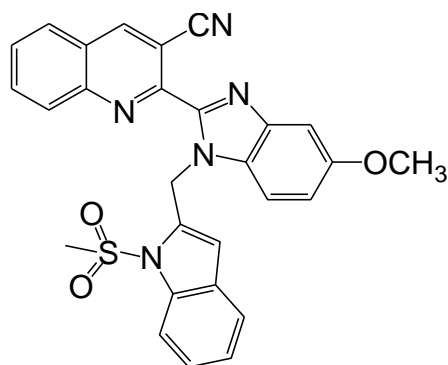
2-(1-((1-(methylsulfonyl)-1H-indol-2-yl)methyl)-1H-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile (5)

A mixture of 1-iodo-2-(methylsulfonyl)benzene (0.01 mmol), 10% Pd/C (0.025 mmol), PPh₃ (0.01 mmol), CuI (0.045 mmol) and triethylamine (2.42 mmol) in ethanol (10 mL) was stirred at rt for 1 h under nitrogen. The acetylenic compound (1.62 mmol) was added slowly to the mixture with stirring. The reaction mixture was then refluxed for the 8 h. The mixture was cooled to rt, diluted with EtOAc and filtered.



¹H NMR(DMSO-d₆, 400MHz): δ 8.53(s, 1H), 8.38(d, 2H), 8.18(d, 2H), 7.80(m, 3H), 7.58(d, 1H), 7.48(m, 1H), 7.39(m, 2H), 7.18(d, 1H), 6.36(s, 1H), 5.83(s, 2H), 2.98(s, 3H); ¹³C NMR(DMSO-d₆, 100MHz): 149.2, 143.8, 134.6, 132.6, 130.1, 129.7, 128.3, 127.8, 126.3, 125.3, 124.3, 119.8, 116.7, 116.6, 107.3, 103.8, 48.2, 45.6;

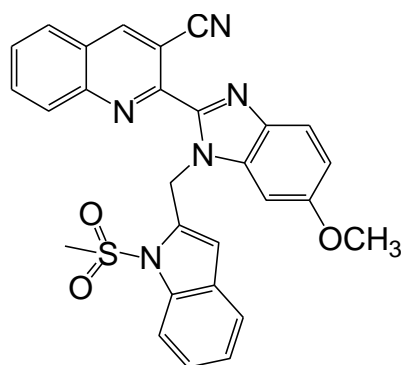
MS: *m/z* 478 [M+H] Yield: 80%.



2-(1-((1-(methylsulfonyl)-1*H*-indol-2-yl)methyl)-(6-methoxy-1*H*-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile

¹H NMR(DMSO-d₆, 400MHz): δ 8.52(s,1H), 8.37(d, 2H), 8.18(d, 2H), 7.80(m, 3H), 7.58(d, 1H), 7.48(m, 1H), 7.39(m, 2H), 6.37(s, 1H), 5.84(s, 2H), 3.81(s, 3H), 2.97(s, 3H); ¹³C NMR(DMSO-d₆, 100MHz): 149.2, 143.8, 134.6, 132.6, 130.1, 129.7, 128.3, 127.8, 126.3, 125.3, 124.3, 119.7, 116.1, 115.8, 108.3, 103.9, 56.4, 48.3, 45.5;

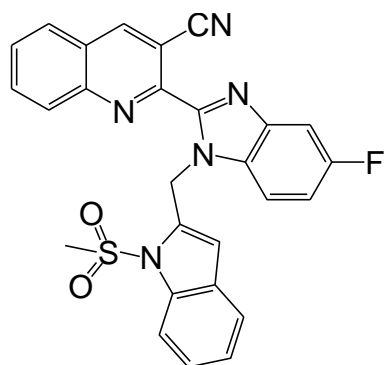
MS: *m/z* 508 [M+H] Yield: 75%.



2-(1-((1-(methylsulfonyl)-1*H*-indol-2-yl)methyl)-(5-methoxy-1*H*-benzo[d]imidazol-2-yl)quinoline-3-carbonitrile

¹H NMR(DMSO-d₆, 400MHz): δ 8.51(s,1H), 8.37(d, 2H), 8.19(d, 2H), 7.80(m, 3H), 7.58(d, 1H), 7.48(m, 1H), 7.38(m, 2H), 6.37(s, 1H), 5.84(s, 2H), 3.81(s, 3H), 2.97(s, 3H); ¹³C NMR(DMSO-d₆, 100MHz): 149.2, 143.8, 134.6, 132.6, 130.1, 129.7, 128.3, 127.8, 126.3, 125.3, 124.2, 119.7, 116.1, 115.8, 108.3, 103.9, 56.4, 48.3, 45.6;

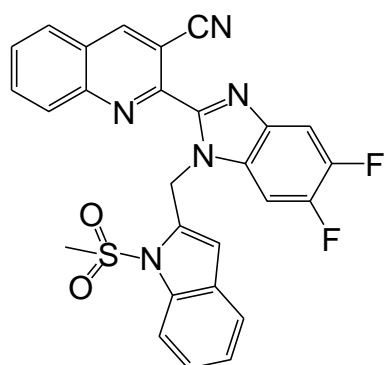
MS: *m/z* 508 [M+H] Yield: 68%.



2-(1-((1-(methylsulfonyl)-1H-indol-2-yl)methyl)-(6-fluoro-1H-benzo[d]imidazol)-2-yl)quinoline-3-carbonitrile

$^1\text{H NMR}$ (DMSO- d_6 , 400MHz): δ 8.90(s, 1H), 8.38(d, 2H), 8.19(d, 2H), 7.89(m, 3H), 7.58(m, 1H), 7.49(m, 1H), 7.39(m, 2H), 6.38(s, 1H), 5.84(s, 2H), 2.98(s, 3H); $^{13}\text{C NMR}$ (DMSO- d_6 , 100MHz): 149.9, 143.9, 134.5, 132.8, 130.2, 129.7, 128.3, 127.8, 126.3, 125.3, 124.3, 120.01, 119.7, 116.1, 115.8, 112.8, 112.1, 108.3, 103.9, 48.3, 45.3;

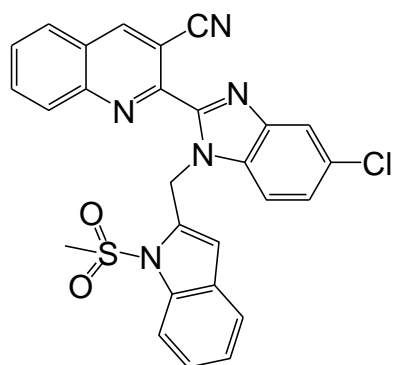
MS: m/z 496 [M+H] Yield: 74%.



2-(1-((1-(methylsulfonyl)-1H-indol-2-yl)methyl)-(5,6-difluoro-1H-benzo[d]imidazol)-2-yl)quinoline-3-carbonitrile

$^1\text{H NMR}$ (DMSO- d_6 , 400MHz): δ 8.92(s,1H), 8.38(d, 2H), 8.20(d, 2H), 7.80(m, 3H), 7.58(m, 1H), 7.49(m, 1H), 7.39(m, 1H), 6.37(s, 1H), 5.84(s, 2H), 2.97(s, 3H); $^{13}\text{C NMR}$ (DMSO- d_6 , 100MHz): 149.2, 143.8, 134.6, 132.6, 130.1, 129.7, 128.3, 127.8, 126.3, 125.3, 124.3, 120.3, 119.8, 116.1, 115.8, 112.6, 112.2, 108.2, 103.9, 48.2, 45.5;

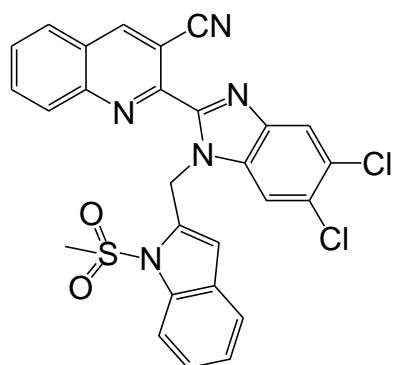
MS: m/z 514 [M+H] Yield: 72%.



2-(1-((1-(methylsulfonyl)-1*H*-indol-2-yl)methyl)-(6-chloro-1*H*-benzo[d]imidazol)-2-yl)quinoline-3-carbonitrile

¹H NMR(DMSO-d₆, 400MHz): δ 8.62(s, 1H), 8.38(d, 2H), 8.20(d, 2H), 7.80(m, 3H), 7.58(d, 1H), 7.48(m, 1H), 7.36(m, 2H), 6.36(s, 1H), 5.84(s, 2H), 2.98(s, 3H); ¹³C NMR(DMSO-d₆, 100MHz): 149.8, 143.8, 134.6, 132.6, 130.1, 129.7, 128.3, 127.8, 126.3, 125.1, 124.3, 119.7, 116.1, 115.5, 108.3, 104.9, 48.3, 45.8;

MS: *m/z* 271 [M+H] Yield: 82%.

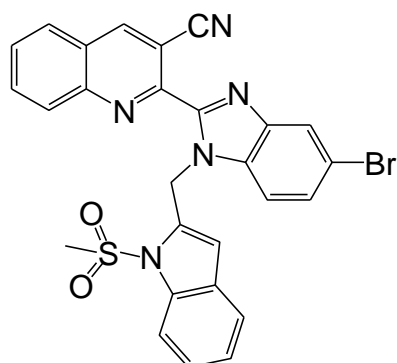


2-(1-((1-(methylsulfonyl)-1*H*-indol-2-yl)methyl)-(5,6-dichloro-1*H*-benzo[d]imidazol)-2-yl)quinoline-3-carbonitrile

¹H NMR(DMSO-d₆, 400MHz): δ 8.62(s, 1H), 8.39(d, 2H), 8.19(d, 2H), 7.80(m, 2H), 7.58(d, 1H), 7.48(m, 1H), 7.35(m, 2H), 6.37(s, 1H), 5.84(s, 2H), 2.98(s, 3H); ¹³C NMR(DMSO-d₆, 100MHz): 149.9, 143.8, 134.6, 132.6, 130.8, 129.7, 128.3, 127.9, 126.3, 125.3, 124.3, 119.7, 116.1, 115.8, 108.3, 103.8, 48.3, 44.9;

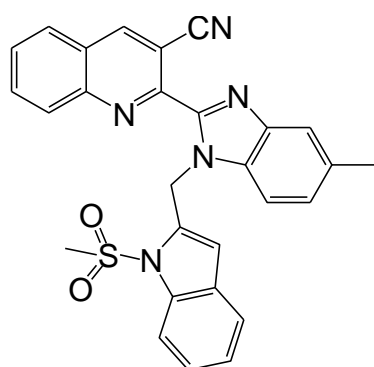
MS: *m/z* 547 [M+H] Yield: 77%.

2-(1-((1-(methylsulfonyl)-1*H*-indol-2-yl)methyl)-(6-bromo-1*H*-benzo[d]imidazol)-2-yl)quinoline-3-carbonitrile



¹H NMR(DMSO-d₆, 400MHz): δ 8.86(s, 1H), 8.39(d, 2H), 8.18(d, 2H), 7.80(m, 3H), 7.58(d, 1H), 7.49(m, 1H), 7.39(m, 2H), 6.35(s, 1H), 5.84(s, 2H), 2.99(s, 3H); **¹³C NMR**(DMSO-d₆, 100MHz): 149.9, 143.8, 134.6, 132.6, 130.1, 129.7, 128.3, 127.8, 126.3, 125.9, 124.3, 119.8, 116.1, 115.8, 108.8, 103.7, 48.3, 45.8;

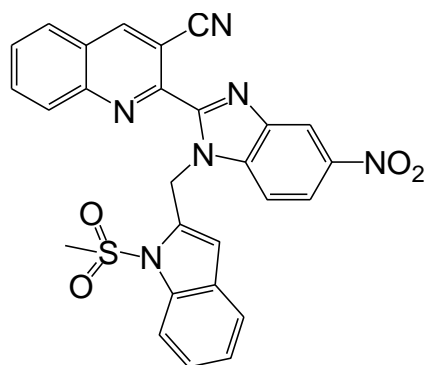
MS: *m/z* 555 [M+H] Yield: 75%.



2-(1-((1-(methylsulfonyl)-1H-indol-2-yl)methyl)-(6-methyl-1H-benzo[d]imidazol)-2-yl)quinoline-3-carbonitrile

¹H NMR(DMSO-d₆, 400MHz): δ 8.91(s, 1H), 8.38(d, 2H), 8.20(d, 2H), 7.81(m, 3H), 7.58(d, 1H), 7.49(m, 1H), 7.38(m, 2H), 6.37(s, 1H), 5.85(s, 2H), 2.98(s, 3H); **¹³C NMR**(DMSO-d₆, 100MHz): 149.5, 143.6, 134.6, 132.6, 130.2, 129.7, 128.3, 127.8, 126.3, 125.3, 124.3, 119.7, 116.1, 115.8, 108.4, 103.8, 48.3, 45.5, 21.7;

MS: *m/z* 592 [M+H] Yield: 74%.



2-(1-((1-(methylsulfonyl)-1*H*-indol-2-yl)methyl)-(6-nitro-1*H*-benzo[d]imidazol)-2-yl)quinoline-3-carbonitrile

¹H NMR(DMSO-d₆, 400MHz): δ 8.86(s, 1H), 8.98(d, 2H), 8.19(d, 2H), 7.80(m, 3H), 7.58(d, 1H), 7.49(m, 1H), 7.39(m, 2H), 6.35(s, 1H), 5.86(s, 2H), 2.98(s, 3H); ¹³C NMR(DMSO-d₆, 100MHz): 149.7, 143.8, 134.6, 132.6, 130.1, 129.7, 128.3, 128.8, 126.3, 125.9, 124.2, 119.8, 116.1, 115.8, 109.8, 103.7, 48.3, 45.9;

MS: *m/z* 523 [M+H] Yield: 73%.

RESULTS AND DISCUSSIONS

Taking into account the importance of Benzimidazole to both medicinal and heterocyclic chemistry, these title compounds are synthesized. The reactions are clear and products are produced in good yield. The structures of the synthesized compounds were confirmed by ¹H NMR, ¹³C NMR and Mass spectral data. They have been screened for their antibacterial activity against four pathogenic strains.

REFERENCES

- [1] Franco, B.E.; Martínez, M.A.; Rodríguez, M.S.; Wertheimer, A.I. 2009, *Infect. Drug Resist.* 2, 1–11.
- [2] Barrett, C.T.; Barrett, J.F. 2003, *Curr. Opin. Biotechnol.* 14, 621–626.
- [3] Cole, S.T. *Philos. Trans. R. Soc. B* 2014, *Biol. Sci.* 369, doi:10.1098/rstb.2013.0430.
- [4] Imperi, F.; Massai, F.; Facchini, M.; Frangipani, E.; Visaggio, D.; Leoni, L.; Bragonzi, A.; Visca, P. 2013, *Proc. Natl. Acad. Sci. USA* 110, 7458–7463.
- [5] Wang, M.; Han, X.; Zhou, Z. (2013–2014). *Expert Opin. Ther. Pat.* 2015, 25, 595–612.

- [6] Soderlind, K.J.; Gorodetsky, B.; Singh, A.K.; Bachur, N.R.; Miller, G.G.; Lown, J.W. 1999, *Anticancer Drug Des.* 14, 19–36.
- [7] Kumar, K.; Awasthi, D.; Lee, S.Y. ; Cummings, J.E. ; Knudson, S.E. ; Slayden, R.A.; Ojima, I. 2013, *Bioorg. Med. Chem.* 21, 3318–3326.
- [8] Mentese, E.; Bektas, H.; Ulker, S.; Bekircan, O.; Kahveci, B. 2014, *J. Enzyme Inhib. Med. Chem.* 29, 64–68.
- [9] HI El-Subbagh; SM Abu-Zaid; MA Mahran; FA Badria; AM Alofaid. 2000, *J. Med.Chem.*, 43, 2915-2921.
- [10] R Gupta; AK Gupta; S Paul. 2000, *Ind. J. Chem.*, 39B, 847.
- [11] AM Farghaly; AA Bekhit; JY Park. 2000, *Arch. Pharm. Med. Chem.*, 333, 53–57.
- [12] AA Bekhit; OA El-Sayed; E Aboulmagd; J. Y. Park. 2004, *Eur. J. Med. Chem.*, 39, 249-55.
- [13] R Vlahov; St Parushev; J Vlahov; P Nickel; G Snatzke. 1990, *Appl. Chem.*, 62 (7), 1303-06.
- [14] L Dalla Via; O Gia; V Gasparotto; MG Ferlin. 2007, *Eur. J. Med. Chem.*, XX, 1-6.
- [15] K Sharma; PS Fernandes. 2005, *Ind. J. Het. Chem.*, 15, 161-168.
- [16] SP Rajendra; R Karvembu 2002., *Ind. J. Chem.*, 41B, 222-224.
- [17] AH Kategaonkar; RU Pokalwar; SS Sonar; VU Gawali. 2010, *Eur. J. Med. Chem.*, 45, 1128–1132.
- [18] M Gupta; S Paul; R Gupta. 2010, *Ind. J. Chem.*, 42B, 475-481.
- [19] Z Zie; K Chai; H Piao; K Kwak; Z Quan. 2005, *Med. Chem. Lett.*, 15, 4803-05.
- [20] R Gupta; AK Gupta; S Paul. 2000, *Ind. J. Chem.*, 39B, 847-852.
- [21] R Vlahov; St Parushev; J Vlahov; P Nickel; G; Snatzke. *Appl. Chem.*, 1990, 62(7), 1303-06.
- [22] L Dalla Via; O Gia; V Gasparotto; MG Ferlin; 2007, *Eur. J. Med. Chem.*, XX, 1-6.
- [23] K Sharma; PS Fernandes; 2005, *Ind. J. Het. Chem.*, 15, 161-168.
- [24] SP Rajendra; R Karvembu. 2002, *Ind. J. Chem.*, 41B, 222-224.

