Supplementary Information

9-Aminoquino[2',3':3,4]pyrrolo[2,1-*b*]quinazolin-11(13*H*)-one

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A) Experimental procedures for the preparation of the starting material, 9-nitroquino[2',3':3,4]pyrrolo[2,1-*b*]quinazolin-11(13*H*)-one (**1**)

B) Spectra of the title compound, 9-aminoquino[2',3':3,4]pyrrolo[2,1-*b*]quinazolin-11(13*H*)-one (**2**)
   a. Figure S1. EI-MS
   b. Figure S2. ^{1}H-NMR
   c. Figure S3. ^{13}C-NMR (APT)
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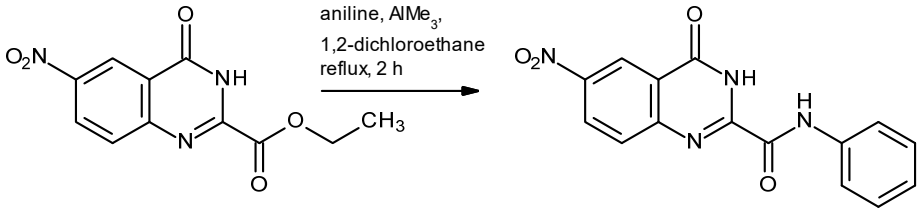
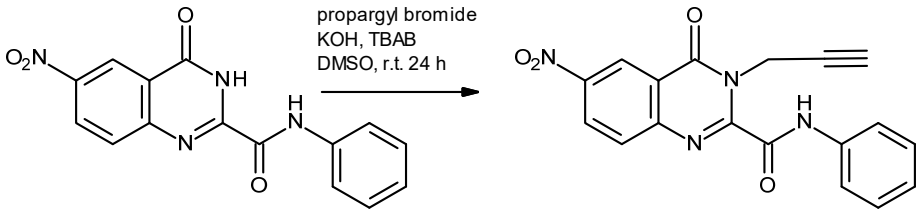
A) Experimental procedures for the preparation of the starting material, 9-nitroquino[2',3':3,4]pyrrolo-[2,1-*b*]quinazolin-11(13*H*)-one (**1**); for general information about equipment, see main text

N-Phenyl-6-nitro-4-oxo-3,4-dihydroquinazoline-2-carboxamide



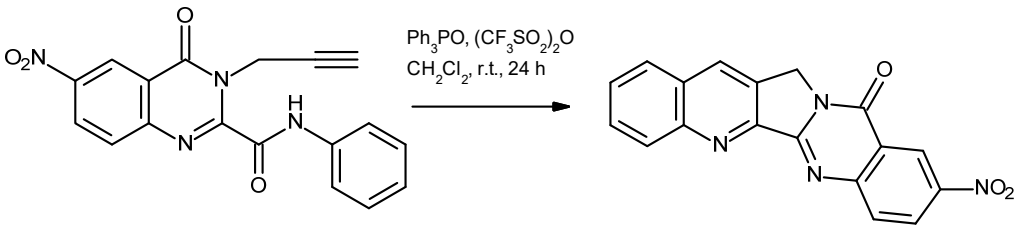
To a solution of aniline (0.745 g, 8 mmol) in dry 1,2-dichloroethane (20 mL) under argon was added dropwise a 2M solution of $AlMe_3$ (4.0 mL, 8 mmol) in heptane. The mixture was stirred for 30 min at room temperature, then ethyl 6-nitro-4-oxo-3,4-dihydroquinazoline-2-carboxylate [1,2] (1.32 g, 5 mmol) was added in one portion, and the mixture was refluxed for 2 h. After cooling to 0 °C, it was then quenched by slow addition of 2 N HCl (20 mL), followed by water (80 mL). The mixture was kept in the refrigerator for 30 min, then the precipitate was collected by filtration and it was washed with 70% EtOH and dried to afford the product (1.48 g, 95%) as almost colorless crystals, m.p. 320–325 °C (DMF/water). .). ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 13.50–12.50 (br, 1H, quinazoline NH), 10.85 (s, 1H, amide NH), 8.85 (d, *J* = 2.6 Hz, 1H, 5-H), 8.62 (dd, *J* = 9.0, 2.7 Hz, 1H, 7-H), 8.05 (d, *J* = 9.0 Hz, 1H, 8-H), 7.88–7.86 (m, 2H, phenyl 2'-H, 6'-H), 7.43–7.39 (m, 2H, phenyl 3'-H, 5'-H), 7.21–7.17 (m, 1H, phenyl 4'-H) ppm. ^{13}C-NMR (100 MHz, DMSO-d_6): δ = 161.4 (4-C), 158.0 (amide C=O), 151.2 (8a-C), 149.6 (2-C), 145.7 (6-C), 137.6 (phenyl 1'-C), 129.3 (8-C), 128.9 (phenyl 3'-C, 5'-C), 128.5 (7-C), 124.8 (phenyl 4'-C), 122.9 (4a-C), 122.1 (5-C), 120.6 (phenyl 2'-C, 6'-C) ppm. MS (EI, 70 eV): *m/z* (%) = 310 (M^+, 54%), 268 (34), 191 (65), 164 (100), 133 (22), 117 (23), 91 (32), 90 (52), 77 (40), 65 (34). HRMS (ESI-TOF) calcd. for $C_{15}H_{10}N_4NaO_4$ ([M+Na]$^+$): 333.0594. Found: 333.0588.

N-Phenyl-6-nitro-4-oxo-3-(prop-2-yn-1-yl)-3,4-dihydroquinazoline-2-carboxamide



To a suspension of finely ground *N*-phenyl-6-nitro-4-oxo-3,4-dihydroquinazoline-2-carboxamide (155 mg, 0.5 mmol) in DMSO (20 mL) were added finely powdered KOH (41 mg, 0.72 mmol) and tetra-*n*-butylammonium bromide (14 mg), and the mixture was sonicated in an ultrasound cleaning bath for 15 min. Then, a solution of propargyl bromide (90 mg of a 80% solution in toluene, 0.6 mmol) in DMSO (10 mL) was dropwise added with vigorous stirring over a period of 2 h. Stirring was continued at room temperature for 24 h, then the mixture was diluted with water (150 mL) and it was kept in the refrigerator for 30 min. The precipitate was collected by filtration, washed with water and dried to give the product (164 mg, 94%) as pale yellow crystals, m.p. 270–273 °C (1-PrOH). ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 11.23 (s, 1H, NH), 8.90 (d, *J* = 2.7 Hz, 1H, 5-H), 8.66 (dd, *J* = 8.9, 2.7 Hz, 1H, 7-H), 8.06 (d, *J* = 8.9 Hz, 1H, 8-H), 7.74 (dd, *J* = 8.6, 1.0 Hz, 2H, phenyl 2'-H, 6'-H), 7.47–7.37 (m, 2H, phenyl 3'-H, 5'-H), 7.24–7.17 (m, 1H, phenyl 4'-H), 5.06 (d, *J* = 2.5 Hz, 2H, NCH_2), 3.39 (t, *J* = 2.5 Hz, 1H, acetylene H) ppm. ^{13}C-NMR (100 MHz, DMSO-d_6): δ = 159.2 (4-C), 158.9 (amide C=O), 151.0 (2-C), 149.9 (8a-C), 146.2 (6-C), 137.5 (phenyl 1'-C), 129.6 (8-C), 129.2 (7-C), 129.0 (phenyl 3'-C, 5'-C), 124.9 (phenyl 4'-C), 122.5 (5-C), 121.3 (4a-C), 120.3 (phenyl 2'-C, 6'-C), 77.7 (propargyl 2-C), 75.6 (propargyl 3-C), 33.7 (propargyl 1-C) ppm. MS (EI, 70 eV): *m/z* (%) = 348 (M^+, 40%), 347 (100), 319 (32), 183 (44), 164 (35), 155 (39), 130 (87), 77 (38). HRMS (ESI-TOF) calcd. for $C_{18}H_{12}N_4NaO_4$ ([M+Na]$^+$): 371.0751. Found: 371.0747.

9-Nitroquino[2',3':3,4]pyrrolo[2,1-b]quinazolin-11(13H)-one (**1**) [3]



To a solution of triphenylphosphine oxide (835 mg, 3 mmol) in dry CH_2Cl_2 (22 mL) was dropwise added trifluoromethanesulfonic anhydride (0.25 mL, 1.5 mmol) at 0 °C under argon, and the mixture was stirred at the same temperature for 15 min. Then, *N*-phenyl-6-nitro-4-oxo-3-(prop-2-yn-1-yl)-3,4-dihydroquinazoline-2-carboxamide (348 mg, 1 mmol) was added in one portion at 0 °C. The mixture was stirred at the same temperature for 15 min, then for 24 h at room temperature. The precipitate was collected by filtration and washed with CH_2Cl_2. It was then resuspended in 10% aq. $NaHCO_3$ and stiirred for 30 min. The solid was filtered off, washed with water and dried to afford the product (263 mg, 79%) as pale yellow crystals, m.p. 336–338 °C (lit. [3]: >300 °C). ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 8.97 (d, *J* = 2.5 Hz, 1H, 10-H), 8.82 (s, 1H, 14-H), 8.66 (dd, *J* = 9.0, 2.5 Hz, 1H, 8-H), 8.31 (d, *J* = 8.1 Hz, 1H, 4-H), 8.21 (d, *J* = 8.9 Hz, 1H, 1-H), 8.15 (d, *J* = 9.0 Hz, 1H, 7-H), 7.98–7.91 (m, 1H, 3-H), 7.84–7.77 (m, 1H, 2-H), 5.38 (s, 2H, 13-CH_2) ppm. MS (EI, 70 eV): *m/z* (%) = 331 (22%), 330 (M^+, 100), 284 (27), 256 (20), 140 (23), 71 (22), 57 (40), 55 (27). HRMS (ESI-TOF) calcd. for $C_{18}H_{10}N_4NaO_3$ ([M+Na]$^+$): 353.06451. Found: 353.0642.

References

1. Althuis, T.H.; Moore, P.F.; Hess, H.-J. Development of ethyl 3,4-dihydro-4-oxopyrimido[4,5-*b*]quinoline-2-carboxylate, a new prototype with oral antiallergy activity. *J. Med. Chem.* **1979**, *22*, 44–48; doi: 10.1021/jm00187a011
2. Gege, C.; Schneider, M.; Chevrier, C.; Deng, H.; Sucholeiki, I.; Gallagher, B.M.; Bosies, M.; Steeneck, C.; Wu, X.; Hochguertel, M.; Nolte, B.; Taveras, A. Preparation of heterobicyclic metalloprotease inhibitors. *PCT Int. Appl.* WO 2008063668.
3. Dallavalle, S.; Merlini, L.; Beretta, G.L.; Tinelli, S.; Zunino, F. Synthesis and cytotoxic activity of substituted Luotonin A derivatives. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 5757–5761; doi:10.1016/j.bmcl.2004.09.039

B) Spectra of the title compound, 9-aminoquino[2',3':3,4]pyrrolo[2,1-*b*]quinazolin-11(13*H*)-one (**2**); for instrumentation details, see main text.

Figure S1. EI-MS of compound **2**.

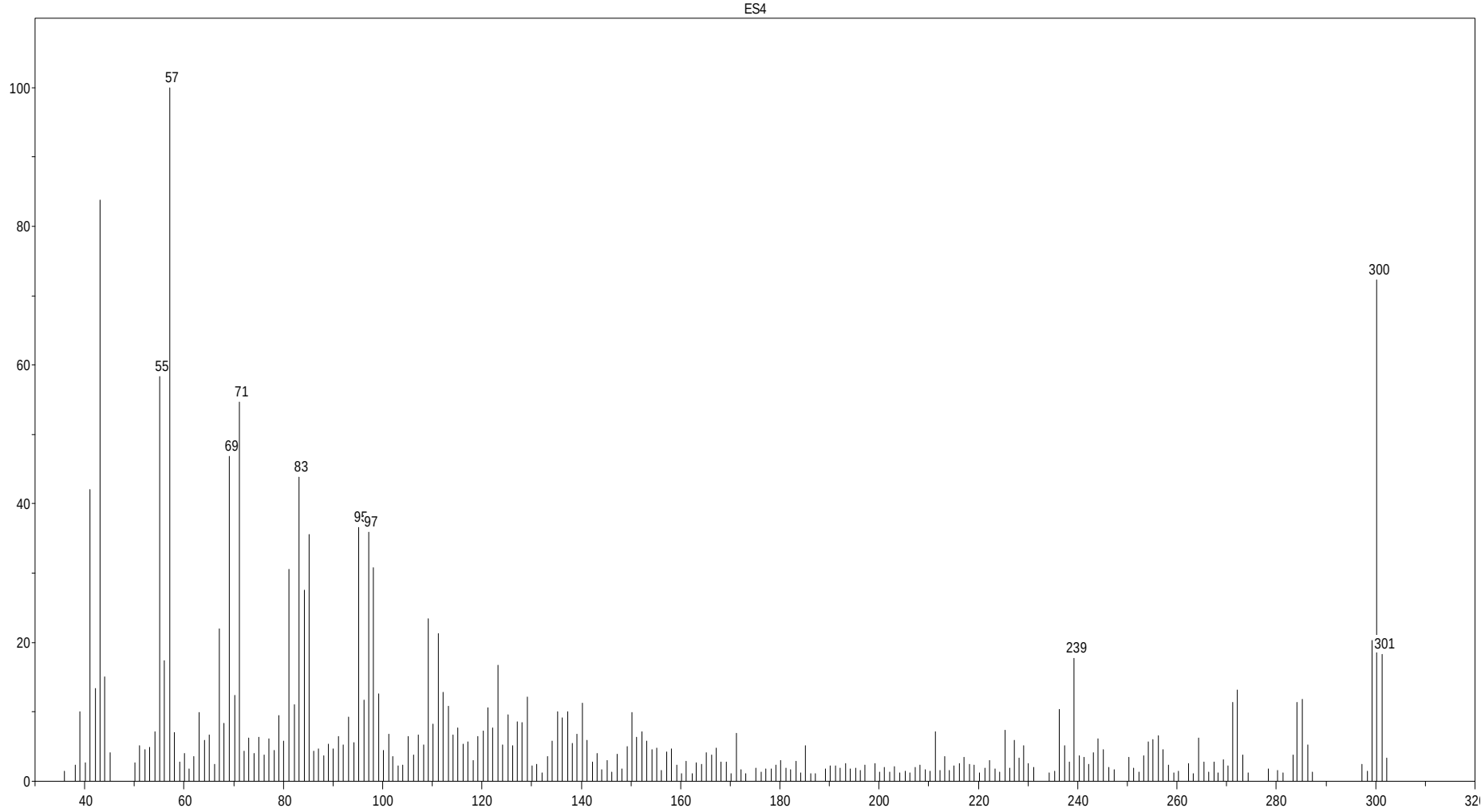


Figure S2. ^{1}H-NMR of compound **2**.

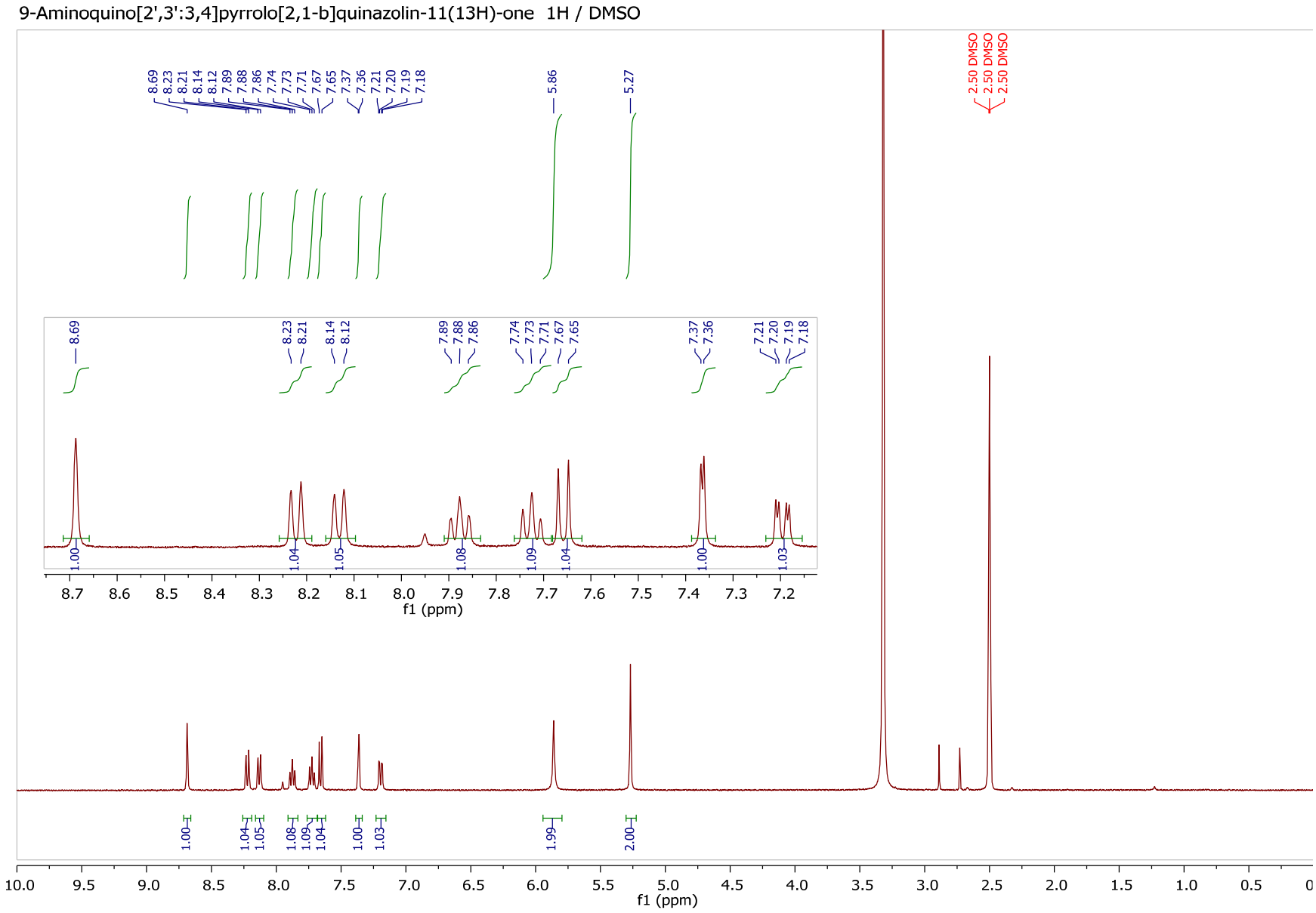


Figure S3. ^{13}C-NMR (APT) of compound **2**.

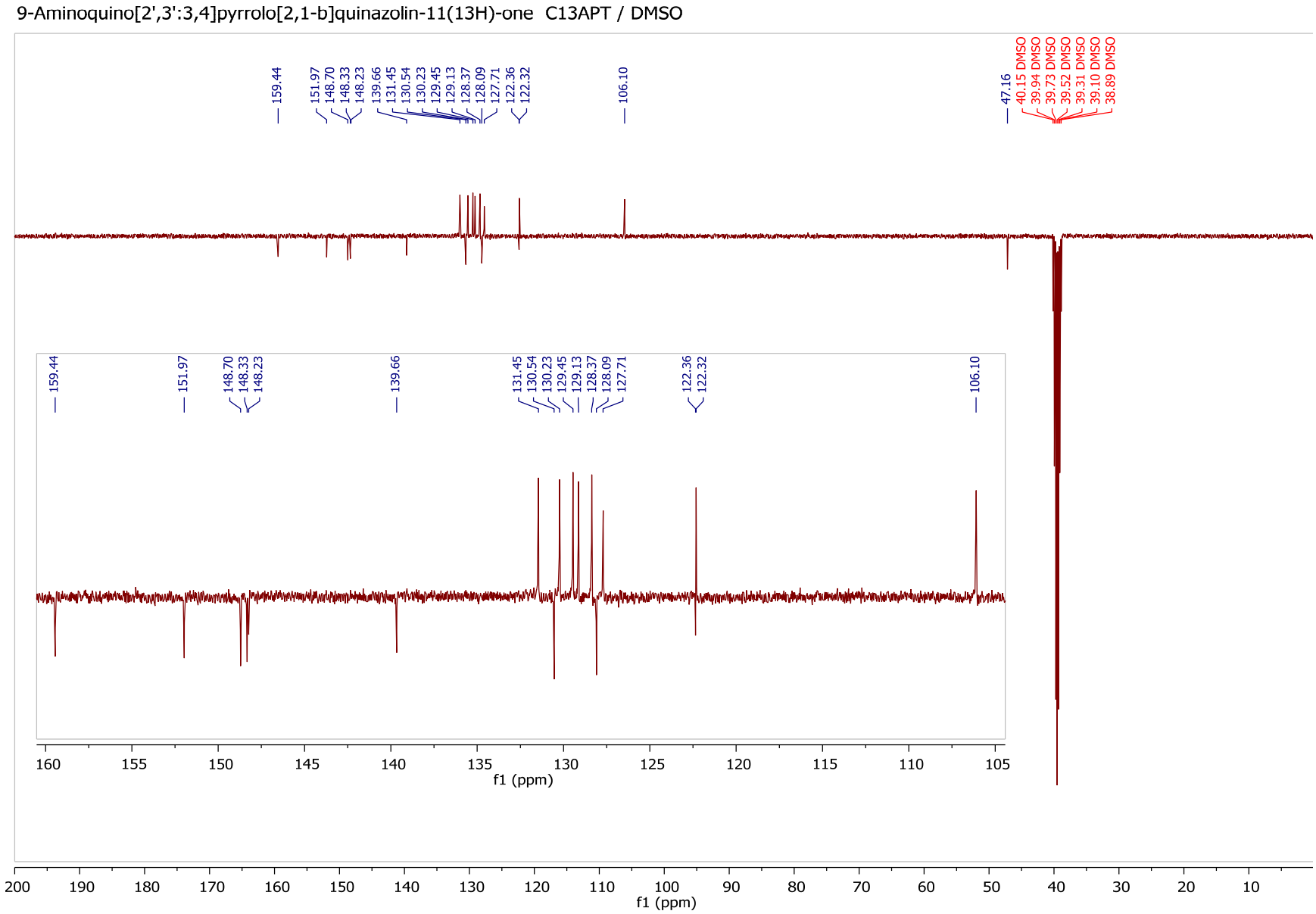


Figure S4. HSQC (overview) of compound **2**.

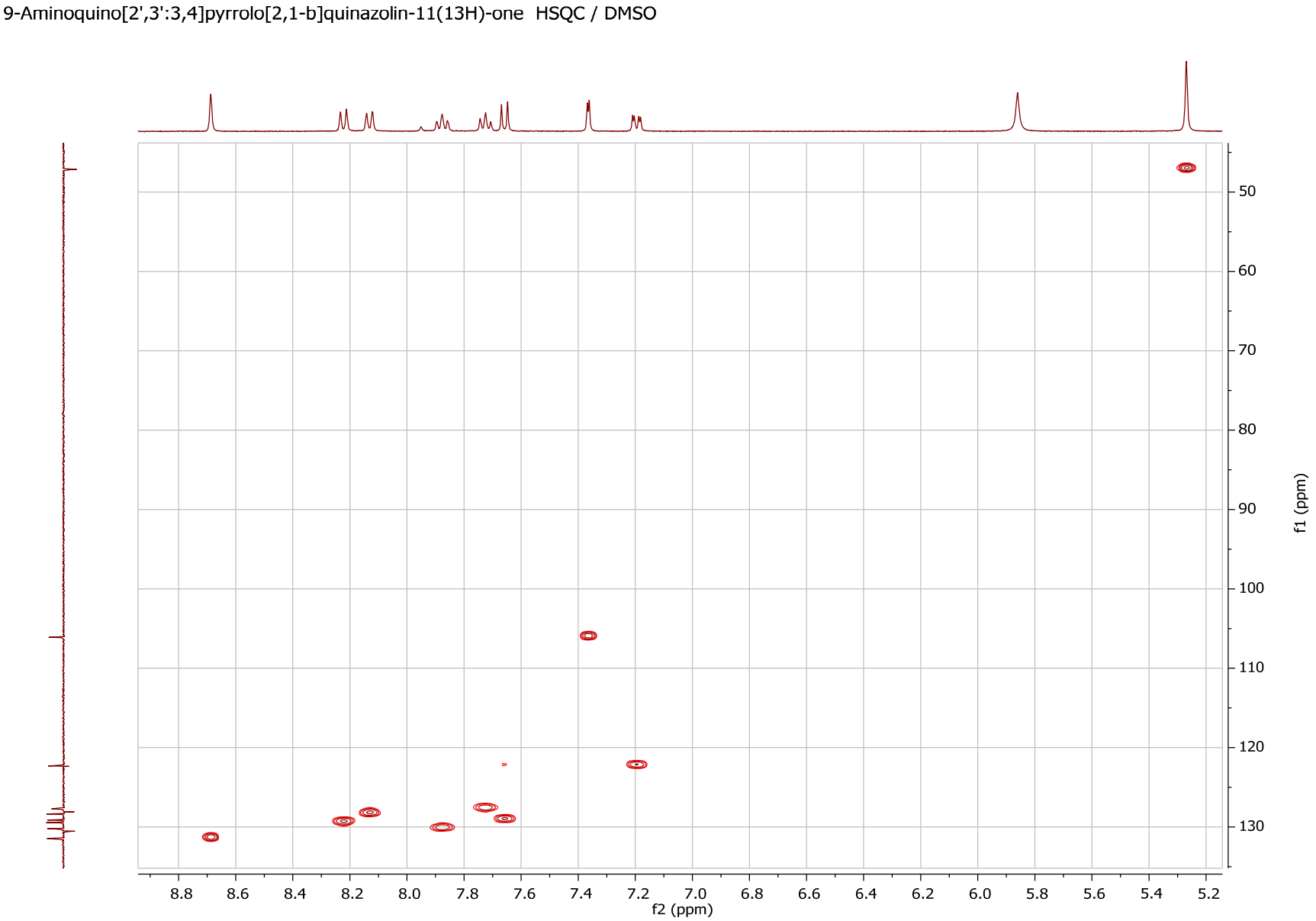


Figure S5. HSQC (expansion) of compound **2**.

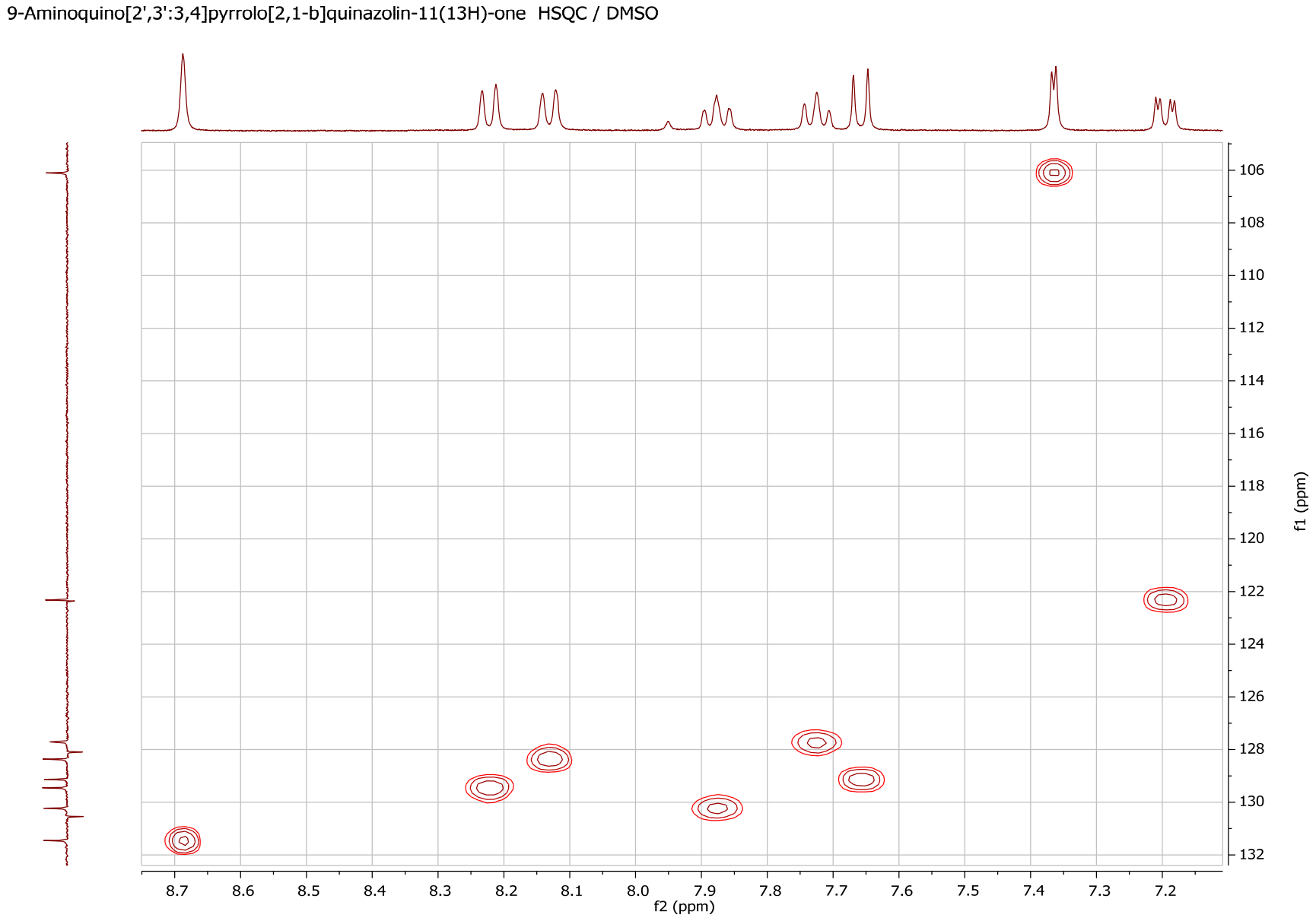


Figure S6. HMBC (overview) of compound **2**.

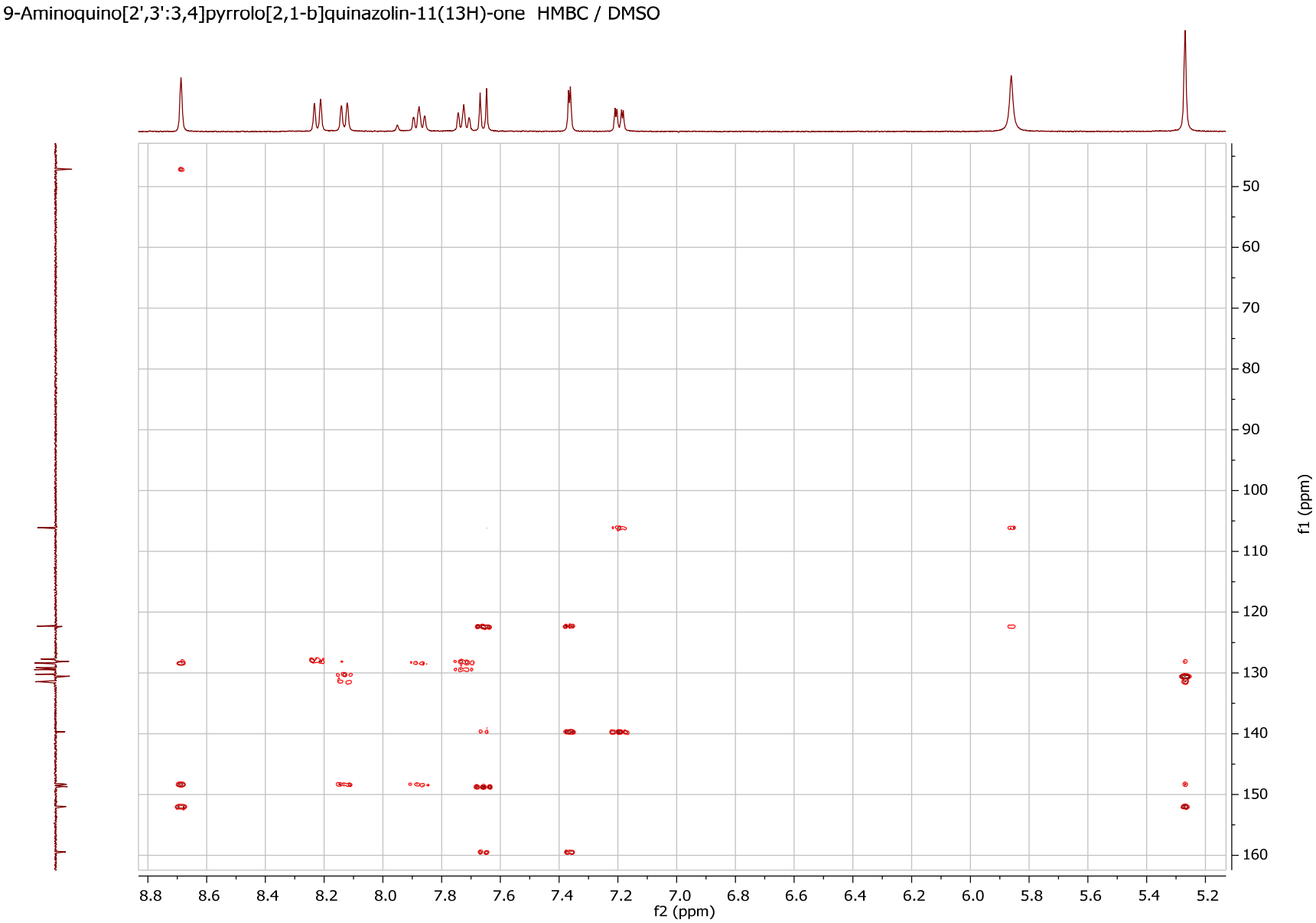


Figure S7. HMBC (expansion) of compound **2**.

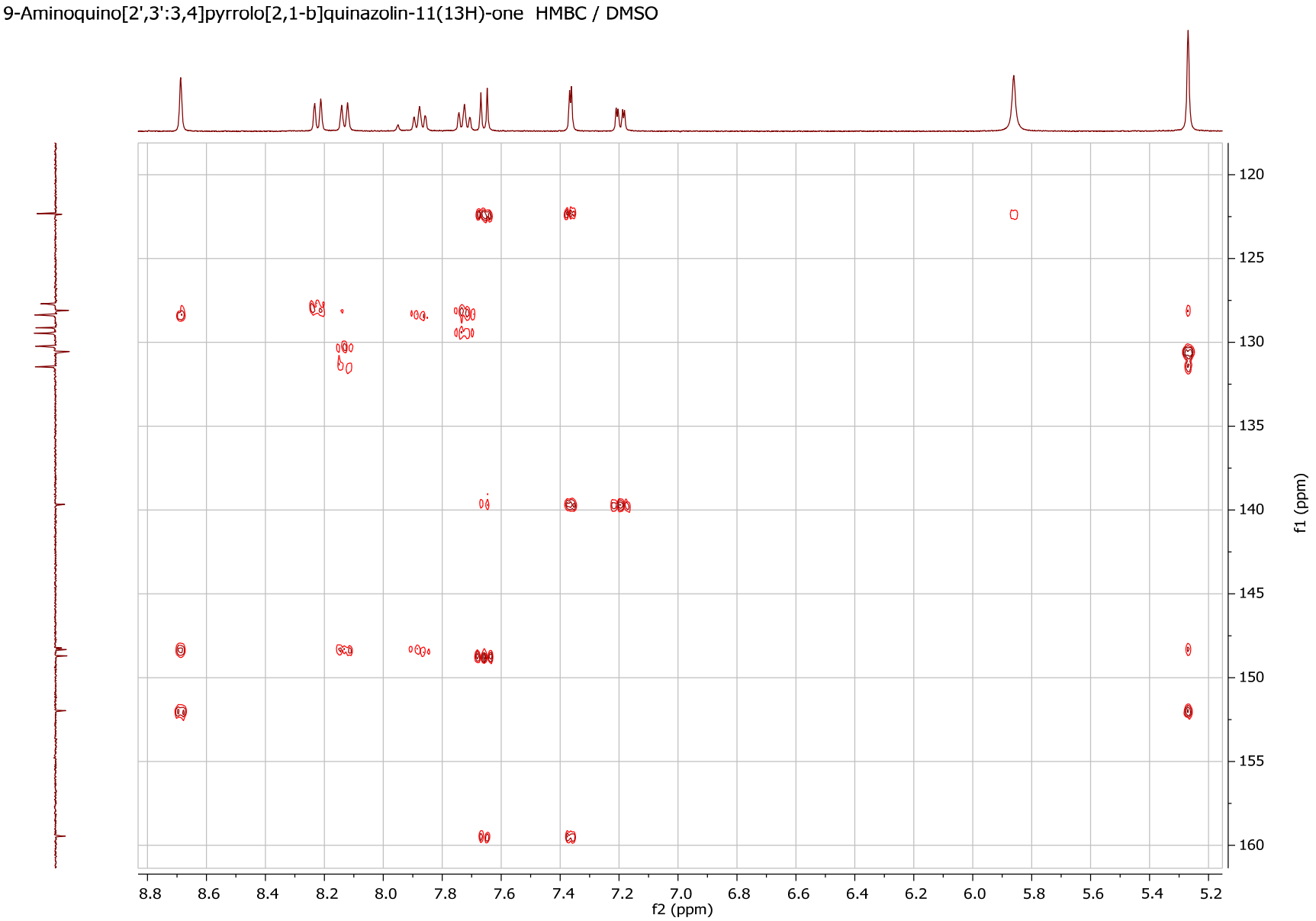


Figure S8. COSY of compound **2**.

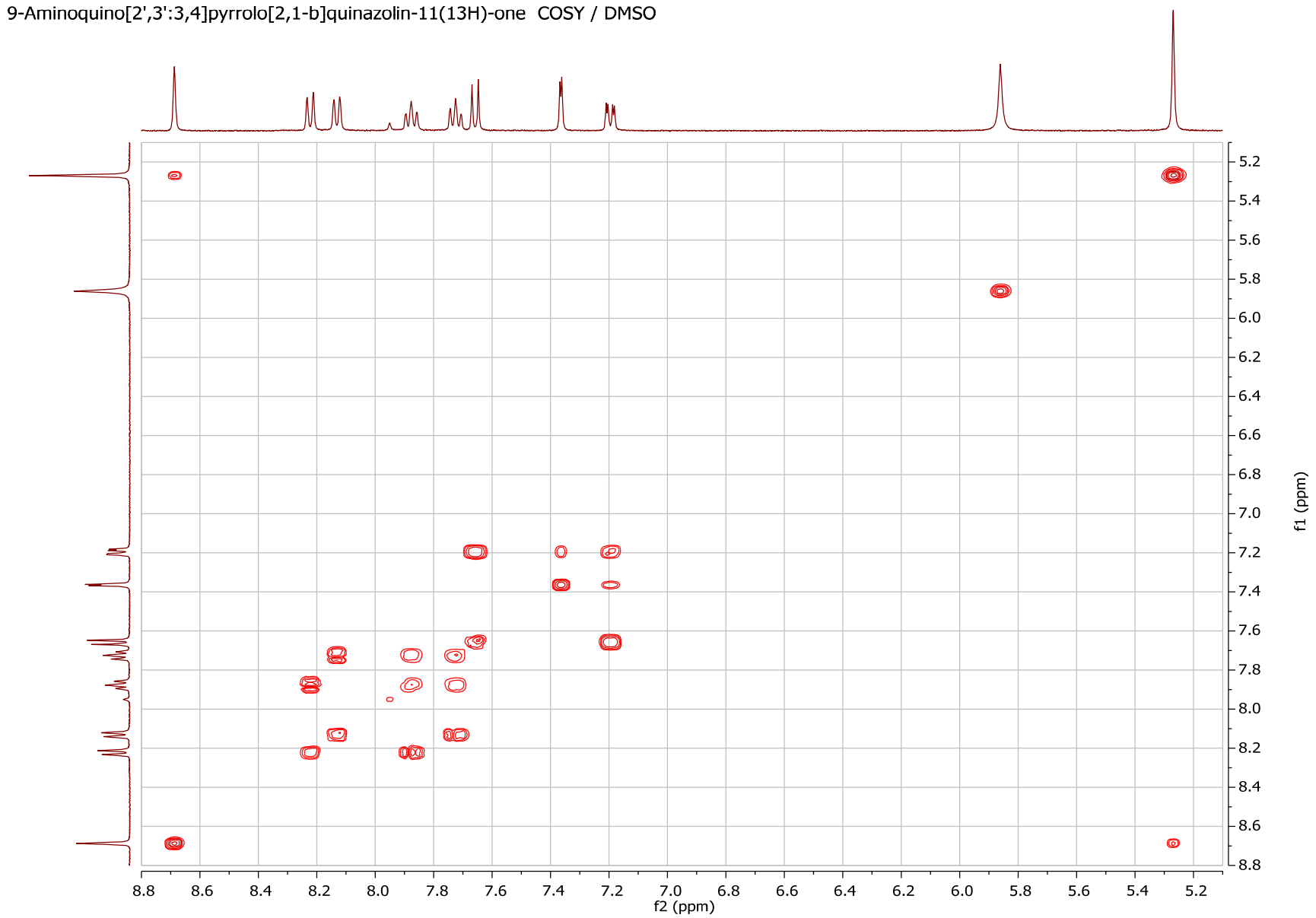


Figure S9. NOESY of compound **2**.