Supporting Information

Practical synthesis of quinolone drugs via novel TsCl-mediated domino reaction sequence

Jie Lei, a Yong Ding, a Hao-Yi Zhou, a Xin-Yan Gao, a Yi-Hua Cao, a Dian-Yong Tang, a Hong-yu Li b, Zhi-Gang Xu a, Zhong-Zhu Chen a

a College of Pharmacy, National & Local Joint Engineering Research Center of Targeted and Innovative Therapeutics, Chongqing Key Laboratory of Kinase Modulators as Innovative Medicine, Chongqing University of Arts and Sciences, Chongqing 402160, China. Email: xzg@cqwu.edu.cn; 18883138277@163.com.

b Department of Pharmaceutical Sciences, College of Pharmacy, University of Arkansas for Medical Sciences, Little Rock, Arkansas 72205, USA. Email: HLi2@uams.edu

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General Experimental

$^1$H and $^{13}$C NMR were recorded on a Bruker 400 spectrometer. $^1$H NMR data are reported as follows: chemical shift in ppm ($\delta$), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constant (Hz), relative intensity. $^{13}$C NMR data are reported as follows: chemical shift in ppm ($\delta$). LC/MS analyses were performed on a Shimadzu-2020 LC-MS instrument using the following conditions: Shim-pack VP-ODS C18 column (reverse phase, 150 x 4.6 mm); a linear gradient from 10% water and 90% acetonitrile to 75% acetonitrile and 25% water over 6.0 min; flow rate of 0.5 mL/min; UV photodiode array detection from 200 to 400 nm. High-resolution mass spectra (HRMS) were recorded on Thermo Scientific Exactive Plus System. UV-VIS spectrophotometer TU-1950. The products were purified by Biotage Isolera™ Spektra Systems and hexane/EtOAc solvent systems. All reagents and solvents were obtained from commercial sources and used without further purification.

General procedures for compound 4

A solution of chromone-3-carboxaldehyde (0.2 mmol), amine (0.22 mmol), sulfochloride (0.2 mmol) and tBuOLi (0.4 mmol) was stirred in toluene (2.0 mL) under 100 °C for 8 h with a sealed system. The reaction mixture was monitored by TLC. When the reaction was completed, the mixture was extracted with EtOAc (15.0 mL), washed with brine. The organic layer was dried over Na$_2$SO$_4$ and concentrated. The residue was purified by silica gel column chromatography using a gradient of ethyl acetate/hexane (0-100%) to afford the relative targeted product.

Transformation from 4a to 4x

A solution of 4a (0.2 mmol) and 1 mol/L of HCl (2.0 equiv.) was stirred in MeCN (5.0 mL) under 80 °C for 6 h in a sealed system. The reaction mixture was monitored by TLC. When the reaction was completed, the mixture was extracted with EtOAc (15.0 mL), washed with brine three times. The organic layer was dried over Na$_2$SO$_4$ and concentrated. The residue was purified by silica gel column chromatography using a gradient of ethyl acetate/hexane (0-100%) to afford 4x with the yield 87%.

General procedures for compounds 5, 8, 11, 12, and 13
4 (0.5 mmol) was treated with \( \text{NH}_2\text{SO}_3\text{H} \) (4.0 equiv.) and \( \text{NaClO}_2 \) (5.0 equiv.) in DCM (5.0 mL) under room temperature for 4 h. The reaction mixture was monitored by TLC. When the reaction was completed, the mixture was extracted with EtOAc (30.0 mL), washed with brine. The organic layer was dried over \( \text{Na}_2\text{SO}_4 \) and concentrated. The crude product was purified by silica gel column chromatography using a gradient of MeOH/DCM (0-10%). For gram scale synthesis of Oxilinic acid: 4e (5.0 mmol) was treated with \( \text{NH}_2\text{SO}_3\text{H} \) (4.0 equiv.) and \( \text{NaClO}_2 \) (5.0 equiv.) under same reaction condition, providing Oxilinic acid with the yield of 80%.

**General procedures for compounds 6, 7, 9, and 10**

A solution of F-substituted quinolone (2.0 mmol) and secondary amine (2.5 equiv.) in DMSO was treated with microwave 120 °C for 30 min. When the reaction was completed, the mixture was cooled to room temperature and washed with MeOH (3x10 mL). The final compound was purified by recrystallization in MeOH/H\(_2\)O (v:v = 1:1).

**General procedures for compound 14**

9a, 5-amino-2,4-di-tert-butylphenol (1.1 equiv.) and Et\(_3\)N (3.0 equiv.) were added into the solvent of DCM at room temperature. Then condensation reagent of TBTU (1.2 equiv.) was added during 10 min. The mixture was stirred at room temperature for 12 h, which was monitored by TLC. When the reaction was completed, the mixture was extracted with EtOAc (30.0 mL), washed with brine. The organic layer was dried over \( \text{Na}_2\text{SO}_4 \) and concentrated. The final compound was purified by silica gel column chromatography using a gradient of ethyl acetate/hexane (0-100%) (14, 93%). For gram scale synthesis: 9a (4.0 mmol), 5-amino-2,4-di-tert-butylphenol (1.1 equiv.) and Et\(_3\)N (3.0 equiv.) TBTU (1.2 equiv.) were treated with the standard condition, affording the desired product 87%.

**General procedures for compound 15**

A solution of chromone-3-carboxaldehyde (0.2 mmol), \( \text{tert-} \)butylamine (0.22 mmol) and \( p\)-toluenesulfonyl chloride (0.2 mmol) was stirred in toluene (2.0 mL) under room temperature for 12 h. The reaction mixture was monitored by TLC. When the reaction was completed, the mixture was extracted with EtOAc (15.0 mL), washed with brine. The organic layer was dried over \( \text{Na}_2\text{SO}_4 \) and concentrated. The residue was purified
by silica gel column chromatography using a gradient of ethyl acetate/hexane (0-100%) to afford the relative targeted product.

**NMR Characterization Data and Figures of Products**

1-(tert-butyl)-4-oxo-1,4-dihydroquinoline-3-carbaldehyde 4a, 86%, light yellow solid, (EA/Hex = 25%, Rf = 0.25), \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 10.37 (s, 1H), 8.66 (s, 1H), 8.56 (d, \(J = 7.9\) Hz, 1H), 7.92 (d, \(J = 8.8\) Hz, 1H), 7.64 (t, \(J = 7.7\) Hz, 1H), 7.42 (t, \(J = 7.5\) Hz, 1H), 1.84 (s, 9H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 188.66, 175.52, 142.13, 138.40, 130.65, 129.94, 126.95, 124.28, 119.37, 115.09, 62.73, 29.83. HRMS (ESI) m/z calcd for C\(_{14}\)H\(_{15}\)NO\(_2\) (M+H)\(^+\) 230.1176, found 230.1177.

1-ethyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde 4b, 81%, light yellow solid, (EA/Hex = 25%, Rf = 0.25), \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 10.36 (s, 1H), 8.48 (dd, \(J = 8.0, 1.1\) Hz, 1H), 8.27 (s, 1H), 7.72 – 7.65 (m, 1H), 7.49 – 7.42 (m, 2H), 4.23 (q, \(J = 7.2\) Hz, 2H), 1.51 (t, \(J = 7.3\) Hz, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 189.49, 176.95, 145.50, 139.13, 133.27, 129.69, 127.64, 125.71, 117.26, 116.15, 49.20, 14.56. HRMS (ESI) m/z calcd for C\(_{12}\)H\(_{12}\)NO\(_2\) (M+H)\(^+\) 202.0863, found 202.0865.
1-(cyclopropylmethyl)-4-oxo-1,4-dihydroquinoline-3-carbaldehyde 4c, 89%, light yellow solid, (EA/Hex = 25%, Rf = 0.25), $^1$H NMR (400 MHz, CDCl$_3$) δ 10.35 (s, 1H), 8.46 (d, $J = 7.9$ Hz, 1H), 8.36 (s, 1H), 7.65 (t, $J = 7.8$ Hz, 1H), 7.49 – 7.40 (m, 2H), 4.86 – 4.73 (m, 1H), 2.62 (dd, $J = 9.6$, 6.3 Hz, 2H), 2.49 – 2.35 (m, 2H), 1.98 – 1.89 (m, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 189.49, 176.88, 141.92, 139.42, 133.02, 129.34, 127.39, 125.80, 116.62, 55.91, 29.83, 14.60. HRMS (ESI) m/z calcd for C$_{14}$H$_{14}$NO$_2$+ (M+H)$^+$ 228.1019, found 228.1022.

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1-(4-methylbenzyl)-4-oxo-1,4-dihydroquinoline-3-carbaldehyde 4d, 77%, light yellow solid, (EA/Hex = 25%, Rf = 0.20), $^1$H NMR (400 MHz, CDCl$_3$) δ 10.47 (d, $J = 1.1$ Hz, 1H), 8.54 (d, $J = 8.0$ Hz, 1H), 8.43 (s, 1H), 7.65 – 7.56 (m, 1H), 7.44 (dd, $J = 16.5$, 8.3 Hz, 2H), 7.17 (d, $J = 7.9$ Hz, 2H), 7.07 (d, $J = 7.8$ Hz, 2H), 5.38 (s, 2H), 2.34 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 189.53, 177.08, 146.63, 139.69, 138.81, 133.23, 130.67, 129.63, 127.39, 126.23, 125.79, 117.22, 57.65, 21.14. HRMS (ESI) m/z calcd for C$_{18}$H$_{16}$NO$_2$+ (M+H)$^+$ 278.1176, found 278.1177.

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1-cyclopropyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde 4e, 85%, light yellow solid, (EA/Hex = 25%, Rf = 0.20), $^1$H NMR (400 MHz, CDCl$_3$) δ 10.33 (d, $J = 1.1$ Hz, 1H), 8.42 (d, $J = 8.0$ Hz, 1H), 8.37 (s, 1H), 7.92 (d, $J = 8.5$ Hz, 1H), 7.69 (dd, $J = 8.4$, 7.2 Hz, 1H), 7.44 (t, $J = 7.6$ Hz, 1H), 3.50 – 3.40 (m, 1H), 1.29 (d, $J = 6.8$ Hz, 2H), 1.12 – 1.03 (m, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 189.40, 177.02, 145.58, 141.05, 133.08,
128.93, 127.13, 125.82, 117.08, 117.01, 34.81, 8.16. HRMS (ESI) m/z calcd for C_{14}H_{14}N_{2}O_{2}^{+} (M+H)^{+} 214.0863, found 214.0865.

4-oxo-1-phenyl-1,4-dihydroquinoline-3-carbaldehyde 4f, 80%, light yellow solid, (EA/Hex = 25%, R_{f} = 0.20), ^{1}H NMR (400 MHz, CDCl_{3}) δ 10.51 (d, J = 1.1 Hz, 1H), 8.58 (d, J = 8.0 Hz, 1H), 8.37 (d, J = 1.1 Hz, 1H), 7.65 (d, J = 5.4 Hz, 3H), 7.60 (dd, J = 8.4, 7.2 Hz, 1H), 7.50 (t, J = 7.5 Hz, 1H), 7.47 – 7.43 (m, 2H), 7.06 (d, J = 8.4 Hz, 1H). ^{13}C NMR (101 MHz, CDCl_{3}) δ 189.62, 177.04, 145.91, 141.11, 140.41, 133.00, 130.55, 130.31, 128.80, 127.22, 126.99, 125.91, 118.36, 117.20. HRMS (ESI) m/z calcd for C_{16}H_{12}N_{2}O_{2}^{+} (M+H)^{+} 250.0863, found 250.0863.

1-(4-methoxyphenyl)-4-oxo-1,4-dihydroquinoline-3-carbaldehyde 4g, 73%, ^{1}H NMR (400 MHz, CDCl_{3}) δ 10.50 (s, 1H), 8.56 (d, J = 8.0 Hz, 1H), 8.36 (s, 1H), 7.59 (t, J = 7.8 Hz, 1H), 7.34 (t, J = 6.1 Hz, 2H), 7.14 – 7.09 (m, 2H), 7.07 (d, J = 8.5 Hz, 1H), 3.94 (s, 3H). ^{13}C NMR (101 MHz, CDCl_{3}) δ 189.66, 177.09, 160.65, 146.31, 141.52, 133.02, 132.96, 128.81, 128.36, 126.92, 125.84, 118.46, 117.12, 115.50, 55.77. HRMS (ESI) m/z calcd for C_{17}H_{14}N_{3}O_{3}^{+} (M+H)^{+} 280.0969, found 280.0967.
5-ethyl-8-oxo-5,8-dihydro-[1,3]dioxolono[4,5-g]quinoline-7-carbaldehyde 4h, 80%, light yellow solid, (EA/Hex = 30%, Rf = 0.15), $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 10.16 (s, 1H), 8.50 (s, 1H), 7.59 (s, 1H), 7.49 (s, 1H), 6.24 (s, 2H), 4.40 (q, J = 7.0 Hz, 2H), 1.35 (t, J = 7.1 Hz, 3H). $^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 189.02, 174.84, 153.03, 146.80, 145.93, 136.63, 125.08, 116.27, 103.14, 97.95, 49.29, 14.96. HRMS (ESI) m/z calcd for C$_{13}$H$_{12}$NO$_2$+ (M+H)$^+$ 246.0761, found 246.0761.

1-ethyl-6-methyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde 4i, 85%, light yellow solid, (EA/Hex = 25%, Rf = 0.25), $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.35 (s, 1H), 8.26 (d, J = 0.8 Hz, 1H), 8.23 (s, 1H), 7.49 (dd, J = 8.6, 2.0 Hz, 1H), 7.35 (d, J = 8.7 Hz, 1H), 4.21 (q, J = 7.3 Hz, 2H), 2.43 (s, 3H), 1.49 (t, J = 7.3 Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 189.58, 176.95, 144.99, 137.08, 136.00, 134.50, 129.53, 127.12, 117.05, 116.08, 49.17, 20.99, 14.59. HRMS (ESI) m/z calcd for C$_{13}$H$_{14}$NO$_2$+ (M+H)$^+$ 216.1019, found 216.1019.

1-ethyl-6-isopropyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, 4j, 73%, light yellow solid, (EA/Hex = 25%, Rf = 0.25), $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.35 (s, 1H), 8.32 (d, J = 2.0 Hz, 1H), 8.24 (s, 1H), 7.55 (dd, J = 8.7, 2.1 Hz, 1H), 7.39 (d, J = 8.7 Hz, 1H), 4.21 (q, J = 7.2 Hz, 2H), 3.01 (dt, J = 13.8, 6.9 Hz, 1H),
1.49 (t, \( J = 7.3 \) Hz, 3H), 1.25 (d, \( J = 6.9 \) Hz, 7H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 189.65, 177.09, 146.85, 144.99, 137.32, 132.16, 129.63, 124.55, 117.01, 116.25, 49.18, 33.79, 23.85, 14.62. HRMS (ESI) m/z calcd for C\(_{15}\)H\(_{18}\)NO\(_2\) (M+H)\(^+\) 244.1332, found 244.1333.

![Chemical structure](image)

\(1\)-isopropyl-6-methyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, 4k. 90%, light yellow solid, (EA/Hex = 25%, \( R_t = 0.25 \)). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 10.37 (s, 1H), 8.39 (s, 1H), 8.30 (s, 1H), 7.52 – 7.43 (m, 2H), 7.20 (s, 1H), 4.85 (dt, \( J = 13.3, 6.6 \) Hz, 1H), 2.43 (s, 3H), 1.55 (d, \( J = 6.6 \) Hz, 6H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 189.56, 176.69, 140.51, 137.70, 135.82, 134.41, 129.65, 127.26, 117.01, 115.47, 51.51, 22.14, 20.86. HRMS (ESI) m/z calcd for C\(_{14}\)H\(_{16}\)NO\(_2\) (M+H)\(^+\) 230.1176, found 230.1177.

![Chemical structure](image)

\(1\)-cyclopropyl-6-methyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, 4l. 84%, light yellow solid, (EA/Hex = 25%, \( R_t = 0.25 \)). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 10.32 (d, \( J = 1.4 \) Hz, 1H), 8.33 (s, 1H), 8.21 (s, 1H), 7.80 (d, \( J = 8.6 \) Hz, 1H), 7.49 (d, \( J = 8.6 \) Hz, 1H), 3.47 – 3.39 (m, 1H), 2.43 (s, 3H), 1.27 (d, \( J = 6.7 \) Hz, 2H), 1.20 (d, \( J = 11.9 \) Hz, 2H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 189.49, 177.01, 145.06, 139.03, 136.08, 134.31, 128.78, 126.64, 116.92, 34.78, 20.98, 8.05. HRMS (ESI) m/z calcd for C\(_{14}\)H\(_{14}\)NO\(_2\) (M+H)\(^+\) 228.1019, found 228.1019.
1-cyclopentyl-6-methyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, 4m, 77%, light yellow solid, (EA/Hex = 25%, Rf = 0.25), 1H NMR (400 MHz, CDCl3) δ 10.36 (s, 1H), 8.35 (s, 1H), 8.27 (s, 1H), 7.55 – 7.45 (m, 2H), 4.88 (ddd, J = 13.2, 7.2, 5.6 Hz, 1H), 2.43 (s, 3H), 2.25 (td, J = 8.4, 7.5, 3.9 Hz, 2H), 1.98 – 1.83 (m, 5H), 1.83 – 1.74 (m, 2H), 1.66 (s, 1H). 13C NMR (101 MHz, CDCl3) δ 189.49, 176.69, 140.94, 138.28, 135.82, 134.22, 129.62, 127.02, 116.29, 61.85, 33.67, 32.31, 23.73, 23.60, 20.87. HRMS (ESI) m/z calcd for C16H18NO2 (M+H)+ 256.1332, found 256.1333.

1-(cyclopropylmethyl)-6-methyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, 4n, 85%, light yellow solid, (EA/Hex = 25%, Rf = 0.25), 1H NMR (400 MHz, CDCl3) δ 10.34 (s, 1H), 8.26 (d, J = 13.6 Hz, 2H), 7.45 (dd, J = 19.8, 8.7 Hz, 2H), 3.97 (d, J = 7.0 Hz, 2H), 2.42 (s, 3H), 1.37 – 1.21 (m, 1H), 0.69 (dd, J = 10.0, 2.9 Hz, 2H), 0.39 (t, J = 5.0 Hz, 2H). 13C NMR (101 MHz, CDCl3) δ 13 C NMR (101 MHz, CDCl3) δ 189.49, 176.92, 144.79, 137.72, 135.97, 134.37, 129.39, 126.95, 116.88, 116.19, 58.18, 20.94, 10.04, 4.66. HRMS (ESI) m/z calcd for C15H16NO2 (M+H)+ 242.1176, found 242.1177.

6-chloro-1-cyclobutyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, 4o, 79%, light yellow solid, (EA/Hex = 25%, Rf = 0.25), 1H NMR (400 MHz, CDCl3) δ 10.30 (s, 1H),
8.44 – 8.31 (m, 2H), 7.87 (d, J = 9.0 Hz, 1H), 7.63 (dd, J = 9.0, 2.4 Hz, 1H), 3.49 – 3.37 (m, 1H), 1.30 (t, J = 6.6 Hz, 2H), 1.20 (d, J = 12.1 Hz, 2H), 1.09 (d, J = 3.3 Hz, 2H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ $^{13}$C NMR (101 MHz, CDCl$_3$) δ 189.05, 175.83, 145.68, 139.47, 133.30, 132.37, 130.06, 126.60, 118.73, 117.25, 34.94, 8.21. HRMS (ESI) m/z calcd for C$_{14}$H$_{13}$NO$_2^+$ (M+H)$^+$ 262.0629 found 262.0629.

![Chemical structure](image)

**1-(tert-butyl)-6-chloro-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, 4p.** 87%, light yellow solid, (EA/Hex = 25%, $R_f = 0.25$), $^1$H NMR (400 MHz, CDCl$_3$) δ 10.34 (d, J = 1.8 Hz, 1H), 8.63 (s, 1H), 8.49 (s, 1H), 7.92 – 7.82 (m, 1H), 7.57 (ddd, J = 9.3, 2.8, 1.8 Hz, 1H), 1.82 (s, 9H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 189.28, 175.28, 143.18, 137.78, 132.33, 131.80, 127.29, 121.93, 116.23, 63.99, 30.81. HRMS (ESI) m/z calcd for C$_{14}$H$_{15}$NO$_2^+$ (M+H)$^+$ 264.0786, found 264.0786.

![Chemical structure](image)

**6-chloro-1-isopropyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, 4q.** 89%, light yellow solid, (EA/Hex = 25%, $R_f = 0.25$), $^1$H NMR (400 MHz, CDCl$_3$) δ 10.42 (d, J = 1.6 Hz, 1H), 8.50 (dd, J = 18.8, 2.0 Hz, 2H), 7.69 (ddd, J = 9.1, 2.5, 1.6 Hz, 1H), 7.60 (d, J = 8.6 Hz, 1H), 4.90 (dt, J = 13.2, 6.6 Hz, 1H), 1.64 (dd, J = 6.6, 1.5 Hz, 6H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 189.16, 175.56, 141.07, 133.37, 131.89, 131.33, 127.16, 117.34, 52.01, 22.13. HRMS (ESI) m/z calcd for C$_{13}$H$_{13}$ClNO$_2^+$ (M+H)$^+$ 250.0629, found 250.0629.
6-bromo-1-(cyclopropylmethyl)-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, 4r, 82%, light yellow solid, (EA/Hex = 25%, R<sub>f</sub> = 0.25), <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 10.32 (d, J = 2.9 Hz, 1H), 8.58 (t, J = 2.5 Hz, 1H), 8.32 (d, J = 2.8 Hz, 1H), 7.75 (dt, J = 9.0, 2.6 Hz, 1H), 7.42 (dd, J = 9.0, 2.7 Hz, 1H), 3.97 (dd, J = 6.9, 2.5 Hz, 2H), 1.28 (dd, J = 7.4, 4.5 Hz, 1H), 0.80 – 0.66 (m, 2H), 0.41 (d, J = 1.8 Hz, 2H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 189.07, 175.63, 145.36, 138.58, 136.06, 130.94, 130.18, 119.84, 118.07, 117.44, 58.37, 9.95, 4.75. HRMS (ESI) m/z calcd for C<sub>14</sub>H<sub>13</sub>BrNO<sub>2</sub>+(M+H)<sup>+</sup> 306.0124, found 306.0125.

6-bromo-1-cyclopropyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, 4s, 85%, light yellow solid, (EA/Hex = 25%, R<sub>f</sub> = 0.25), <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 10.29 (s, 1H), 8.52 (d, J = 2.1 Hz, 1H), 8.35 (s, 1H), 7.87 – 7.71 (m, 2H), 7.31 – 3.34 (m, 1H), 1.30 (q, J = 6.8 Hz, 2H), 1.09 (q, J = 6.6 Hz, 2H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 188.96, 175.64, 145.66, 139.88, 136.03, 130.29, 129.76, 120.03, 118.88, 117.39, 34.87, 8.19. HRMS (ESI) m/z calcd for C<sub>13</sub>H<sub>11</sub>BrNO<sub>2</sub>+(M+H)<sup>+</sup> 291.9968, found 291.9969.

7-chloro-1-cyclobutyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, 4aa, 78%, light yellow solid, (EA/Hex = 25%, R<sub>f</sub> = 0.25), <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 10.41 (d,
$J = 1.6$ Hz, 1H), 8.43 (d, $J = 1.6$ Hz, 1H), 8.27 (d, $J = 8.8$ Hz, 1H), 7.61 (dd, $J = 5.7$, 1.6 Hz, 1H), 4.81 (td, $J = 8.4$, 7.5, 2.1 Hz, 1H), 2.82 – 2.63 (m, 2H), 2.51 (ddd, $J = 11.3$, 7.0, 2.1 Hz, 2H), 2.14 – 1.97 (m, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 188.98, 175.35, 157.08, 154.57, 142.20, 135.97, 129.68, 127.55, 119.21, 116.29, 113.87, 56.11, 29.76, 14.53. HRMS (ESI) m/z calcd for C$_{14}$H$_{12}$ClFNO$_2^+$ (M+H)$^+$ 280.0535, found 280.0535.

7-chloro-1-ethyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, 4ab, 77%, light yellow solid, (EA/Hex = 25%, $R_f = 0.25$), $^1$H NMR (400 MHz, CDCl$_3$) δ 10.31 (s, 1H), 8.25 (s, 1H), 8.19 (d, $J = 8.8$ Hz, 1H), 7.53 (d, $J = 5.6$ Hz, 1H), 4.20 (q, $J = 7.3$ Hz, 2H), 1.52 (t, $J = 7.3$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ $^{13}$C NMR (101 MHz, CDCl$_3$) δ 188.93, 175.40, 157.00, 154.49, 145.68, 135.79, 129.90, 118.69, 117.00, 114.08, 49.54, 14.48. HRMS (ESI) m/z calcd for C$_{12}$H$_{10}$ClFNO$_2^+$ (M+H)$^+$ 254.0379, found 254.0380.

7-chloro-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, 4ac, 81%, light yellow solid, (EA/Hex = 25%, $R_f = 0.25$), $^1$H NMR (400 MHz, CDCl$_3$) δ 10.36 (s, 1H), 8.42 (s, 1H), 8.21 (d, $J = 8.7$ Hz, 1H), 8.06 (d, $J = 5.8$ Hz, 1H), 3.50 (dt, $J = 7.0$, 3.8 Hz, 1H), 1.41 (d, $J = 6.8$ Hz, 2H), 1.18 (d, $J = 2.1$ Hz, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 188.87, 175.49, 157.23, 154.73, 145.87, 137.66, 129.14, 127.70, 119.60, 116.74, 113.62, 35.08, 8.29. HRMS (ESI) m/z calcd for C$_{13}$H$_{10}$ClFNO$_2^+$ (M+H)$^+$ 266.0379, found 266.0381.
7-chloro-1-(cyclopropylmethyl)-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, **4ad**, 85%, light yellow solid, (EA/Hex = 25%, Rf = 0.25), $^1$H NMR (400 MHz, CDCl$_3$) δ 10.41 (s, 1H), 8.42 (s, 1H), 8.28 (d, $J$ = 8.8 Hz, 1H), 7.71 (d, $J$ = 5.6 Hz, 1H), 4.05 (d, $J$ = 7.0 Hz, 2H), 1.48 – 1.31 (m, 1H), 0.85 (d, $J$ = 8.1 Hz, 2H), 0.52 (d, $J$ = 5.2 Hz, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 188.94, 175.45, 157.02, 154.52, 145.41, 136.39, 129.82, 127.77, 118.84, 116.77, 113.71, 58.65, 9.83, 4.87. HRMS (ESI) m/z calcd for C$_{14}$H$_{12}$ClFNO$_2$+ (M+H)$^+$ 280.0535, found 280.0537.

1-cyclopropyl-6,7-difluoro-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, **4ae**, 79%, light yellow solid, (EA/Hex = 25%, Rf = 0.25), $^1$H NMR (400 MHz, CDCl$_3$) δ 10.36 (s, 1H), 8.43 (s, 1H), 8.27 (dd, $J$ = 9.7, 9.0 Hz, 1H), 7.80 (dd, $J$ = 11.2, 6.4 Hz, 1H), 3.53 – 3.44 (m, 1H), 1.40 (q, $J$ = 6.7 Hz, 2H), 1.18 (q, $J$ = 6.6 Hz, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 188.96, 175.38, 154.97, 150.13, 147.75, 145.94, 138.06, 126.11, 116.80, 115.08, 106.37, 35.12, 8.24. HRMS (ESI) m/z calcd for C$_{13}$H$_{16}$ClFNO$_2$+ (M+H)$^+$ 250.0674, found 250.0675.

1-ethyl-6,7-difluoro-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, **4af**, 76%, light yellow solid, (EA/Hex = 25%, Rf = 0.25) $^1$H NMR (400 MHz, DMSO-d$_6$) δ 10.14 (s,
1H), 8.64 (s, 1H), 8.19 − 8.04 (m, 2H), 4.43 (q, J = 7.1 Hz, 2H), 1.37 (t, J = 7.1 Hz, 3H). $^{13}$C NMR (101 MHz, DMSO- $d_6$) δ 188.24, 174.48, 148.16, 137.02, 126.74, 116.53, 114.06, 113.88, 108.23, 108.01, 49.32, 14.92. HRMS (ESI) m/z calcd for C$_{12}$H$_{10}$F$_2$NO$_2^+$ (M+H)$^+$ 280.0674, found 280.0675.

7-bromo-1-cyclopropyl-8-methyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, 4ag. 80%, light yellow solid, (EA/Hex = 25%, R$_f$ = 0.25) $^1$H NMR (400 MHz, DMSO- $d_6$) δ 10.09 (s, 1H), 8.51 (s, 1H), 7.99 (d, J = 8.5 Hz, 1H), 7.75 (d, J = 8.5 Hz, 1H), 4.26 (dt, J = 10.7, 3.5 Hz, 1H), 2.29 (s, 3H), 1.16 (d, J = 5.8 Hz, 2H), 0.86 (d, J = 1.5 Hz, 2H). $^{13}$C NMR (101 MHz, DMSO- $d_6$) δ 188.29, 175.65, 151.95, 146.59, 130.29, 128.99, 125.28, 117.17, 41.04, 22.90, 21.26, 10.86. HRMS (ESI) m/z calcd for C$_{14}$H$_{13}$BrNO$_2^+$ (M+H)$^+$ 306.0124, found 306.0125.

4-oxo-1,4-dihydroquinoline-3-carbaldehyde, 4ah. 75%, light yellow solid, (EA/Hex = 25%, R$_f$ = 0.25), $^1$H NMR (400 MHz, DMSO- $d_6$) δ 12.71 (s, 1H), 10.20 (s, 1H), 8.49 (s, 1H), 8.22 (dd, J = 8.0, 1.1 Hz, 1H), 7.76 (dd, J = 7.1, 1.3 Hz, 1H), 7.67 (d, J = 8.1 Hz, 1H), 7.52 − 7.43 (m, 1H). $^{13}$C NMR (101 MHz, DMSO- $d_6$) δ 189.18, 176.69, 143.67, 139.84, 133.55, 128.20, 125.87, 119.87, 116.77. HRMS (ESI) m/z calcd for C$_{10}$H$_{8}$NO$_2^+$ (M+H)$^+$ 174.0550, found 174.0551.
ethyl (E)-3-(1-cyclopropyl-3-formyl-4-oxo-1,4-dihydroquinolin-6-yl)acrylate, 4ai. 73%, light yellow solid, (EA/Hex = 30%, Rf = 0.2), $^1$H NMR (400 MHz, CDCl$_3$) δ 10.33 (s, 1H), 8.54 (d, $J$ = 1.8 Hz, 1H), 8.36 (s, 1H), 7.93 (d, $J$ = 8.8 Hz, 1H), 7.81 (dd, $J$ = 8.8, 1.9 Hz, 1H), 7.72 (d, $J$ = 16.0 Hz, 1H), 6.52 (d, $J$ = 16.0 Hz, 1H), 3.77 (s, 3H), 3.45 (qd, $J$ = 7.6, 3.9 Hz, 1H), 1.31 (q, $J$ = 6.7 Hz, 2H), 1.10 (q, $J$ = 6.6 Hz, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 189.11, 176.61, 166.96, 145.67, 142.74, 141.90, 132.02, 129.12, 126.95, 119.73, 117.79, 117.57, 51.87, 34.92, 8.23. HRMS (ESI) m/z calcd for C$_{18}$H$_{18}$NO$_4$+ (M+H)$^+$ 312.1230, found 312.1231.

6-((3-((6,7-bis(2-methoxyethoxy)quinazolin-4-yl)amino)phenyl)ethynyl)-1-cyclopropyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, 4aj. 76%, white solid, (EA/Hex = 60%, Rf = 0.25). $^1$H NMR (400 MHz, CDCl$_3$) δ 10.37 (s, 1H), 8.61 (s, 1H), 8.27 (d, $J$ = 19.4 Hz, 3H), 7.98 (d, $J$ = 7.9 Hz, 1H), 7.81 (d, $J$ = 8.7 Hz, 1H), 7.70 – 7.60 (m, 2H), 7.48 (s, 1H), 7.28 (d, $J$ = 7.9 Hz, 1H), 7.18 – 7.11 (m, 2H), 4.20 (dd, $J$ = 19.0, 14.5 Hz, 4H), 3.79 – 3.71 (m, 4H), 3.37 (d, $J$ = 3.5 Hz, 7H), 1.21 (dd, $J$ = 10.0, 4.9 Hz, 4H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 189.45, 176.61, 166.96, 156.48, 154.51, 153.47, 149.07, 147.41, 145.95, 140.32, 139.39, 135.58, 130.06, 129.09, 128.55, 126.73, 124.41, 122.93, 122.26, 120.82, 117.32, 109.56, 108.61, 102.67, 90.84, 87.82, 70.84, 69.02, 68.34, 59.24, 35.05, 29.68, 8.05. HRMS (ESI) m/z calcd for C$_{35}$H$_{33}$N$_4$O$_6$+ (M+H)$^+$ 605.2395, found 605.2396.
1-cyclopropyl-6,7-difluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid, 5, 91%, light yellow solid, (MeOH/DCM=10%, Rf = 0.2). 1H NMR (400 MHz, DMSO-d6) δ 14.74 (s, 1H), 8.77 (s, 1H), 8.39 (dd, J = 12.0, 6.8 Hz, 1H), 8.34 – 8.20 (m, 1H), 3.86 – 3.76 (m, 1H), 1.33 (d, J = 5.7 Hz, 2H), 1.25 – 1.21 (m, 2H). 13C NMR (101 MHz, DMSO-d6) δ 177.15, 165.89, 150.06, 139.30, 123.13, 113.87, 108.86, 107.91, 37.10, 8.04. HRMS (ESI) m/z calcd for C13H10F2NO3+ (M+H)+ 266.0623, found 266.0625.

1-cyclopropyl-6-fluoro-4-oxo-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid, 6, 91%, light yellow solid, (MeOH/DCM=15%, Rf = 0.15). 1H NMR (400 MHz, D2O) δ 8.29 (s, 1H), 7.23 (d, J = 7.1 Hz, 1H), 7.02 (d, J = 12.9 Hz, 1H), 3.47 (s, 5H), 3.38 (s, 4H), 1.28 (d, J = 6.5 Hz, 2H), 1.00 (s, 2H). 13C NMR (101 MHz, D2O) δ 175.28 (s), 168.41, 154.31, 151.81, 147.84, 144.50, 138.62, 118.20, 110.39, 106.25, 105.24, 46.18, 46.13, 43.09, 36.02, 7.40. HRMS (ESI) m/z calcd for C17H19FN3O3+ (M+H)+ 332.1405, found 332.1408.

1-cyclopropyl-6-fluoro-7-(3-methylpiperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid, 7, 87%, light yellow solid, (MeOH/DCM=15%, Rf = 0.15). 1H NMR (400 MHz, DMSO-d6) δ 8.64 (s, 1H), 7.87 (d, J = 13.4 Hz, 1H), 7.53 (d, J = 7.3 Hz,
1H), 3.84 (s, 1H), 3.60 (d, J = 9.9 Hz, 2H), 3.35 (s, 1H), 3.13 – 2.93 (m, 4H), 2.66 (t, J = 11.0 Hz, 1H), 1.32 (d, J = 5.6 Hz, 2H), 1.18 (s, 2H), 1.11 (d, J = 6.2 Hz, 3H). 13C NMR (101 MHz, DMSO-d6) δ 176.75, 166.40, 154.64, 152.16, 148.39, 145.66, 139.67, 118.95, 111.53, 107.15, 56.21, 50.48, 49.47, 44.91, 36.33, 18.86, 8.01. HRMS (ESI) m/z calcd for C18H21FN3O3+ (M+H)+ 346.1561, found 346.1560.

![Image of a chemical structure](image1.png)

1-ethyl-6,7-difluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid, 8, 89%, light yellow solid, (MeOH/DCM=10%, Rf = 0.2), 1H NMR (400 MHz, CDCl3), 1H NMR (400 MHz, DMSO-d6) δ 14.87 (s, 1H), 9.09 (s, 1H), 8.39 – 8.25 (m, 2H), 4.58 (q, J = 6.9 Hz, 2H), 1.39 (d, J = 6.9 Hz, 3H). 13C NMR (101 MHz, DMSO-d6) δ 176.91, 166.06, 150.29, 137.36, 123.77, 113.96, 108.45, 108.22, 50.04, 14.98. HRMS (ESI) m/z calcd for C12H10FNO3+ (M+H)+ 254.0623, found 254.0625.

![Image of a chemical structure](image2.png)

1-ethyl-6-fluoro-4-oxo-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid, 9, 92%, light yellow solid, (MeOH/DCM=15%, Rf = 0.15), 1H NMR (400 MHz, DMSO-d6) δ 8.93 (s, 1H), 7.84 (d, J = 13.5 Hz, 1H), 7.12 (d, J = 7.3 Hz, 1H), 4.58 (q, J = 7.0 Hz, 2H), 3.33 – 3.12 (m, 4H), 2.98 – 2.80 (m, 4H), 1.42 (t, J = 7.1 Hz, 3H). 13C NMR (101 MHz, DMSO-d6) δ 175.54, 166.61, 154.58 152.10, 148.82, 146.53, 137.66, 119.43, 111.62, 107.48, 105.93, 51.29, 49.47, 45.87, 14.79. HRMS (ESI) m/z calcd for C16H19FNO3+ (M+H)+ 320.1405, found 320.1408.
1-ethyl-6-fluoro-7-(4-methylpiperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid, 10, 90%, light yellow solid, (MeOH/DCM=15%, Rf = 0.15), $^1$H NMR (400 MHz, DMSO-$d_6$) δ 8.95 (s, 1H), 7.90 (d, $J = 13.4$ Hz, 1H), 7.17 (d, $J = 7.2$ Hz, 1H), 4.59 (q, $J = 6.9$ Hz, 2H), 3.33 (d, $J = 4.2$ Hz, 4H), 2.53 (s, 4H), 2.26 (s, 3H), 1.42 (t, $J = 7.0$ Hz, 3H). $^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 176.62, 166.61, 148.98, 145.89, 137.67, 119.65, 111.73, 107.51, 106.28, 54.76, 49.76, 49.51, 46.16, 14.84. HRMS (ESI) m/z calcd for C$_{17}$H$_{21}$FN$_3$O$_3$+ (M+H)$^+$ 334.1561, found 334.1564.

5-ethyl-8-oxo-5,8-dihydro-[1,3]dioxolo[4,5-g]quinoline-7-carboxylic acid, 11, 88%, light yellow solid, (MeOH/DCM=10%, Rf = 0.2), $^1$H NMR (400 MHz, DMSO-$d_6$) δ 15.70 (s, 1H), 8.90 (s, 1H), 7.62 (d, $J = 11.1$ Hz, 2H), 6.30 (s, 2H), 4.54 (d, $J = 7.1$ Hz, 2H), 1.38 (t, $J = 7.1$ Hz, 3H). $^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 176.62, 166.79, 154.20, 147.57, 137.42, 103.74, 102.33, 97.71, 50.04, 15.09. HRMS (ESI) m/z calcd for C$_{13}$H$_{12}$NO$_5$+ (M+H)$^+$ 262.0710, found 262.0715.

7-bromo-1-cyclopropyl-8-methyl-4-oxo-1,4-dihydroquinoline-3-carboxylic acid, 12, 91%, light yellow solid, (MeOH/DCM=10%, Rf = 0.2), $^1$H NMR (400 MHz, DMSO-$d_6$) δ 14.68 (s, 1H), 8.87 (s, 1H), 8.06 (d, $J = 8.6$ Hz, 1H), 7.85 (d, $J = 8.6$ Hz, 1H), 4.48 – 4.31 (m, 1H), 2.92 (s, 3H), 1.22 (d, $J = 6.3$ Hz, 2H), 0.93 (s, 2H). $^{13}$C NMR (101 MHz,
DMSO-$d_6$ $\delta$ 178.16, 165.79, 153.50, 143.18, 133.92, 131.06, 125.11, 108.50, 55.40, 41.95, 23.12, 11.01. HRMS (ESI) m/z calcd for $C_{14}H_{13}BrNO_3^+$ (M+H)$^+$ 322.0073, found 322.0073.

4-oxo-1,4-dihydroquinoline-3-carboxylic acid, 13, 92%, light yellow solid, (MeOH/DCM=10%, $R_f$ = 0.2). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 15.37 (s, 1H), 13.51 (s, 1H), 8.90 (s, 1H), 8.40 – 8.22 (m, 1H), 8.01 – 7.75 (m, 2H), 7.61 (dd, $J$ = 11.1, 3.9 Hz, 1H). $^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 178.81, 166.87, 145.64, 139.92, 134.42, 126.69, 125.52, 124.86, 120.14, 108.03. HRMS (ESI) m/z calcd for $C_{10}H_8NO_3^+$ (M+H)$^+$ 190.0499, found 190.0498.

$N$-(2,4-di-tert-butyl-5-hydroxyphenyl)-4-oxo-1,4-dihydroquinoline-3-carboxamide, 14, 93%, light yellow solid, (EA/Hex = 25%, $R_f$ = 0.25). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 12.89 (s, 1H), 11.82 (s, 1H), 9.21 (s, 1H), 8.87 (s, 1H), 8.33 (d, $J$ = 8.1 Hz, 1H), 7.78 (dd, $J$ = 19.3, 7.7 Hz, 2H), 7.52 (t, $J$ = 7.5 Hz, 1H), 7.13 (d, $J$ = 26.1 Hz, 2H), 1.37 (d, $J$ = 6.7 Hz, 18H). $^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 176.87, 163.29, 153.75, 144.64, 139.63, 134.00, 133.40, 132.75, 131.97, 126.46, 125.62, 124.23, 119.60, 116.42, 111.35, 34.80, 34.44, 31.03, 29.88. HRMS (ESI) m/z calcd for $C_{24}H_{29}N_2O_3^+$ (M+H)$^+$ 393.2173, found 393.2174.
2-(3-(tert-butylamino)-2-formylacryloyl)phenyl 4-methylbenzenesulfonate, 15, 97%, light yellow solid, (EA/Hex = 20%, Rf = 0.2), ¹H NMR (400 MHz, CDCl₃) δ 11.40 (s, 1H), 9.31 (s, 0.6H), 9.04 (s, 0.4H), 8.13 (d, J = 14.7 Hz, 0.4H), 7.97 (s, 0.6H), 7.64 (t, J = 8.6 Hz, 2H), 7.41 (dd, J = 14.0, 6.0 Hz, 1H), 7.34 – 7.29 (m, 1H), 7.24 (dd, J = 12.5, 6.9 Hz, 4H), 2.43 (s, 3H), 1.46 (s, 4H), 1.40 (s, 5H). ¹³C NMR (101 MHz, CDCl₃) δ 191.78, 190.84, 189.46, 188.43, 156.09, 145.95, 145.53, 133.76, 132.46, 131.09, 129.74, 128.51, 127.13, 123.27, 110.18, 54.85, 29.52, 21.74. HRMS (ESI) m/z calcd for C₂₁H₂₄N₂O₅S⁺ (M+H)⁺ 402.1370, found 402.1370.
NMR Figures of Products

1H NMR spectrum of 4a

13C NMR spectrum of 4a
$^1$H NMR spectrum of 4b

$^{13}$C NMR spectrum of 4b
DEP 135° spectrum of 4b
$^1$H NMR spectrum of 4c

$^{13}$C NMR spectrum of 4c
DEP 135° spectrum of 4c
\( ^1\text{H NMR spectrum of 4d} \)

\( ^{13}\text{C NMR spectrum of 4d} \)
$^{1}H$ NMR spectrum of 4e

$^{13}C$ NMR spectrum of 4e
$^{13}$C NMR spectrum of $4f$

$^{13}$C NMR spectrum of $4f$
$^{1}$H NMR spectrum of 4g

$^{13}$C NMR spectrum of 4g
$^1$H NMR spectrum of 4h

$^{13}$C NMR spectrum of 4h
DEP 135° spectrum of 4h
$^1\text{H}$ NMR spectrum of 4i

$^{13}\text{C}$ NMR spectrum of 4i
DEP135° spectrum of 4i
$^{1}H$ NMR spectrum of 4j

$^{13}C$ NMR spectrum of 4j
DEP 135° spectrum of 4j
$^1$H NMR spectrum of 4k

$^{13}$C NMR spectrum of 4k
$^1$H NMR spectrum of 4I

$^{13}$C NMR spectrum of 4I
DEP 135° spectrum of 41
$^1$H NMR spectrum of 4m

$^{13}$C NMR spectrum of 4m
$^1$H NMR spectrum of 4n

$^{13}$C NMR spectrum of 4n
DEP 135° spectrum of 4n
$^1$H NMR spectrum of 4o

$^{13}$C NMR spectrum of 4o
DEP 135° spectrum of 4o
$^1$H NMR spectrum of 4p

$^{13}$C NMR spectrum of 4p
$^1$H NMR spectrum of 4q

$^{13}$C NMR spectrum of 4q
$^1$H NMR spectrum of 4r

$^{13}$C NMR spectrum of 4r
DEP 135° spectrum of 4r
DEP $135^\circ$ spectrum of 4s
$^1$H NMR spectrum of 4aa

$^{13}$C NMR spectrum of 4aa
$^{19}\text{F} \text{NMR spectrum of 4aa}$
$^1$H NMR spectrum of 4ab

$^{13}$C NMR spectrum of 4ab
DEP 135° spectrum of 4ab

19F NMR spectrum of 4ab
$^1$H NMR spectrum of 4ac

$^{13}$C NMR spectrum of 4ac
$^{19}$F NMR spectrum of 4ac
$^1$H NMR spectrum of 4ad

$^{13}$C NMR spectrum of 4ad
19F NMR spectrum of 4ad
$^1$H NMR spectrum of 4ae

$^{13}$C NMR spectrum of 4ae
$^{19}$F NMR spectrum of 4ae
\textit{H} NMR spectrum of 4af

$^{13}$C NMR spectrum of 4af
$^{19}$F NMR spectrum of 4af
$^{1} \text{H NMR spectrum of 4ag}$

$^{13} \text{C NMR spectrum of 4ag}$
$^1$H NMR spectrum of 4ah

$^{13}$C NMR spectrum of 4ah
$^1$H NMR spectrum of 4ai

$^{13}$C NMR spectrum of 4ai
DEP 135° spectrum of 4ai
$^1$H NMR spectrum of 4aj

$^{13}$C NMR spectrum of 4aj
$^1$H NMR spectrum of 5

$^{13}$C NMR spectrum of 5
$^{19}$F NMR spectrum of 5
$^1$H NMR spectrum of 6

$^{13}$C NMR spectrum of 6
$^1$H NMR spectrum of 7

$^{13}$C NMR spectrum of 7
$^{19}$F NMR spectrum of 7
\(^1\)H NMR spectrum of 8

\(^1^3\)C NMR spectrum of 8
$^1$H NMR spectrum of 9

$^{13}$C NMR spectrum of 9
$^1$H NMR spectrum of 10

$^{13}$C NMR spectrum of 10
$^{19}$F NMR spectrum of 10
$^1$H NMR spectrum of 11

$^{13}$C NMR spectrum of 11
The image contains two NMR spectra of compound 12.

**1H NMR spectrum of 12**

- Peaks at various ppm values, with labels indicating chemical shifts.

**13C NMR spectrum of 12**

- Peaks at various ppm values, with labels indicating chemical shifts.

The structures of compound 12 are also shown, depicting the positions of the chemical shifts in the NMR spectra.
"H NMR spectrum of 13

\[ \begin{array}{c}
\text{NMR spectrum of 13} \\
\text{13C NMR spectrum of 13}
\end{array} \]
$^1$H NMR spectrum of 14

$^{13}$C NMR spectrum of 14
$^1$H NMR spectrum of 15

$^{13}$C NMR spectrum of 15
DEPT 135' spectrum of 15