Anticancer sulfonamide hybrids that inhibit bladder cancer cells growth and migration as tubulin polymerization inhibitors

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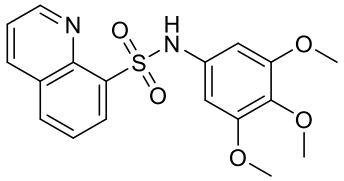
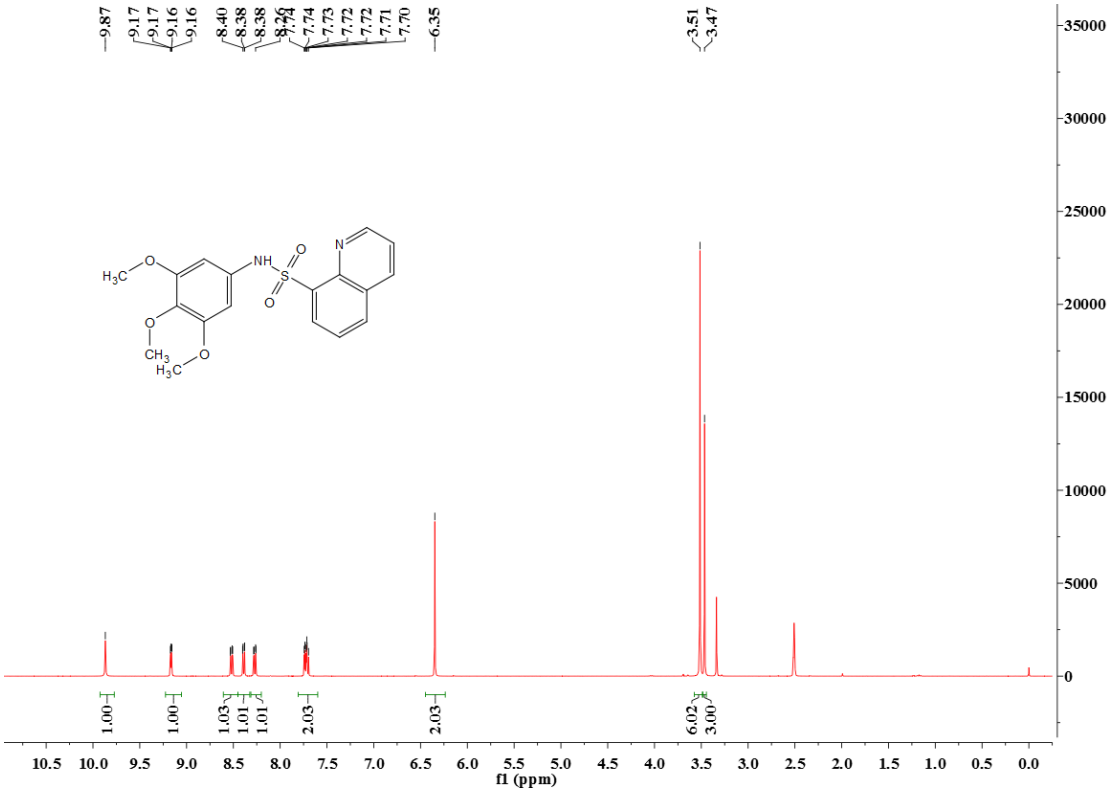
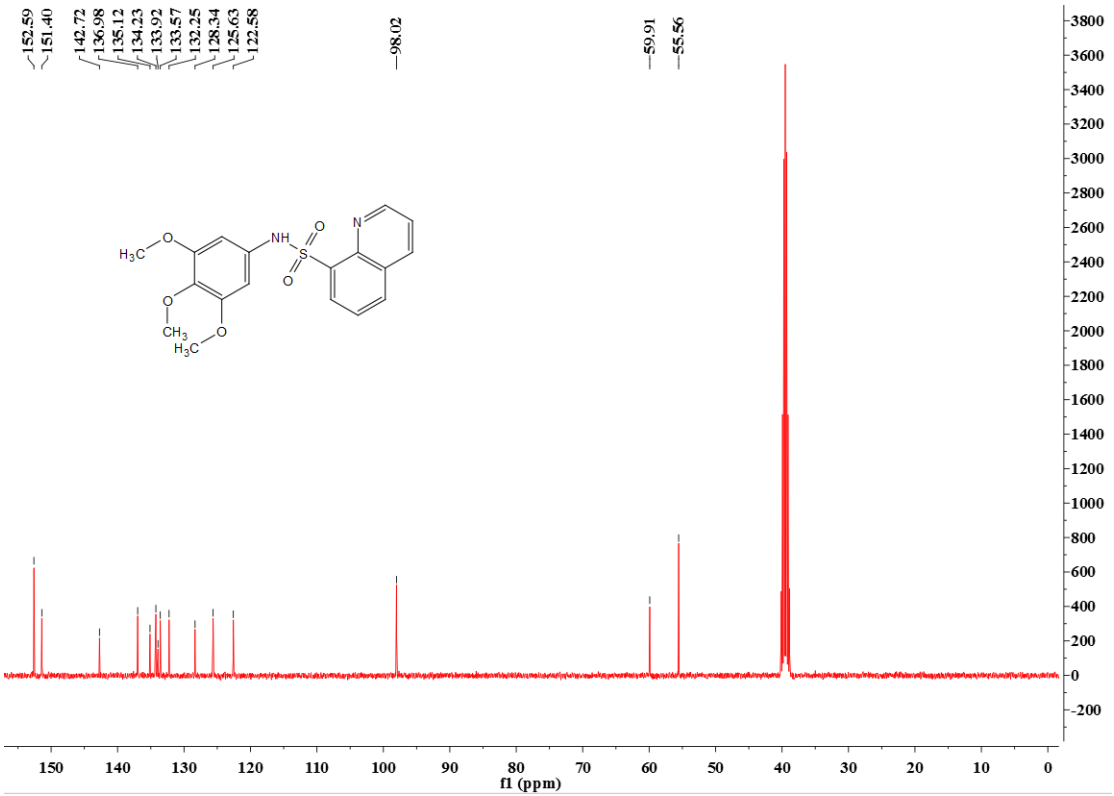
N-(3,4,5-trimethoxyphenyl)quinoline-8-sulfonamide (11)

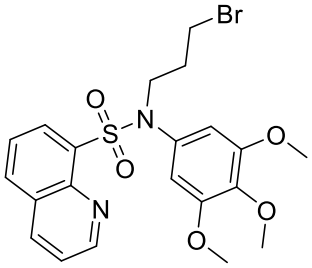


White solid, yield:94%, m.p.:181~183 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.87 (s, 1H), 9.16 (dd, J = 4.2, 1.7 Hz, 1H), 8.52 (dd, J = 8.4, 1.7 Hz, 1H), 8.39 (dd, J = 7.3, 1.3 Hz, 1H), 8.27 (dd, J = 8.2, 1.3 Hz, 1H), 7.81 – 7.60 (m, 2H), 6.35 (s, 2H), 3.51 (s, 6H), 3.47 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 152.6, 151.4, 142.7, 136.0, 135.1, 134.2, 133.9, 133.6, 132.3, 128.3, 125.6, 122.6, 98.0, 59.9, 55.6. HRMS (m/z): Calcd. $C_{18}H_{19}N_2O_5S$, $[M+H]^+$m/z: 375.1015, found: 375.1018.

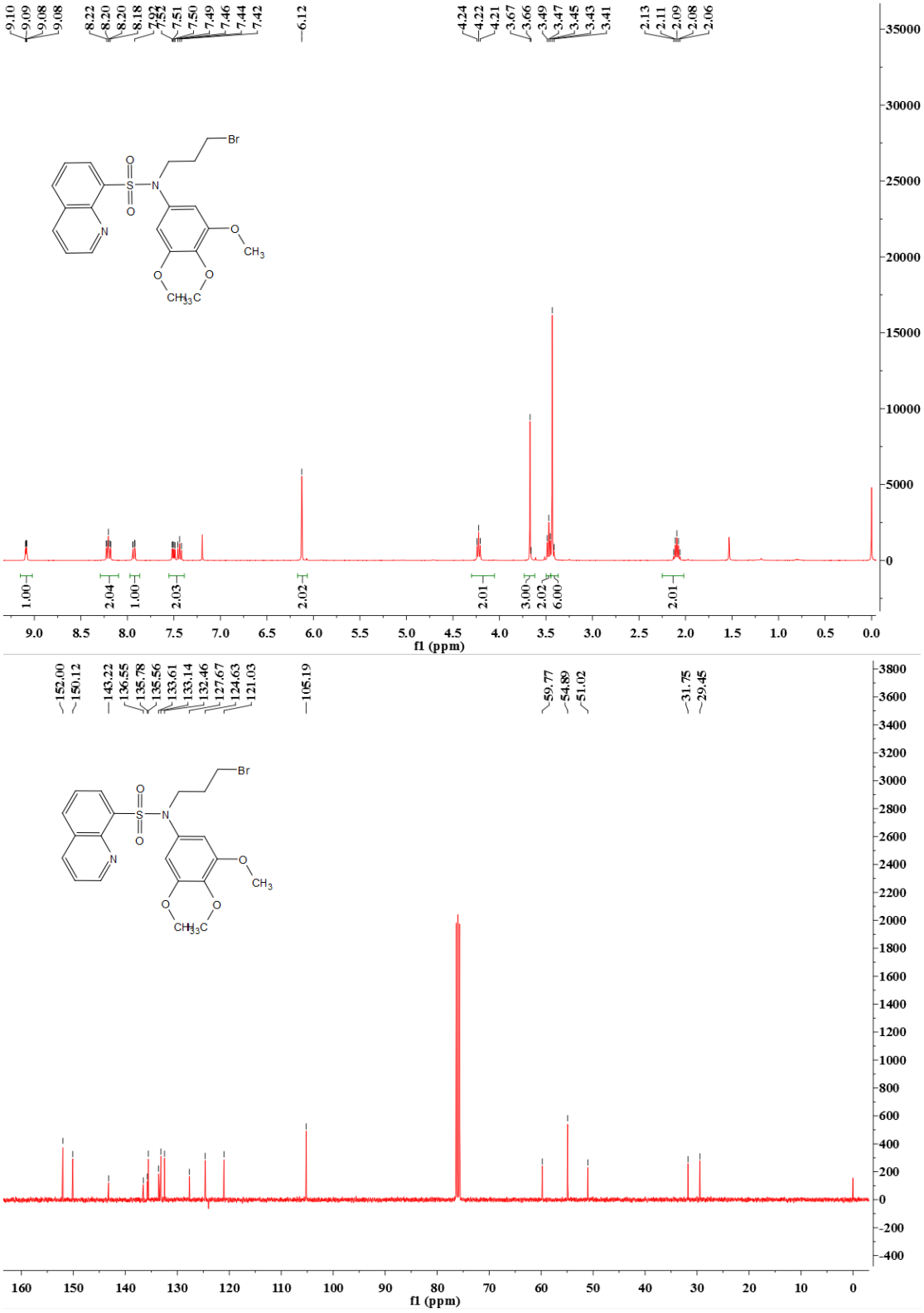




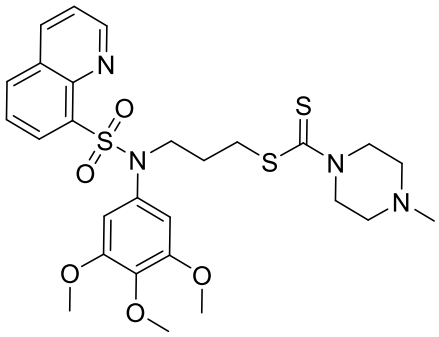
N-(3-bromopropyl)-N-(3,4,5-trimethoxyphenyl)quinoline-8-sulfonamide (12)



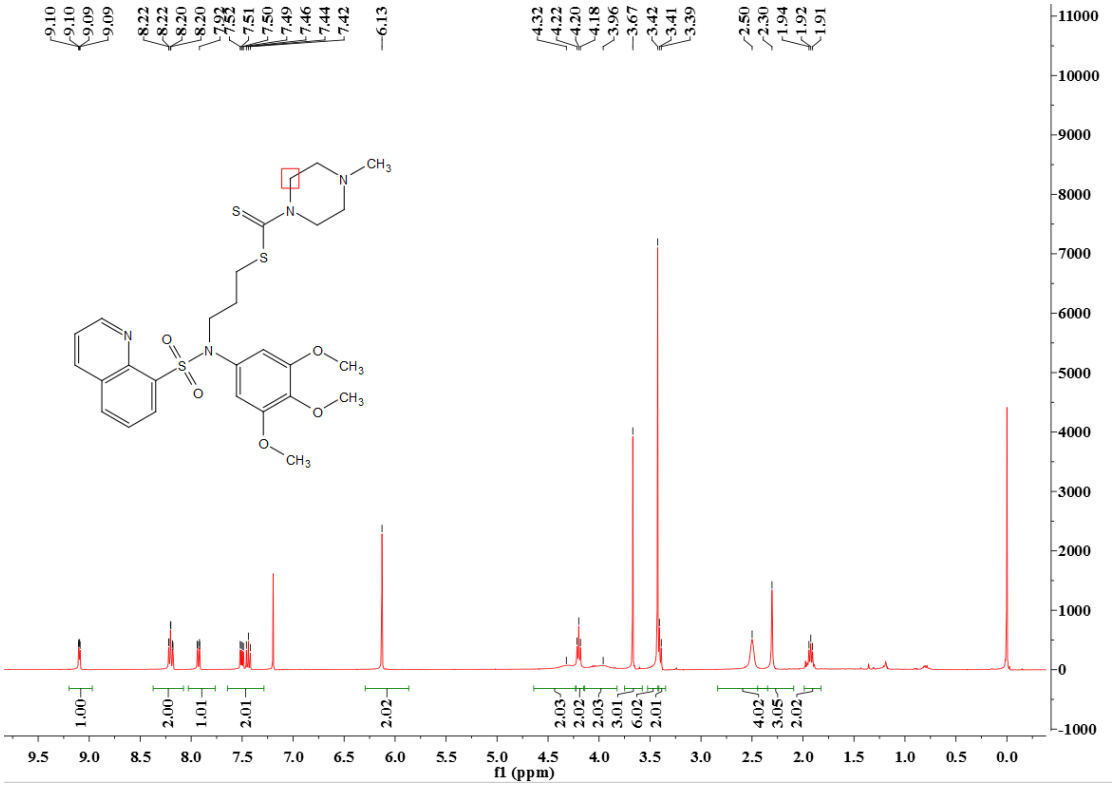
White solid, yield:82%, m.p.:129~131°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.20 (td, *J* = 8.6, 1.5 Hz, 2H), 7.93 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.55 – 7.39 (m, 2H), 6.12 (s, 2H), 4.22 (t, *J* = 6.8 Hz, 2H), 3.67 (d, *J* = 4.6 Hz, 3H), 3.47 (t, *J* = 6.8 Hz, 2H), 3.42 (d, *J* = 8.3 Hz, 6H), 2.09 (p, *J* = 6.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 150.1, 143.2, 136.6, 135.8, 135.6, 133.6, 133.1, 132.5, 127.7, 124.6, 121.0, 105.2, 59.8, 54.9, 51.0, 31.8, 29.5. HRMS (m/z): Calcd. $C_{21}H_{24}BrN_2O_5S$, $[M+H]^+$m/z: 495.0589, found: 495.0593.

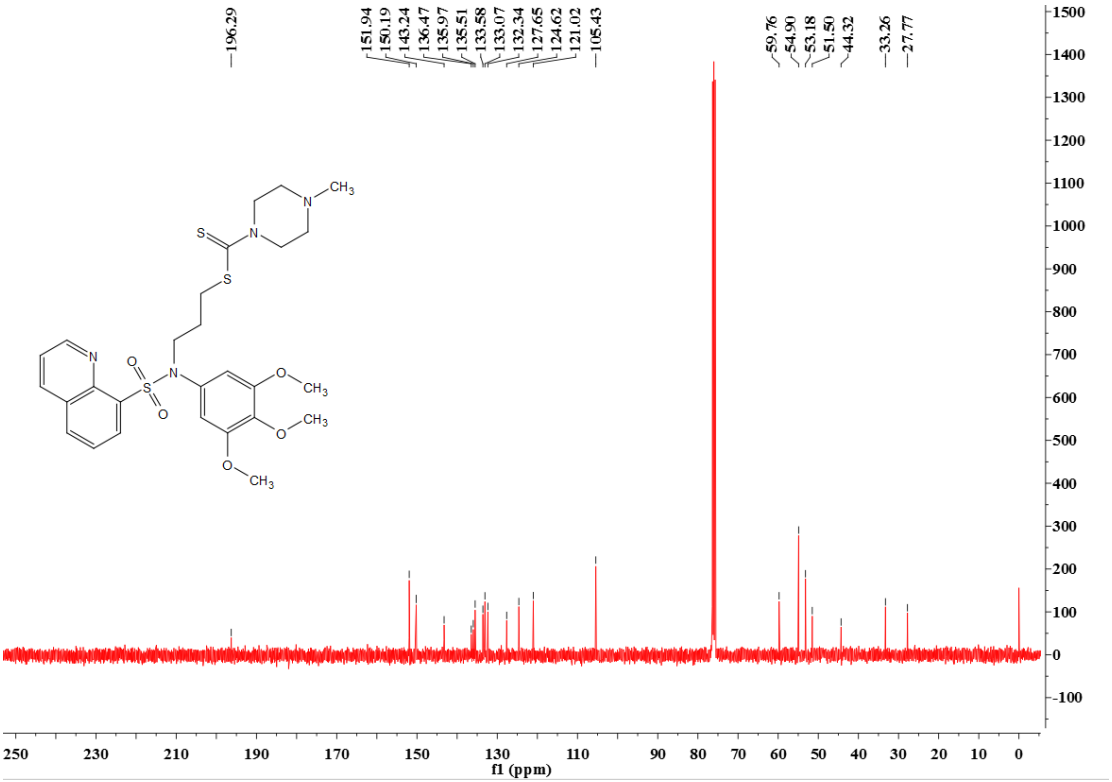


3-(N-(3,4,5-trimethoxyphenyl)quinoline-8-sulfonamido)propyl-4-methylpiperazine-1-carbodithioate (13a)

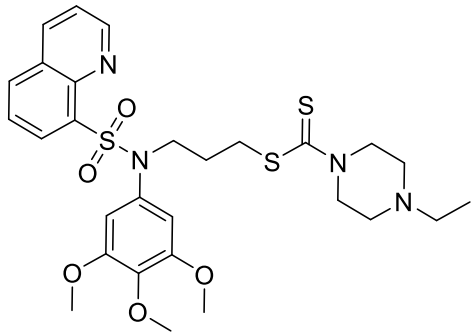


White solid, yield:76%, m.p.:96~98ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.10 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.37 – 8.08 (m, 2H), 7.93 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.64 – 7.29 (m, 2H), 6.13 (s, 2H), 4.32 (s, 2H), 4.20 (t, *J* = 6.8 Hz, 2H), 3.96 (s, 2H), 3.67 (s, 3H), 3.42 (s, 6H), 3.40 (d, *J* = 7.3 Hz, 2H), 2.50 (s, 4H), 2.30 (s, 3H), 1.99 – 1.82 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.9, 150.2, 143.2, 136.5, 136.0, 135.5, 133.6, 133.1, 132.3, 127.7, 124.6, 121.0, 105.4, 59.8, 54.9, 53.2, 51.5, 44.3, 33.3, 27.8. HRMS (m/z): Calcd. $C_{27}H_{35}N_4O_5S_3$, $[M+H]^+$m/z: 591.1770, found: 591.1776.

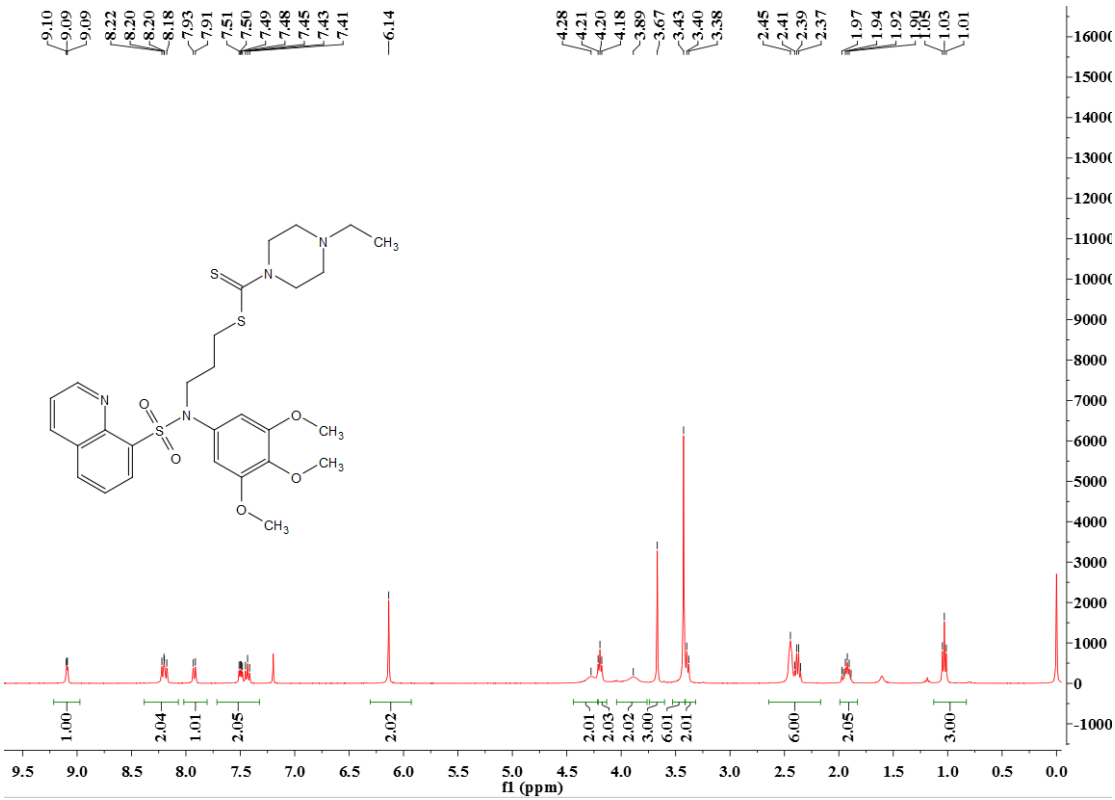


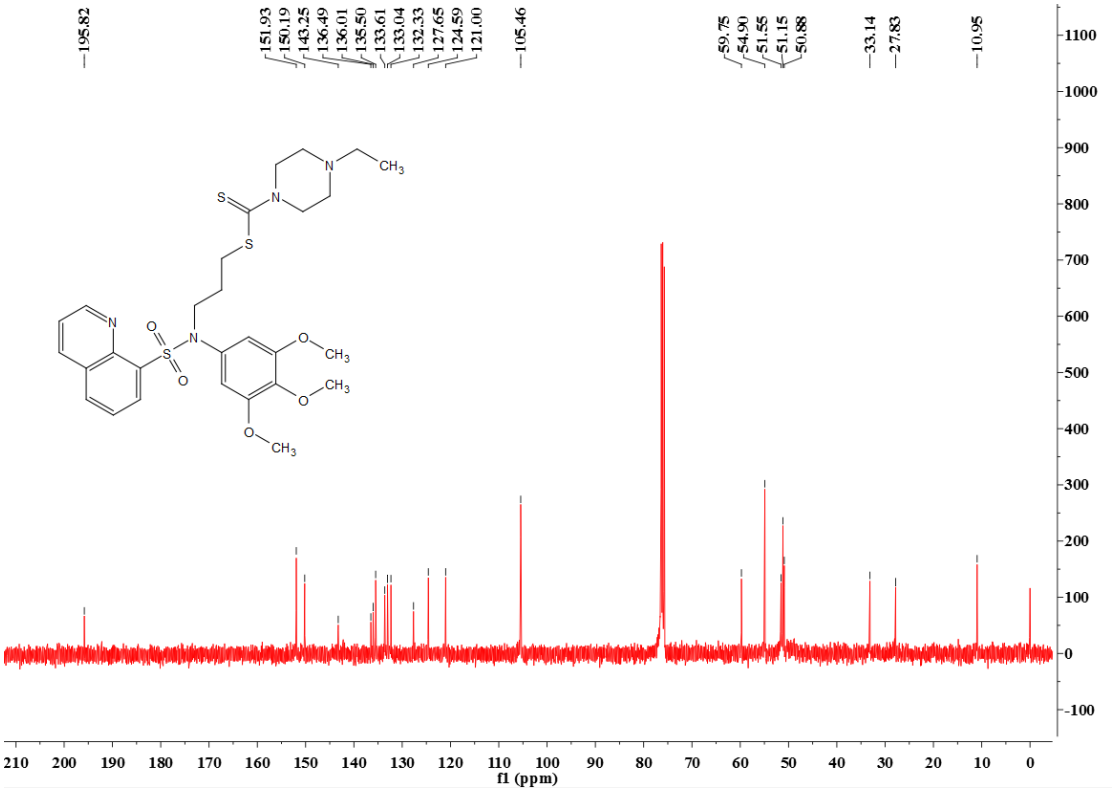


3-(N-(3,4,5-trimethoxyphenyl)quinoline-8-sulfonamido)propyl-4-ethylpiperazine-1-carbodithioate(13b)

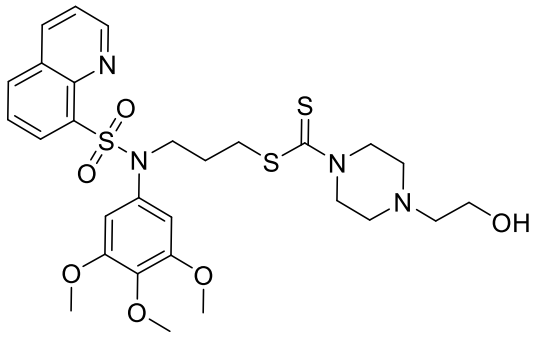


White solid, yield:84%, m.p.:131~133°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.21 – 8.97 (m, 1H), 8.20 (dd, *J* = 9.8, 8.1 Hz, 2H), 7.92 (d, *J* = 7.7 Hz, 1H), 7.72 – 7.32 (m, 2H), 6.14 (s, 2H), 4.24 (d, *J* = 26.0 Hz, 2H), 4.20 (t, *J* = 6.7 Hz, 2H), 3.89 (s, 2H), 3.67 (s, 3H), 3.43 (s, 6H), 3.39 (d, *J* = 7.3 Hz, 2H), 2.64 – 2.17 (m, 6H), 1.99 – 1.83 (m, 2H), 1.03 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.8, 151.9, 150.2, 143.3, 136.5, 136.0, 135.5, 133.6, 133.0, 132.3, 127.7, 124.6, 121.0, 105.5, 59.8, 54.9, 51.6, 51.2, 50.9, 33.1, 27.8, 11.0. HRMS (m/z): Calcd. $C_{28}H_{37}N_4O_5S_3$, $[M+H]^+$m/z: 605.1926, found: 605.1929.

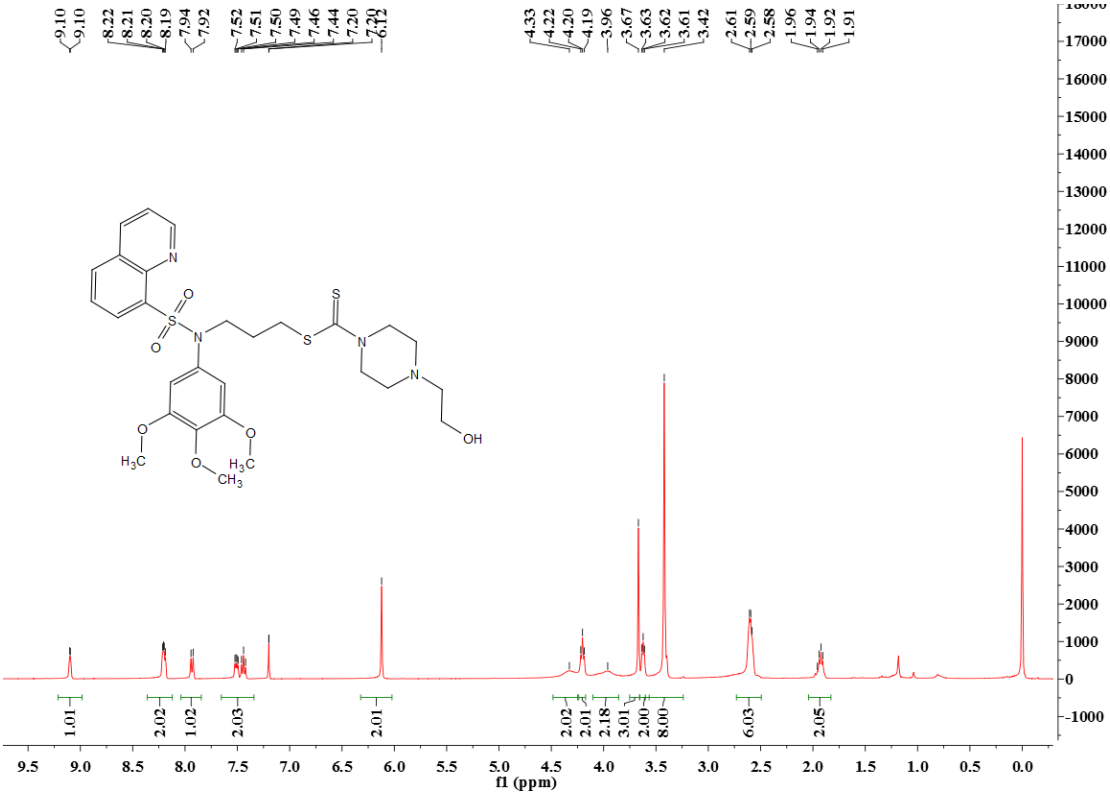


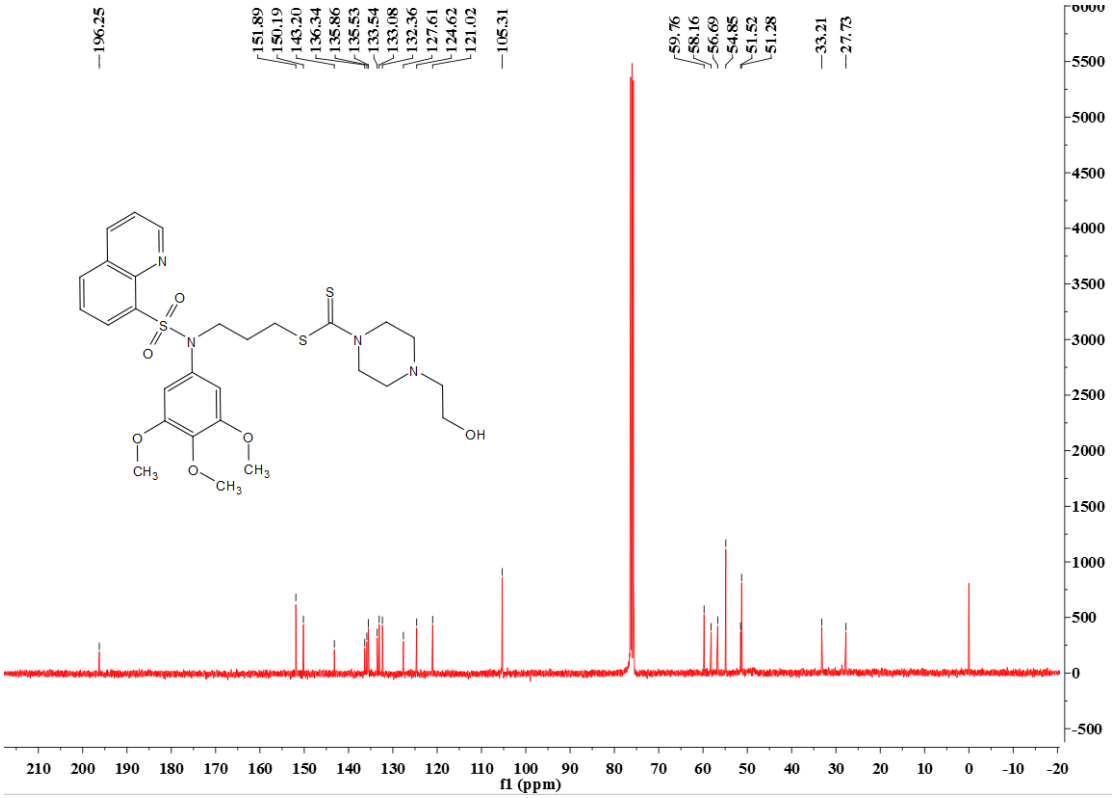


3-(N-(3,4,5-trimethoxyphenyl)quinoline-8-sulfonamido)propyl-4-(2-hydroxyethyl)piperazine-1-carbodithioate(13c)

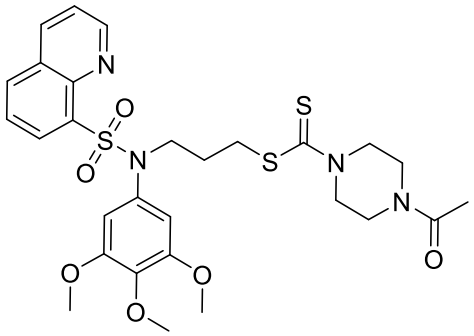


White solid, yield:75%, m.p.:106~108°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.10 (d, *J* = 2.1 Hz, 1H), 8.20 (dd, *J* = 6.8, 3.9 Hz, 2H), 7.93 (d, *J* = 8.1 Hz, 1H), 7.65 – 7.34 (m, 2H), 6.12 (s, 2H), 4.33 (s, 2H), 4.20 (t, *J* = 6.6 Hz, 2H), 3.96 (s, 2H), 3.67 (s, 3H), 3.66 – 3.57 (m, 2H), 3.42 (s, 8H), 2.73 – 2.49 (m, 6H), 1.93 (dd, *J* = 13.7, 6.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.3, 151.9, 150.2, 143.2, 136.3, 135.9, 135.5, 133.5, 133.1, 132.4, 127.6, 124.6, 121.0, 105.3, 59.8, 58.2, 56.7, 54.9, 51.5, 51.3, 33.2, 27.7. HRMS (m/z): Calcd. $C_{28}H_{37}N_4O_6S_3$, $[M+H]^+$m/z: 621.1875, found: 621.1878.

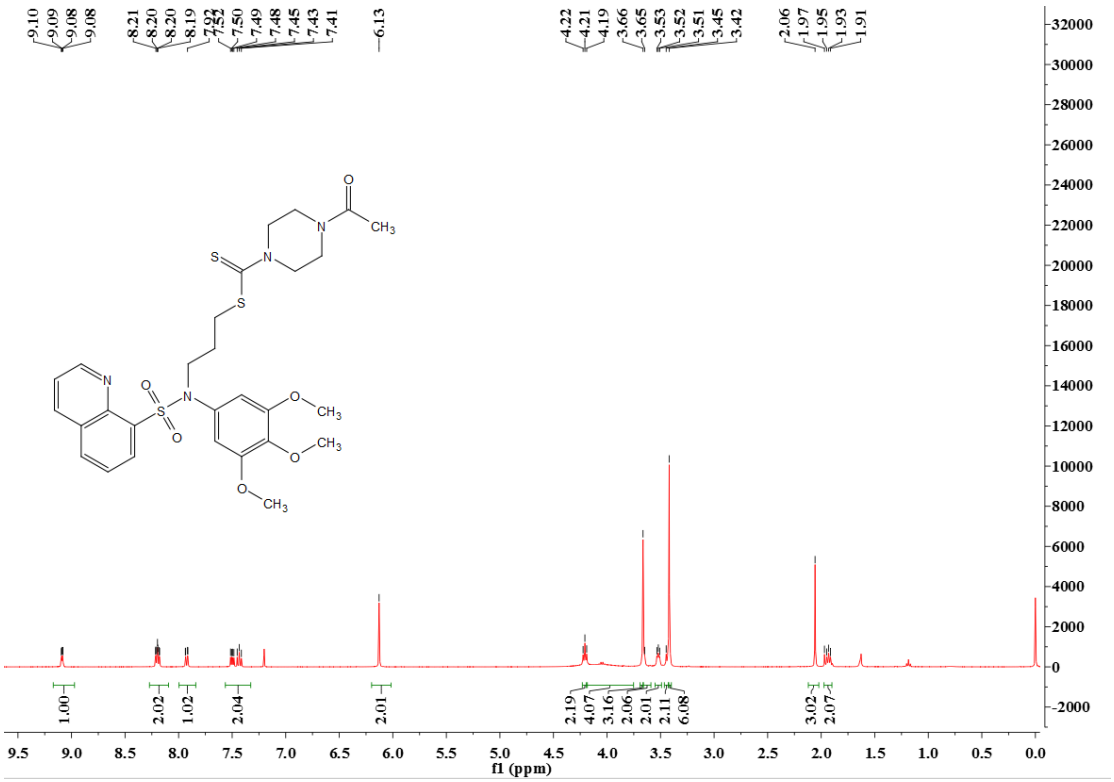




3-(N-(3,4,5-trimethoxyphenyl)quinoline-8-sulfonamido)propyl-4-acetylpiperazine-1-carbodithioate (13d)



White solid, yield:90%, m.p.:128~129°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.27 – 8.09 (m, 2H), 7.93 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.56 – 7.33 (m, 2H), 6.13 (s, 2H), 4.21 (t, *J* = 6.7 Hz, 2H), 4.19 (s, 4H), 3.66 (s, 3H), 3.65 (s, 2H), 3.55 – 3.49 (m, 2H), 3.45 (s, 2H), 3.42 (s, 6H), 2.06 (s, 3H), 1.94 (dd, *J* = 14.9, 7.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.0, 168.4, 152.0, 150.2, 143.2, 136.5, 135.9, 135.6, 133.5, 133.1, 132.4, 127.6, 124.6, 121.0, 105.4, 59.8, 54.9, 51.6, 44.2, 39.6, 33.2, 27.7, 20.4. HRMS (m/z): Calcd. $C_{28}H_{35}N_4O_6S_3$, $[M+H]^+$m/z: 619.1719, found: 619.1726.


9.10
9.09
9.08
9.08
8.21
8.20
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8.19
7.52
7.50
7.49
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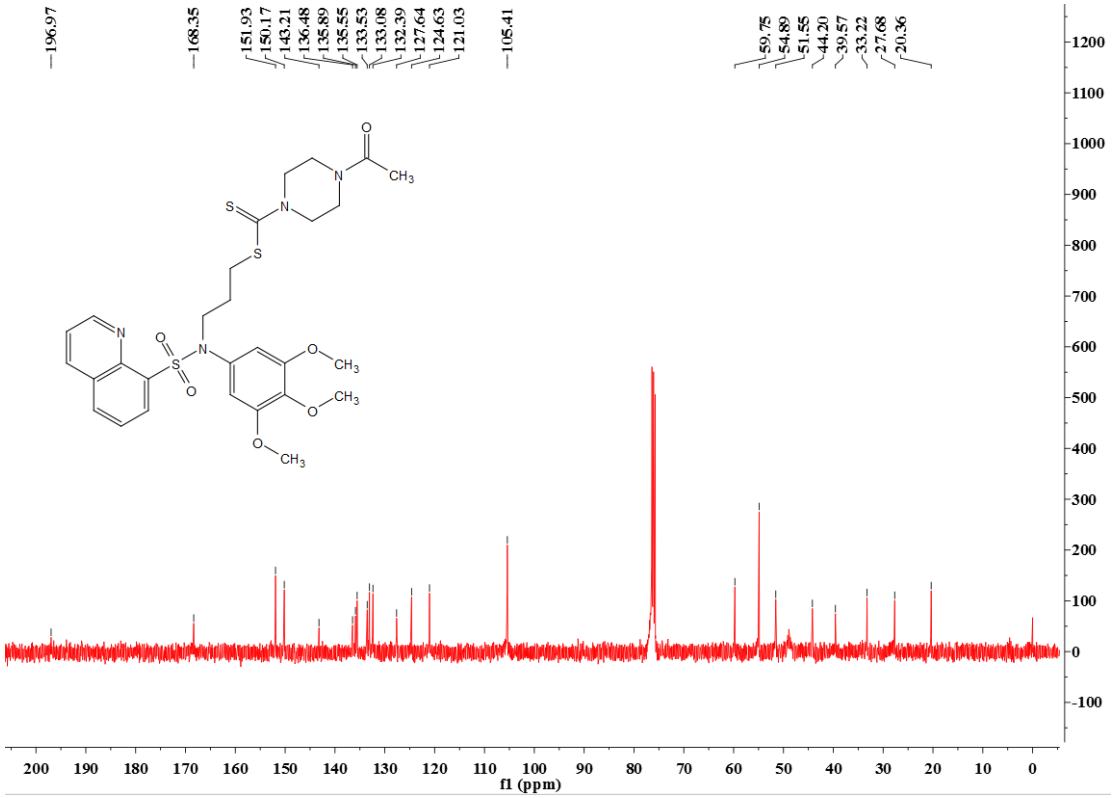
3.02
2.07
f1 (ppm)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150.17
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135.89
135.55
133.53
133.08
132.39
127.64
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121.03
105.41
59.75
54.89
51.55
44.20
39.57
33.22
27.68
20.36
f1 (ppm)