Supporting Information

Copper-Mediated Cross-Coupling Approach for the Synthesis of 3-Heteroaryl Quinolone and Related Analogues

Sanghye Shin, Yechan Kim, Kiho Kim, and Sungwoo Hong*

Department of Chemistry, Korea Advance Institute of Science and Technology (KAIST), Daejeon 305-701, Korea

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Spectral Copies of $^1$H- and $^{13}$C-NMR Data Obtained in this Study

I. General Methods and Materials

Unless stated otherwise, reactions were performed in flame-dried glassware under a positive pressure of nitrogen using freshly distilled solvents. Analytical thin layer chromatography (TLC) was performed on precoated silica gel 60 F254 plates and visualization on TLC was achieved by UV light (254 and 354 nm). Flash column chromatography was undertaken on silica gel (400-630 mesh). $^1$H NMR was recorded on 400 MHz and chemical shifts were quoted in parts per million (ppm) referenced to the appropriate solvent peak or 0.0 ppm for tetramethylsilane. The following abbreviations were used to describe peak splitting patterns when appropriate: br = broad, s = single, d = double, t = triplet, q = quartet, m = multiplet, dd = doublet of doublet. Coupling constants, $J$, were reported in hertz unit (Hz). $^{13}$C NMR was recorded on 100 MHz and was fully decoupled by broad band proton decoupling. Chemical shifts were reported in ppm referenced to the center line of a triplet at 77.0 ppm of chloroform-$d$. Mass spectral data were obtained by using EI method. Commercial grade reagents and solvents were used without further purification.

II. Experimental Procedures

General procedure for the preparation of 1-benzyl-3-ido-4-quinolone derivatives

1. Synthesis of 4-quinolones

According to the literature procedure, trimethyl orthoformate (25.0 equiv) and Meldrum’s acid (1.5 equiv) were refluxed at 115 °C for 2 hours under N₂, and then cooled slightly. An appropriate aniline (1.0 equiv) was then added to the mixture and the resulting mixture reheated to reflux for 2 hours. The mixture was cooled to room temperature and the solvent was removed under vacuo. The resulting precipitated product was filtered with MeOH washing and dried under vacuo. Without any purification, the resulted intermediate was sealed in a glass tube with diphenyl ether and a magnetic stir bar. The sealed tube was heated to 250 °C for 5-10 minutes with 300 Watts of power, then cooled down to room temperature. The resulting mixture was diluted with excess hexanes, a precipitated product was collected by filtration, washed with hexanes, and dried under vacuo to give the corresponding 4-quinolones which was used for the next step without further purification. (ref. Synthesis, 2009, 1, 69)
2. **Synthesis of 1-benzyl-4-quinolones**

Benzyl bromide (1.5 equiv) was added dropwise to a solution of a 4-quinolone compound (1 equiv) and K$_2$CO$_3$ (1.5 equiv) in THF. The reaction mixture was refluxed overnight. After cooled to room temperature, THF was removed under vacuo. The resulting mixture was diluted with CH$_2$Cl$_2$ and then organic layer was extracted with aqueous NH$_4$Cl. The organic layer was dried over MgSO$_4$. After removal of solvent, the residue was purified by flash chromatography on silica gel (3% MeOH/CH$_2$Cl$_2$, v/v) to give desired product.

3. **Synthesis of 1-benzyl-3-iodo-4-quinolones**

A mixture of 1-benzyl-4-quinolone (1 equiv), NH$_4$I (2 equiv), Cu(NO$_3$)$_2$.3H$_2$O (2 equiv), AcOH (2 equiv) in 1,4-dioxane was heated to 100 °C for 1 hour. After cooled to room temperature, 1,4-dioxane was removed under vacuo. The residue was diluted with CH$_2$Cl$_2$ and then added aqueous sodium thiosulfate and aqueous NH$_4$Cl. When the residue was changed from dark red to pale yellow, it was extracted three times with CH$_2$Cl$_2$. After removal of solvent, the residue was purified by flash chromatography on silica gel (0~2% MeOH/CH$_2$Cl$_2$, v/v) to give 1-benzyl-3-iodo-4-quinolone derivatives.
3-(benzo[d]thiazol-2-yl)-1-benzylquinolin-4(1H)-one (3a)

400 MHz, $^1$H NMR in DMSO-$d_6$

100 MHz, $^{13}$C NMR in DMSO-$d_6$
1-benzyl-3-(6-methylbenzo[d]thiazol-2-yl)quinolin-4(1H)-one (3b)

400 MHz, $^1$H NMR in CDCl$_3$

100 MHz, $^{13}$C NMR in CDCl$_3$
1-benzyl-3-(6-methoxybenzo[d]thiazol-2-yl)quinolin-4(1H)-one (3c)

400 MHz, $^1$H NMR in CDCl$_3$

100 MHz, $^{13}$C NMR in CDCl$_3$
1-benzyl-3-(6-chlorobenzo[d]thiazol-2-yl)quinolin-4(1H)-one (3d)

400 MHz, $^1$H NMR in CDCl₃

100 MHz, $^{13}$C NMR in CDCl₃
1-benzyl-3-(6-phenylbenzo[d]thiazol-2-yl)quinolin-4(1H)-one (3e)

400 MHz, $^1$H NMR in CDCl$_3$

100 MHz, $^{13}$C NMR in CDCl$_3$
1-benzyl-3-(4,5-dimethylthiazol-2-yl)quinolin-4(1H)-one (3f)

400 MHz, $^1$H NMR in CDCl$_3$

100 MHz, $^{13}$C NMR in CDCl$_3$
1-benzyl-3-(5-phenylthiazol-2-yl)quinolin-4(1H)-one (3g)

400 MHz, $^1$H NMR in CDCl$_3$

100 MHz, $^{13}$C NMR in CDCl$_3$
3-(benzo[d]oxazol-2-yl)-1-benzylquinolin-4(1H)-one (3h)

400 MHz, $^1$H NMR in CDCl$_3$

100 MHz, $^{13}$C NMR in CDCl$_3$
1-benzyl-3-(5-methoxybenzo[d]oxazol-2-yl)quinolin-4(1H)-one (3i)

400 MHz, $^1$H NMR in CDCl$_3$

100 MHz, $^{13}$C NMR in CDCl$_3$
1-benzyl-3-(6-chlorobenzo[d]oxazol-2-yl)quinolin-4(1H)-one (3j)

400 MHz, $^1$H NMR in CDCl$_3$

100 MHz, $^{13}$C NMR in CDCl$_3$
1-benzyl-3-(5-phenyloxazol-2-yl)quinolin-4(1H)-one (3k)

400 MHz, $^1$H NMR in CDCl$_3$

100 MHz, $^{13}$C NMR in CDCl$_3$
1-benzyl-3-(5-phenyl-1,3,4-oxadiazol-2-yl)quinolin-4(1H)-one (3l)

400 MHz, $^1$H NMR in CDCl$_3$

100 MHz, $^{13}$C NMR in CDCl$_3$
1-benzyl-3-(1-benzyl-1H-benzo[d]imidazol-2-yl)quinolin-4(1H)-one (3m)

400 MHz, $^1$H NMR in CDCl$_3$

100 MHz, $^{13}$C NMR in DMSO-$d_6$
8-(1-benzyl-4-oxo-1,4-dihydroquinolin-3-yl)-1,3,7-trimethyl-1H-purine-2,6(3H,7H)-dione (3n)

400 MHz, $^1$H NMR in CDCl$_3$

100 MHz, $^{13}$C NMR in CDCl$_3$
3-(benzo[d]thiazol-2-yl)-1-benzyl-6-methylquinolin-4(1H)-one (4a)

400 MHz, $^1$H NMR in CDCl$_3$

100 MHz, $^{13}$C NMR in CDCl$_3$
3-(benzo[d]thiazol-2-yl)-1-benzyl-6-methoxyquinolin-4(1H)-one (4b)

400 MHz, $^1$H NMR in CDCl$_3$

100 MHz, $^{13}$C NMR in CDCl$_3$
3-(benzo[d]thiazol-2-yl)-1-benzyl-6-fluoroquinolin-4(1H)-one (4c)

400 MHz, $^1$H NMR in CDCl$_3$

100 MHz, $^{13}$C NMR in CDCl$_3$
3-(benzo[d]thiazol-2-yl)-1-benzyl-6-chloroquinolin-4(1H)-one (4d)

400 MHz, $^1$H NMR in CDCl$_3$

100 MHz, $^{13}$C NMR in CDCl$_3$
3-(benzo[d]thiazol-2-yl)-1-benzyl-6-bromoquinolin-4(1H)-one (4e)

400 MHz, $^1$H NMR in CDCl$_3$

100 MHz, $^{13}$C NMR in CDCl$_3$
3-(benzo[d]thiazol-2-yl)-1-benzyl-6-phenylquinolin-4(1H)-one (4f)

400 MHz, $^1$H NMR in CDCl$_3$

100 MHz, $^{13}$C NMR in CDCl$_3$
3-(benzo[d]thiazol-2-yl)-1-benzyl-8-methoxyquinolin-4(1H)-one (4g)

400 MHz, $^1$H NMR in CDCl$_3$

100 MHz, $^{13}$C NMR in CDCl$_3$
3-(benzo[d]thiazol-2-yl)-1-benzyl-8-fluoroquinolin-4(1H)-one (4h)

400 MHz, $^1$H NMR in DMSO-$d_6$

100 MHz, $^{13}$C NMR in DMSO-$d_6$
3-(benzo[d]thiazol-2-yl)-1-methylquinolin-4(1H)-one (4i)

400 MHz, $^1$H NMR in DMSO-$d_6$

100 MHz, $^{13}$C NMR in DMSO-$d_6$
3-(benzo[d]thiazol-2-yl)-1-benzylpyridin-4(1H)-one (4j)

400 MHz, $^1$H NMR in DMSO-$d_6$

100 MHz, $^{13}$C NMR in DMSO-$d_6$
5-(benzo[d]thiazol-2-yl)-1,3-dimethylpyrimidine-2,4(1H,3H)-dione (4k)

400 MHz, $^1$H NMR in CDCl$_3$

100 MHz, $^{13}$C NMR in CDCl$_3$
3-(benzo[d]thiazol-2-yl)-1-methylquinolin-2(1H)-one (4l)

400 MHz, $^1$H NMR in CDCl$_3$

100 MHz, $^{13}$C NMR in CDCl$_3$
3-(benzo[d]thiazol-2-yl)-1-ethyl-7-methyl-1,8-naphthyridin-4(1H)-one (4m)

400 MHz, $^1$H NMR in CDCl$_3$

100 MHz, $^{13}$C NMR in CDCl$_3$
4-(benzo[d]thiazol-2-yl)-2-methylisoquinolin-1(2H)-one (4n)

\[\text{400 MHz, } ^1\text{H NMR in CDCl}_3\]

\[\text{100 MHz, } ^{13}\text{C NMR in CDCl}_3\]
3-(benzo[d]thiazol-2-yl)-4H-chromen-4-one (4o)

400 MHz, $^1$H NMR in CDCl$_3$

100 MHz, $^{13}$C NMR in CDCl$_3$