

Supporting Information

Synthesis and *in vitro* antiprotozoal evaluation of novel Knoevenagel hydroxychloroquine derivatives

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Spectroscopic data of compounds **4**, **5** and Knoevenagel adducts **7a-o**

The compounds were obtained through purification in a chromatographic column using silica gel (0.063-0.2 mm / 70-230 mesh ASTM, Macherey-Nagel™) as the stationary phase and CH₂Cl₂:MeOH mixtures up to a ratio of 97:3 as eluent. After the fractions containing the desired product were dried in a vacuum pump and stored at -20 °C.

2-((4-((7-chloroquinolin-4-yl)amino)pentyl)(ethyl)amino)ethan-1-ol (**4**). Colorless transparent oil. Yield 97%. FT-IR (KBr, ν_{\max} cm⁻¹) 3320, 3110, 2967, 2870, 1612, 1577, 1454, 1380, 1332, 1150, 1049, 908, 877, 807, 758, 647, 602. ¹H NMR (400 MHz, CDCl₃, δ ppm) 1.01 (t, 3H, $J = 7.1$ Hz, NCH₂CH₃), 1.31 (d, 3H, $J = 6.4$ Hz, CHCH₃), 1.51–1.79 (m, 4H, CH₂CH₂), 2.42–2.67 (m, 6H, CH₂N), 3.56 (t, 2 H, $J = 5.5$ Hz, NCH₂CH₂O), 3.65–3.77 (m, 1H, CHCH₃) 5.02 (d, 1H, $J = 7.5$ Hz, NH), 6.40 (d, 1H, $J = 5.5$ Hz, CHQn), 7.33 (dd, 1H, $J = 2.2, 9.0$ Hz, CHQn), 7.71 (d, 1H, $J = 9.0$ Hz, CHQn), 7.94 (d, 1H, $J = 2.1$ Hz, CHQn), 8.50 (d, 1H, $J = 5.4$ Hz, CHQn). ¹³C NMR (100 MHz, CDCl₃, δ ppm) 11.9 (NCH₂CH₃), 20.5 (CHCH₃), 24.2 (CH₂CH₂), 34.5 (CH₂CH₂), 47.6 (NCH₂CH₃), 48.4 (CHCH₃), 53.2 (CH₂CH₂CH₂N), 55.0 (NCH₂CH₂O), 58.6 (NCH₂CH₂O), 99.3 (CHQn), 117.4 (CQn), 121.2 (CHQn), 125.2 (CHQn), 128.9 (CHQn), 134.9 (CQn), 149.1 (CQn), 149.5 (CQn), 152.1 (CHQn).

2-((4-((7-chloroquinolin-4-yl)amino)pentyl)(ethyl)amino)ethyl 3-oxobutanoate (**5**). Yellow viscous oil. Yield 77%. FT-IR (KBr, ν_{\max} cm⁻¹) 3406, 2971, 2868, 1741, 1716, 1575, 1454, 1378, 1332, 1148, 1078, 1033, 881, 809, 647. ¹H NMR (400 MHz, CDCl₃, δ ppm) 0.99 (t, 3H, $J = 7.1$ Hz, NCH₂CH₃), 1.32 (d, 3H, $J = 6.3$ Hz, CHCH₃), 1.51–1.79 (m, 4H, CH₂CH₂), 2.23 (s, 3 H, COCH₃), 2.48 (t, 2H, $J = 6.8$ Hz, CH₂CH₂CH₂N), 2.55

(q, 2H, $J = 7.1$ Hz, NCH_2CH_3), 2.69 (t, 2H, $J = 6.0$ Hz, $\text{NCH}_2\text{CH}_2\text{O}$), 3.43 (s, 2H, COCH_2), 3.65 – 3.77 (m, 1H, CHCH_3), 4.20 (t, 2H, $J = 6.0$ Hz, $\text{NCH}_2\text{CH}_2\text{O}$), 5.25 (d, 1H, $J = 7.5$ Hz, NH), 6.42 (d, 1H, $J = 5.5$ Hz, CHQn), 7.33 (dd, 1H, $J = 2.1, 9.0$ Hz, CHQn), 7.75 (d, 1H, $J = 9.0$ Hz, CHQn), 7.94 (d, 1H, $J = 2.1$ Hz, CHQn), 8.50 (d, 1H, $J = 5.4$ Hz, CHQn). ^{13}C NMR (100 MHz, CDCl_3 , δ ppm) 11.7 (NCH_2CH_3), 20.3 (CHCH_3), 24.1 (CH_2CH_2), 30.3 (COCH_3), 34.3 (CH_2CH_2), 48.2 (NCH_2CH_3), 48.4 (CHCH_3), 50.2 (COCH_2), 51.6 ($\text{NCH}_2\text{CH}_2\text{O}$), 53.7 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 63.4 ($\text{NCH}_2\text{CH}_2\text{O}$), 99.3 (CHQn), 117.4 (CQn), 121.38 (CHQn), 125.1 (CHQn), 128.7 (CHQn), 134.9 (ClCQn), 149.2 (CQnN), 149.4 (CQnN), 152.0 (CHQn), 167.1 (C=O), 200.76 ($\text{CH}_3\text{C=O}$). HRMS $\text{C}_{22}\text{H}_{30}\text{ClN}_3\text{O}_3$ $[\text{M}+\text{H}]^+$ 420.2049; found, 420.2059.

(*E/Z*)-2-((4-((7-chloroquinolin-4-yl)amino)pentyl)(ethyl)amino)ethyl 2-acetyl-5-methylhex-2-enoate (**7a**). Brown viscous oil. Yield 89%. FT-IR (KBr, ν_{max} cm^{-1}) 3400, 2961, 2868, 1716, 1575, 1538, 1454, 1378, 1335, 1220, 1148, 1076, 1020, 908, 877, 811, 733, 647. ^1H NMR (400 MHz, CDCl_3 , δ ppm) 0.92 **isomer a/b** (t, $J = 7.0$ Hz, 6H, CH_3CHCH_3), 0.95-1.06 **isomer a/b** (m, 3H, NCH_2CH_3), 1.31 **isomer a/b** (d, $J = 6.1$ Hz, 3H, CHCH_3), 1.39-1.86 **isomer a/b** (m, 4H, CH_2CH_2), 1.39-1.86 **isomer a/b** (m, 1H, CH_3CHCH_3), 2.06-2.27 **isomer a/b** (m, 2H, C=CHCH_2), 2.30 **isomer a**, 2.36 **isomer b** (s, 3H, COCH_3), 2.39-2.62 **isomer a/b** (m, 2H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 2.39-2.62 **isomer a/b** (m, 2H, NCH_2CH_3), 2.62-2.81 **isomer a/b** (m, 2H, $\text{NCH}_2\text{CH}_2\text{O}$), 3.63-3.78 **isomer a/b** (m, 1H, CHCH_3), 4.25 **isomer a** (t, $J = 6.0$ Hz, 2H, $\text{NCH}_2\text{CH}_2\text{O}$), 4.30 **isomer b** (td, $J = 6.0, 2.0$ Hz, 2H, $\text{NCH}_2\text{CH}_2\text{O}$), 5.32 **isomer a/b** (d, $J = 6.4$ Hz, 1H, NH), 6.42 **isomer a/b** (d, $J = 4.0$ Hz, 1H, CHQn), 6.82 **isomer a**, 6.92 **isomer b** (t, $J = 7.8$ Hz, 1H, C=CH), 7.32 **isomer a/b** (d, $J = 8.6$ Hz, 1H, CHQn), 7.78 **isomer a/b** (t, $J = 8.7$ Hz, 1H, CHQn), 7.94 **isomer a/b** (s, 1H, CHQn), 8.50 **isomer a/b** (d, $J = 4.5$ Hz, 1H,

CHQ_n). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 11.7 **isomer a**, 11.9 **isomer b** (NCH_2CH_3), 20.3 **isomer a/b** ($CHCH_3$), 22.4 **isomer a/b** (CH_3CHCH_3), 22.5 **isomer a/b** (CH_3CHCH_3), 24.2 **isomer a**, 24.3 **isomer b** (CH_2CH_2), 26.8 **isomer a** ($COCH_3$), 28.2 **isomer a**, 28.3 **isomer b** (CH_3CHCH_3), 31.4 **isomer b** ($COCH_3$), 34.2 **isomer a**, 34.3 **isomer b** (CH_2CH_2), 38.2 **isomer a**, 38.9 **isomer b** ($C=CHCH_2$), 48.1 **isomer a/b** (NCH_2CH_3), 48.5 **isomer a/b** ($CHCH_3$), 51.6 **isomer a**, 51.7 **isomer b** (NCH_2CH_2O), 53.6 **isomer a**, 53.7 **isomer b** ($CH_2CH_2CH_2N$), 63.2 **isomer a/b** (NCH_2CH_2O), 99.2 **isomer a/b** (CHQ_n), 117.4 **isomer a/b** (CQ_n), 121.5 **isomer a/b** (CHQ_n), 125.1 **isomer a/b** (CHQ_n), 128.6 **isomer a/b** (CHQ_n), 134.9 **isomer a/b** ($ClCQ_n$), 136.3 **isomer a**, 137.9 **isomer b** ($C=CH$), 147.8 **isomer a/b** ($C=CH$), 149.2 **isomer a/b** (CQ_nN), 149.3 **isomer a/b** (CQ_nN), 151.8 **isomer a/b** (CHQ_n), 164.4 **isomer a**, 166.6 **isomer b** ($C=O$), 195.4 **isomer a**, 201.5 **isomer b** ($CH_3C=O$). HRMS $C_{27}H_{38}ClN_3O_3$ $[M+H]^+$ 488.2675; found, 488.2681.

(E/Z)-2-((4-((7-chloroquinolin-4-yl)amino)pentyl)(ethyl)amino)ethyl 2-benzylidene-3-oxobutanoate (**7b**). Yellow viscous oil. Yield 86%. FT-IR (KBr, ν_{max} cm^{-1}) 3402, 2971, 2870, 1729, 1665, 1581, 1538, 1452, 1378, 1335, 1250, 1201, 1148, 1078, 1039, 908, 877, 809, 735, 692, 647. 1H NMR (600 MHz, $CDCl_3$, δ ppm) 0.95 **isomer a**, 1.01 **isomer b** (t, $J = 7.1$ Hz, 3H, NCH_2CH_3), 1.27 **isomer a**, 1.31 **isomer b** (d, $J = 6.4$ Hz, 3H, $CHCH_3$), 1.49-1.77 **isomer a/b** (m, 4H, CH_2CH_2), 2.35 **isomer a**, 2.40 **isomer b** (s, 3H, $COCH_3$), 2.46 **isomer a**, 2.50 **isomer b** (t, $J = 6.9$ Hz, 2H, $CH_2CH_2CH_2N$), 2.51 **isomer a**, 2.56 **isomer b** (q, $J = 7.1$ Hz, 2H, NCH_2CH_3), 2.70 **isomer a** (td, $J = 6.0, 3.1$ Hz, 2H, NCH_2CH_2O), 2.74 **isomer b** (t, $J = 5.9$ Hz, 2H, NCH_2CH_2O), 3.62-3.76 **isomer a/b** (m, 1H, $CHCH_3$), 4.31 **isomer a** (t, $J = 5.9$ Hz, 2H, NCH_2CH_2O), 4.33 **isomer b** (td, $J = 6.0, 2.7$ Hz, 2H, NCH_2CH_2O), 5.17 **isomer a**, 5.31 **isomer b** (d, $J = 7.5$ Hz, 1H,

NH), 6.38 **isomer a**, 6.41 **isomer b** (d, $J = 5.6$ Hz, 1H, CHQn), 7.26 **isomer a**, 7.28 **isomer b** (dd, $J = 8.9, 2.2$ Hz, 1H, CHQn), 7.31-7.46 **isomer a/b** (m, 5H, CHAr), 7.51 **isomer a**, 7.67 **isomer b** (s, 1H, C=CH), 7.68 **isomer a**, 7.76 **isomer b** (d, $J = 9.0$ Hz, 1H, CHQn), 7.92 **isomer a**, 7.93 **isomer b** (d, $J = 2.2$ Hz, 1H, CHQn), 8.48 **isomer a**, 8.49 **isomer b** (d, $J = 1.9$ Hz, 1H, CHQn). ^{13}C NMR (100 MHz, CDCl_3 , δ ppm) 11.6 **isomer a**, 12.0 **isomer b** (NCH₂CH₃), 20.2 **isomer a**, 20.3 **isomer b** (CHCH₃), 24.1 **isomer a**, 24.4 **isomer b** (CH₂CH₂), 26.5 **isomer a**, 31.4 **isomer b** (COCH₃), 34.3 **isomer a**, 34.4 **isomer b** (CH₂CH₂), 48.1 **isomer a**, 48.2 **isomer b** (NCH₂CH₃), 48.4 **isomer a**, 48.5 **isomer b** (CHCH₃), 51.5 **isomer a**, 51.6 **isomer b** (NCH₂CH₂O), 53.5 **isomer a**, 53.8 **isomer b** (CH₂CH₂CH₂N), 63.73 **isomer a**, 63.77 **isomer b** (NCH₂CH₂O) 99.2 **isomer a**, 99.3 **isomer b** (CHQn), 117.4 **isomer a**, 117.5 **isomer b** (CQn), 121.3 **isomer a**, 121.4 **isomer b** (CHQn), 125.0 **isomer a**, 125.1 **isomer b** (CHQn), 128.7 **isomer a**, 128.8 **isomer b** (CHQn), 129.0 **isomer a**, 129.1 **isomer b** (2CHAr), 129.7 **isomer a**, 129.8 **isomer b** (2CHAr), 130.7 **isomer a**, 130.9 **isomer b** (CHAr), 132.8 **isomer a**, 132.9 **isomer b** (CAr), 133.9 **isomer a**, 134.7 **isomer b** (C=CH), 134.8 **isomer a**, 134.9 **isomer b** (ClCQn), 141.0 **isomer a**, 141.6 **isomer b** (C=CH), 149.2 **isomer a**, 149.3 **isomer b** (CQnN), 149.4 **isomer a**, 149.5 **isomer b** (CQnN), 152.1 **isomer a/b** (CHQn), 164.5 **isomer a**, 167.9 **isomer b** (C=O), 195.1 **isomer a**, 203.7 **isomer b** (CH₃C=O). HRMS C₂₉H₃₄ClN₃O₃ [M+H]⁺ 508.2362; found, 508.2345.

(*E/Z*)-2-((4-((7-chloroquinolin-4-yl)amino)pentyl)(ethyl)amino)ethyl 2-(4-(dimethylamino)benzylidene)-3-oxobutanoate (**7c**). Orange viscous oil. Yield 47%. FT-IR (KBr, ν_{max} cm⁻¹) 3394, 2969, 2811, 1716, 1649, 1575, 1528, 1450, 1371, 1328, 1263, 1218, 1166, 1064, 1039, 977, 947, 908, 879, 813, 762, 733, 647, 532. ^1H NMR (400

MHz, CDCl₃, δ ppm) 0.98 **isomer a**, 1.01 **isomer b** (t, $J = 7.1$ Hz, 3H, NCH₂CH₃), 1.26 **isomer a**, 1.30 **isomer b** (d, $J = 6.3$ Hz, 3H, CHCH₃), 1.46-1.79 **isomer a/b** (m, 4H, CH₂CH₂), 2.35 **isomer a**, 2.41 **isomer b** (s, 3H, COCH₃), 2.45-2.52 **isomer a/b** (m, 2H, CH₂CH₂CH₂N), 2.55 **isomer a/b** (q, $J = 7.1$ Hz, 2H, NCH₂CH₃), 2.73 **isomer a** (t, $J = 5.8$ Hz, 2H, NCH₂CH₂O), 2.77 **isomer b** (td, $J = 6.0, 3.7$ Hz, 2H, NCH₂CH₂O), 2.99 **isomer a**, 3.01 **isomer b** (s, 6H, ArCN(CH₃)₂), 3.59-3.77 **isomer a/b** (m, 1H, CHCH₃), 4.28 **isomer a** (td, $J = 5.8, 3.0$ Hz, 2H, NCH₂CH₂O), 4.38 **isomer b** (t, $J = 6.0$ Hz, 2H, NCH₂CH₂O), 5.36 **isomer a**, 5.49 **isomer b** (d, $J = 7.5$ Hz, 1H, NH), 6.37 **isomer a**, 6.40 **isomer b** (d, $J = 5.5$ Hz, 1H, CHQn), 6.57 **isomer a**, 6.60 **isomer b** (d, $J = 2.0$ Hz, 2H, CHAr), 7.20 **isomer a**, 7.24 **isomer b** (dd, $J = 9.0, 2.0$ Hz, 1H, CHQn), 7.26 **isomer a/b** (d, $J = 7.0$ Hz, 1H, CHAr), 7.34 **isomer a/b** (d, $J = 9.0$ Hz, 1H, CHAr), 7.41 **isomer a**, 7.57 **isomer b** (s, 1H, C=CH), 7.73 **isomer a**, 7.81 **isomer b** (d, $J = 9.0$ Hz, 1H, CHQn), 7.88-7.92 **isomer a/b** (m, 1H, CHQn), 8.46 **isomer a**, 8.48 **isomer b** (d, $J = 2.4$ Hz, 1H, CHQn). ¹³C NMR (100 MHz, CDCl₃, δ ppm) 11.6 **isomer a**, 11.9 **isomer b** (NCH₂CH₃), 20.1 **isomer a**, 20.2 **isomer b** (CHCH₃), 24.1 **isomer a**, 24.3 **isomer b** (CH₂CH₂), 26.2 **isomer a**, 31.5 **isomer b** (COCH₃), 34.3 **isomer a/b** (CH₂CH₂), 39.99 **isomer a/b** ArCN(CH₃)₂, 48.1 **isomer a**, 48.2 **isomer b** (NCH₂CH₃), 48.4 **isomer a**, 48.5 **isomer b** (CHCH₃), 51.5 **isomer a**, 51.6 **isomer b** (NCH₂CH₂O), 53.5 **isomer a**, 53.7 **isomer b** (CH₂CH₂CH₂N), 63.1 **isomer a**, 63.5 **isomer b** (NCH₂CH₂O), 99.2 **isomer a/b** (CHQn), 111.7 **isomer a/b** (2CHAR), 117.4 **isomer a**, 117.5 **isomer b** (CQn), 119.7 **isomer a**, 120.0 **isomer b** (CAr), 121.6 **isomer a**, 121.7 **isomer b** (CHQn), 125.0 **isomer a/b** (CHQn), 127.6 **isomer a** (C=CH), 128.5 **isomer a/b** (CHQn), 129.1 **isomer b** (C=CH), 132.2 **isomer a**, 132.3 **isomer b** (2CHAR), 134.7 **isomer a**, 134.8 **isomer b** (ClCQn), 141.9 **isomer a**, 142.6 **isomer b** (C=CH), 149.3 **isomer a/b** (CQnN), 149.4 **isomer a/b** (CQnN), 151.9 **isomer a/b** (CHQn), 152.2

isomer a/b (ArCN(CH₃)₂), 165.3 **isomer a**, 169.2 **isomer b** (C=O), 195.1 **isomer a**, 205.2 **isomer b** (CH₃C=O). HRMS C₃₁H₃₉ClN₄O₃ [M+H]⁺ 551.2784; found, 551.2783.

(E/Z)-2-((4-((7-chloroquinolin-4-yl)amino)pentyl)(ethyl)amino)ethyl 2-(4-methoxybenzylidene)-3-oxobutanoate (7d). Yellow viscous oil. Yield 75%. FT-IR (KBr, ν_{\max} cm⁻¹) 3402, 2969, 2839, 1718, 1655, 1601, 1577, 1513, 1454, 1425, 1378, 1332, 1259, 1203, 1174, 1078, 1029, 908, 879, 829, 758, 647, 540. ¹H NMR (600 MHz, CDCl₃, δ ppm) 0.97 **isomer a**, 1.01 **isomer b** (t, J = 7.1 Hz, 3H, NCH₂CH₃), 1.26 **isomer a**, 1.31 **isomer b** (d, J = 6.4 Hz, 3H, CHCH₃), 1.49-1.78 **isomer a/b** (m, 4H, CH₂CH₂), 2.38 **isomer a/b** (s, 3H, COCH₃), 2.47 **isomer a**, 2.49 **isomer b** (t, J = 6.5 Hz, 2H, CH₂CH₂CH₂N), 2.54 **isomer a**, 2.55 **isomer b** (q, J = 7.1 Hz, 2H, NCH₂CH₃), 2.70-2.79 **isomer a/b** (m, 2H, NCH₂CH₂O), 3.61-3.75 **isomer a/b** (m, 1H, CHCH₃), 3.81 **isomer a**, 3.82 **isomer b** (s, 3H, ArOCH₃), 4.29 **isomer a** (t, J = 6.0 Hz, 2H, NCH₂CH₂O), 4.36 **isomer b** (td, J = 6.0, 1.0 Hz, 2H, NCH₂CH₂O), 5.27 **isomer a**, 5.39 **isomer b** (d, J = 7.5 Hz, 1H, NH), 6.38 **isomer a**, 6.41 **isomer b** (d, J = 5.5 Hz, 1H, CHQn), 6.85 **isomer a**, 6.87 **isomer b** (d, J = 3.4 Hz, 2H, CHAr), 7.23 **isomer a**, 7.26 **isomer b** (dd, J = 2.2, 8.9 Hz, 1H, CHQn), 7.31 **isomer a**, 7.40 **isomer b** (d, J = 8.8 Hz, 2H, CHAr), 7.44 **isomer a**, 7.60 **isomer b** (s, 1H, C=CH), 7.71 **isomer a**, 7.78 **isomer b** (d, J = 9.0 Hz, 1H, CHQn), 7.91 **isomer a**, 7.92 **isomer b** (d, J = 2.3 Hz, 1H, CHQn), 8.47 **isomer a**, 8.48 **isomer b** (d, J = 4.0 Hz, 1H, CHQn). ¹³C NMR (150 MHz, CDCl₃, δ ppm) δ 11.5 **isomer a**, 11.9 **isomer b** (NCH₂CH₃), 20.2 **isomer a/b** (CHCH₃), 24.1 **isomer a**, 24.3 **isomer b** (CH₂CH₂), 26.4 **isomer a**, 31.4 **isomer b** (COCH₃), 34.2 **isomer a**, 34.3 **isomer b** (CH₂CH₂), 48.1 **isomer a/b** (NCH₂CH₃), 48.4 **isomer a**, 48.5 **isomer b** (CHCH₃), 51.5 **isomer a**, 51.6 **isomer b** (NCH₂CH₂O), 53.5 **isomer a**, 53.7 **isomer b** (CH₂CH₂CH₂N), 55.5 **isomer a/b** (ArOCH₃), 63.5 **isomer a**, 63.7 **isomer b**

(NCH₂CH₂O), 99.2 **isomer a/b** (CHQn), 114.5 **isomer a/b** (2CHAr), 117.3 **isomer a**, 117.4 **isomer b** (CQn), 121.5 **isomer a**, 121.6 **isomer b** (CHQn), 125.0 **isomer a**, 125.1 **isomer b** (CHQn), 125.2 **isomer a**, 125.3 **isomer b** (CAr), 128.6 **isomer a/b** (CHQn), 131.2 **isomer a** (C=CH), 131.8 **isomer a**, 131.9 **isomer b** (CHAr), 132.3 **isomer b** (C=CH), 134.7 **isomer a**, 134.8 **isomer b** (ClCQn), 140.8 **isomer a**, 141.4 **isomer b** (C=CH), 149.2 **isomer a/b** (CQnN), 149.3 **isomer a/b** (CQnN), 151.9 **isomer a/b** (CHQn), 161.7 **isomer a**, 161.9 **isomer b** (ArCOCH₃), 164.8 **isomer a**, 168.3 **isomer b** (C=O), 195.1 **isomer a**, 204.3 **isomer b** (CH₃C=O). HRMS C₃₀H₃₆ClN₃O₄ [M+H]⁺ 538.2467; found, 538.2478.

(E/Z)-2-((4-((7-chloroquinolin-4-yl)amino)pentyl)(ethyl)amino)ethyl 2-(3,4-dimethoxybenzylidene)-3-oxobutanoate (7e). Yellow viscous oil. Yield 64%. FT-IR (KBr, ν_{\max} cm⁻¹) 3400, 2967, 2837, 1723, 1659, 1575, 1517, 1454, 1378, 1335, 1252, 1226, 1146, 1078, 1022, 908, 852, 809, 731, 647, 600, 550. ¹H NMR (400 MHz, CDCl₃, δ ppm) 0.96 **isomer a**, 1.01 **isomer b** (t, *J* = 7.1 Hz, 3H, NCH₂CH₃), 1.26 **isomer a**, 1.31 **isomer b** (d, *J* = 6.2 Hz, 3H, CHCH₃), 1.45-1.81 **isomer a/b** (m, 4H, CH₂CH₂), 2.38 **isomer a/b** (s, 3H, COCH₃), 2.42-2.61 **isomer a/b** (m, 4H, CH₂CH₂CH₂N and NCH₂CH₃), 2.74 **isomer a/b** (t, *J* = 5.8 Hz, 2H, NCH₂CH₂O), 3.60-3.78 **isomer a/b** (m, 1H, CHCH₃), 3.82 **isomer a**, 3.85 **isomer b** (s, 3H, ArOCH₃), 3.90 **isomer a/b** (s, 3H, ArOCH₃), 4.30 **isomer a** (t, *J* = 5.9 Hz, 2H, NCH₂CH₂O), 4.32-4.41 **isomer b** (m, 2H, NCH₂CH₂O), 5.29 **isomer a**, 5.36 **isomer b** (d, *J* = 7.0 Hz, 1H, NH), 6.39 **isomer a**, 6.42 **isomer b** (d, *J* = 5.5 Hz, 1H, CHQn), 6.82 **isomer a**, 6.84 **isomer b** (d, *J* = 9.0 Hz, 1H, CHAr), 6.89 **isomer a** (s, 1H, CHAr), 6.98 **isomer a** (d, *J* = 8.5 Hz, 1H, CHAr), 7.00 **isomer b** (s, 1H, CHAr), 7.07 **isomer b** (d, *J* = 8.5 Hz, 1H CHAr), 7.22-7.29 **isomer a/b** (m, 1H, CHQn), 7.44 **isomer a**, 7.59 **isomer b** (s, 1H, C=CH), 7.74 **isomer**

a, 7.78 **isomer b** (d, $J = 9.0$ Hz, 1H, CHQn), 7.88-7.96 **isomer a/b** (m, 1H, CHQn), 8.49 **isomer a/b** (d, $J = 5.3$ Hz, 1H, CHQn). ^{13}C NMR (100 MHz, CDCl_3 , δ ppm) δ 11.5 **isomer a**, 11.9 **isomer b** (NCH_2CH_3), 20.1 **isomer a**, 20.2 **isomer b** (CHCH_3), 24.0 **isomer a**, 24.3 **isomer b** (CH_2CH_2), 26.3 **isomer a**, 31.5 **isomer b** (COCH_3), 34.3 **isomer a/b** (CH_2CH_2), 48.1 **isomer a/b** (NCH_2CH_3), 48.3 **isomer a**, 48.4 **isomer b** (CHCH_3), 51.5 **isomer a**, 51.6 **isomer b** ($\text{NCH}_2\text{CH}_2\text{O}$), 53.5 **isomer a**, 53.7 **isomer b** ($\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 55.9 **isomer a/b** (ArOCH_3), 56.0 **isomer a/b** (ArOCH_3), 63.5 **isomer a**, 63.9 **isomer b** ($\text{NCH}_2\text{CH}_2\text{O}$), 99.2 **isomer a/b** (CHQn), 111.1 **isomer a/b** (CHAr), 111.9 **isomer a**, 112.2 **isomer b** (CHAr), 117.3 **isomer a**, 117.4 **isomer b** (CQn), 121.5 **isomer a/b** (CHQn), 124.2 **isomer a**, 124.6 **isomer b** (CHAr), 125.0 **isomer a/b** (CHQn), 125.5 **isomer a/b** (CAr), 128.7 **isomer a/b** (CHQn), 131.5 **isomer a**, 132.6 **isomer b** ($\text{C}=\text{CH}$), 134.7 **isomer a/b** (ClCQn), 140.9 **isomer a**, 141.5 **isomer b** ($\text{C}=\text{CH}$), 149.1 **isomer a/b** (CQnN), 149.2 **isomer a/b** (CQnN), 149.4 **isomer a/b** (ArCOCH_3), 151.4 **isomer a**, 151.6 **isomer b** (ArCOCH_3), 152.0 **isomer a/b** (CHQn), 164.7 **isomer a**, 168.3 **isomer b** ($\text{C}=\text{O}$), 195.0 **isomer a**, 204.2 **isomer b** ($\text{CH}_3\text{C}=\text{O}$). HRMS $\text{C}_{31}\text{H}_{38}\text{ClN}_3\text{O}_5$ $[\text{M}+\text{H}]^+$ 568.2573; found, 568.2621.

(*E/Z*)-2-((4-((7-chloroquinolin-4-yl)amino)pentyl)(ethyl)amino)ethyl 2-(4-fluorobenzylidene)-3-oxobutanoate (**7f**). Yellow viscous oil. Yield 73%. FT-IR (KBr, ν_{max} cm^{-1}) 3402, 2969, 2870, 1729, 1698, 1665, 1575, 1509, 1454, 1378, 1332, 1240, 1199, 1162, 1078, 1039, 905, 879, 834, 758, 647, 522. ^1H NMR (600 MHz, CDCl_3 , δ ppm) 0.96 **isomer a**, 1.01 **isomer b** (t, $J = 7.1$ Hz, 3H, NCH_2CH_3), 1.27 **isomer a**, 1.31 **isomer b** (d, $J = 6.4$ Hz, 3H, CHCH_3), 1.48-1.77 **isomer a/b** (m, 4H, CH_2CH_2), 2.35 **isomer a**, 2.39 **isomer b** (s, 3H, COCH_3), 2.46 **isomer a**, 2.49 **isomer b** (t, $J = 6.6$ Hz, 2H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 2.53 **isomer a**, 2.56 **isomer b** (q, $J = 7.1$ Hz, 2H, NCH_2CH_3), 2.71

isomer a (td, $J = 6.0, 2.0$ Hz, 2H, $\text{NCH}_2\text{CH}_2\text{O}$), 2.74 **isomer b** (t, $J = 6.0$ Hz, 2H, $\text{NCH}_2\text{CH}_2\text{O}$), 3.63-3.76 **isomer a/b** (m, 1H, CHCH_3), 4.30 **isomer a**, 4.33 **isomer b** (t, $J = 6.0$ Hz, 2H, $\text{NCH}_2\text{CH}_2\text{O}$), 5.16-5.25 **isomer a**, 5.25-5.34 **isomer b** (m, 1H, NH), 6.39 **isomer a**, 6.42 **isomer b** (d, $J = 5.5$ Hz, 1H, CHQn), 7.04 **isomer a/b** (t, $J = 8.5$ Hz, 2H, CHAr), 7.23-7.30 **isomer a/b** (m, 1H, CHQn), 7.34 **isomer a**, 7.36 **isomer b** (d, $J = 5.3$ Hz, 1H, CHAr), 7.43 **isomer a**, 7.44 **isomer b** (d, $J = 5.3$ Hz, 1H, CHAr), 7.45 **isomer a**, 7.60 **isomer b** (s, 1H, C=CH), 7.68-7.73 **isomer a**, 7.74-7.81 **isomer b** (m, 1H, CHQn), 7.91 **isomer a**, 7.92 **isomer b** (d, $J = 2.2$ Hz, 1H, CHQn), 8.48 **isomer a**, 8.49 **isomer b** (d, $J = 4.5$ Hz, 1H, CHQn). ^{13}C NMR (100 MHz, CDCl_3 , δ ppm) 11.5 **isomer a**, 11.8 **isomer b** (NCH_2CH_3), 20.1 **isomer a**, 20.2 **isomer b** (CHCH_3), 23.9 **isomer a**, 24.2 **isomer b** (CH_2CH_2), 26.4 **isomer a**, 31.3 **isomer b** (COCH_3), 34.1 **isomer a**, 34.2 **isomer b** (CH_2CH_2), 47.9 **isomer a**, 48.0 **isomer b** (NCH_2CH_3), 48.3 **isomer a**, 48.4 **isomer b** (CHCH_3), 51.4 **isomer a**, 51.5 **isomer b** ($\text{NCH}_2\text{CH}_2\text{O}$), 53.4 **isomer a**, 53.6 **isomer b** ($\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 63.6 **isomer a**, 63.7 **isomer b** ($\text{NCH}_2\text{CH}_2\text{O}$), 99.1 **isomer a/b** (CHQn), 115.9 **isomer a**, 116.0 **isomer b** (CHAr), 116.2 **isomer a**, 116.3 **isomer b** (CHAr), 117.3 **isomer a**, 117.4 **isomer b** (CQn), 121.4 **isomer a**, 121.5 **isomer b** (CHQn), 124.8 **isomer a**, 124.9 **isomer b** (CHQn), 128.5 **isomer a/b** (CHQn), 128.9 **isomer a**, 129.0 **isomer b** (d, $J = 3.3$ Hz, CAr), 131.7 **isomer a/b** (CHAr), 131.8 **isomer a/b** (CHAr), 133.5 **isomer a**, 134.3 **isomer b** (C=CH), 134.7 **isomer a/b** (ClCQn), 139.5 **isomer a**, 140.1 **isomer b** (C=CH), 149.1 **isomer a**, 149.2 **isomer b** (CQnN), 149.3 **isomer a/b** (CQnN), 151.9 **isomer a/b** (CHQn), 162.6 **isomer a** (d, $J = 12.7$ Hz, FCAr), 164.3 **isomer a** (C=O), 165.1 **isomer b** (d, $J = 12.7$ Hz, FCAr), 167.6 **isomer b** (C=O), 194.8 **isomer a**, 203.4 **isomer b** ($\text{CH}_3\text{C=O}$). HRMS $\text{C}_{29}\text{H}_{33}\text{ClFN}_3\text{O}_3$ $[\text{M}+\text{H}]^+$ 526.2267; found, 526.2259.

(*E/Z*)-2-((4-((7-chloroquinolin-4-yl)amino)pentyl)(ethyl)amino)ethyl 2-(2-chlorobenzylidene)-3-oxobutanoate (**7g**). Yellow viscous oil. Yield 78%. FT-IR (KBr, ν_{\max} cm^{-1}) 3406, 2969, 2868, 1727, 1702, 1577, 1538, 1452, 1378, 1335, 1244, 1201, 1131, 1043, 953, 877, 809, 756, 694. ^1H NMR (600 MHz, CDCl_3 , δ ppm) 0.93 **isomer a**, 1.02 **isomer b** (t, $J = 7.1$ Hz, 3H, NCH_2CH_3), 1.29 **isomer a**, 1.31 **isomer b** (d, $J = 6.3$ Hz, 3H, CHCH_3), 1.45-1.79 **isomer a/b** (m, 4H, CH_2CH_2), 2.23 **isomer a** (s, 3H, COCH_3), 2.41 **isomer a** (t, $J = 6.9$ Hz, 2H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 2.45 **isomer b** (s, 3H, COCH_3), 2.46 **isomer a** (q, $J = 7.1$ Hz, 2H, NCH_2CH_3), 2.51 **isomer b** (t, $J = 6.9$ Hz, 2H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 2.57 **isomer b** (q, $J = 7.1$ Hz, 2H, NCH_2CH_3), 2.61 **isomer a** (td, $J = 6.0, 3.6$ Hz, 2H, $\text{NCH}_2\text{CH}_2\text{O}$), 2.76 **isomer b** (t, $J = 6.0$ Hz, 2H, $\text{NCH}_2\text{CH}_2\text{O}$), 3.64-3.75 **isomer a/b** (m, 1H, CHCH_3), 4.23 **isomer a** (td, $J = 6.0, 2.0$ Hz, 2H, $\text{NCH}_2\text{CH}_2\text{O}$), 4.32 **isomer b** (td, $J = 6.0, 1.0$ Hz, 2H, $\text{NCH}_2\text{CH}_2\text{O}$), 5.13 **isomer a**, 5.23 **isomer b** (d, $J = 7.0$ Hz, 1H, NH), 6.40 **isomer a**, 6.41 **isomer b** (d, $J = 5.5$ Hz, 1H, CHQn), 7.19-7.24 **isomer a/b** (m, 1H, CHAr), 7.24-7.39 **isomer a/b** (m, 3H, CHAr , CHQn), 7.39-7.48 **isomer a/b** (m, 1H, CHAr), 7.68 **isomer a**, 7.74 **isomer b** (d, $J = 9.0$ Hz, 1H, CHQn), 7.84 **isomer a** (s, 1H, C=CH), 7.92 **isomer a**, 7.94 **isomer b** (d, $J = 2.0$ Hz, 1H, CHQn), 7.95 **isomer b** (s, 1H, C=CH), 8.49 **isomer a**, 8.50 **isomer b** (d, $J = 3.7$ Hz, 1H, CHQn). ^{13}C NMR (100 MHz, CDCl_3 , δ ppm) 11.5 **isomer a**, 11.8 **isomer b** (NCH_2CH_3), 20.1 **isomer a/b** (CHCH_3), 24.0 **isomer a**, 24.2 **isomer b** (CH_2CH_2), 26.6 **isomer a**, 31.3 **isomer b** (COCH_3), 34.1 **isomer a/b** (CH_2CH_2), 47.9 **isomer a**, 48.0 **isomer b** (NCH_2CH_3), 48.2 **isomer a**, 48.3 **isomer b** (CHCH_3), 51.1 **isomer a**, 51.4 **isomer b** ($\text{NCH}_2\text{CH}_2\text{O}$), 53.4 **isomer a**, 53.6 **isomer b** ($\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 63.6 **isomer a**, 63.7 **isomer b** ($\text{NCH}_2\text{CH}_2\text{O}$), 99.1 **isomer a/b** (CHQn), 117.3 **isomer a/b** (CQn), 121.5 **isomer a/b** (CHQn), 124.9 **isomer a/b** (CHQn), 126.9 **isomer a**, 127.0 **isomer b** (CHAr), 128.3 **isomer a/b** (CHQn), 129.2 **isomer a**, 129.8 **isomer b** (CHAr), 129.9

isomer a/b (CHAr), 131.3 **isomer a**, 131.4 **isomer b** (CHAr), 131.5, 131.8, 134.4, 134.6 (3C), 136.0, 136.5 **isomer a/b** (C=CH, ClCQn, ClCAr, CAr), 137.7 **isomer a**, 138.4 **isomer b** (C=CH), 149.1 **isomer a/b** (2CQnN), 151.7 **isomer a/b** (CHQn), 164.0 **isomer a**, 166.7 **isomer b** (C=O), 194.9 **isomer a**, 202.2 **isomer b** (CH₃C=O). HRMS C₂₉H₃₃Cl₂N₃O₃ [M+H]⁺ 542.1972; found, 542.1960.

(*E/Z*)-2-((4-((7-chloroquinolin-4-yl)amino)pentyl)(ethyl)amino)ethyl 2-(3-chlorobenzylidene)-3-oxobutanoate (**7h**). Yellow viscous oil. Yield 76%. FT-IR (KBr, ν_{\max} cm⁻¹) 3408, 2969, 2868, 1729, 1698, 1667, 1575, 1536, 1454, 1378, 1332, 1246, 1199, 1150, 1082, 1039, 901, 879, 807, 786, 758, 686, 645, 546. ¹H NMR (600 MHz, CDCl₃, δ ppm) 0.96 **isomer a**, 1.01 **isomer b** (t, *J* = 7.1 Hz, 3H, NCH₂CH₃), 1.28 **isomer a**, 1.31 **isomer b** (d, *J* = 6.3 Hz, 3H, CHCH₃), 1.47-1.77 **isomer a/b** (m, 4H, CH₂CH₂), 2.34 **isomer a**, 2.39 **isomer b** (s, 3H, COCH₃), 2.46 **isomer a**, 2.50 **isomer b** (t, *J* = 6.9 Hz, 2H, CH₂CH₂CH₂N), 2.52 **isomer a**, 2.56 **isomer b** (q, *J* = 7.1 Hz, 2H, NCH₂CH₃), 2.71 **isomer a** (td, *J* = 6.0, 1.0 Hz, 2H, NCH₂CH₂O), 2.74 **isomer b** (t, *J* = 6.0 Hz, 2H, NCH₂CH₂O), 3.62-3.76 **isomer a/b** (m, 1H, CHCH₃), 4.31 **isomer a** (t, *J* = 5.9 Hz, 2H, NCH₂CH₂O), 4.33 **isomer b** (td, *J* = 6.0, 1 Hz, 2H, NCH₂CH₂O), 5.10-5.24 **isomer a**, 5.24-5.35 **isomer b** (m, 1H, NH), 6.39 **isomer a**, 6.42 **isomer b** (d, *J* = 5.5 Hz, 1H, CHQn), 7.19-7.23 **isomer a/b** (m, 1H, CHQn), 7.26-7.41 **isomer a/b** (m, 4H, CHAr), 7.42 **isomer a**, 7.57 **isomer b** (s, 1H, C=CH), 7.69 **isomer a**, 7.76 **isomer b** (dd, *J* = 9.0, 1.6 Hz, 1H, CHQn), 7.92 **isomer a**, 7.93 **isomer b** (d, *J* = 2.1 Hz, 1H, CHQn), 8.48 **isomer a**, 8.49 **isomer b** (d, *J* = 2.8 Hz, 1H, CHQn). ¹³C NMR (100 MHz, CDCl₃, δ ppm) 11.5 **isomer a**, 11.8 **isomer b** (NCH₂CH₃), 20.1 **isomer a**, 20.2 **isomer b** (CHCH₃), 24.0 **isomer a**, 24.2 **isomer b** (CH₂CH₂), 26.5 **isomer a**, 31.3 **isomer b** (COCH₃), 34.1 **isomer a**, 34.2 **isomer b** (CH₂CH₂), 48.0 **isomer a/b** (NCH₂CH₃), 48.3

isomer a, 48.4 **isomer b** (CHCH₃), 51.3 **isomer a**, 51.5 **isomer b** (NCH₂CH₂O), 53.5 **isomer a**, 53.6 **isomer b** (CH₂CH₂CH₂N), 63.7 **isomer a**, 63.8 **isomer b** (NCH₂CH₂O) 99.2 **isomer a/b** (CHQn), 117.2 **isomer a**, 117.3 **isomer b** (CQn), 121.3 **isomer a**, 121.4 **isomer b** (CHQn), 124.9 **isomer a**, 125.0 **isomer b** (CHAr), 127.4 **isomer a**, 127.7 **isomer b** (CHQn), 128.6 **isomer a/b** (CHQn), 129.0 **isomer a**, 129.5 **isomer b** (CHAr), 130.1 **isomer a**, 130.2 **isomer b** (CHAr), 130.5 **isomer a**, 130.6 **isomer b** (CHAr), 134.5, 134.6, 134.7, 134.8 (2C), 134.9, 135.2, 135.7 **isomer a/b** (C=CH, ClCQn, ClCAr, CAr), 139.1 **isomer a**, 139.7 **isomer b** (C=CH), 149.0 **isomer a**, 149.1 **isomer b** (CQnN), 149.2 **isomer a**, 149.3 **isomer b** (CQnN), 151.9 **isomer a/b** (CHQn), 164.1 **isomer a**, 167.2 **isomer b** (C=O), 194.6 **isomer a**, 202.9 **isomer b** (CH₃C=O). HRMS C₂₉H₃₃Cl₂N₃O₃ [M+H]⁺ 542.1972; found, 542.1972.

(*E/Z*)-2-((4-((7-chloroquinolin-4-yl)amino)pentyl)(ethyl)amino)ethyl 2-(4-chlorobenzylidene)-3-oxobutanoate (**7i**). Yellow viscous oil. Yield 74%. FT-IR (KBr, ν_{\max} cm⁻¹) 3402, 2969, 2870, 1729, 1698, 1612, 1575, 1538, 1452, 1378, 1332, 1248, 1201, 1150, 1092, 1014, 905, 879, 819, 758, 647. ¹H NMR (600 MHz, CDCl₃, δ ppm) 0.96 **isomer a**, 1.01 **isomer b** (t, *J* = 7.1 Hz, 3H, NCH₂CH₃), 1.27 **isomer a**, 1.31 **isomer b** (d, *J* = 6.3 Hz, 3H, CHCH₃), 1.48-1.78 **isomer a/b** (m, 4H, CH₂CH₂), 2.34 **isomer a**, 2.39 **isomer b** (s, 3H, COCH₃), 2.46 **isomer a**, 2.49 **isomer b** (t, *J* = 6.9 Hz, 2H, CH₂CH₂CH₂N), 2.52 **isomer a**, 2.55 **isomer b** (q, *J* = 7.1 Hz, 2H, NCH₂CH₃), 2.70 **isomer a** (td, *J* = 6.0, 1.9 Hz, 2H, NCH₂CH₂O), 2.73 **isomer b** (t, *J* = 6.0 Hz, 2H, NCH₂CH₂O), 3.61-3.76 **isomer a/b** (m, 1H, CHCH₃), 4.30 **isomer a**, 4.32 **isomer b** (t, *J* = 6.0 Hz, 2H, NCH₂CH₂O), 5.19 **isomer a**, 5.28 **isomer b** (d, *J* = 7.5 Hz, 1H, NH), 6.39 **isomer a**, 6.41 **isomer b** (d, *J* = 5.5 Hz, 1H, CHQn), 7.24-7.38 **isomer a/b** (m, 5H, CHQn and CHAr), 7.43 **isomer a**, 7.58 **isomer b** (s, 1H, C=CH), 7.69 **isomer a**, 7.75

isomer b (d, $J = 9.0$ Hz, 1H, CHQn), 7.91 **isomer a**, 7.92 **isomer b** (d, $J = 2.2$ Hz, 1H, CHQn), 8.48 **isomer a**, 8.49 **isomer b** (d, $J = 3.6$ Hz, 1H, CHQn). ^{13}C NMR (100 MHz, CDCl_3 , δ ppm) 11.5 **isomer a**, 11.9 **isomer b** (NCH_2CH_3), 20.2 **isomer a**, 20.3 **isomer b** (CHCH_3), 24.1 **isomer a**, 24.3 **isomer b** (CH_2CH_2), 26.5 **isomer a**, 31.4 **isomer b** (COCH_3), 34.2 **isomer a**, 34.3 **isomer b** (CH_2CH_2), 48.0 **isomer a**, 48.1 **isomer b** (NCH_2CH_3), 48.3 **isomer a**, 48.4 **isomer b** (CHCH_3), 51.5 **isomer a**, 51.6 **isomer b** ($\text{NCH}_2\text{CH}_2\text{O}$), 53.5 **isomer a**, 53.7 **isomer b** ($\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 63.7 **isomer a**, 63.8 **isomer b** ($\text{NCH}_2\text{CH}_2\text{O}$), 99.3 **isomer a/b** (CHQn), 117.3 **isomer a**, 117.4 **isomer b** (CQn), 121.3 **isomer a**, 121.4 **isomer b** (CHQn), 125.0 **isomer a**, 125.1 **isomer b** (CHAR), 128.8 **isomer a/b** (2CHQn), 129.2 **isomer a**, 129.3 **isomer b** (2CHAR), 130.8 **isomer a**, 130.9 **isomer b** (2CHAR), 131.2 **isomer a**, 131.4 **isomer b** (CAr), 134.4, 134.8 (2C), 135.0 **isomer a/b** ($\text{C}=\text{CH}$, ClCQn), 136.8 **isomer a**, 137.0 **isomer b** (ClCAr), 139.4 **isomer a**, 140.0 **isomer b** ($\text{C}=\text{CH}$), 149.1 **isomer a**, 149.2 **isomer b** (CQnN), 149.4 **isomer a**, 149.5 **isomer b** (CQnN), 152.1 **isomer a/b** (CHQn), 164.3 **isomer a**, 167.6 **isomer b** ($\text{C}=\text{O}$), 194.8 **isomer a**, 203.3 **isomer b** ($\text{CH}_3\text{C}=\text{O}$). HRMS $\text{C}_{29}\text{H}_{33}\text{Cl}_2\text{N}_3\text{O}_3$ $[\text{M}+\text{H}]^+$ 542.1972; found, 542.1963.

(*E/Z*)-2-((4-((7-chloroquinolin-4-yl)amino)pentyl)(ethyl)amino)ethyl 2-(2-nitrobenzylidene)-3-oxobutanoate (**7j**). Yellowish brown viscous oil. Yield 78%. FT-IR (KBr, ν_{max} cm^{-1}) 3408, 2969, 2864, 1731, 1698, 1608, 1575, 1532, 1454, 1378, 1345, 1244, 1201, 1150, 1078, 905, 879, 854, 811, 756, 700, 676. ^1H NMR (600 MHz, CDCl_3 , δ ppm) 0.90 **isomer a**, 1.02 **isomer b** (t, $J = 7.1$ Hz, 3H, NCH_2CH_3), 1.29 **isomer a**, 1.31 **isomer b** (d, $J = 6.4$ Hz, 3H, CHCH_3), 1.42-1.79 **isomer a/b** (m, 4H, CH_2CH_2), 2.18 **isomer a** (s, 3H, COCH_3), 2.36 **isomer a** (t, $J = 7.0$ Hz, 2H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 2.40 **isomer a** (q, $J = 7.1$ Hz, 2H, NCH_2CH_3), 2.45 **isomer a** (t, $J = 6.1$ Hz, 2H,

$\text{NCH}_2\text{CH}_2\text{O}$), 2.47 **isomer b** (s, 3H, COCH_3), 2.52 **isomer b** (t, $J = 6.8$ Hz, 2H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 2.58 **isomer b** (q, $J = 7.1$ Hz, 2H, NCH_2CH_3), 2.77 **isomer b** (t, $J = 5.9$ Hz, 2H, $\text{NCH}_2\text{CH}_2\text{O}$), 3.64-3.78 **isomer a/b** (m, 1H, CHCH_3), 4.05 **isomer a** (t, $J = 6.2$ Hz, 2H, $\text{NCH}_2\text{CH}_2\text{O}$), 4.28-4.40 **isomer b** (m, 2H, $\text{NCH}_2\text{CH}_2\text{O}$), 5.15 **isomer a**, 5.23 **isomer b** (d, $J = 7.5$ Hz, 1H, NH), 6.41 **isomer a/b** (t, $J = 5.3$ Hz, 1H, CHQn), 7.24-7.28 **isomer a** (m, 1H, CHAr), 7.29 **isomer a**, 7.33 **isomer b** (dd, $J = 9.0, 2.1$ Hz, 1H, CHQn), 7.39-7.43 **isomer b** (m, 1H, CHAr), 7.49-7.56 **isomer a/b** (m, 1H, CHAr), 7.56-7.64 **isomer a/b** (m, 1H, CHAr), 7.72 **isomer a**, 7.73 **isomer b** (d, $J = 5.5$ Hz, 1H, CHQn), 7.90 **isomer a**, 7.93 **isomer b** (d, $J = 2.1$ Hz, 1H, CHQn), 8.02 **isomer a**, 8.05 **isomer b** (s, 1H, $\text{C}=\text{CH}$), 8.16 **isomer a**, 8.19 **isomer b** (dd, $J = 8.0, 1.0$ Hz, 1H, CHAr), 8.48 **isomer a**, 8.50 **isomer b** (d, $J = 5.5$ Hz, 1H, CHQn). ^{13}C NMR (150 MHz, CDCl_3 , δ ppm) 11.7 **isomer a**, 11.9 **isomer b** (NCH_2CH_3), 20.2 **isomer**, 20.3 **isomer b** (CHCH_3), 24.1 **isomer a**, 24.3 **isomer b** (CH_2CH_2), 27.2 **isomer a**, 31.4 **isomer b** (COCH_3), 34.3 **isomer a/b** (CH_2CH_2), 48.0 **isomer a**, 48.1 **isomer b** (NCH_2CH_3), 48.4 **isomer a**, 48.5 **isomer b** (CHCH_3), 51.2 **isomer a**, 51.6 **isomer b** ($\text{NCH}_2\text{CH}_2\text{O}$), 53.6 **isomer a**, 53.7 **isomer b** ($\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 63.6 **isomer a**, 63.9 **isomer b** ($\text{NCH}_2\text{CH}_2\text{O}$), 99.3 **isomer a/b** (CHQn), 117.4 **isomer a/b** (CQn), 121.3 **isomer a**, 121.4 **isomer b** (CHQn), 125.1 **isomer a/b** (CHQn), 125.2 **isomer a/b** (CHAr), 128.7 **isomer a**, 128.8 **isomer b** (CHQn), 130.0 **isomer a** (CAr), 130.1 **isomer a** (CHAr), 130.3 **isomer a**, 130.4 **isomer b** (CHAr), 130.7 **isomer b** (CAr), 131.0 **isomer b** (CHAr), 134.0 **isomer a/b** (CHAr), 134.8 **isomer a**, 134.9 **isomer b** (ClCQn), 136.1 **isomer a**, 136.6 **isomer b** ($\text{C}=\text{CH}$), 139.5 **isomer a**, 140.4 **isomer b** ($\text{C}=\text{CH}$), 147.0 **isomer a**, 147.2 **isomer b** (ArCNO_2), 149.2 **isomer a/b** (CQnN), 149.4 **isomer a/b** (CQnN), 152.0 **isomer a/b** (CHQn), 163.9 **isomer a**, 165.8 **isomer b** ($\text{C}=\text{O}$), 194.8 **isomer a**, 200.8 **isomer b** ($\text{CH}_3\text{C}=\text{O}$). HRMS $\text{C}_{29}\text{H}_{33}\text{ClN}_4\text{O}_5$ $[\text{M}+\text{H}]^+$ 553.2212; found, 553.2291.

(*E/Z*)-2-((4-((7-chloroquinolin-4-yl)amino)pentyl)(ethylamino)ethyl 2-(3-nitrobenzylidene)-3-oxobutanoate (**7k**). Yellowish viscous oil. Yield 59%. FT-IR (KBr, ν_{\max} cm^{-1}) 3408, 2969, 2868, 1731, 1706, 1614, 1575, 1532, 1452, 1351, 1279, 1248, 1201, 1152, 1080, 908, 809, 733, 678, 647. ^1H NMR (600 MHz, CDCl_3 , δ ppm) 0.92 **isomer a**, 0.98 **isomer b** (t, $J = 7.1$ Hz, 3H, NCH_2CH_3), 1.24 **isomer a**, 1.28 **isomer b** (d, $J = 6.4$ Hz, 3H, CHCH_3), 1.45-1.75 **isomer a/b** (m, 4H, CH_2CH_2), 2.34 **isomer a**, 2.39 **isomer b** (s, 3H, COCH_3), 2.43 **isomer a**, 2.46 **isomer b** (t, $J = 6.9$ Hz, 2H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 2.49 **isomer a**, 2.53 **isomer b** (q, $J = 7.1$ Hz, 2H, NCH_2CH_3), 2.69 **isomer a**, 2.71 **isomer b** (t, $J = 6.1$ Hz, 2H, $\text{NCH}_2\text{CH}_2\text{O}$), 3.59-3.72 **isomer a/b** (m, 1H, CHCH_3), 4.29 **isomer a** (td, $J = 6.0, 1.0$ Hz, 2H, $\text{NCH}_2\text{CH}_2\text{O}$), 4.32 **isomer b** (t, $J = 6.2$ Hz, 2H, $\text{NCH}_2\text{CH}_2\text{O}$), 5.30 **isomer a**, 5.33 **isomer b** (d, $J = 7.5$ Hz, 1H, NH), 6.36 **isomer a**, 6.38 **isomer b** (d, $J = 5.6$ Hz, 1H, CHQn), 7.18-7.23 **isomer a/b** (m, 1H, CHQn), 7.44-7.52 **isomer a/b** (m, 1H, CHAr), 7.47 **isomer a** (s, 1H, $\text{C}=\text{CH}$), 7.56-7.58 **isomer a** (m, 1H, CHAr), 7.59 **isomer b** (s, 1H, $\text{C}=\text{CH}$), 7.66-7.69 **isomer b** (m, 1H, CHAr), 7.70 **isomer a**, 7.73 **isomer b** (d, $J = 9.0$ Hz, 1H, CHQn), 7.83 **isomer a**, 7.84 **isomer b** (d, $J = 2.2$ Hz, 1H, CHQn), 8.12-8.15 **isomer a**, 8.15-8.17 **isomer b** (m, 1H, CHAr), 8.20-8.23 **isomer a**, **isomer b** (m, 1H, CHAr), 8.42 **isomer a**, 8.43 **isomer b** (d, $J = 3.0$ Hz, 1H, CHQn). ^{13}C NMR (150 MHz, CDCl_3 , δ ppm) 11.5 **isomer a**, 11.8 **isomer b** (NCH_2CH_3), 20.1 **isomer a**, 20.2 **isomer b** (CHCH_3), 23.9 **isomer a**, 24.1 **isomer b** (CH_2CH_2), 26.7 **isomer a**, 31.3 **isomer b** (COCH_3), 34.0 **isomer a**, 34.1 **isomer b** (CH_2CH_2), 48.0 **isomer a**, 48.1 **isomer b** (NCH_2CH_3), 48.2 **isomer a**, 48.3 **isomer b** (CHCH_3), 51.3 **isomer a**, 51.5 **isomer b** ($\text{NCH}_2\text{CH}_2\text{O}$), 53.5 **isomer a/b** ($\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 63.9 **isomer a**, 64.0 **isomer b** ($\text{NCH}_2\text{CH}_2\text{O}$), 99.2 **isomer a/b** (CHQn), 117.3 **isomer a/b** (CQn), 121.4 **isomer a**, 121.5 **isomer b** (CHQn), 123.5

isomer a, 124.2 **isomer b** (CHAr), 124.7 **isomer a/b** (CAr), 124.9 **isomer a/b** (CHQn), 128.4 **isomer a/b** (CHQn), 130.0 **isomer a/b** (CHAr), 134.3 **isomer a**, 134.5 **isomer b** (ClCQn), 134.7 **isomer a**, 134.8 **isomer b** (CHAr), 135.3 **isomer a/b** (CHAr), 136.6 **isomer a**, 136.7 **isomer b** (C=CH), 137.9 **isomer a**, 138.2 **isomer b** (C=CH), 148.3 **isomer a/b** (ArCNO₂), 149.1 **isomer a/b** (CQnN), 149.2 **isomer a/b** (CQnN), 151.8 **isomer a/b** (CHQn), 163.8 **isomer a**, 166.8 **isomer b** (C=O), 194.4 **isomer a**, 202.2 **isomer b** (CH₃C=O). HRMS C₂₉H₃₃ClN₄O₅ [M+H]⁺ 553.2212; found, 553.2220.

(E/Z)-2-((4-((7-chloroquinolin-4-yl)amino)pentyl)(ethyl)amino)ethyl 2-(4-nitrobenzylidene)-3-oxobutanoate (7I). Yellowish viscous oil. Yield 59%. FT-IR (KBr, ν_{\max} cm⁻¹) 3410, 2971, 2868, 1731, 1714, 1575, 1519, 1454, 1347, 1244, 1199, 1078, 910, 854, 813, 733, 647. ¹H NMR (400 MHz, CDCl₃, δ ppm) 0.95 **isomer a**, 1.02 **isomer b** (t, $J = 7.1$ Hz, 3H, NCH₂CH₃), 1.28 **isomer a**, 1.32 **isomer b** (d, $J = 6.3$ Hz, 3H, CHCH₃), 1.39-1.81 **isomer a/b** (m, 4H, CH₂CH₂), 2.35 **isomer a**, 2.43 **isomer b** (s, 3H, COCH₃), 2.44-2.62 **isomer a/b** (m, 2H, CH₂CH₂CH₂N and NCH₂CH₃), 2.68 **isomer a**, 2.75 **isomer b** (t, $J = 5.9$ Hz, 2H, NCH₂CH₂O), 3.57-3.80 **isomer a/b** (m, 1H, CHCH₃), 4.24-4.42 **isomer a/b** (m, 2H, NCH₂CH₂O), 5.28 **isomer a**, 5.35 **isomer b** (d, $J = 7.5$ Hz, 1H, NH), 6.39 **isomer a**, 6.42 **isomer b** (d, $J = 5.5$ Hz, 1H, CHQn), 7.25 **isomer a**, 7.27 **isomer b** (d, $J = 1.8$ Hz, 1H, CHQn), 7.47 **isomer a** (d, $J = 8.7$ Hz, 2H, CHAr), 7.51 **isomer a** (s, 1H, C=CH), 7.56 **isomer b** (d, $J = 8.7$ Hz, 2H, CHAr), 7.63 **isomer b** (s, 1H, C=CH), 7.72 **isomer a**, 7.77 **isomer b** (d, $J = 9.0$ Hz, 1H, CHQn), 7.89 **isomer a**, 7.90 **isomer b** (d, $J = 2.2$ Hz, 1H, CHQn), 8.15 **isomer a**, 8.18 **isomer b** (d, $J = 2.2$ Hz, 2H, CHAr), 8.47 **isomer a/b** (d, $J = 6$ Hz, 1H, CHQn). ¹³C NMR (100 MHz, CDCl₃, δ ppm) δ 11.4 **isomer a**, 11.8 **isomer b** (NCH₂CH₃), 20.1 **isomer**, 20.2 **isomer b** (CHCH₃), 24.0 **isomer a**, 24.2 **isomer b** (CH₂CH₂), 26.7 **isomer a**, 31.3

isomer b (COCH₃), 34.2 **isomer a/b** (CH₂CH₂), 47.9 **isomer a**, 48.0 **isomer b** (NCH₂CH₃), 48.3 **isomer a**, 48.4 **isomer b** (CHCH₃), 51.5 **isomer a/b** (NCH₂CH₂O), 53.5 **isomer a**, 53.6 **isomer b** (CH₂CH₂CH₂N), 64.0 **isomer a/b** (NCH₂CH₂O), 99.2 **isomer a/b** (CHQn), 117.2 **isomer a**, 117.3 **isomer b** (CQn), 121.4 **isomer a/b** (CHQn), 123.9 **isomer a**, 124.0 **isomer b** (2CHAr), 125.0 **isomer a/b** (CHQn), 128.4 **isomer a/b** (CHQn), 130.1 **isomer a**, 130.2 **isomer b** (2CHAr), 134.8 **isomer a/b** (ClCQn), 137.4 **isomer a/b** (C=CH), 137.9 **isomer a**, 138.3 **isomer b** (C=CH), 139.0 **isomer a**, 139.3 **isomer b** (CAr), 148.4 **isomer a/b** (ArCNO₂), 149.1 **isomer a/b** (CQnN), 149.2 **isomer a**, 149.3 **isomer b** (CQnN), 151.8 **isomer a/b** (CHQn), 163.7 **isomer a**, 166.8 **isomer b** (C=O), 194.4 **isomer a**, 202.2 **isomer b** (CH₃C=O). HRMS C₂₉H₃₃ClN₄O₅ [M+H]⁺ 553.2212; found, 553.2278.

(E/Z)-2-((4-((7-chloroquinolin-4-yl)amino)pentyl)(ethyl)amino)ethyl *2-acetyl-5-phenylpenta-2,4-dienoate (7m)*. Yellow viscous oil. Yield 62%. FT-IR (KBr, ν_{\max} cm⁻¹) 3400, 3061, 2969, 2870, 1714, 1614, 1575, 1538, 1450, 1378, 1332, 1281, 1228, 1152, 1078, 1027, 977, 908, 879, 809, 751, 733, 690, 645. ¹H NMR (400 MHz, CDCl₃, δ ppm) 1.02 **isomer a/b** (t, $J = 7.0$ Hz, 3H, NCH₂CH₃), 1.25 **isomer a**, 1.30 **isomer b** (d, $J = 6.3$ Hz, 3H, CHCH₃), 1.49-1.78 **isomer a/b** (m, 4H, CH₂CH₂), 2.39 **isomer a**, 2.46 **isomer b** (s, 3H, COCH₃), 2.48-2.54 **isomer a/b** (m, 2H, CH₂CH₂CH₂N), 2.54-2.64 **isomer a/b** (m, 2H, NCH₂CH₃), 2.75 **isomer a**, 2.80 **isomer b** (t, $J = 5.8$ Hz, 2H, NCH₂CH₂O), 3.57-3.77 **isomer a/b** (m, 1H, CHCH₃), 4.31 **isomer a**, 4.39 **isomer b** (t, $J = 5.8$ Hz, 2H, NCH₂CH₂O), 5.09 **isomer a**, 5.20 **isomer b** (d, $J = 7.5$ Hz, 1H, NH), 6.35 **isomer a**, 6.41 **isomer b** (d, $J = 5.5$ Hz, 1H, CHQn), 6.98 **isomer a** (d, $J = 15.5$ Hz, 1H, HC=CHPh), 7.02 **isomer b** (d, $J = 14.4$ Hz, 1H, HC=CHPh), 7.18-7.56 **isomer a/b** (m, 1H, CHQn), 7.18-7.56 **isomer a/b** (m, 5H, CHAr), 7.18-7.56 **isomer a/b** (m,

1H, C=CH), 7.18-7.56 **isomer a/b** (m, 1H, CH=CH=CH), 7.68 **isomer a**, 7.75 **isomer b** (d, $J = 9.0$ Hz, 1H, CHQn), 7.89-7.97 **isomer a/b** (m, 1H, CHQn), 8.47 **isomer a**, 8.49 **isomer b** (d, $J = 5.5$ Hz, 1H, CHQn). ¹³C NMR (100 MHz, CDCl₃, δ ppm) 11.6 **isomer a**, 11.9 **isomer b** (NCH₂CH₃), 20.3 **isomer a/b** (CHCH₃), 24.2 **isomer a**, 24.3 **isomer b** (CH₂CH₂), 27.9 **isomer a**, 31.4 **isomer b** (COCH₃), 34.4 **isomer a/b** (CH₂CH₂), 48.1 **isomer a**, 48.2 **isomer b** (NCH₂CH₃), 48.3 **isomer a**, 48.4 **isomer b** (CHCH₃), 51.8 **isomer a/b** (NCH₂CH₂O), 53.7 **isomer a/b** (CH₂CH₂CH₂N), 63.2 **isomer a**, 63.3 **isomer b** (NCH₂CH₂O), 99.3 **isomer a/b** (CHQn), 117.3 **isomer a**, 117.4 **isomer b** (CQn), 121.3 **isomer a/b** (CHQn), 123.4 **isomer a**, 123.8 **isomer b** (CH=CH=CH), 125.1 **isomer a/b** (CHQn), 128.0 **isomer a/b** (2CHAr), 128.8 **isomer a/b** (CHQn), 129.0 **isomer a/b** (2CHAr), 130.1 **isomer a/b** (CHAr), 131.8 **isomer a**, 132.5 **isomer b** (C=CH), 134.8 **isomer a/b** (ClCQn), 135.5 **isomer a**, 135.6 **isomer b** (CAr), 144.9 **isomer a**, 145.3 **isomer b** (HC=CHPh), 145.9 **isomer a/b** (C=CH), 149.1 **isomer a/b** (CQnN), 149.4 **isomer a**, 149.5 **isomer b** (CQnN), 152.1 **isomer a/b** (CHQn), 165.4 **isomer a**, 166.4 **isomer b** (C=O), 195.8 **isomer a**, 200.7 **isomer b** (CH₃C=O). HRMS C₃₁H₃₆ClN₃O₃ [M+H]⁺ 534.2518; found, 534.2530.

(*E/Z*)-2-((4-((7-chloroquinolin-4-yl)amino)pentyl)(ethyl)amino)ethyl 2-(furan-2-ylmethylene)-3-oxobutanoate (**7n**). Brown viscous oil. Yield 77%. FT-IR (KBr, ν_{\max} cm⁻¹) 3400, 3123, 2969, 2868, 1714, 1661, 1622, 1575, 1538, 1454, 1378, 1335, 1252, 1207, 1150, 1080, 1020, 930, 908, 885, 852, 811, 756, 733, 647, 591, 558. ¹H NMR (400 MHz, CDCl₃, δ ppm) 0.99 **isomer a**, 1.00 **isomer b** (t, $J = 7.1$ Hz, 3H, NCH₂CH₃), 1.28 **isomer a**, 1.30 **isomer b** (d, $J = 6.4$ Hz, 3H, CHCH₃), 1.47-1.78 **isomer a/b** (m, 4H, CH₂CH₂), 2.34 **isomer a**, 2.47 **isomer b** (s, 3H, COCH₃), 2.47-2.64 **isomer a/b** (m, 4H, CH₂CH₂CH₂N and NCH₂CH₃), 2.72 **isomer a** (t, $J = 5.8$ Hz, 2H, NCH₂CH₂O), 2.80

isomer b (t, $J = 6.2$ Hz, 2H, $\text{NCH}_2\text{CH}_2\text{O}$) 3.61-3.77 **isomer a/b** (m, 1H, CHCH_3), 4.28 **isomer a** (t, $J = 5.8$ Hz, 2H, $\text{NCH}_2\text{CH}_2\text{O}$), 4.41 **isomer b** (t, $J = 6.2$ Hz, 2H, $\text{NCH}_2\text{CH}_2\text{O}$), 5.15-5.27 **isomer a**, 5.28-5.39 **isomer b** (m, 1H, NH), 6.40 **isomer a/b** (t, $J = 5.4$ Hz, 1H, CHQn), 6.46-6.53 **isomer a/b** (m, 1H, CHAr), 6.71 **isomer a**, 6.81 **isomer b** (d, $J = 3.5$ Hz, 1H, CHAr), 7.23 **isomer a** (s, 1H, CHAr), 7.24-7.31 **isomer a**, **isomer b** (m, 1H, CHQn), 7.35 **isomer b** (s, 1H, CHAr), 7.46-7.54 **isomer a/b** (m, 1H, C=CH), 7.71 **isomer a**, 7.77 **isomer b** (d, $J = 9.0$ Hz, 1H, CHQn), 7.88-7.96 **isomer a/b** (m, 1H, CHQn), 8.49 **isomer a/b** (d, $J = 5.4$ Hz, 1H, CHQn). ^{13}C NMR (100 MHz, CDCl_3 , δ ppm) 11.7 **isomer a**, 12.0 **isomer b** (NCH_2CH_3), 20.3 **isomer a/b** (CHCH_3), 24.1 **isomer a**, 24.4 **isomer b** (CH_2CH_2), 26.4 **isomer a**, 31.3 **isomer b** (COCH_3), 34.3 **isomer a**, 34.4 **isomer b** (CH_2CH_2), 48.2 **isomer a**, 48.3 **isomer b** (NCH_2CH_3), 48.4 **isomer a**, 48.5 **isomer b** (CHCH_3), 51.5 **isomer a**, 51.6 **isomer b** ($\text{NCH}_2\text{CH}_2\text{O}$), 53.6 **isomer a**, 53.7 **isomer b** ($\text{CH}_2\text{CH}_2\text{CH}_2\text{N}$), 63.6 **isomer a**, 63.7 **isomer b** ($\text{NCH}_2\text{CH}_2\text{O}$), 99.3 **isomer a/b** (CHQn), 112.9 **isomer a**, 113.1 **isomer b** (CHAr), 117.4 **isomer a**, 117.5 **isomer b** (CQn), 118.1 **isomer a**, 119.0 **isomer b** (CHAr), 121.4 **isomer a**, 121.5 **isomer b** (CHQn), 125.0 **isomer a**, 125.1 **isomer b** (CHQn), 126.3 **isomer a**, 126.8 **isomer b** (CHAr), 128.8 **isomer a/b** (CHQn), 129.5 **isomer a**, 130.1 **isomer b** (C=CH), 134.8 **isomer a**, 134.9 **isomer b** (ClCQn), 146.4 **isomer a**, 146.6 **isomer b** (C=CH), 148.9, 149.2 (2C), 149.3, 149.5 **isomer a/b** (2CQnN, CAr), 152.1 **isomer a/b** (CHQn), 164.6 **isomer a**, 167.5 **isomer b** (C=O), 194.3 **isomer a**, 202.4 **isomer b** ($\text{CH}_3\text{C=O}$). HRMS $\text{C}_{27}\text{H}_{32}\text{ClN}_3\text{O}_4$ $[\text{M}+\text{H}]^+$ 498.2154; found, 498.2181.

(*E/Z*)-2-((4-((7-chloroquinolin-4-yl)amino)pentyl)(ethyl)amino)ethyl 3-oxo-2-(thiophen-2-ylmethylene)butanoate (**o**). Yellow viscous oil. Yield 62%. FT-IR (KBr, ν_{max} cm^{-1}) 3402, 3104, 2969, 2868, 1716, 1659, 1610, 1577, 1538, 1452, 1421, 1378, 1335, 1246,

1203, 1152, 1078, 1055, 975, 908, 879, 856, 809, 731, 647. ¹H NMR (400 MHz, CDCl₃, δ ppm) 1.00 **isomer a/b** (q, *J* = 7.0 Hz, 3H, NCH₂CH₃), 1.27 **isomer a**, 1.30 **isomer b** (d, *J* = 6.4 Hz, 3H, CHCH₃), 1.46-1.78 **isomer a/b** (m, 4H, CH₂CH₂), 2.36 **isomer a** (s, 3H, COCH₃), 2.45-2.52 **isomer a/b** (m, 2H, CH₂CH₂CH₂N), 2.48 **isomer b** (s, 3H, COCH₃), 2.55 **isomer a**, 2.56 **isomer b** (q, *J* = 7.1 Hz, 2H, NCH₂CH₃), 2.73 **isomer a**, 2.80 **isomer b** (t, *J* = 6.0 Hz, 2H, NCH₂CH₂O), 3.60-3.77 **isomer a/b** (m, 1H, CHCH₃), 4.30 **isomer a** (t, *J* = 6.0 Hz, 2H, NCH₂CH₂O), 4.41 **isomer b** (td, *J* = 6.0, 1.8 Hz, 2H, NCH₂CH₂O), 5.32 **isomer a**, 5.37 **isomer b** (d, *J* = 7.5 Hz, 1H, NH), 6.39 **isomer a**, 6.41 **isomer b** (d, *J* = 5.6 Hz, 1H, CHQn), 7.06 **isomer a**, 7.07 **isomer b** (t, *J* = 3.6 Hz, 1H, CHAr), 7.24 **isomer a**, 7.26 **isomer b** (dd, *J* = 8.7, 2.2 Hz, 1H, CHQn), 7.30-7.33 **isomer a**, 7.36-7.42 **isomer b** (m, 1H, CHAr), 7.49-7.52 **isomer a**, 7.52-7.57 **isomer b** (m, 1H, CHAr), 7.65 **isomer a** (s, 1H, C=CH), 7.74 **isomer a**, 7.80 **isomer b** (d, *J* = 9.0 Hz, 1H, CHQn), 7.76 **isomer b** (s, 1H, C=CH), 7.92 **isomer a/b** (t, *J* = 2 Hz, 1H, CHQn), 8.47 **isomer a**, 8.49 **isomer b** (d, *J* = 1.4 Hz, 1H, CHQn). ¹³C NMR (100 MHz, CDCl₃, δ ppm) 11.6 **isomer a**, 11.9 **isomer b** (NCH₂CH₃), 20.1 **isomer a**, 20.2 **isomer b** (CHCH₃), 24.1 **isomer a**, 24.3 **isomer b** (CH₂CH₂), 26.7 **isomer a**, 31.0 **isomer b** (COCH₃), 34.2 **isomer a/b** (CH₂CH₂), 48.0 **isomer a**, 48.1 **isomer b** (NCH₂CH₃), 48.3 **isomer a**, 48.4 **isomer b** (CHCH₃), 51.5 **isomer a**, 51.6 **isomer b** (NCH₂CH₂O), 53.5 **isomer a**, 53.7 **isomer b** (CH₂CH₂CH₂N), 63.5 **isomer a**, 63.9 **isomer b** (NCH₂CH₂O), 99.2 **isomer a/b** (CHQn), 117.4 **isomer a/b** (CQn), 121.5 **isomer a/b** (CHQn), 125.0 **isomer a/b** (CHQn), 128.0 **isomer a**, 128.1 **isomer b** (CHAr), 128.6 **isomer a/b** (CHQn), 129.4 **isomer a**, 130.5 **isomer b** (C=CH), 132.2 **isomer a**, 132.5 **isomer b** (CHAr), 134.3 **isomer a/b** (C=CH) 134.7 **isomer a/b** (ClCQn), 135.1 **isomer a**, 135.3 **isomer b** (CHAr), 135.9 **isomer a**, 136.1 **isomer b** (CAr), 149.2 **isomer a/b** (CQnN), 149.4 **isomer a/b** (CQnN), 152.0 **isomer a/b** (CHQn), 164.8 **isomer a**, 167.3 **isomer b**

(C=O), 194.7 **isomer a**, 202.6 **isomer b** (CH₃C=O). HRMS C₂₇H₃₂ClN₃O₃S [M+H]⁺
514.1926; found, 514.1910.

Selected ^1H and ^{13}C NMR spectra

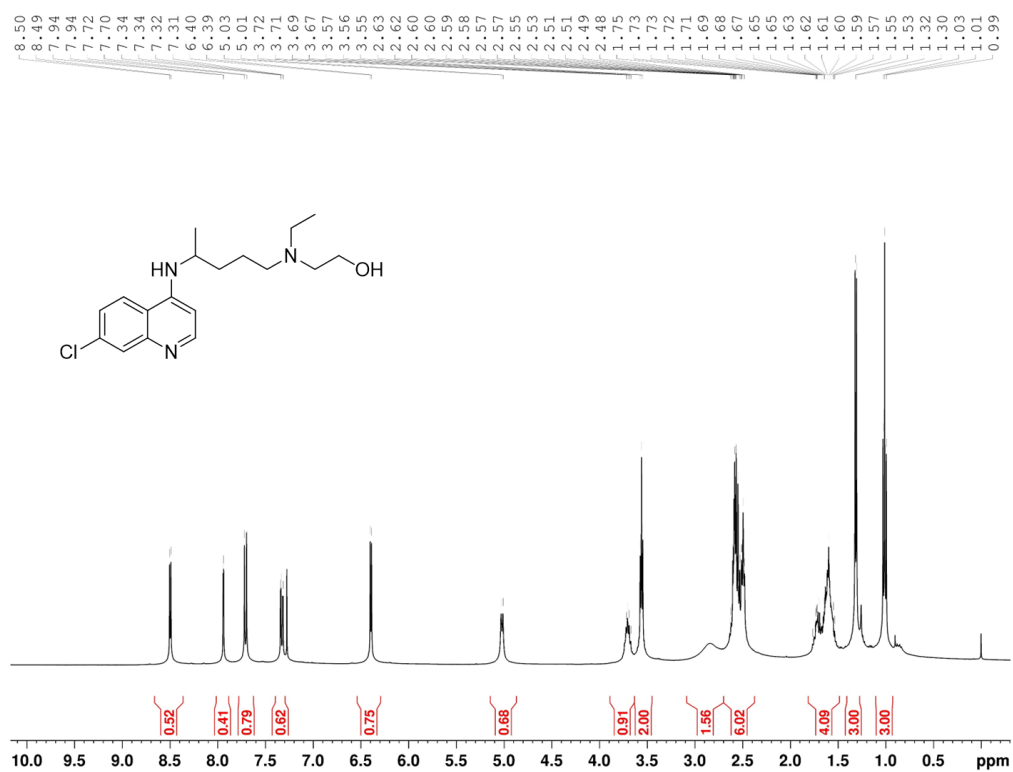


Figure S1. ^1H NMR (400 MHz, CDCl_3) spectrum of **4**.

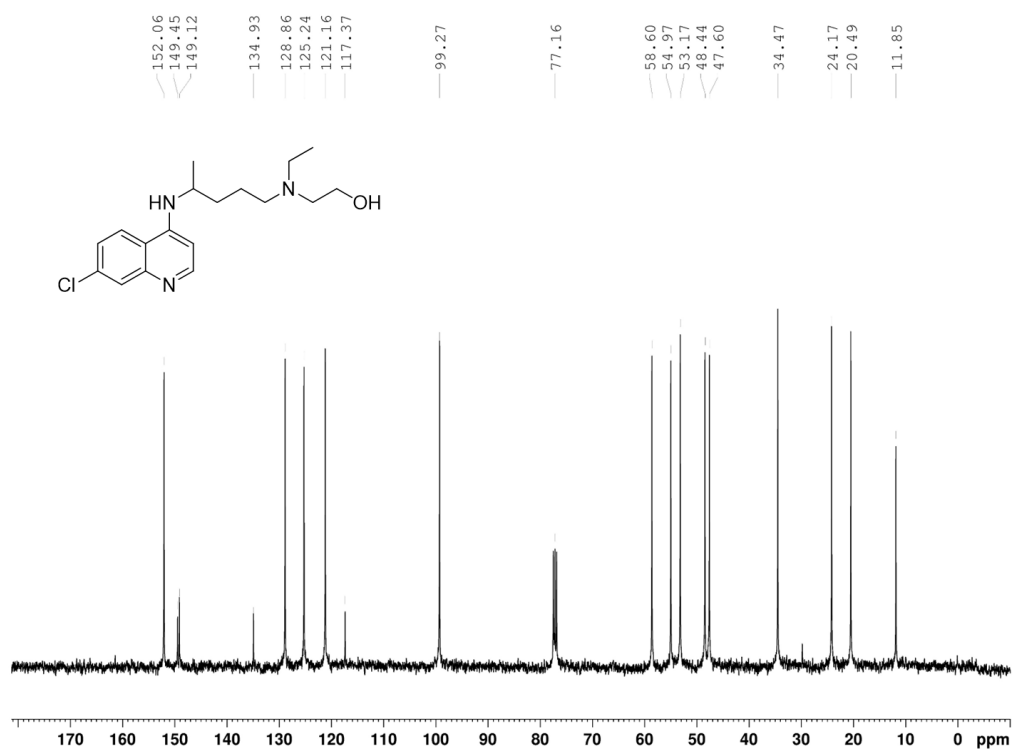


Figure S2. ^{13}C NMR (100 MHz, CDCl_3) spectrum of **4**.

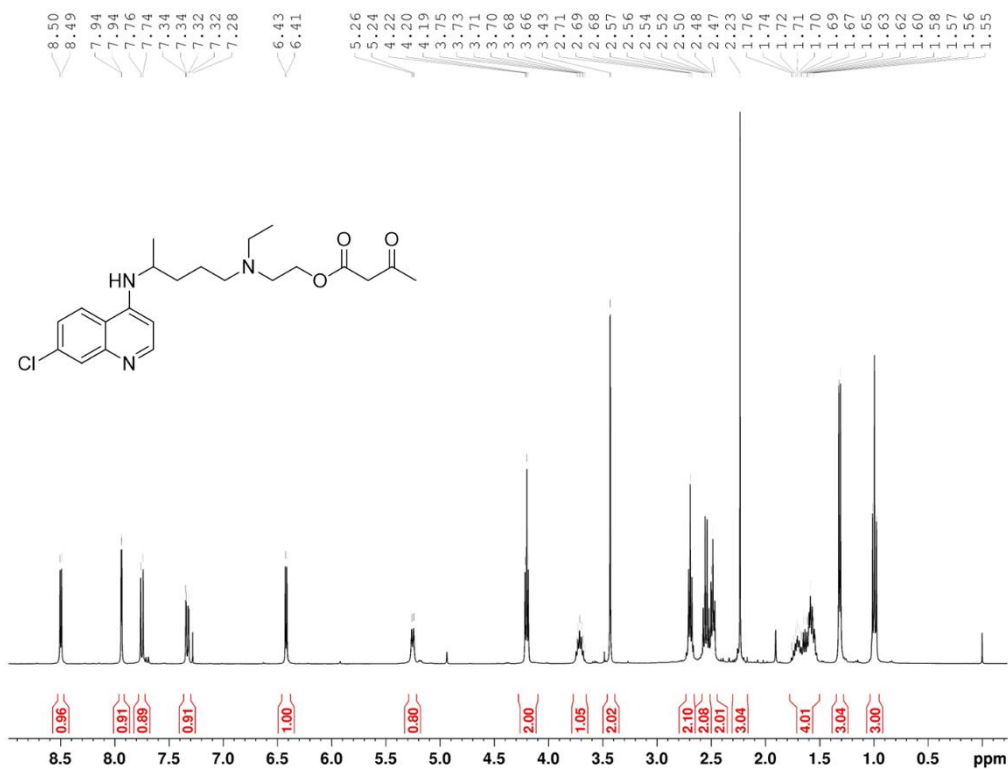


Figure S3. ¹H NMR (400 MHz, CDCl₃) spectrum of 5.

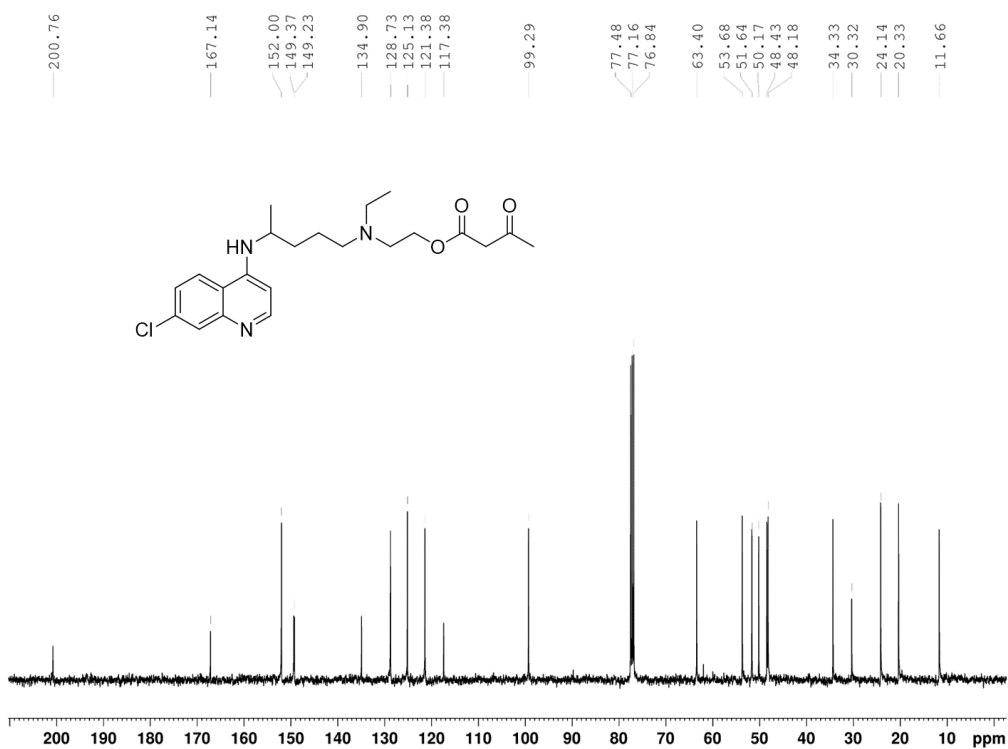


Figure S4. ¹³C NMR (100 MHz, CDCl₃) spectrum of 5.

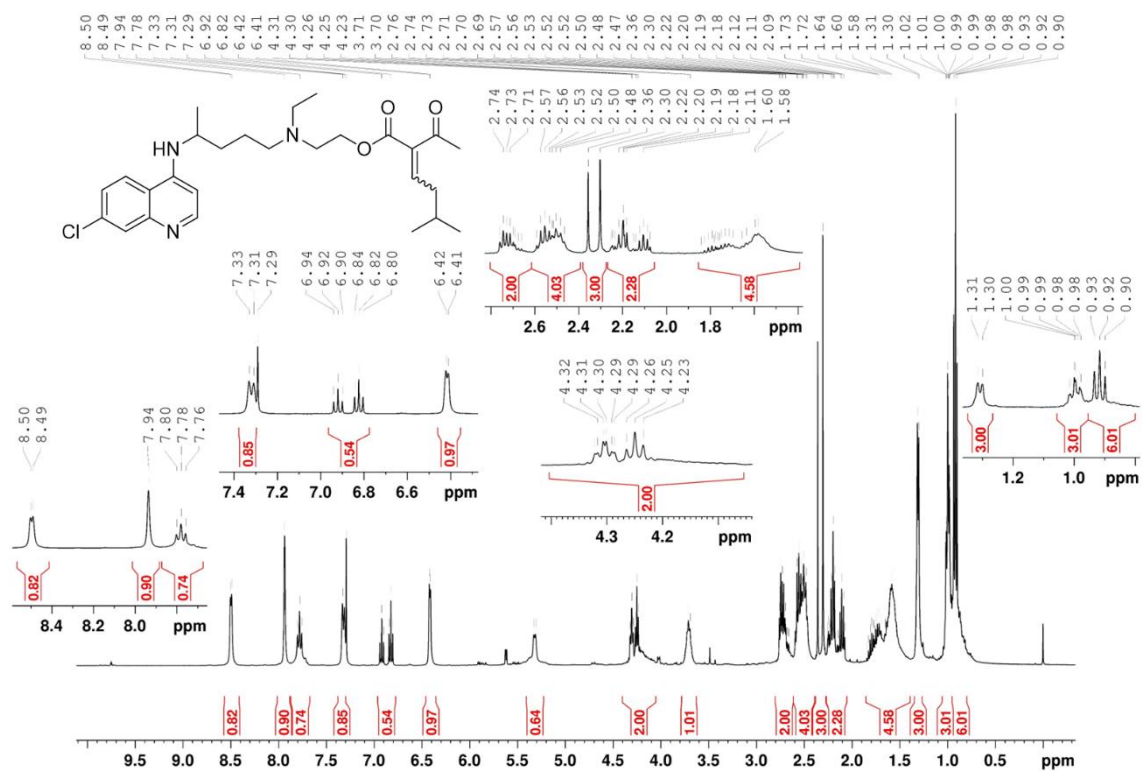


Figure S5. ^1H NMR (400 MHz, CDCl_3) spectrum of (E/Z)-7a.

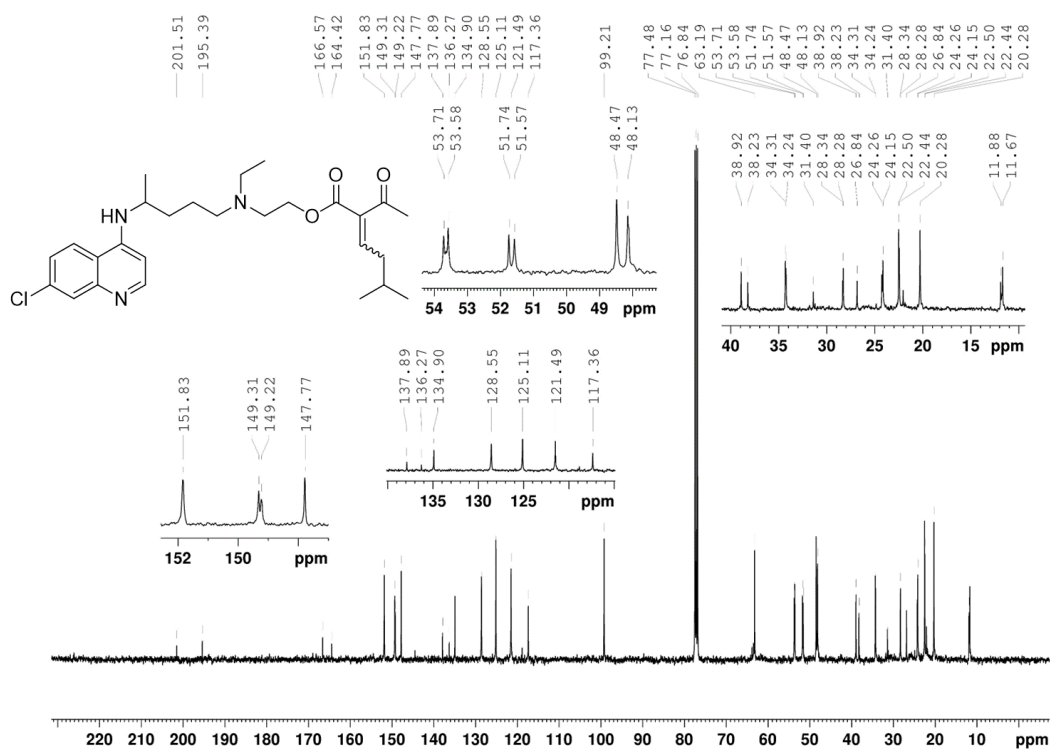
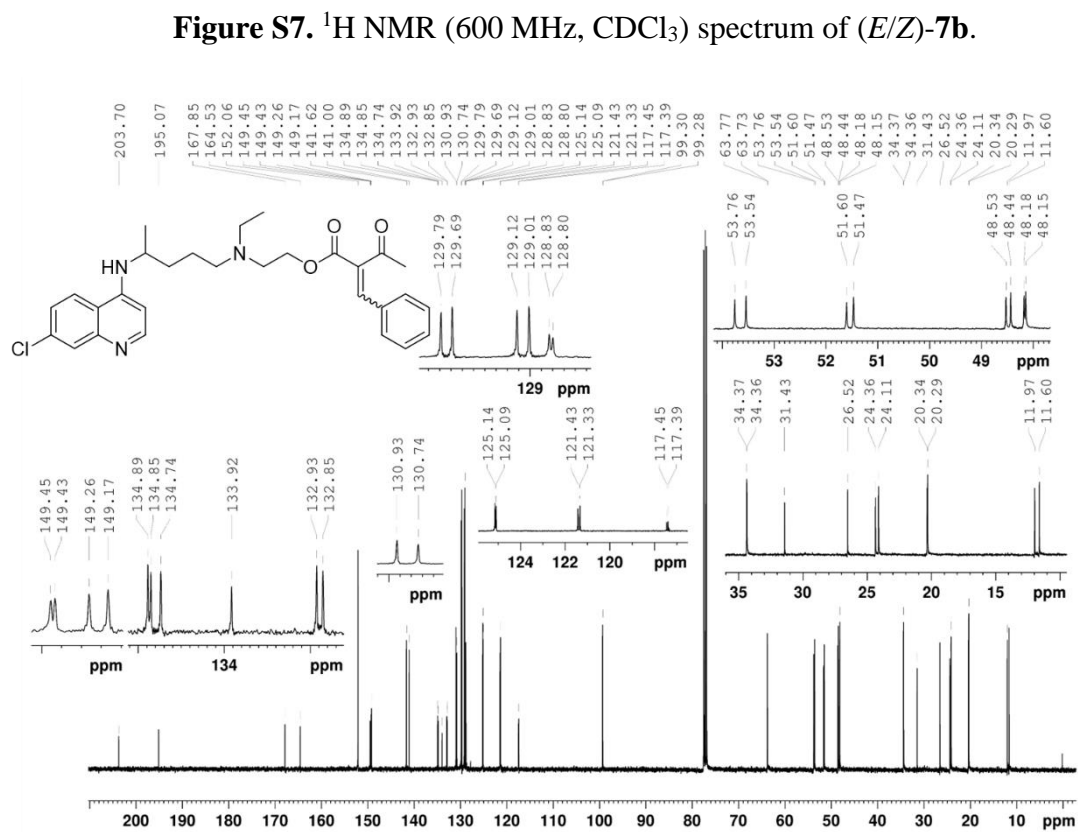
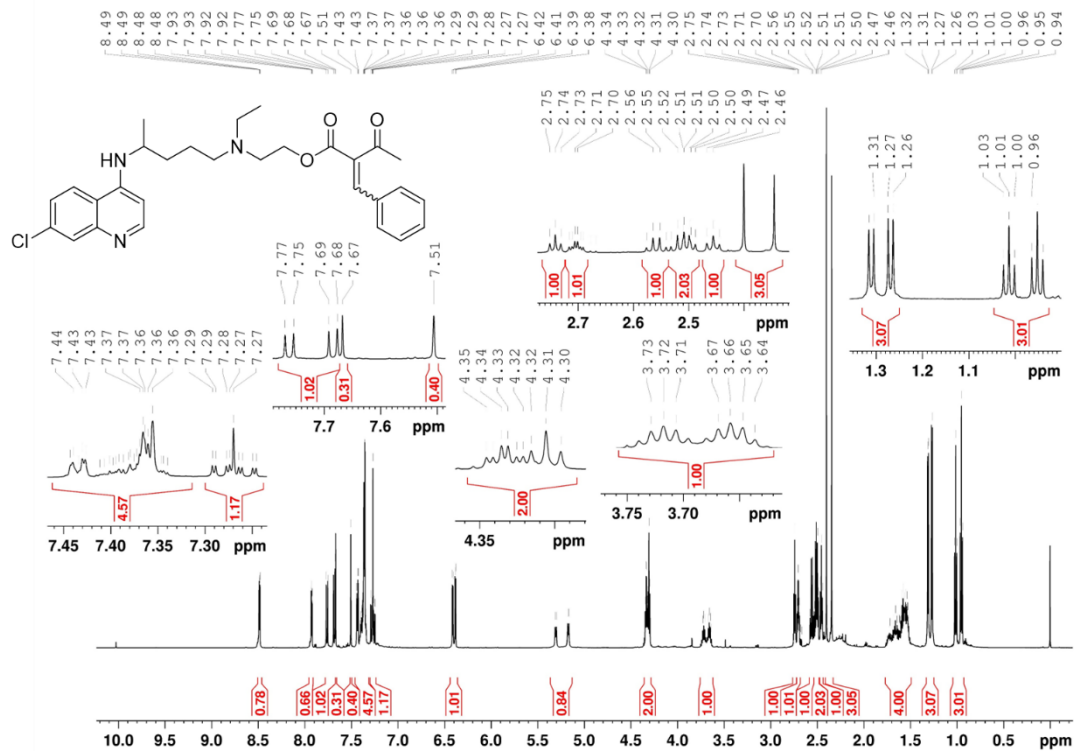


Figure S6. ^{13}C NMR (100 MHz, CDCl_3) spectrum of (E/Z)-7a.



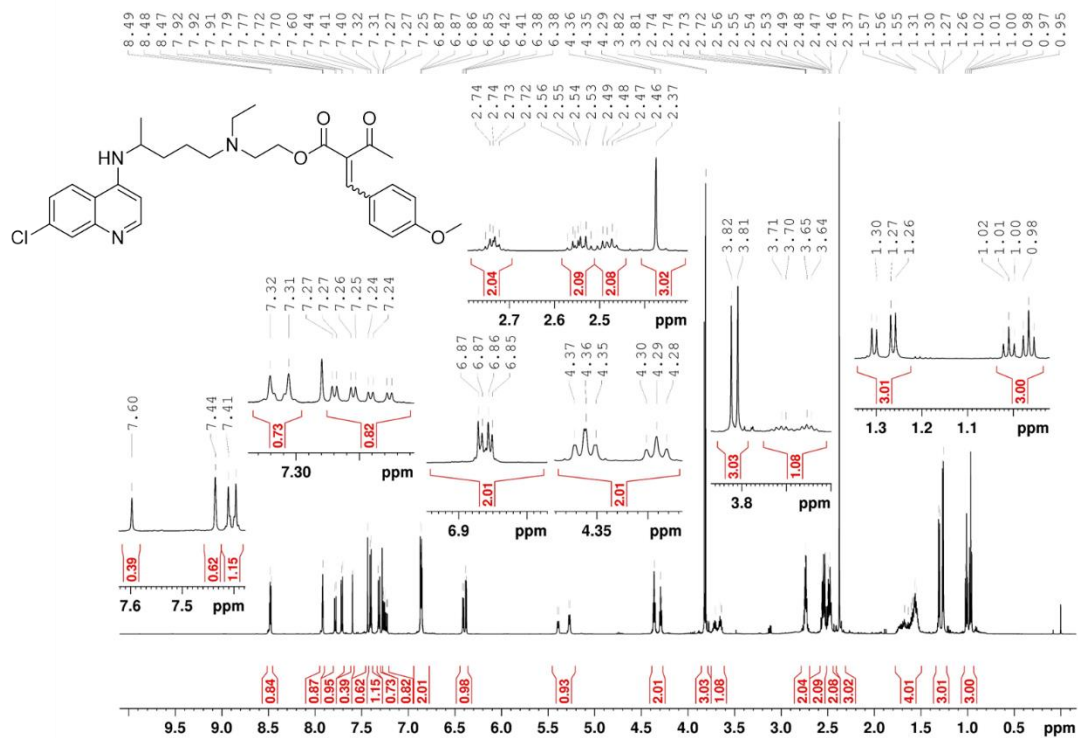


Figure S11. ^1H NMR (600 MHz, CDCl_3) spectrum of (*E/Z*)-7d.

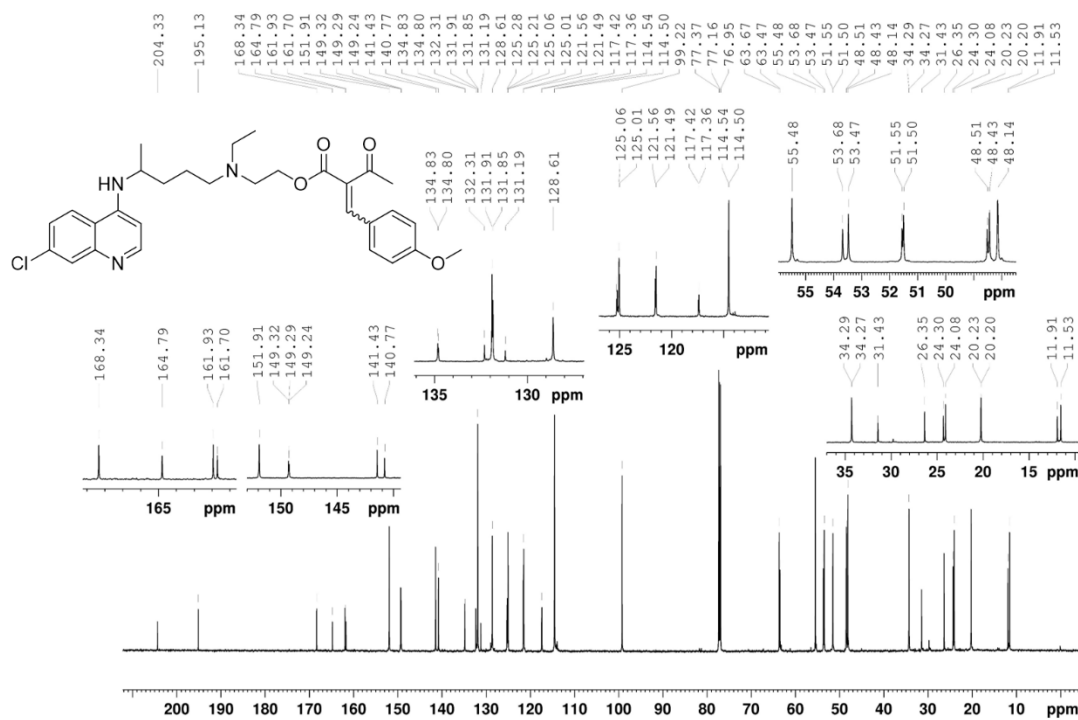
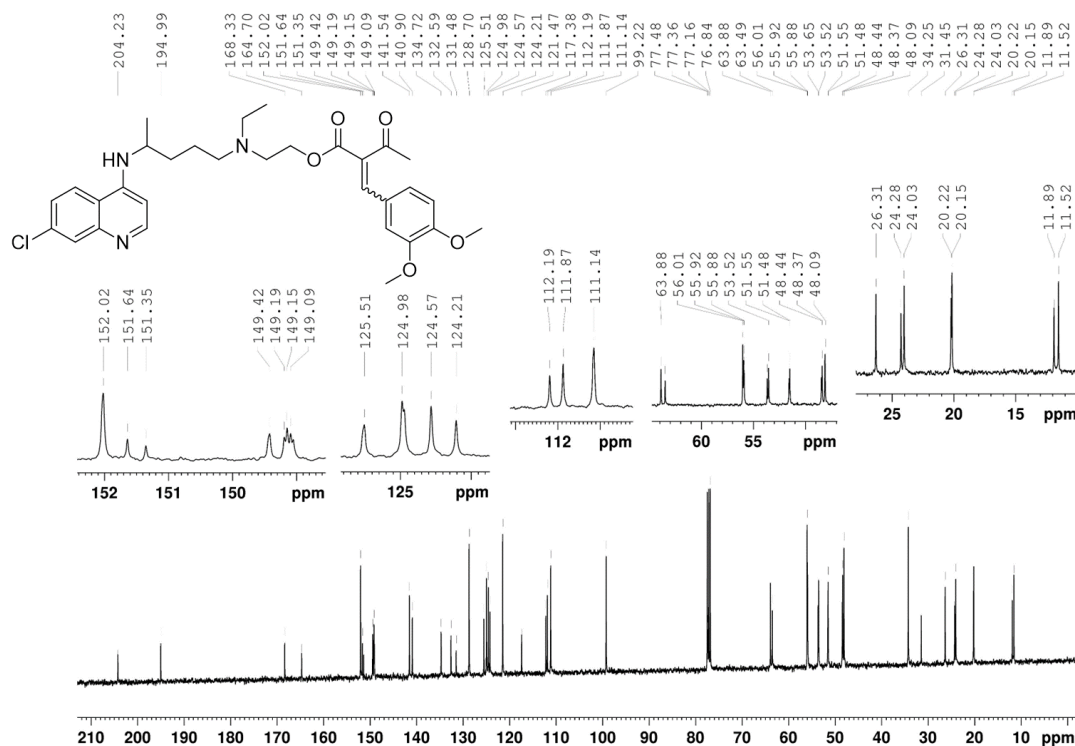
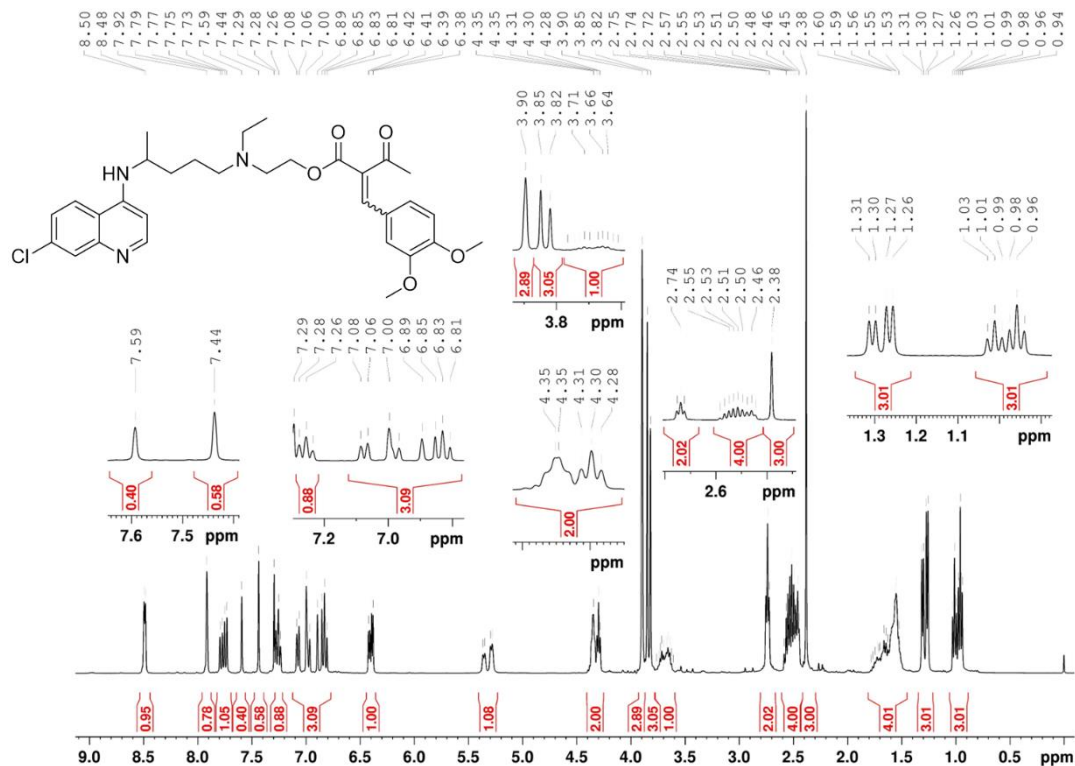


Figure S12. ^{13}C NMR (150 MHz, CDCl_3) spectrum of (*E/Z*)-7d.



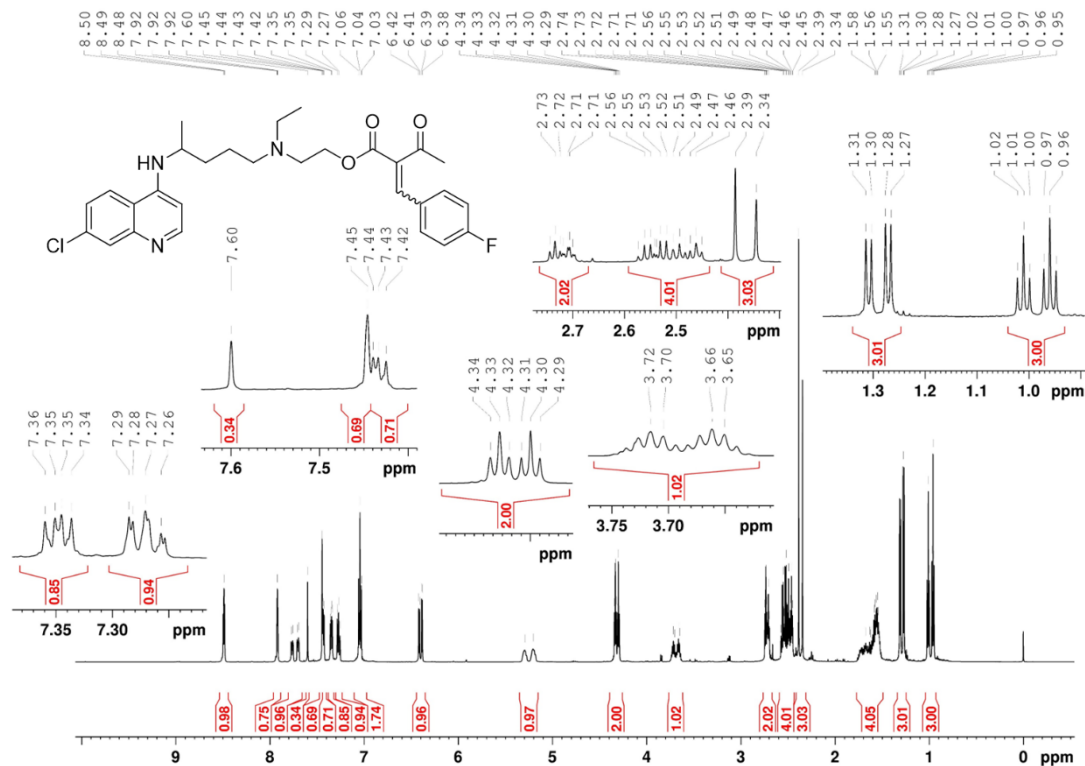


Figure S15. ¹H NMR (600 MHz, CDCl₃) spectrum of (E/Z)-7f.

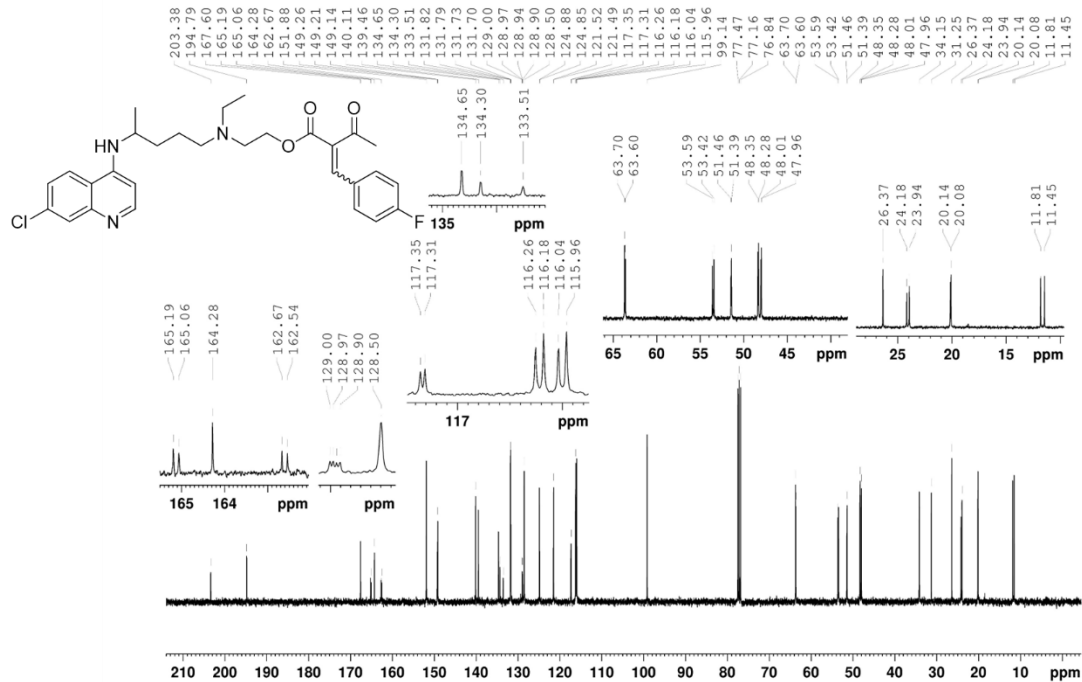


Figure S16. ¹³C NMR (100 MHz, CDCl₃) spectrum of (E/Z)-7f.

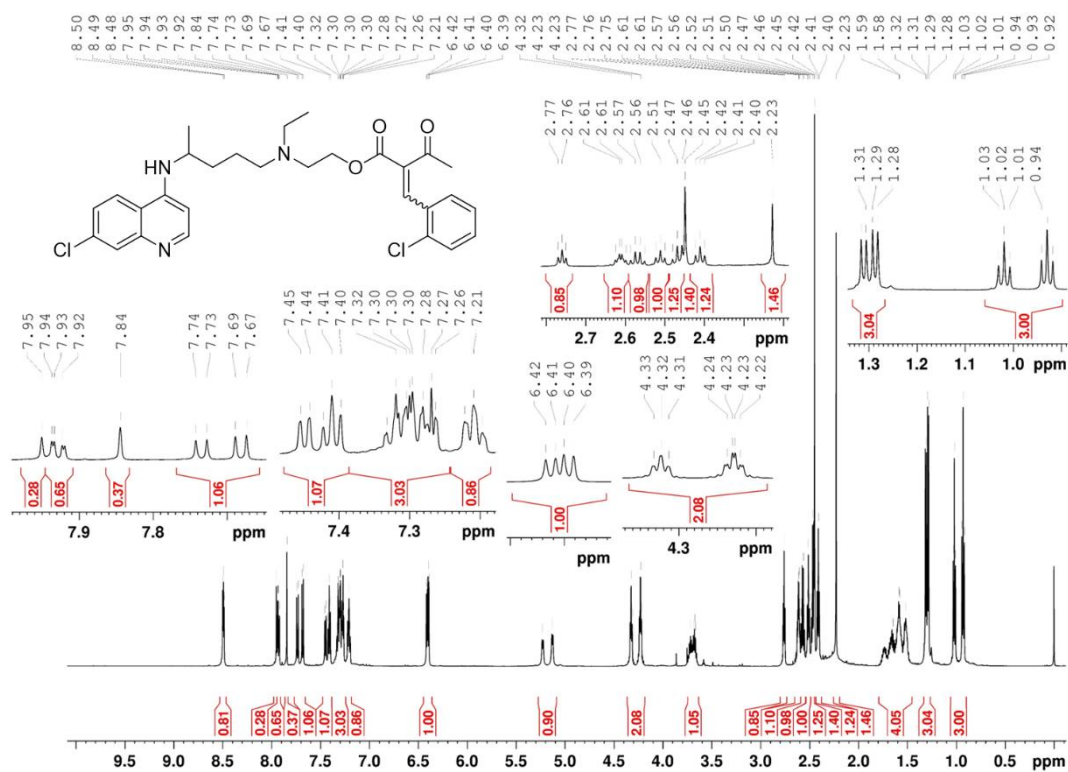


Figure S17. ^1H NMR (600 MHz, CDCl_3) spectrum of (*E/Z*)-**7g**.

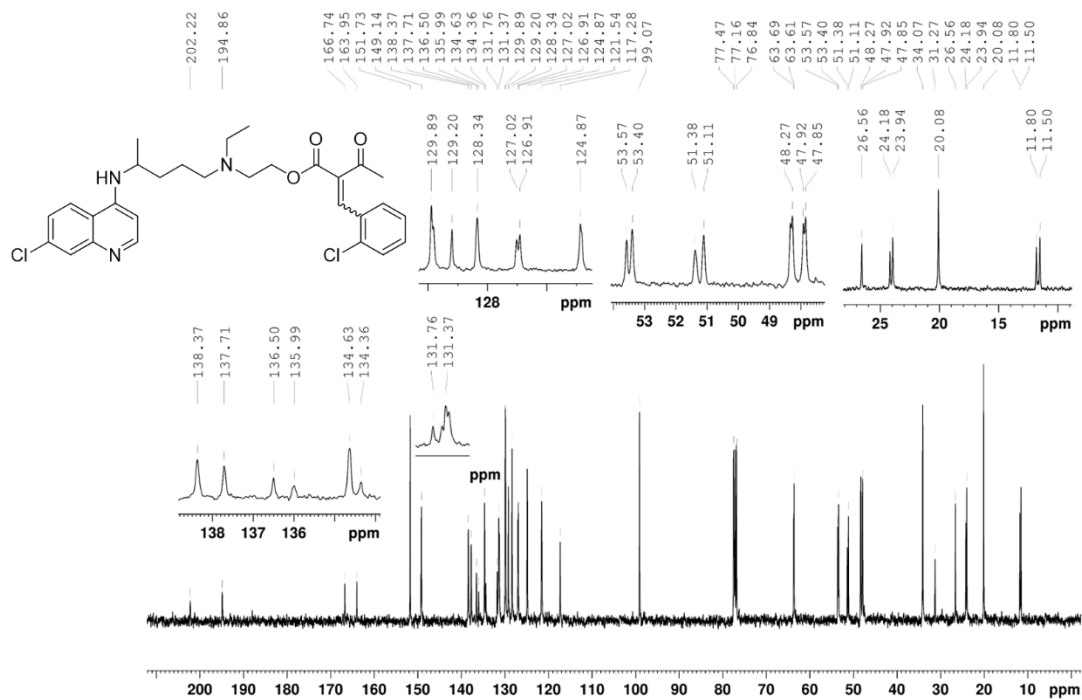
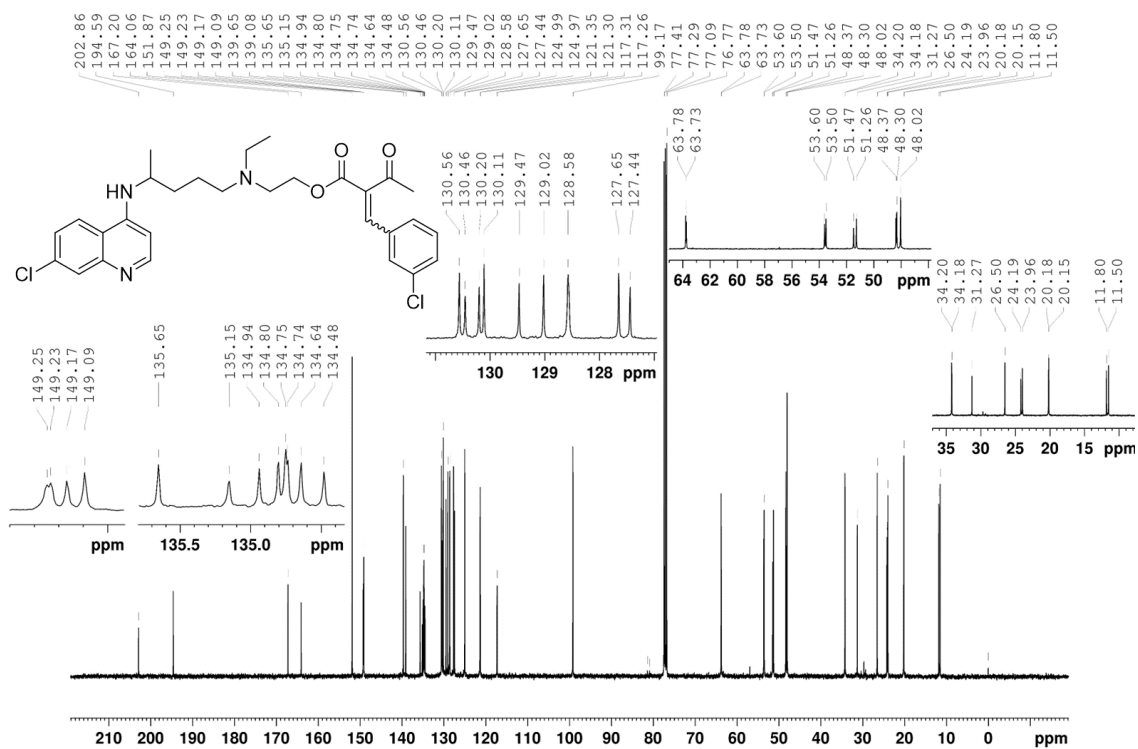
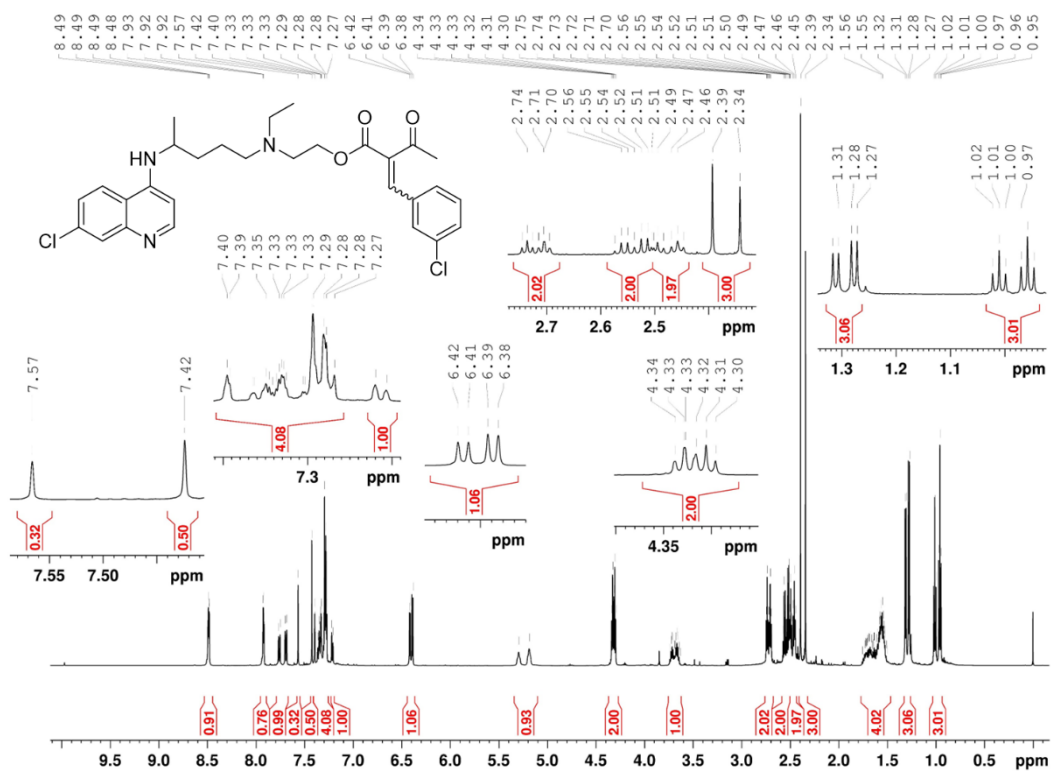
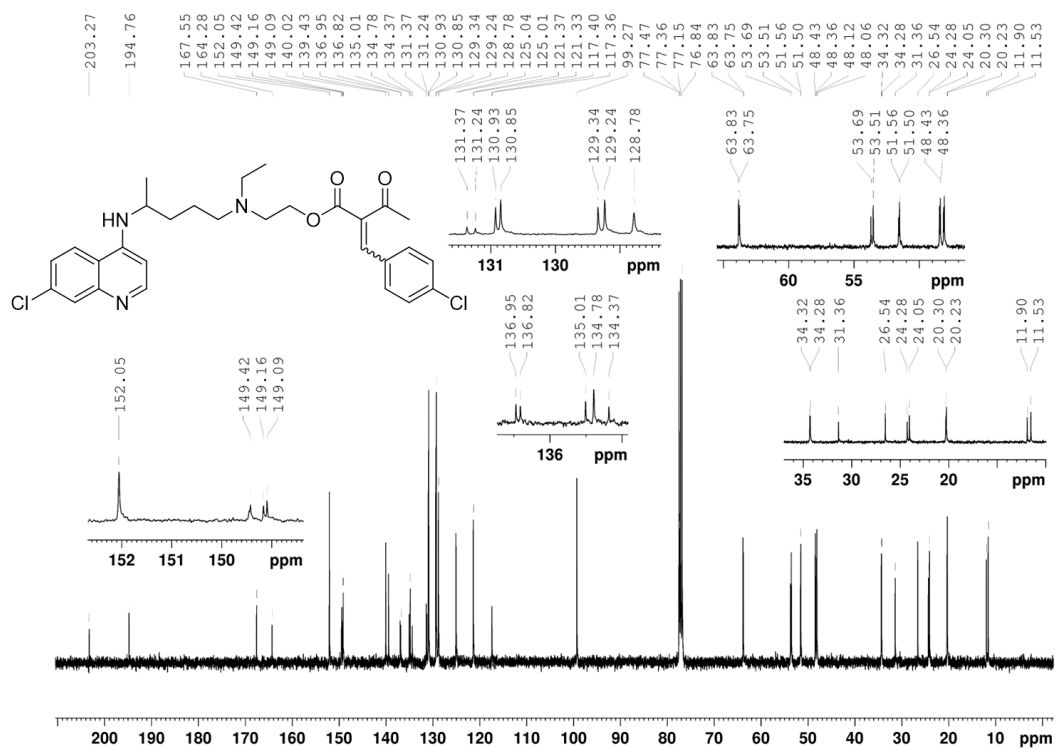
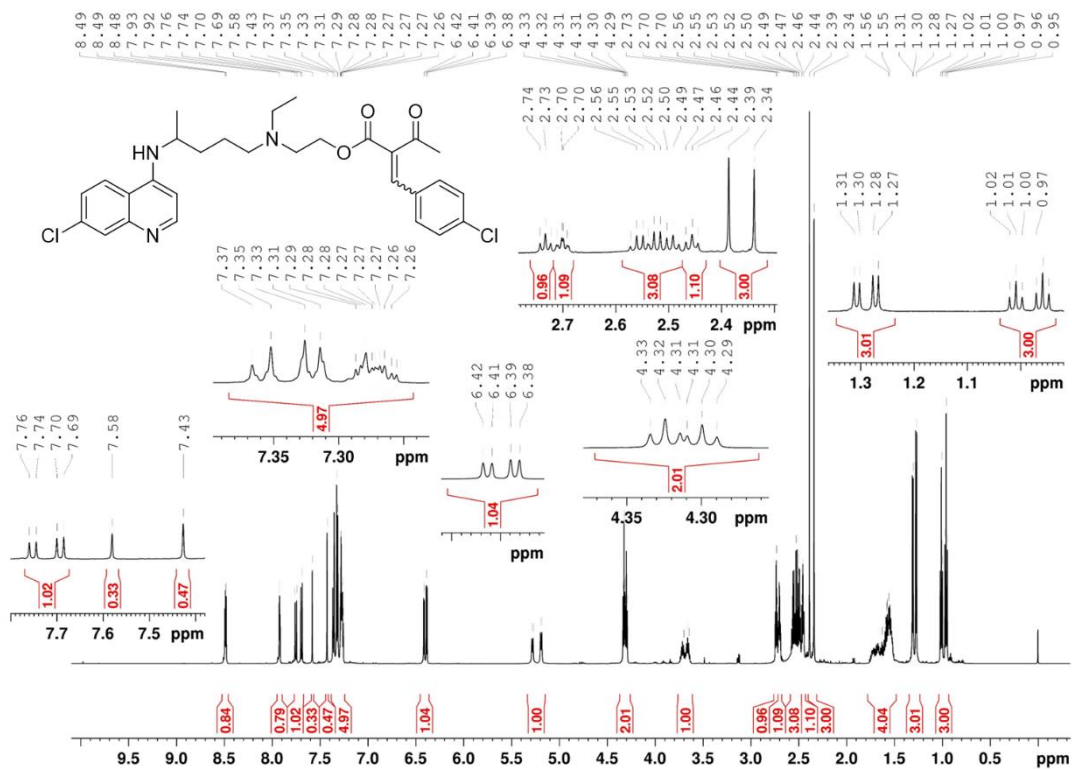
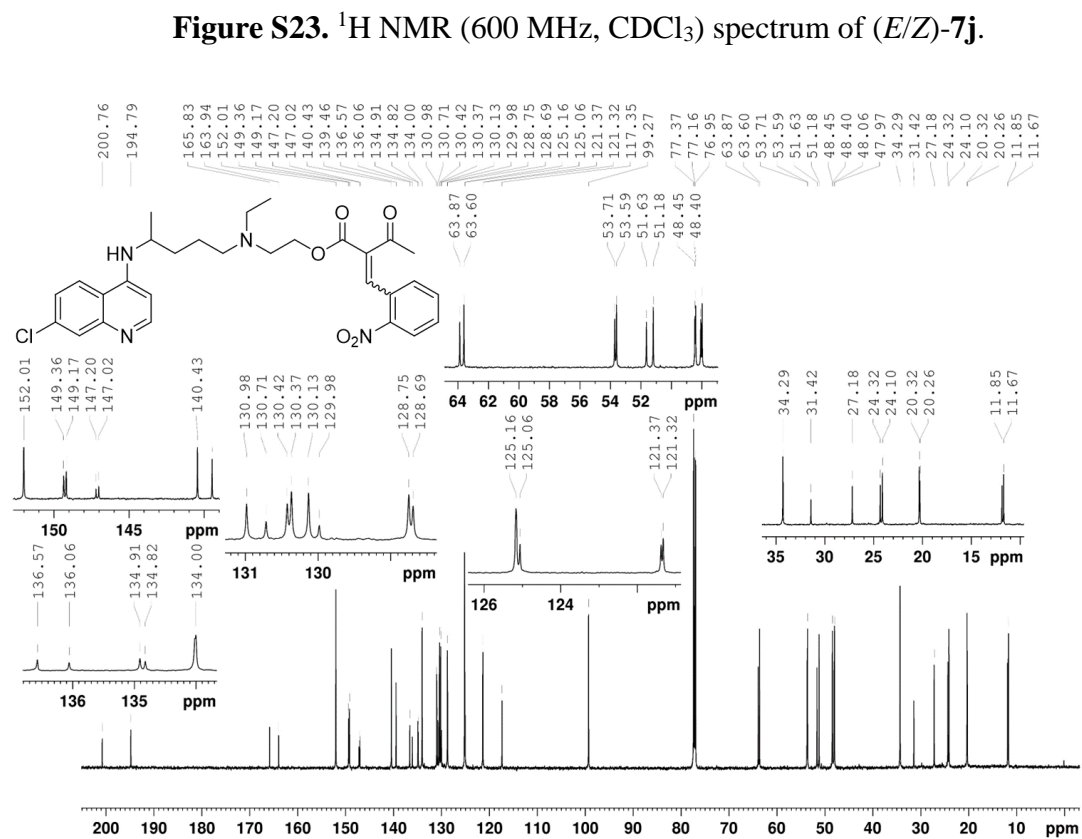
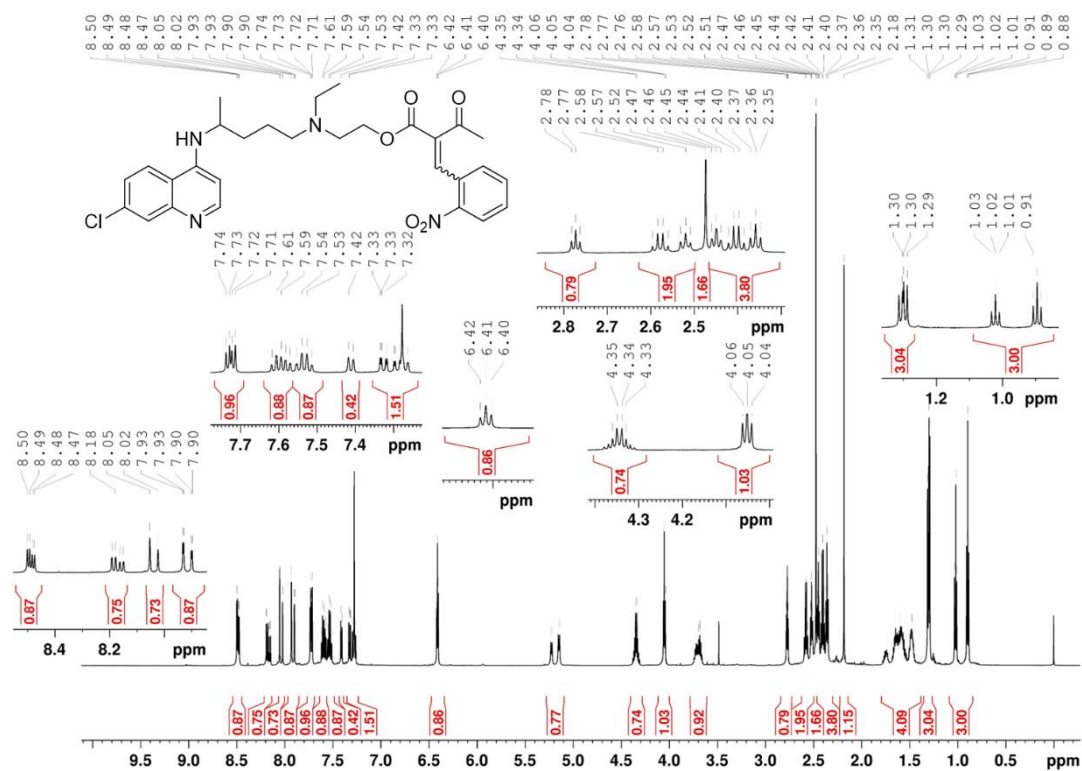
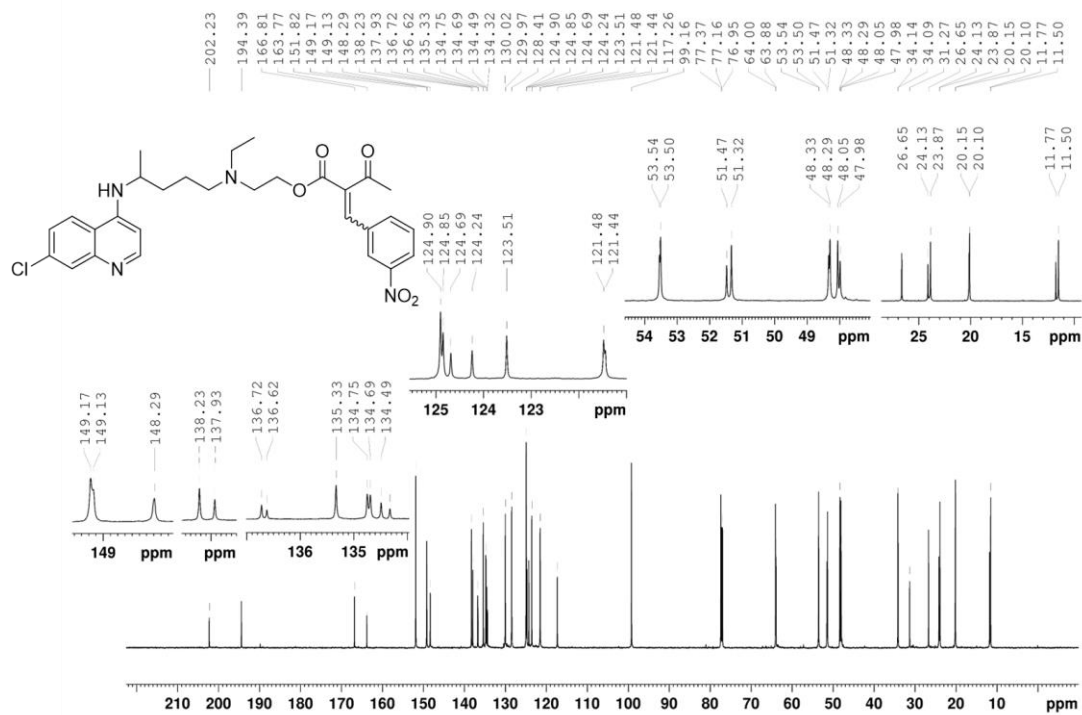
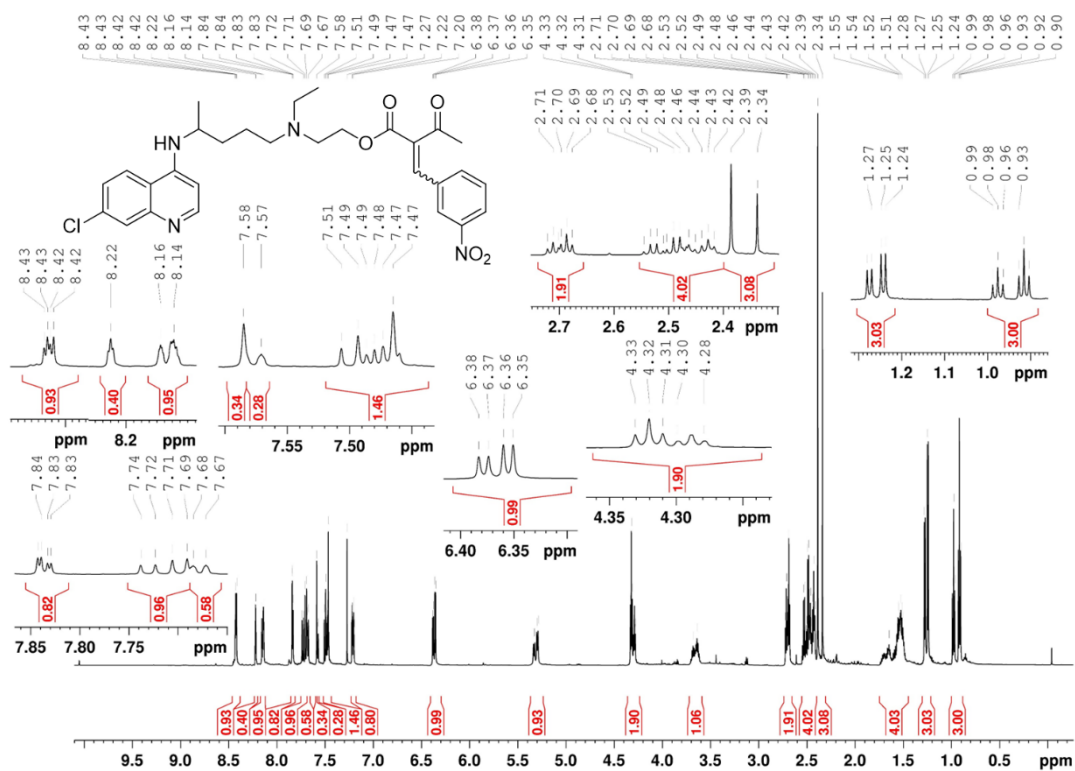


Figure S18. ^{13}C NMR (100 MHz, CDCl_3) spectrum of (*E/Z*)-**7g**.









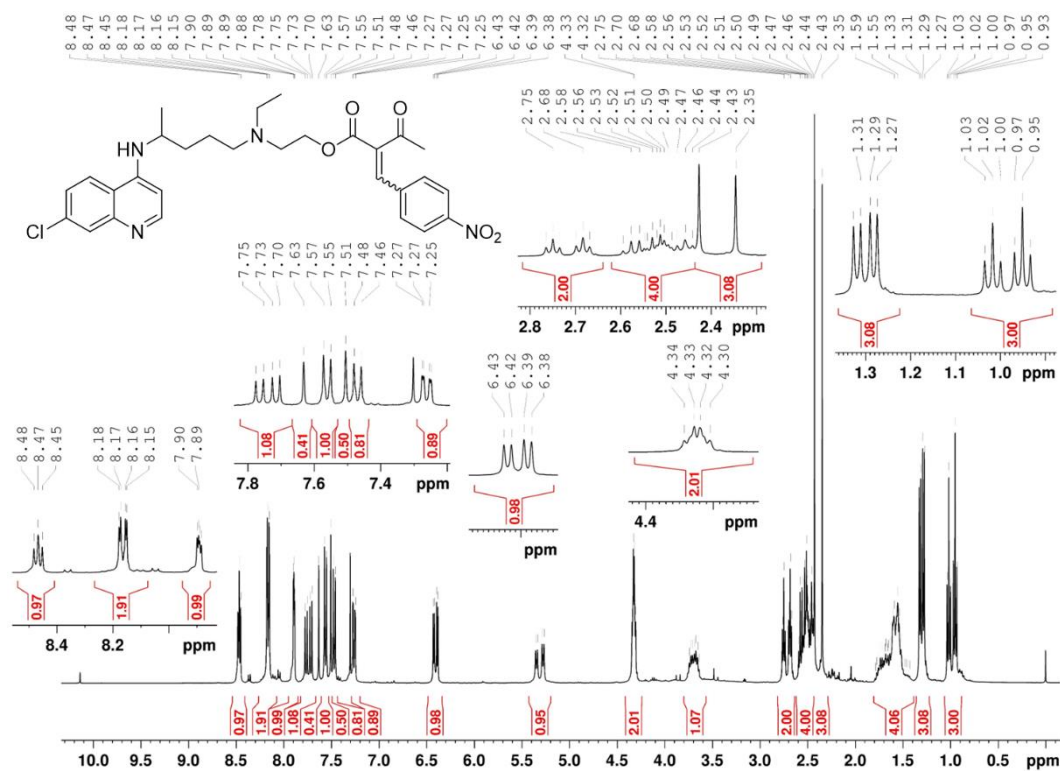


Figure S27. ¹H NMR (400 MHz, CDCl₃) spectrum of *(E/Z)*-71.

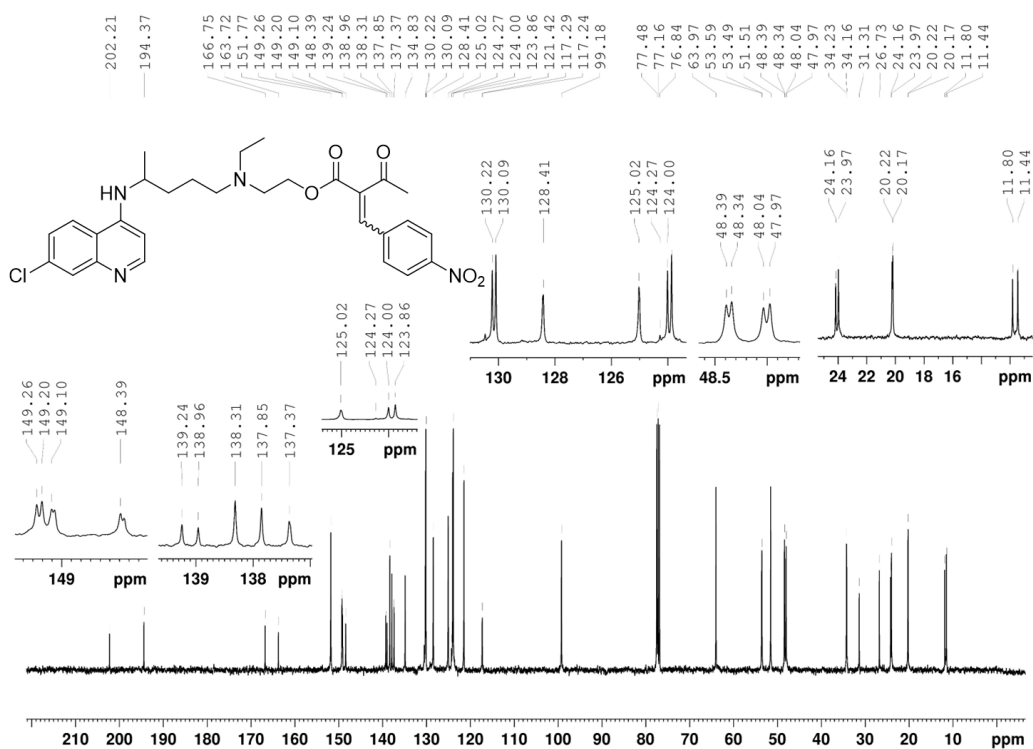


Figure S28. ¹³C NMR (100 MHz, CDCl₃) spectrum of *(E/Z)*-71.

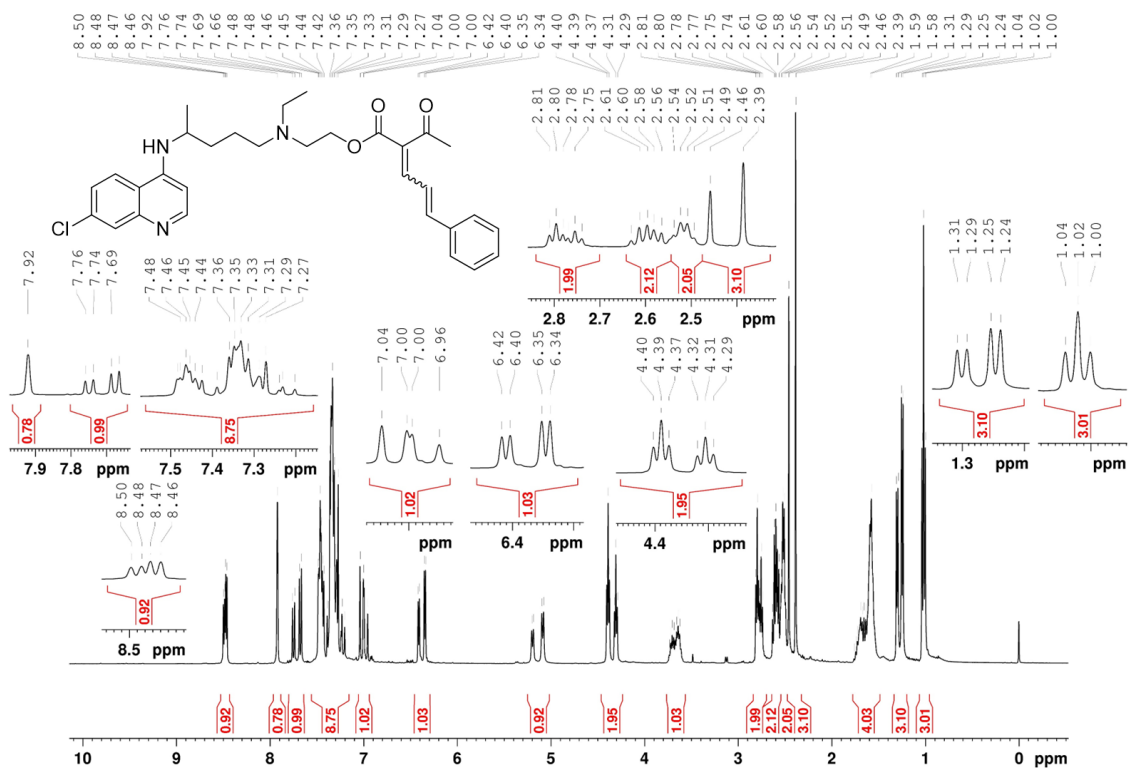


Figure S29. ^1H NMR (400 MHz, CDCl_3) spectrum of (*E/Z*)-7m.

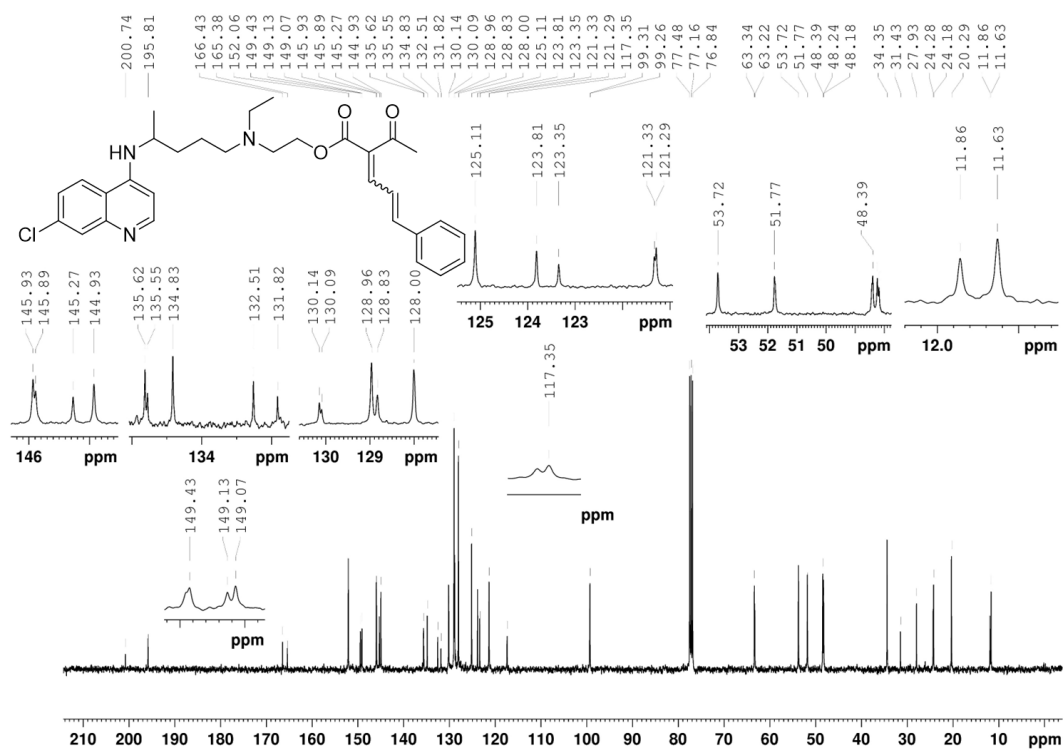
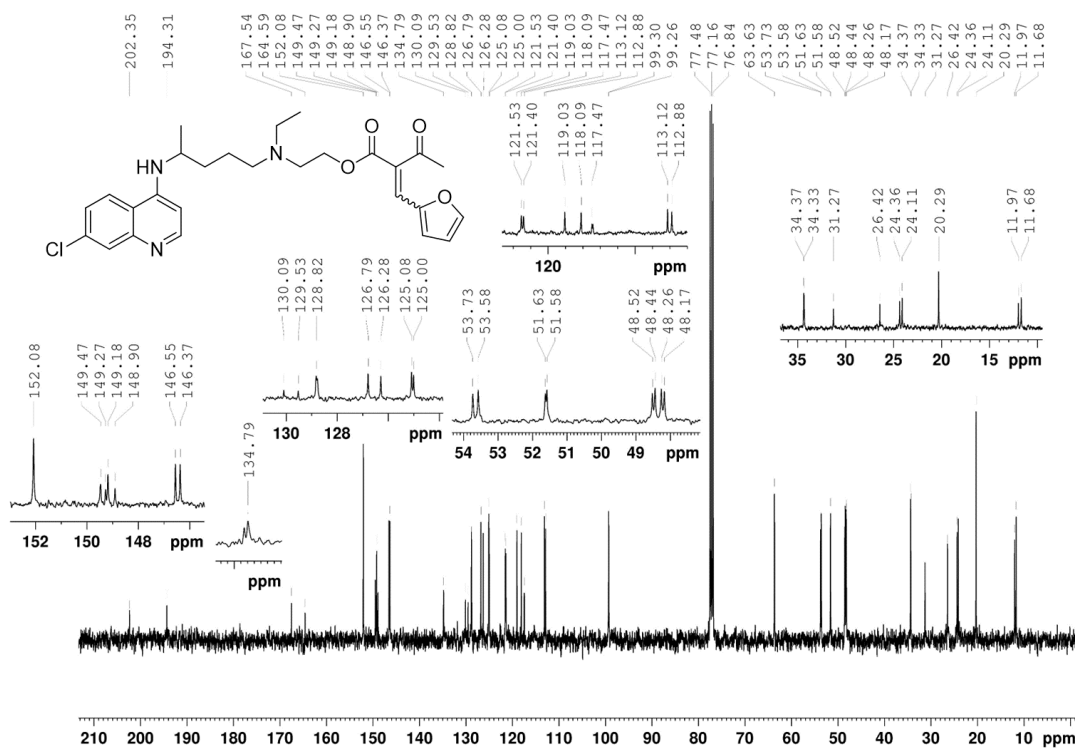
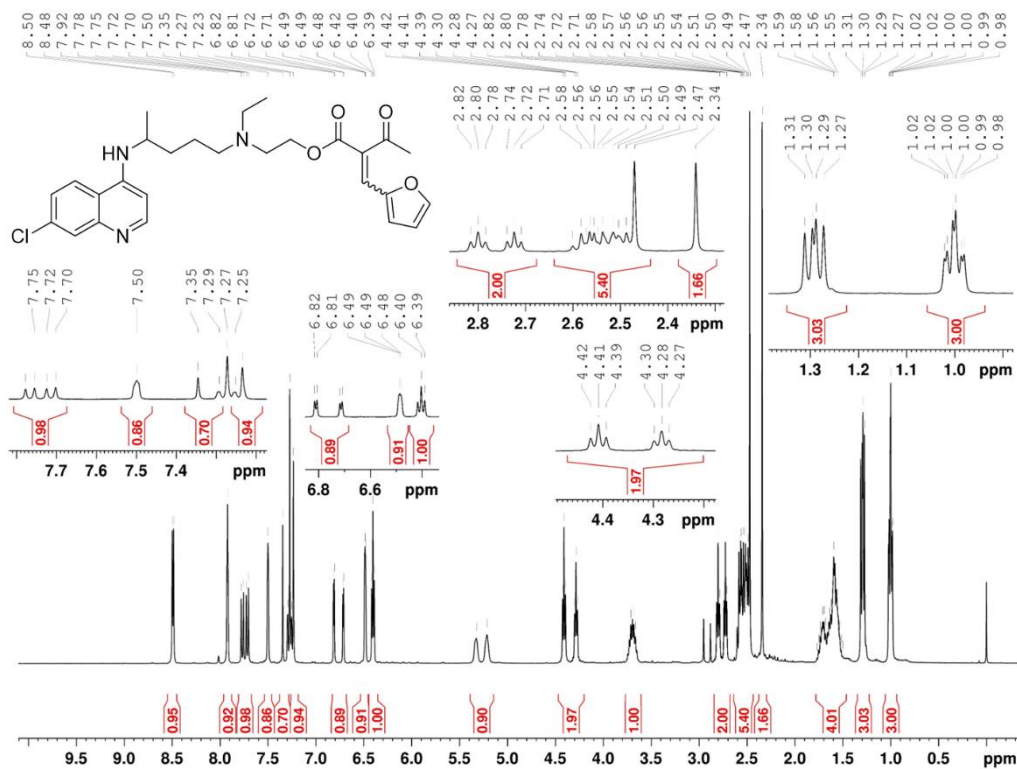


Figure S30. ^{13}C NMR (100 MHz, CDCl_3) spectrum of (*E/Z*)-7m.



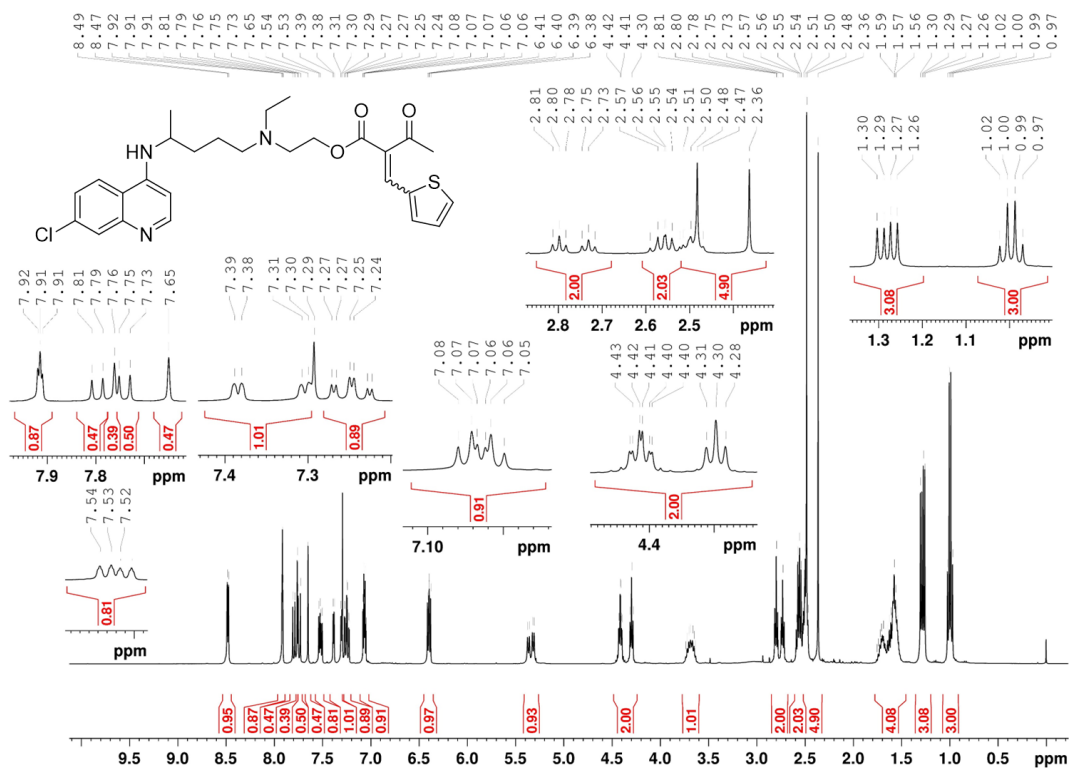


Figure S33. ¹H NMR (400 MHz, CDCl₃) spectrum of (E/Z)-7o.

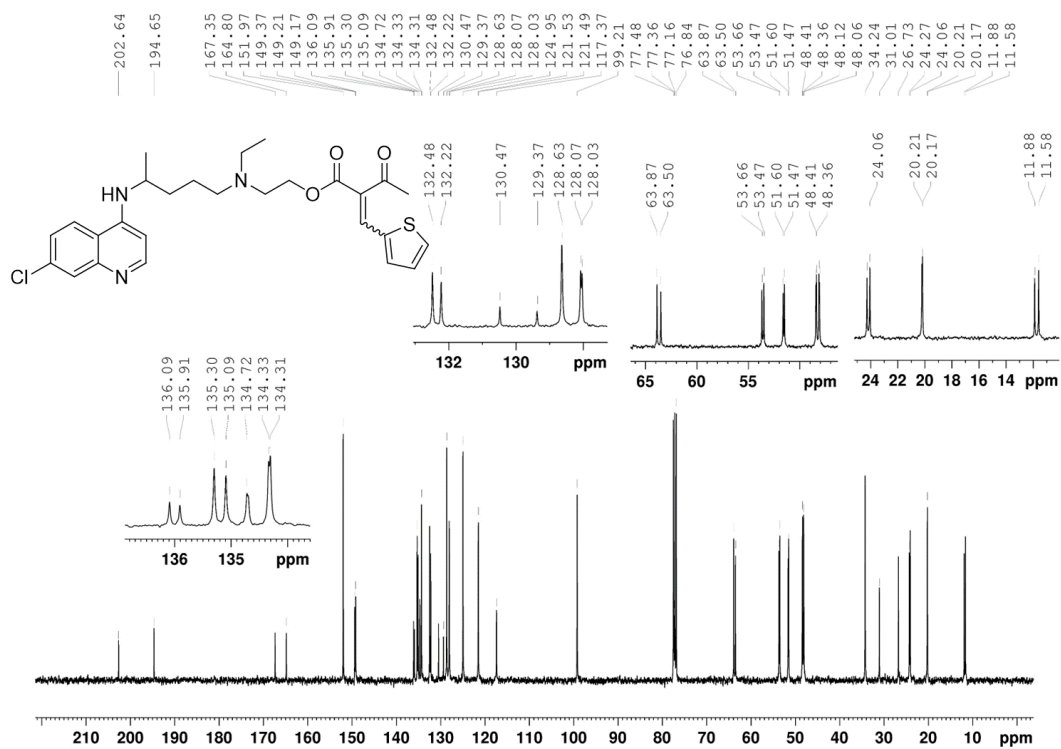


Figure S34. ¹³C NMR (100 MHz, CDCl₃) spectrum of (E/Z)-7o.

Selected HSQC and HMBC spectra

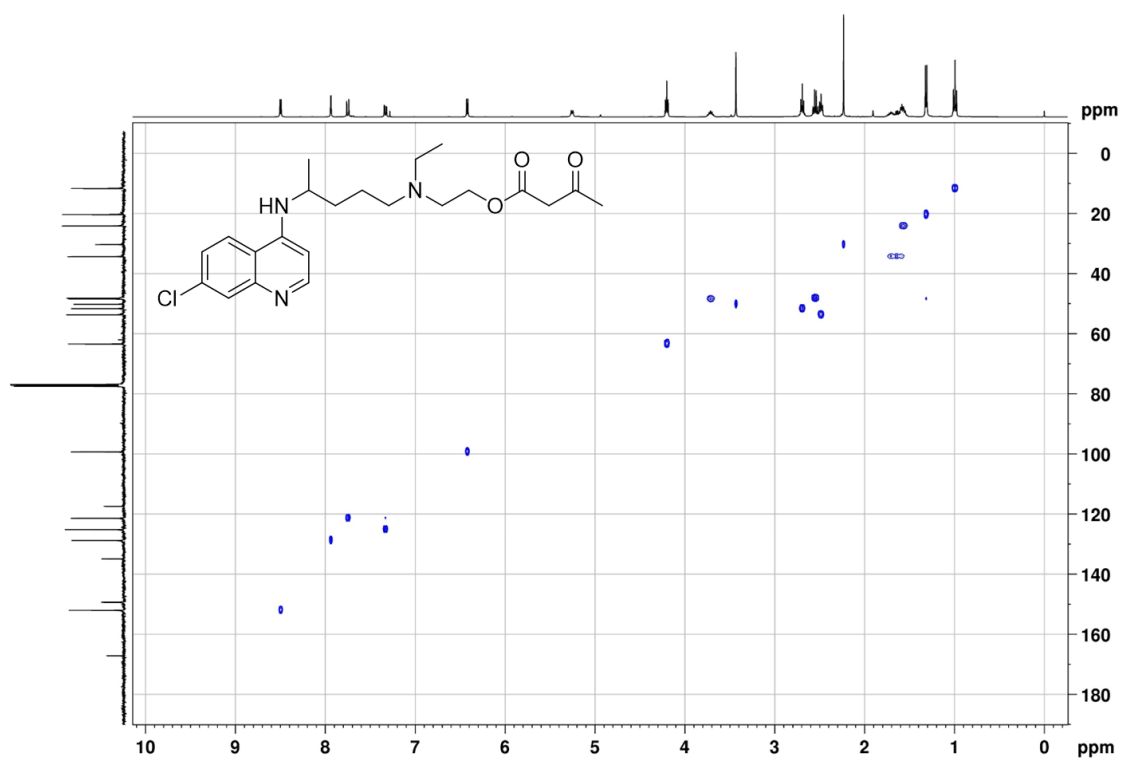


Figure S35. Heteronuclear correlation of a ^1H - ^{13}C bond (HSQC) in CDCl_3 of **5**.

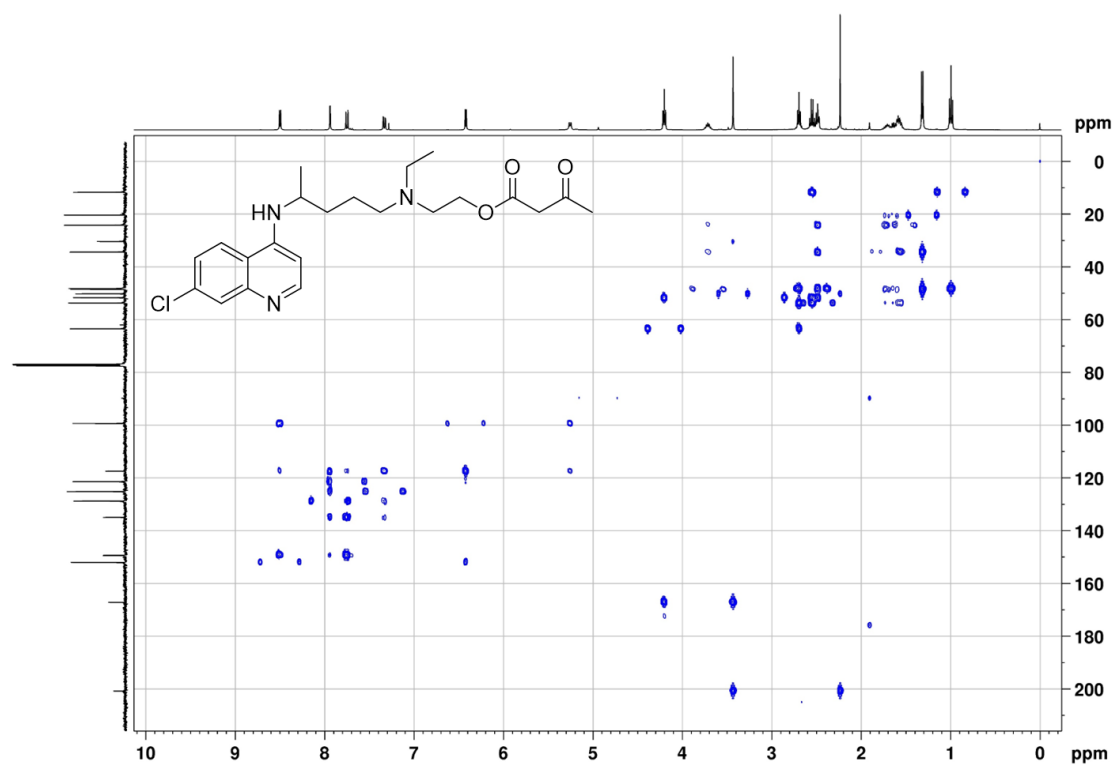


Figure S36. Heteronuclear correlation of a ^1H - ^{13}C bond (HMBC) in CDCl_3 of **5**.

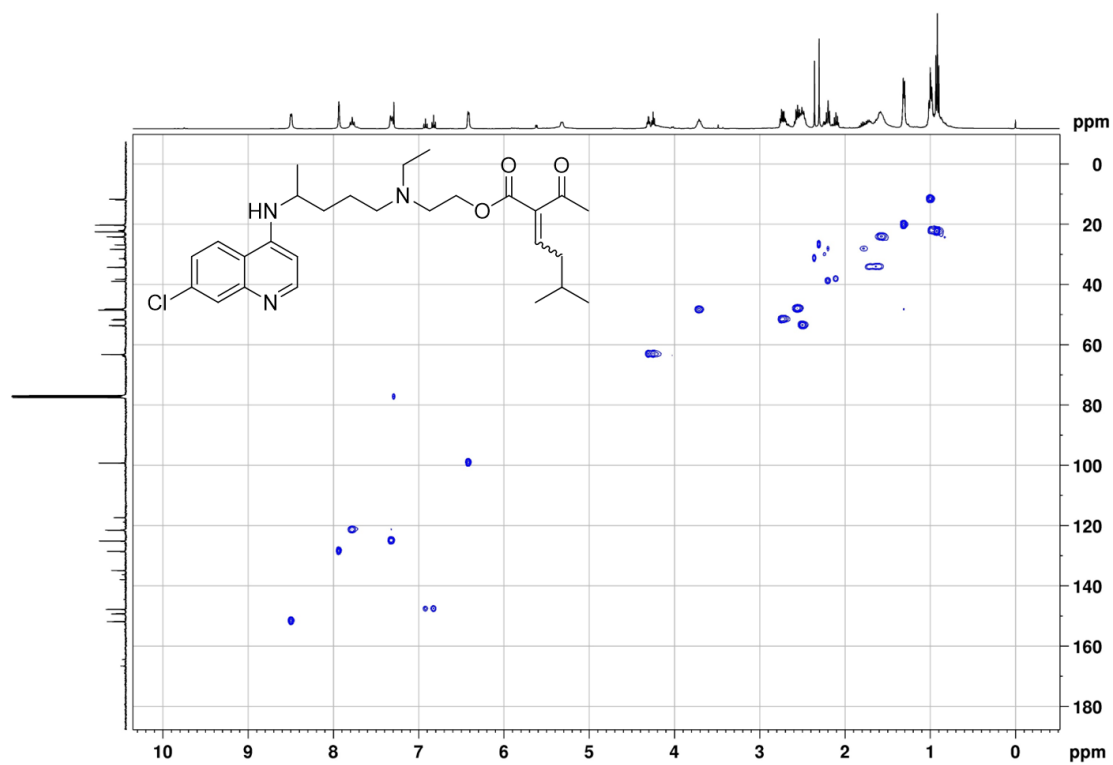


Figure S37. Heteronuclear correlation of a ^1H - ^{13}C bond (HSQC) in CDCl_3 of (*E/Z*)-**7a**.

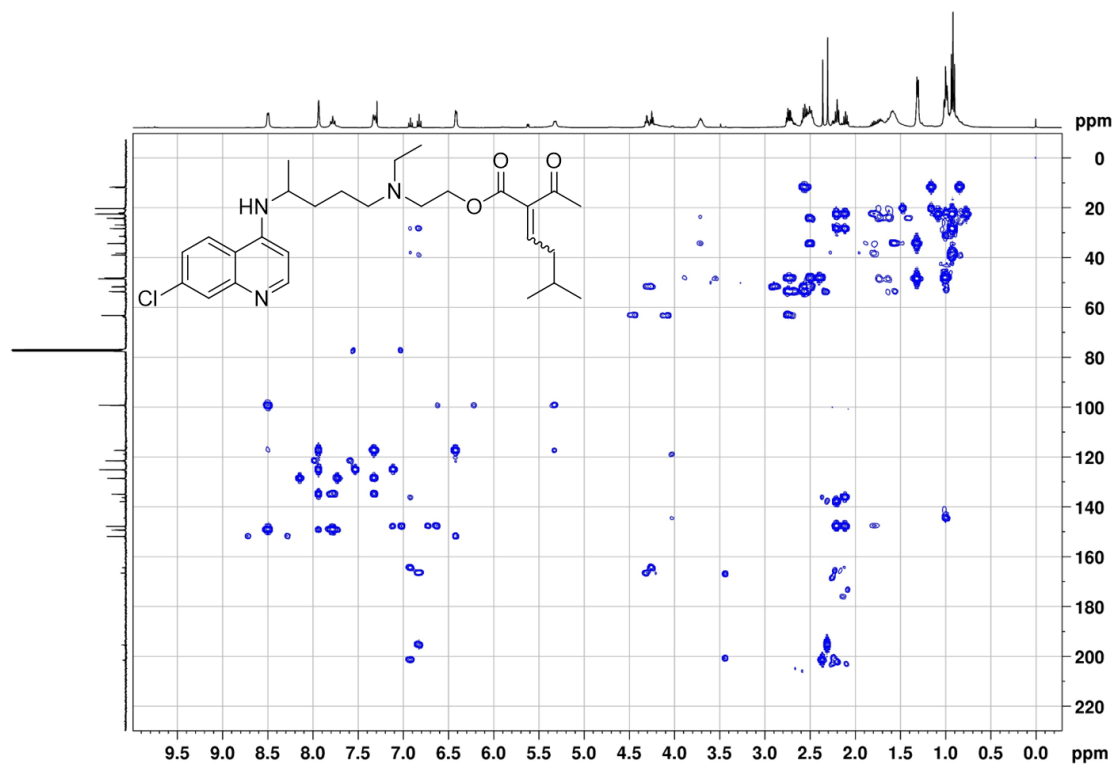


Figure S38. Heteronuclear correlation of a ^1H - ^{13}C bond (HMBC) in CDCl_3 of (*E/Z*)-**7a**.

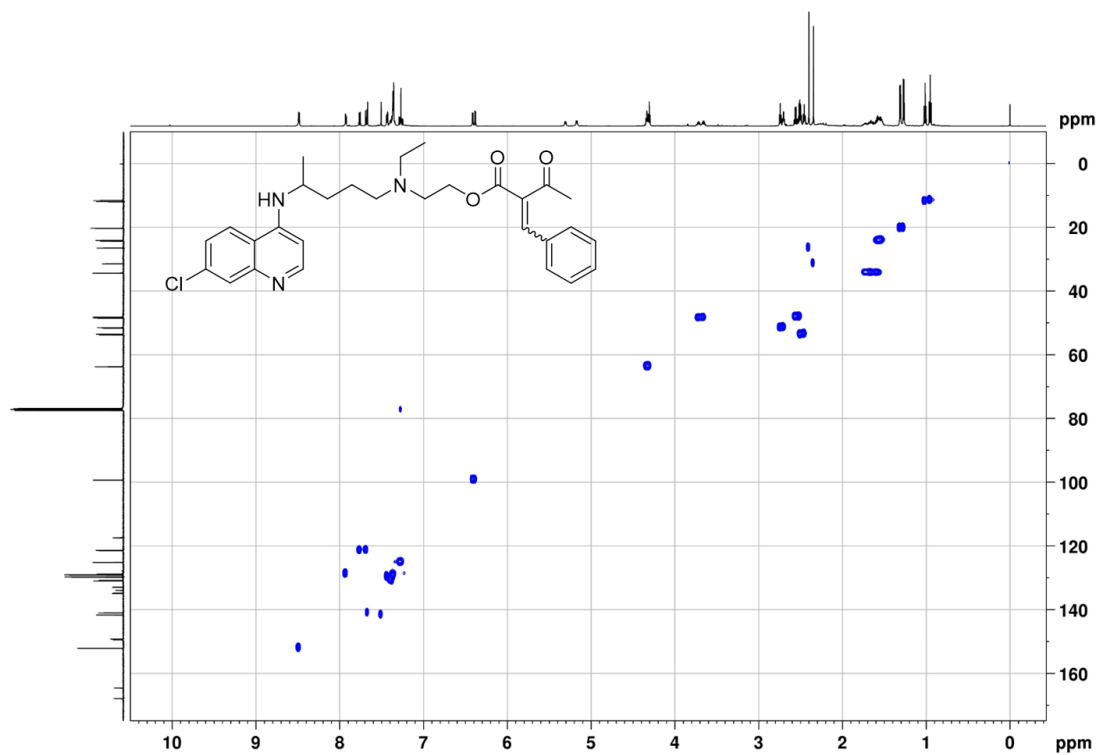


Figure S39. Heteronuclear correlation of a ¹H-¹³C bond (HSQC) in CDCl₃ of *(E/Z)*-7b.

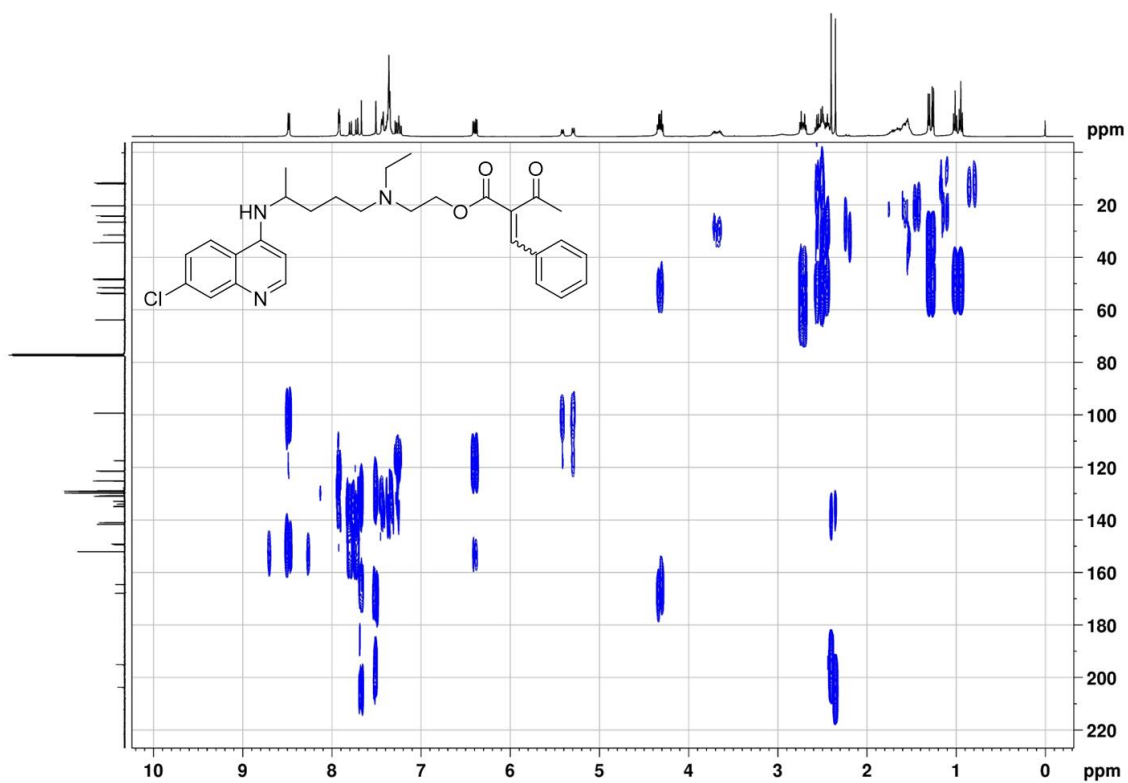


Figure S40. Heteronuclear correlation of a ¹H-¹³C bond (HMBC) in CDCl₃ of *(E/Z)*-7b.

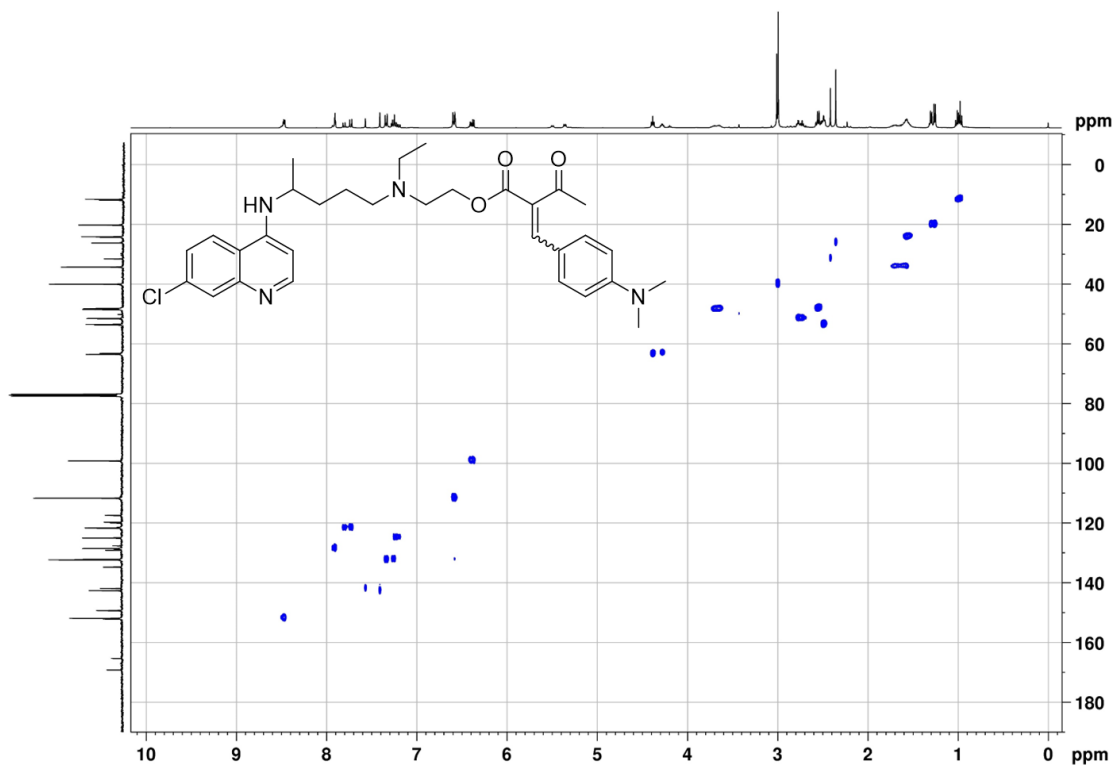


Figure S41. Heteronuclear correlation of a ^1H - ^{13}C bond (HSQC) in CDCl_3 of (*E/Z*)-**7c**.

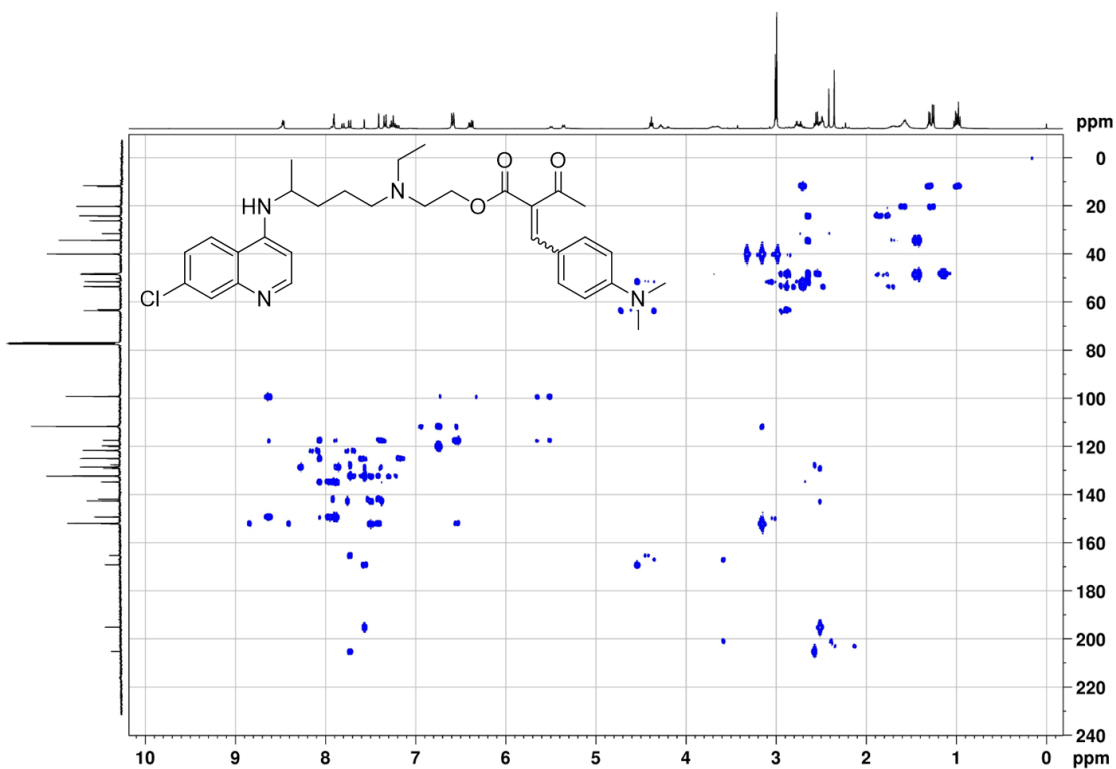


Figure S42. Heteronuclear correlation of a ^1H - ^{13}C bond (HMBC) in CDCl_3 of (*E/Z*)-**7c**.

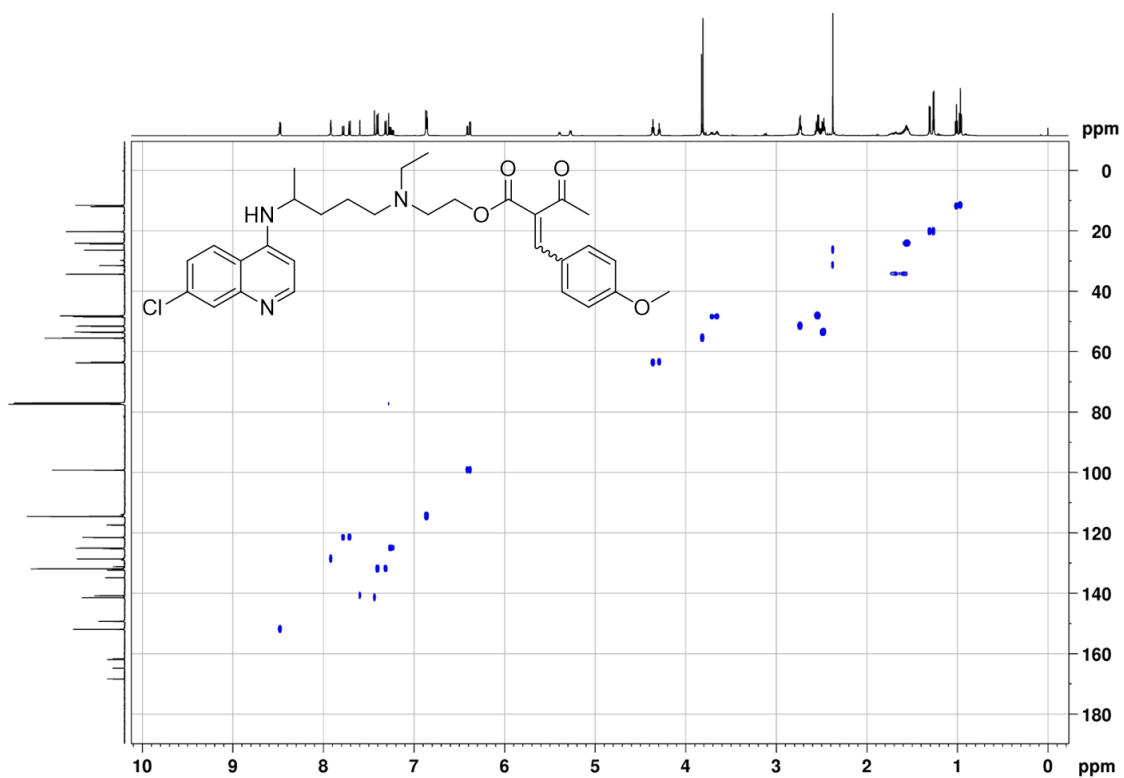


Figure S43. Heteronuclear correlation of a ^1H - ^{13}C bond (HSQC) in CDCl_3 of (*E/Z*)-**7d**.

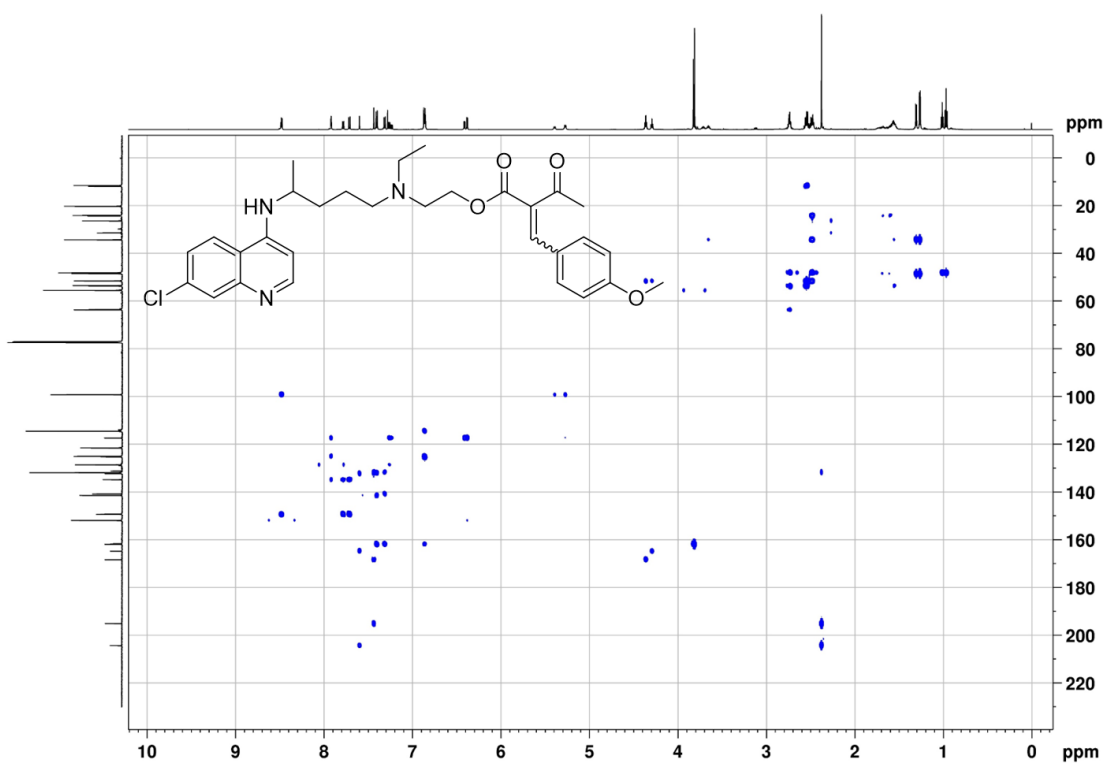


Figure S44. Heteronuclear correlation of a ^1H - ^{13}C bond (HMBC) in CDCl_3 of (*E/Z*)-**7d**.

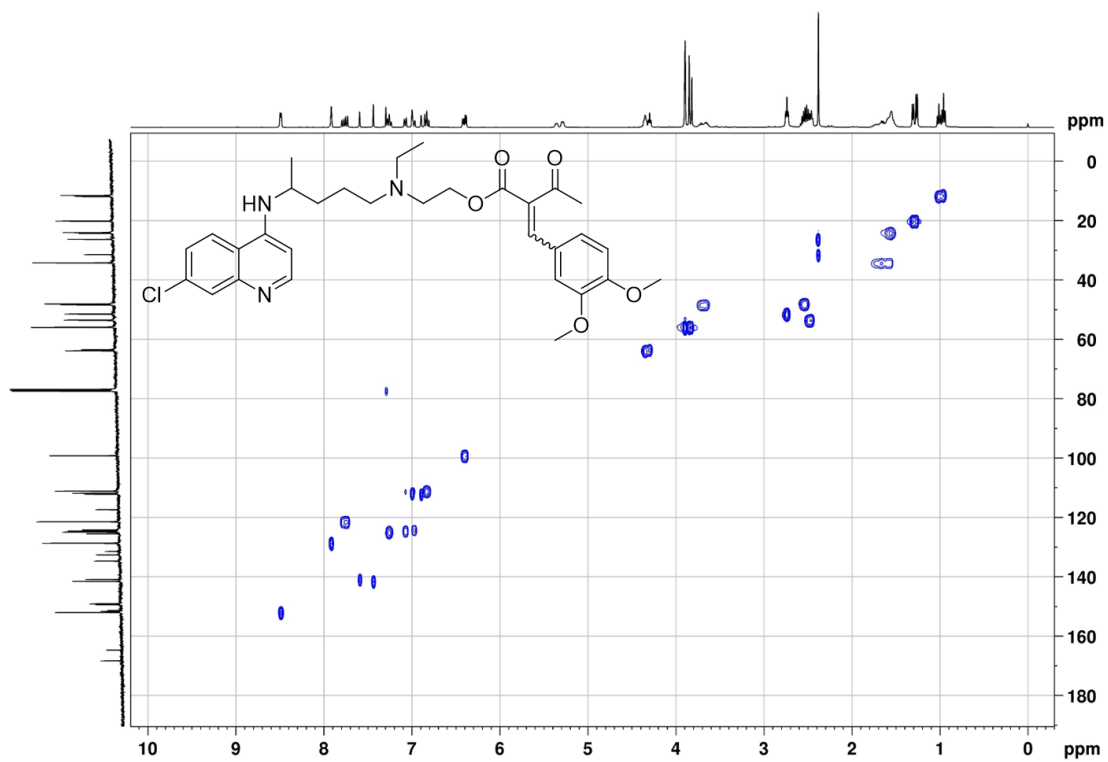


Figure S45. Heteronuclear correlation of a ¹H-¹³C bond (HSQC) in CDCl₃ of *(E/Z)*-7e.

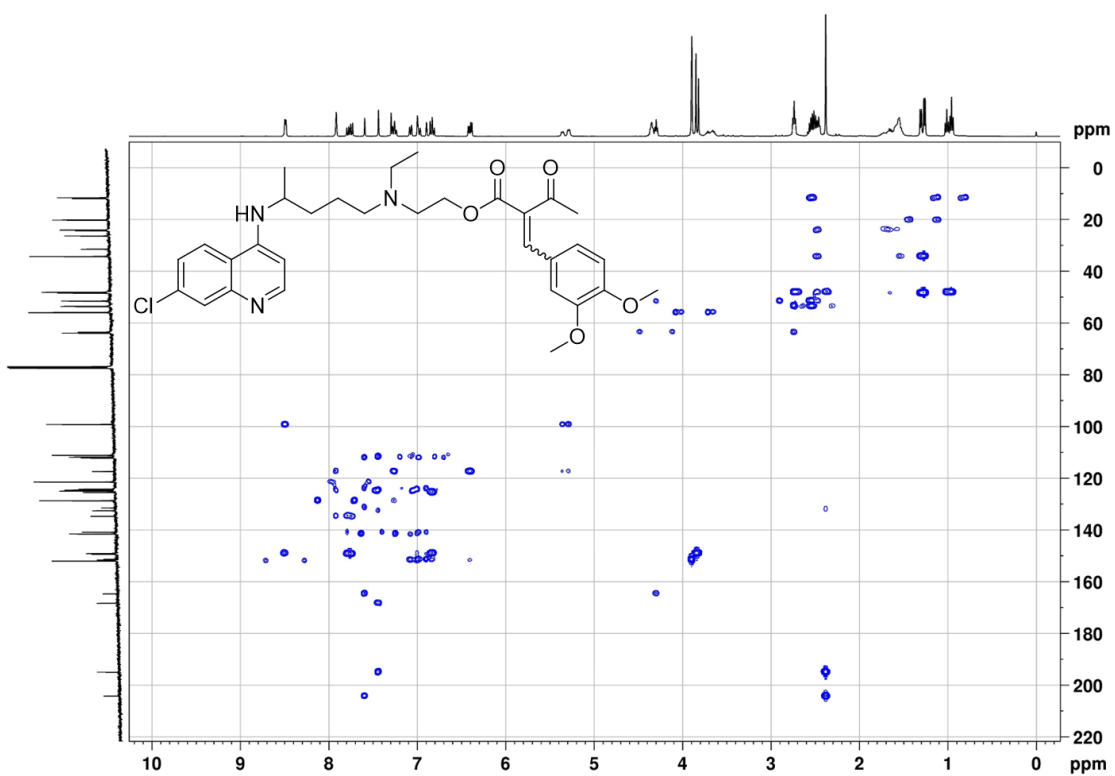


Figure S46. Heteronuclear correlation of a ¹H-¹³C bond (HMBC) in CDCl₃ of *(E/Z)*-7e.

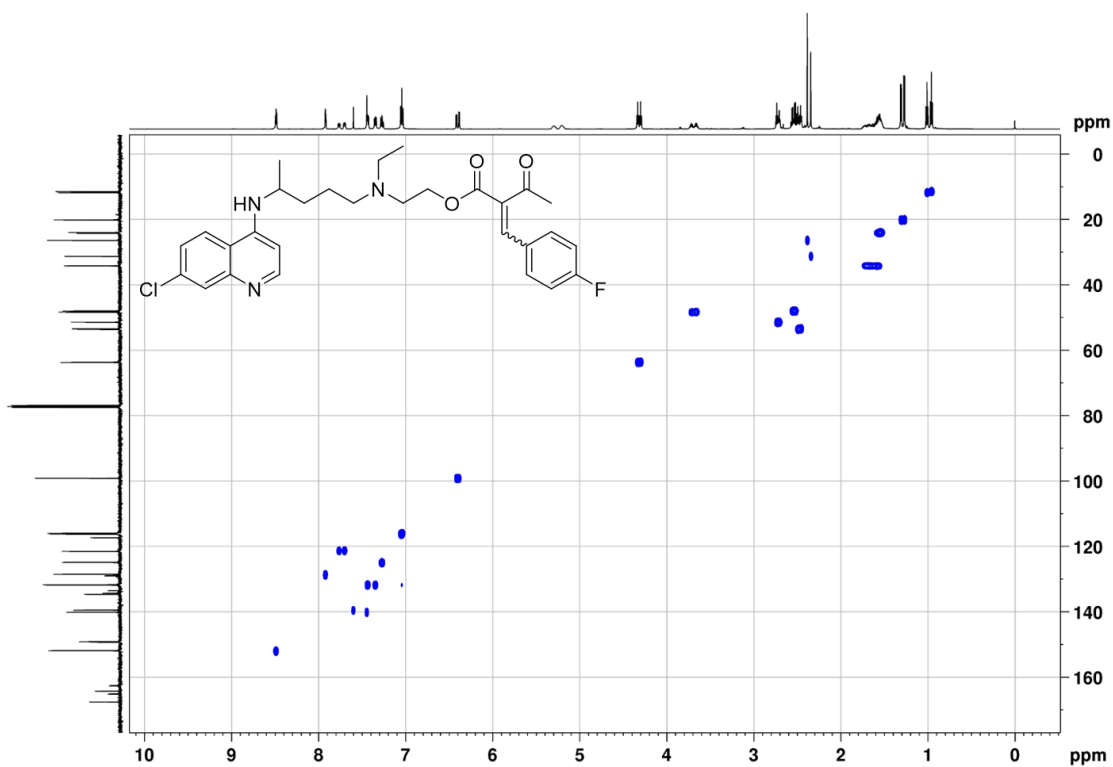


Figure S47. Heteronuclear correlation of a ¹H-¹³C bond (HSQC) in CDCl₃ of (E/Z)-7f.

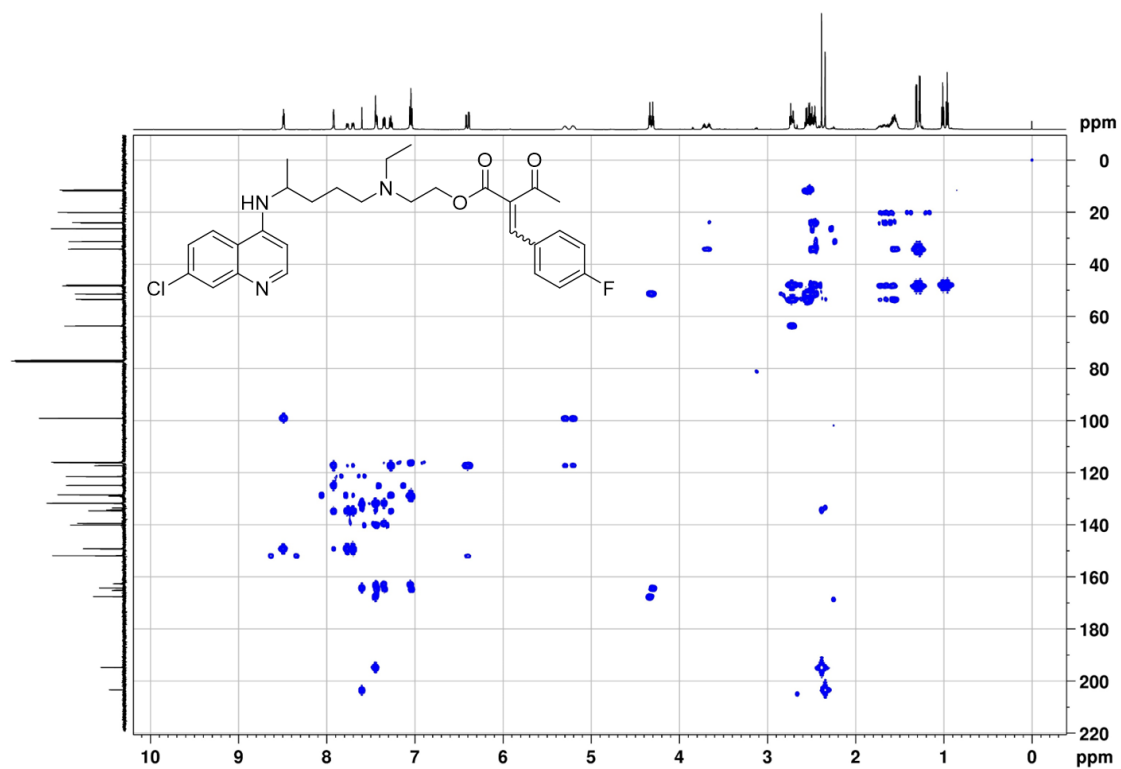


Figure S48. Heteronuclear correlation of a ¹H-¹³C bond (HMBC) in CDCl₃ of (E/Z)-7f.

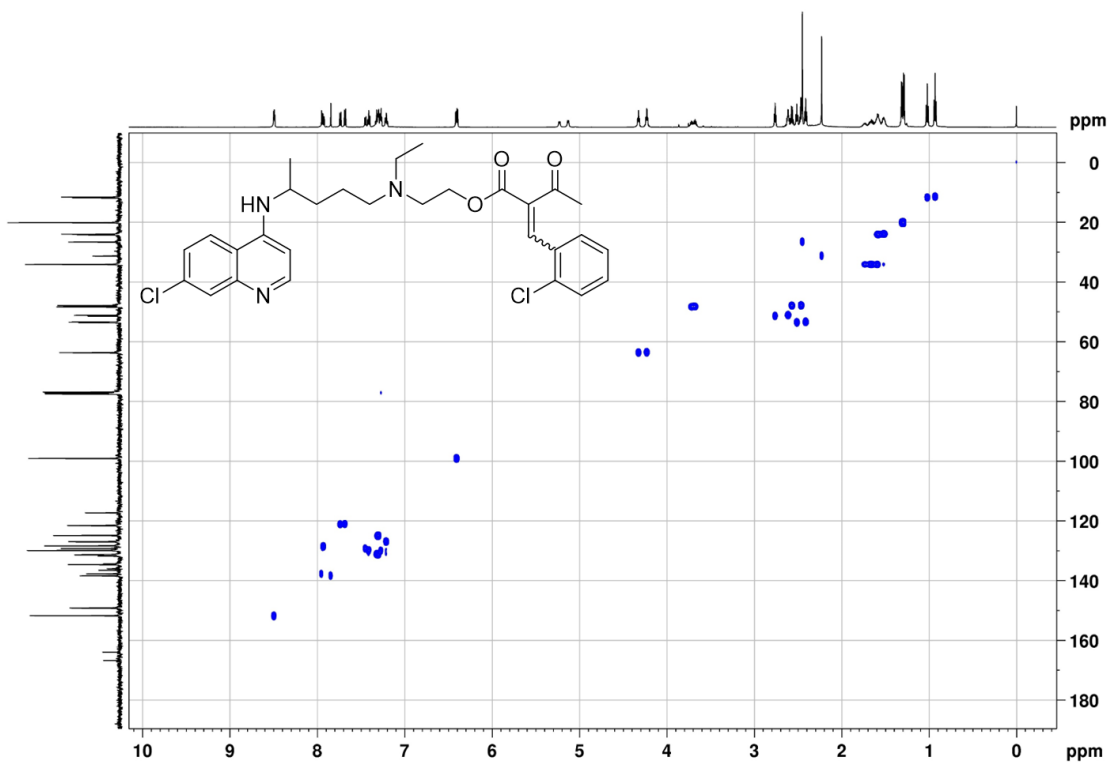


Figure S49. Heteronuclear correlation of a ¹H-¹³C bond (HSQC) in CDCl₃ of *(E/Z)*-7g.

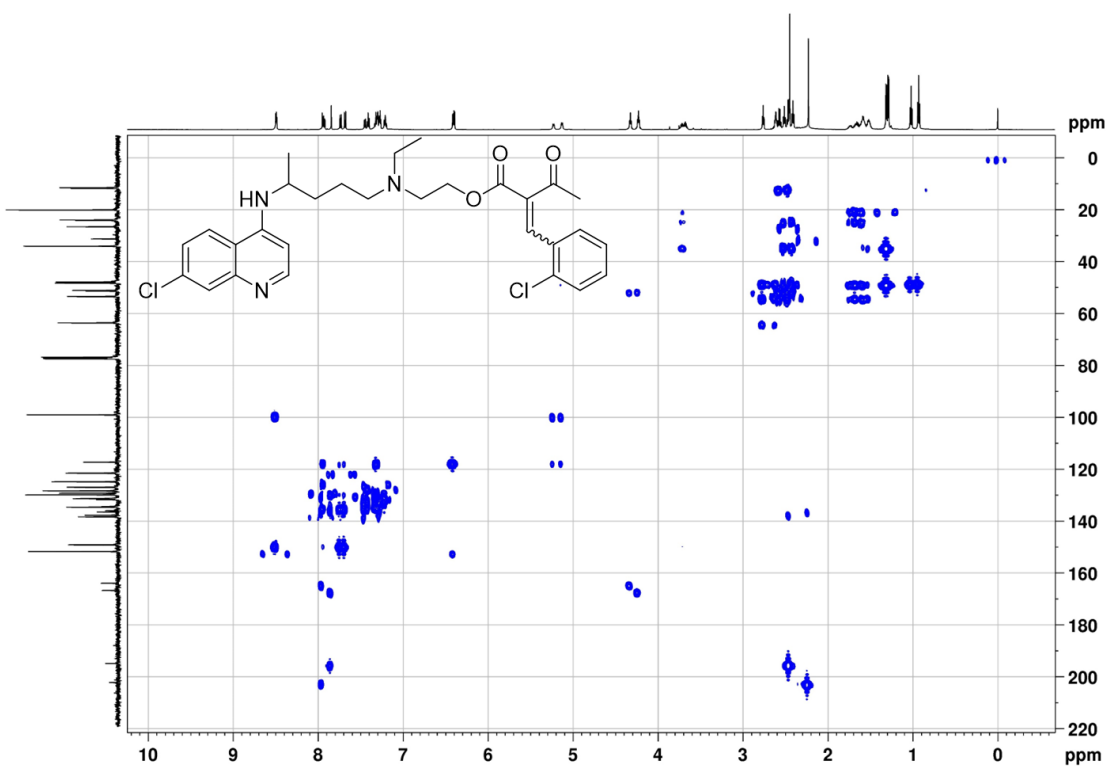


Figure S50. Heteronuclear correlation of a ¹H-¹³C bond (HMBC) in CDCl₃ of *(E/Z)*-7g.

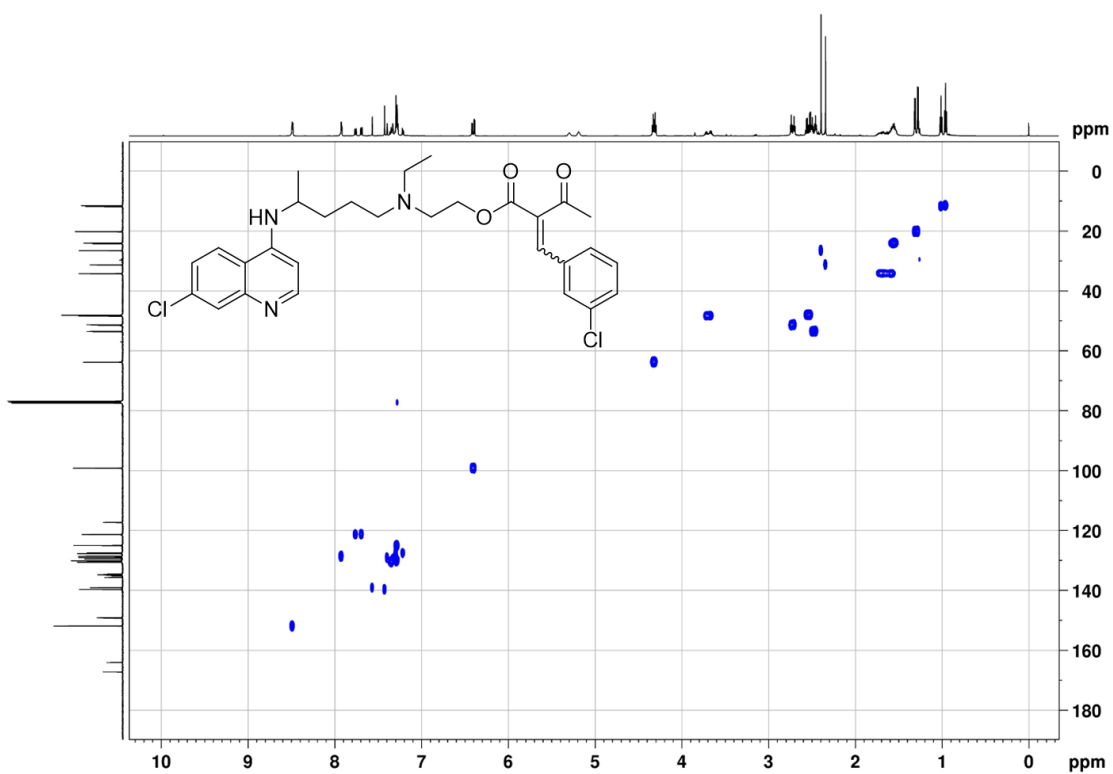


Figure S51. Heteronuclear correlation of a ^1H - ^{13}C bond (HSQC) in CDCl_3 of (*E/Z*)-**7h**.

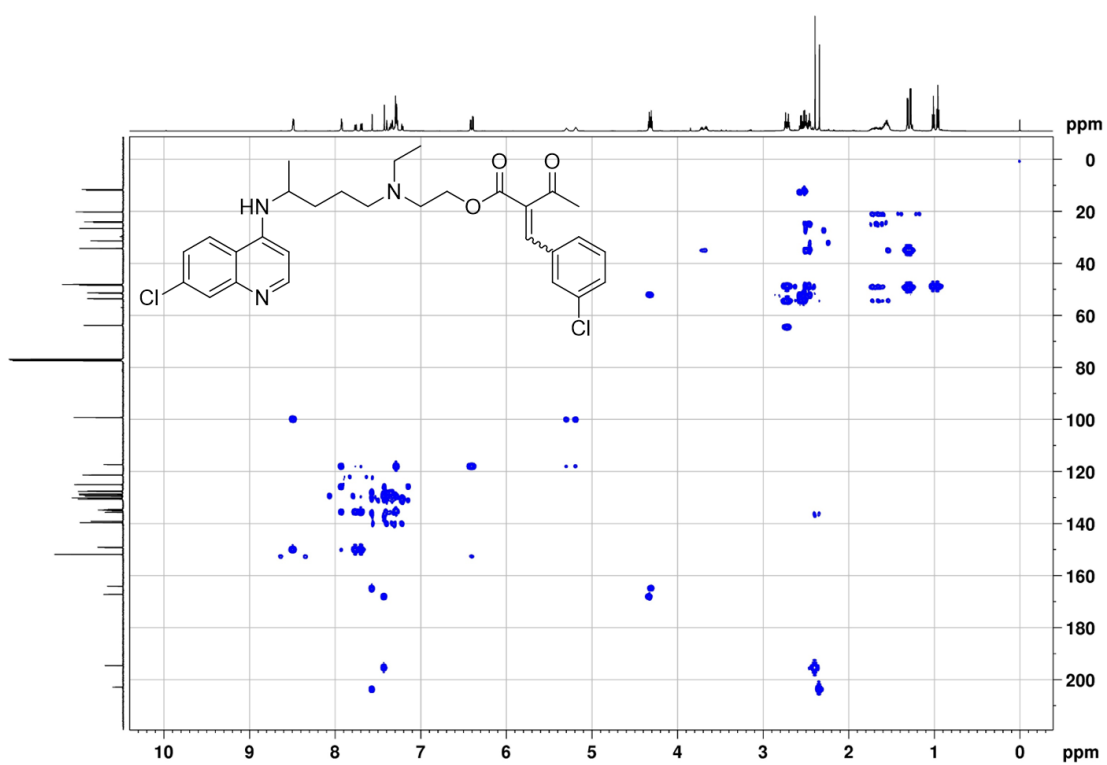


Figure S52. Heteronuclear correlation of a ^1H - ^{13}C bond (HMBC) in CDCl_3 of (*E/Z*)-**7h**.

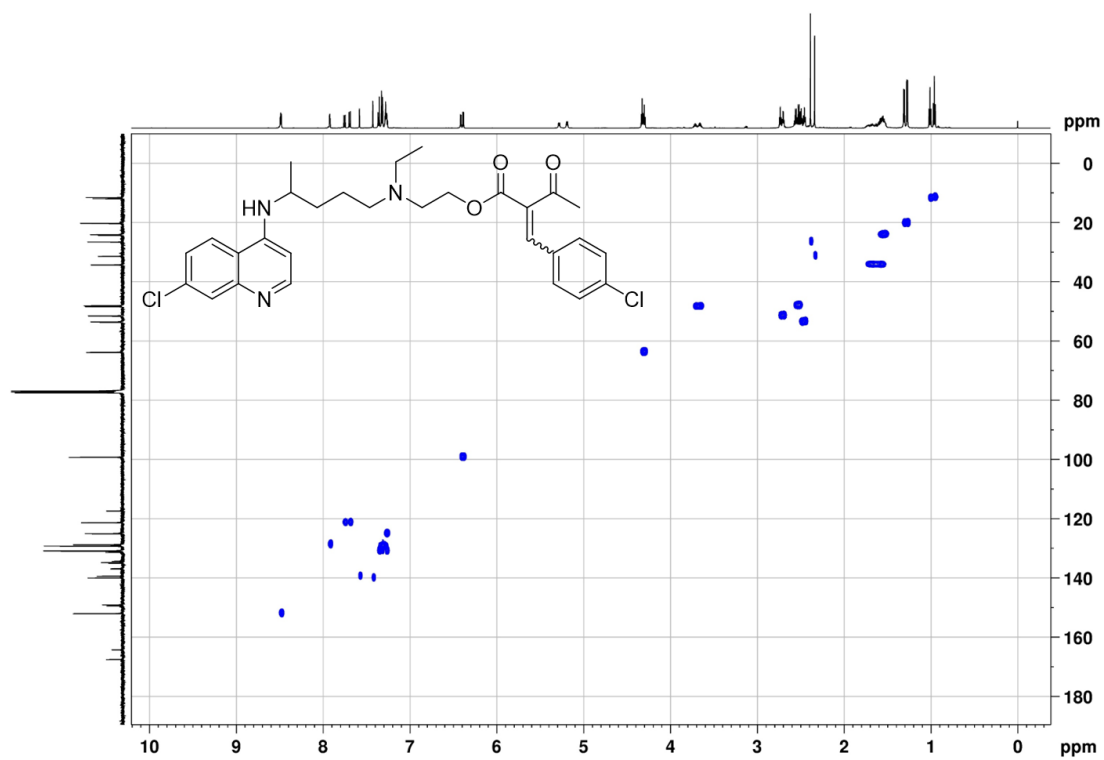


Figure S53. Heteronuclear correlation of a ^1H - ^{13}C bond (HSQC) in CDCl_3 of (*E/Z*)-**7i**.

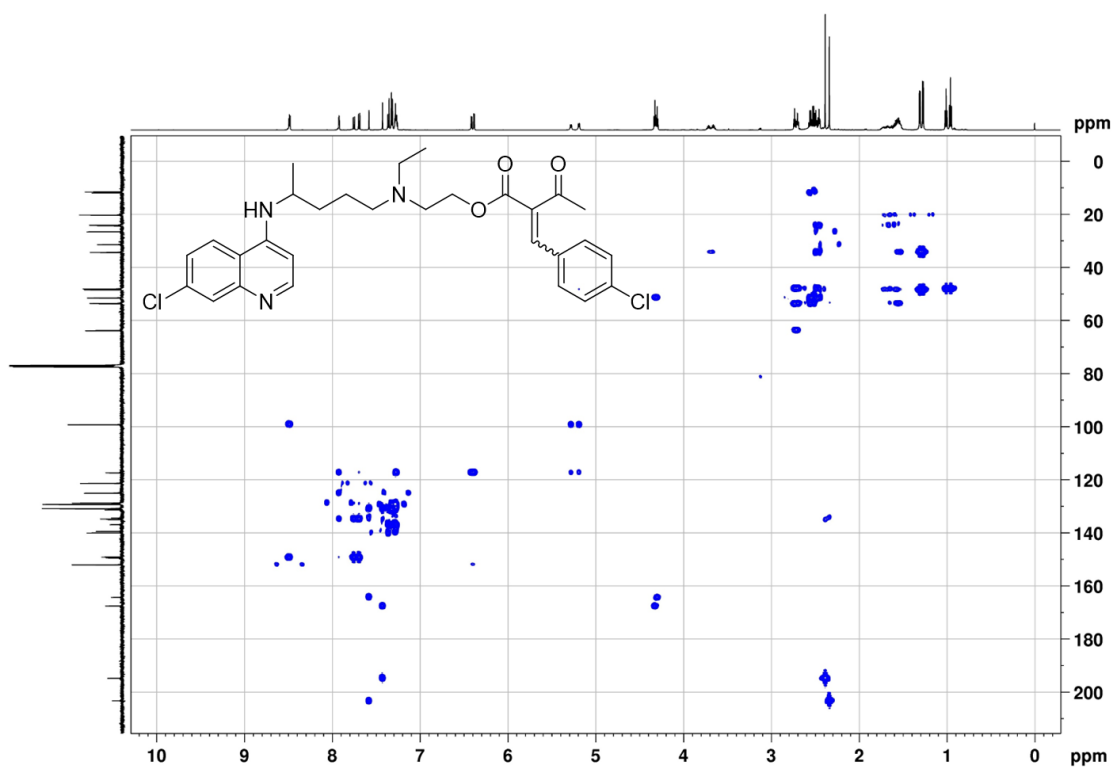


Figure S54. Heteronuclear correlation of a ^1H - ^{13}C bond (HMBC) in CDCl_3 of (*E/Z*)-**7i**.

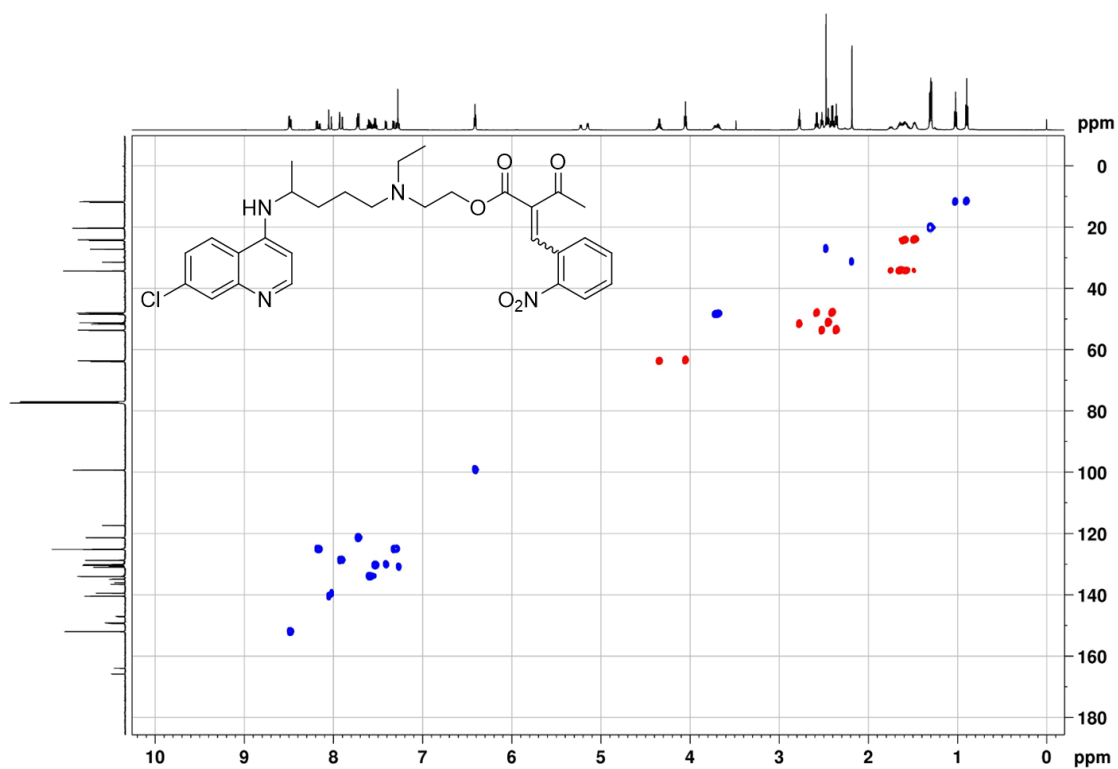


Figure S55. Heteronuclear correlation of a ¹H-¹³C bond (HSQC) in CDCl₃ of *(E/Z)*-7j.

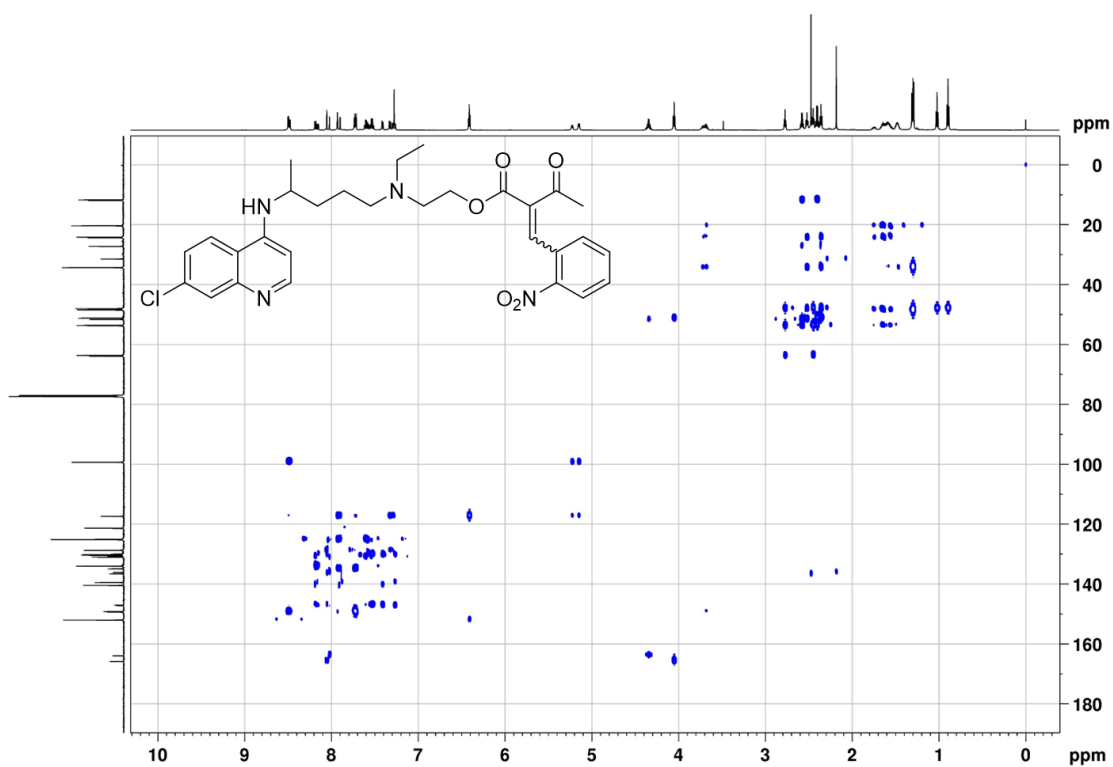


Figure S56. Heteronuclear correlation of a ¹H-¹³C bond (HMBC) in CDCl₃ of *(E/Z)*-7j.

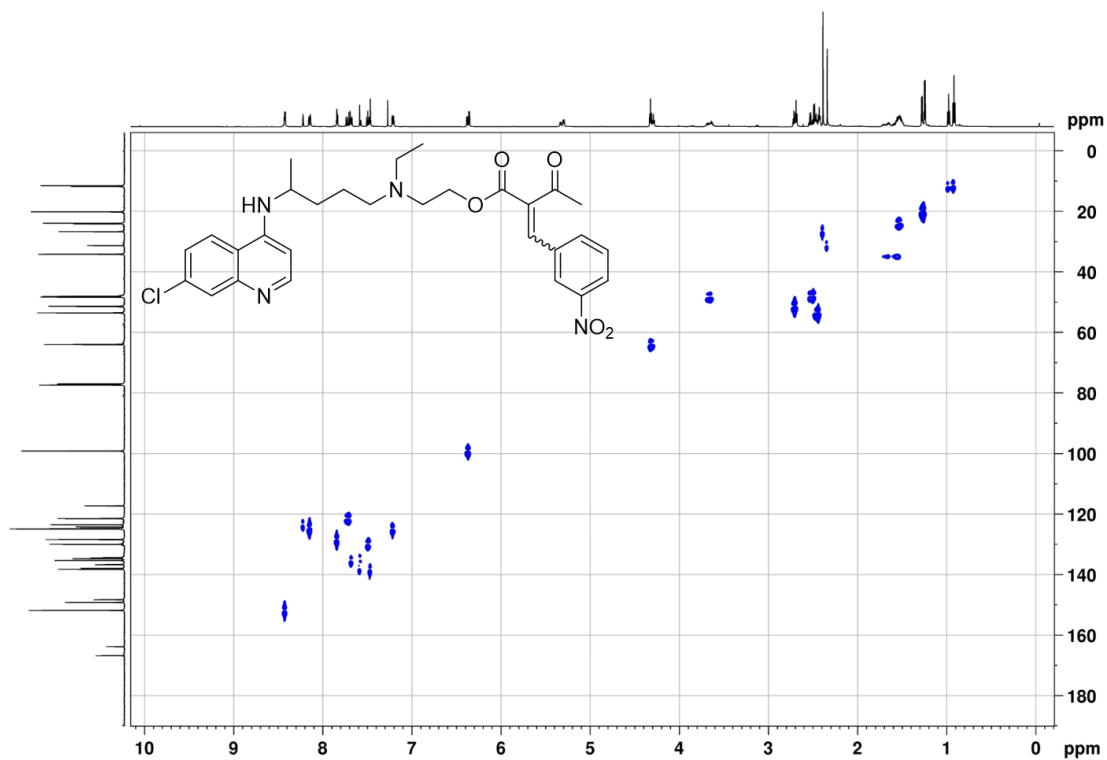


Figure S57. Heteronuclear correlation of a ^1H - ^{13}C bond (HSQC) in CDCl_3 of (E/Z) -7k.

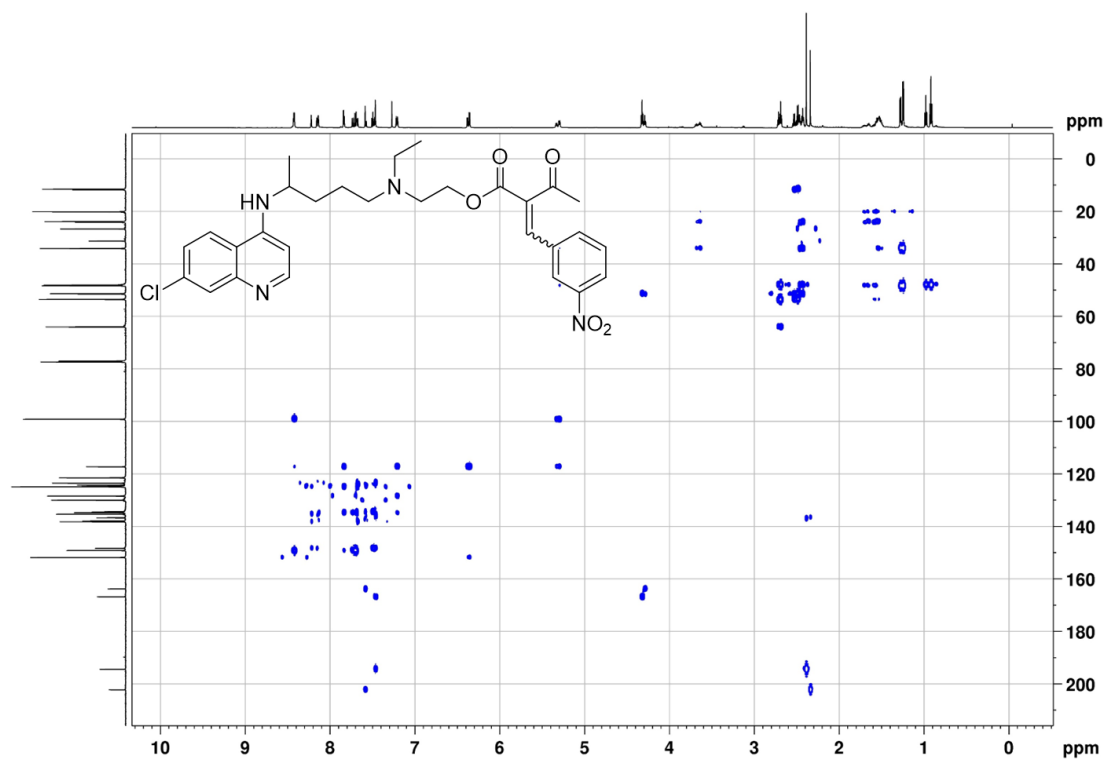


Figure S58. Heteronuclear correlation of a ^1H - ^{13}C bond (HMBC) in CDCl_3 of (E/Z) -7k.

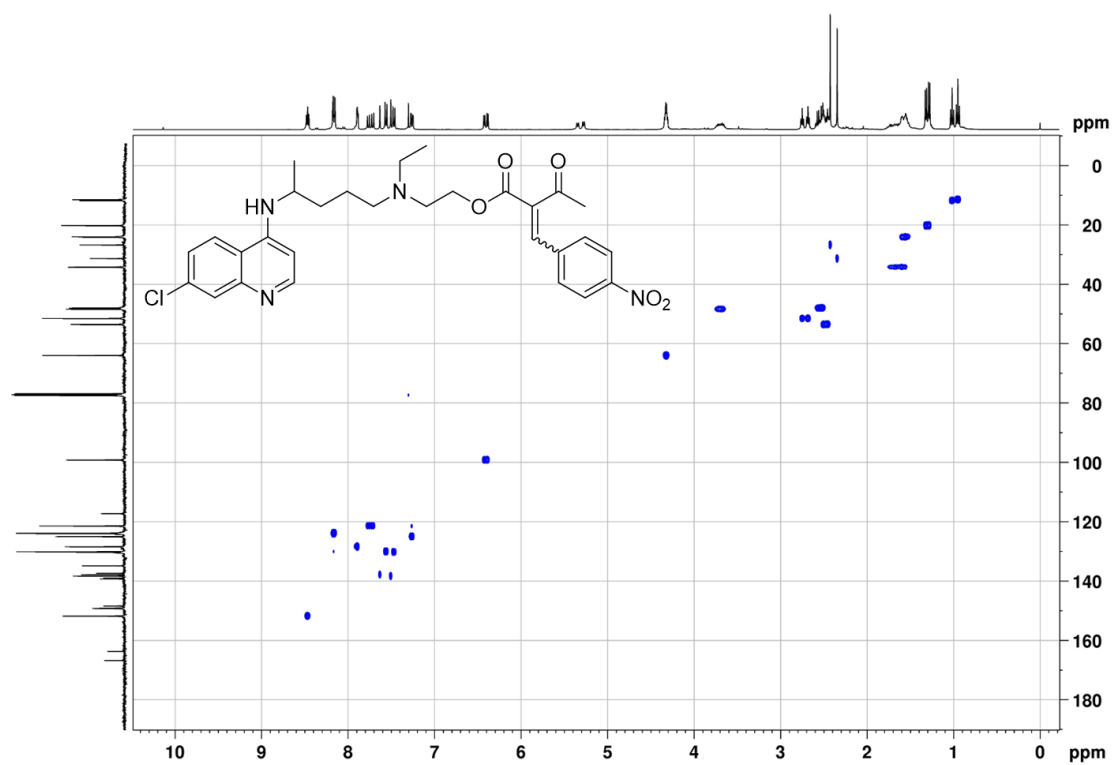


Figure S59. Heteronuclear correlation of a ^1H - ^{13}C bond (HSQC) in CDCl_3 of (*E/Z*)-**71**.

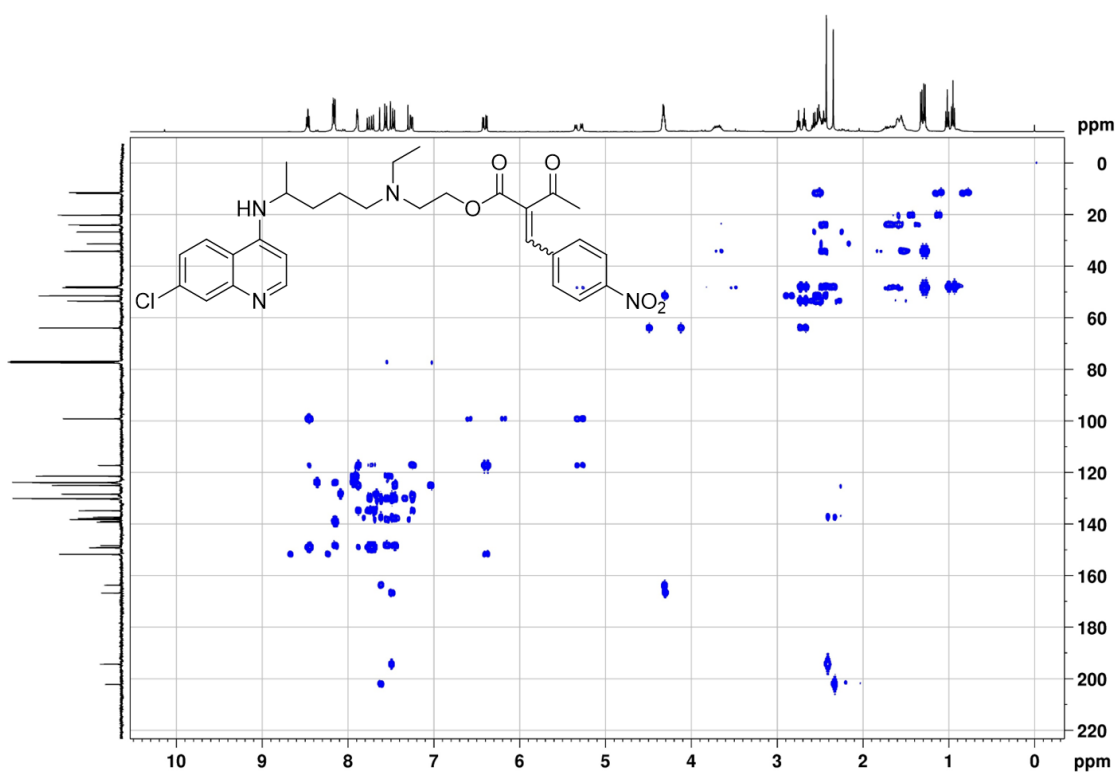


Figure S60. Heteronuclear correlation of a ^1H - ^{13}C bond (HMBC) in CDCl_3 of (*E/Z*)-**71**.

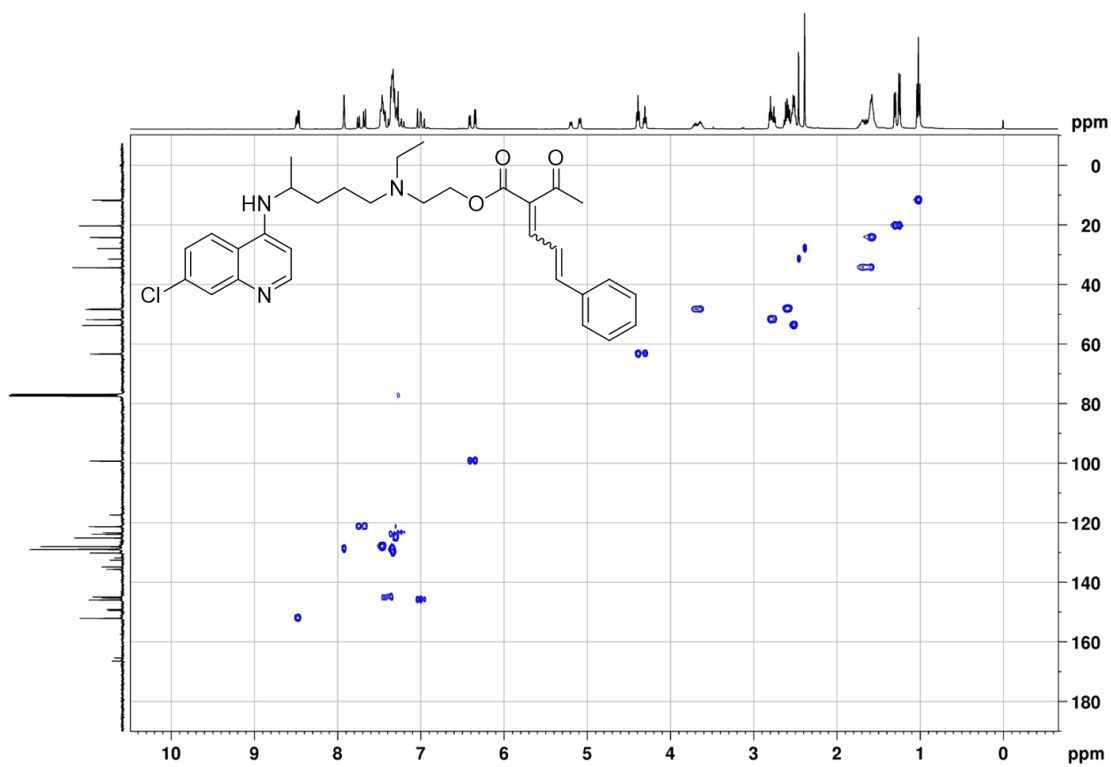


Figure S61. Heteronuclear correlation of a ^1H - ^{13}C bond (HSQC) in CDCl_3 of (*E/Z*)-**7m**.

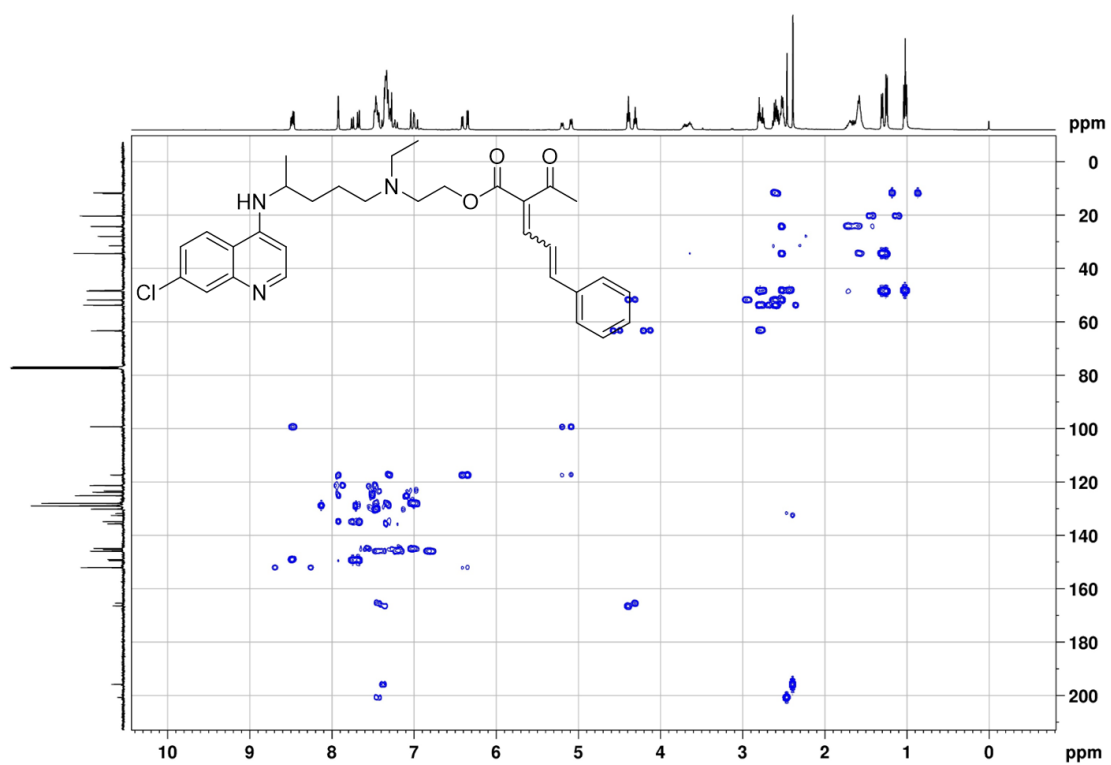


Figure S62. Heteronuclear correlation of a ^1H - ^{13}C bond (HMBC) in CDCl_3 of (*E/Z*)-**7m**.

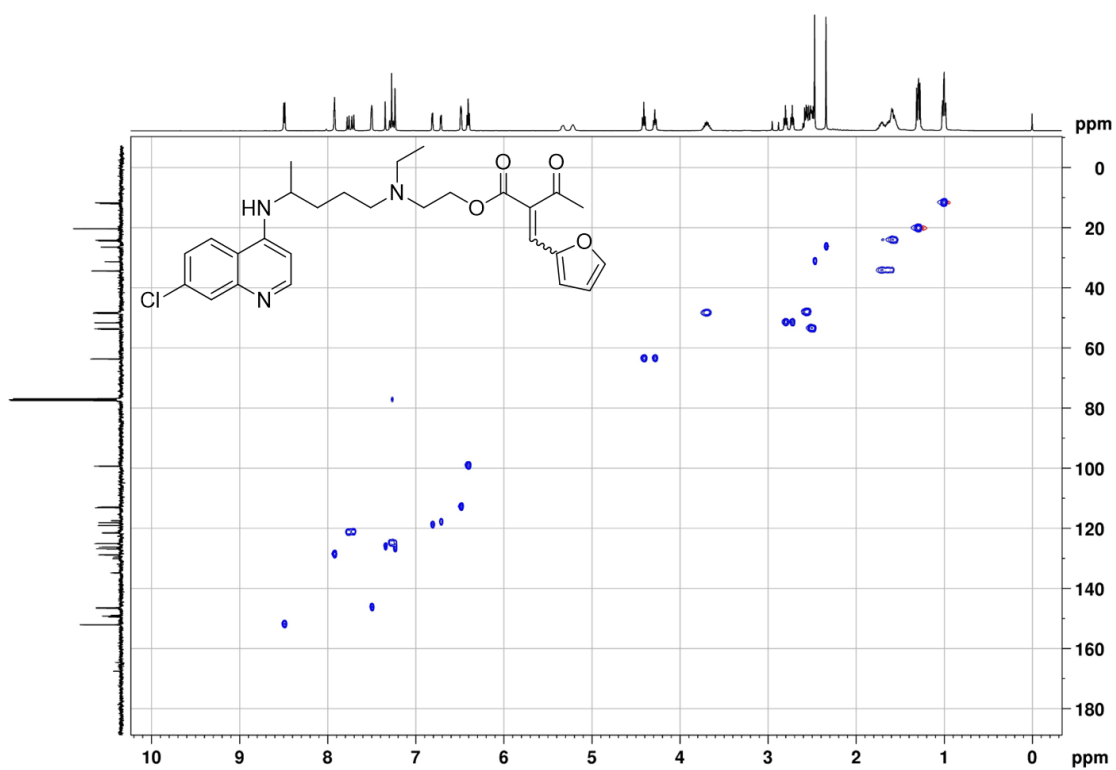


Figure S63. Heteronuclear correlation of a ¹H-¹³C bond (HSQC) in CDCl₃ of (E/Z)-7n.

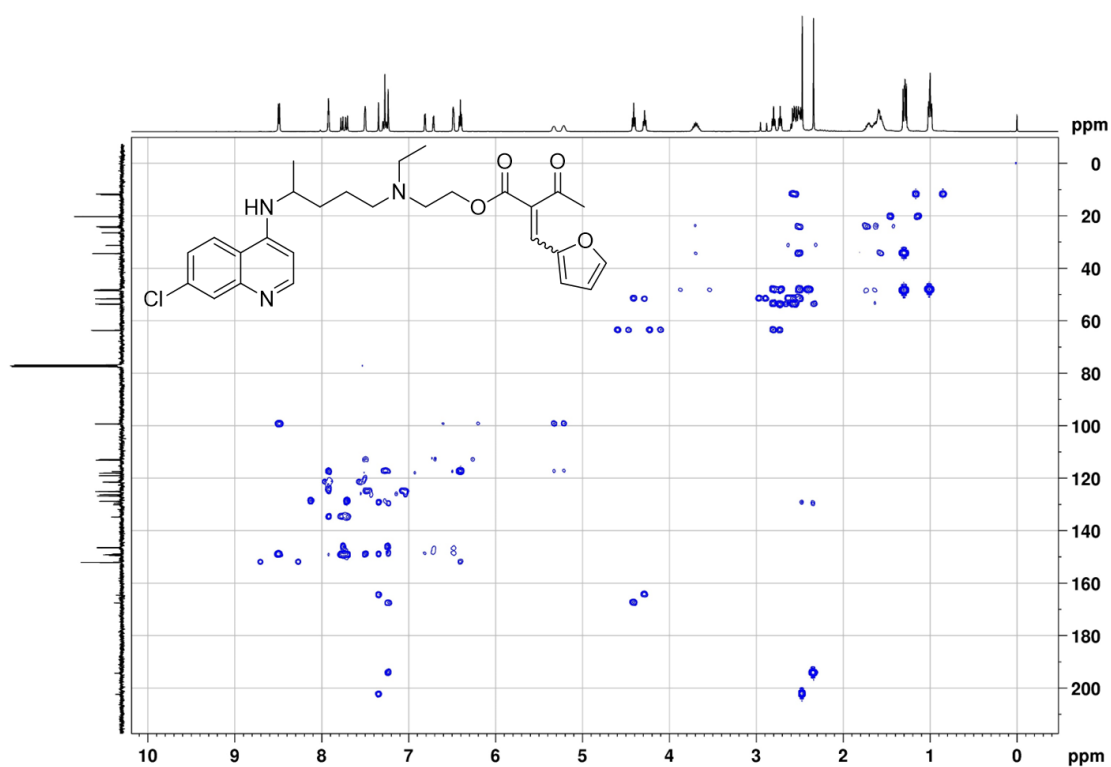


Figure S64. Heteronuclear correlation of a ¹H-¹³C bond (HMBC) in CDCl₃ of (E/Z)-7n.

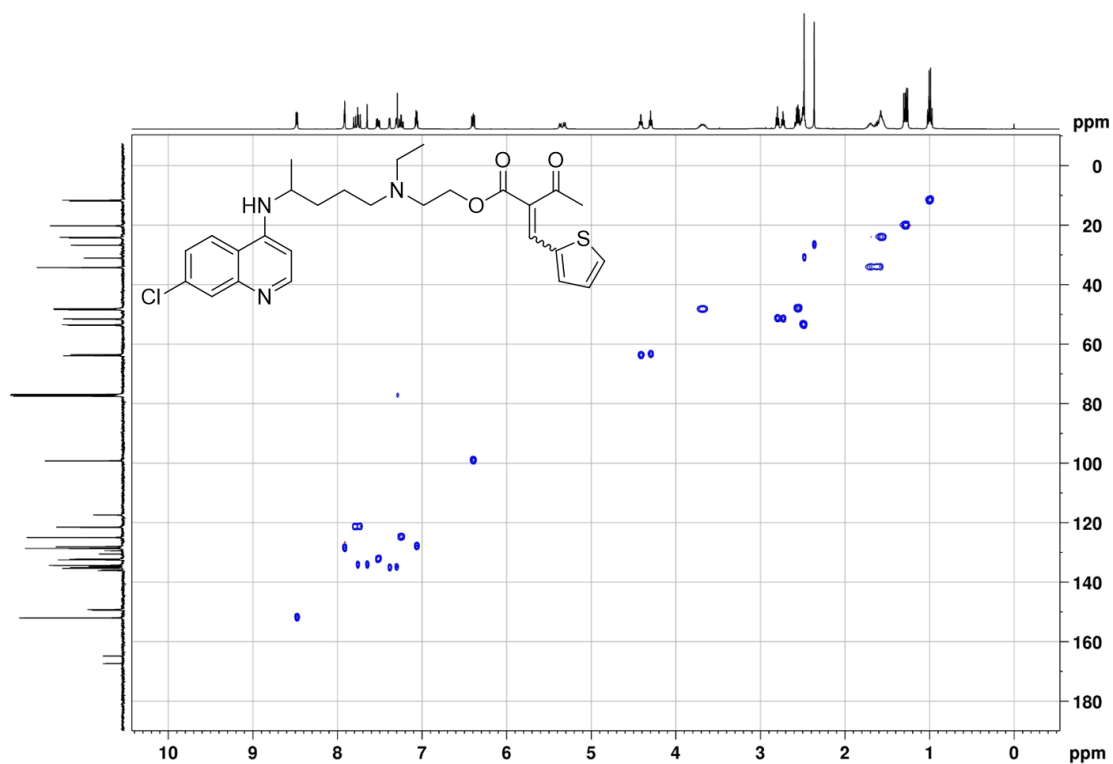


Figure S65. Heteronuclear correlation of a ^1H - ^{13}C bond (HSQC) in CDCl_3 of (*E/Z*)-**7o**.

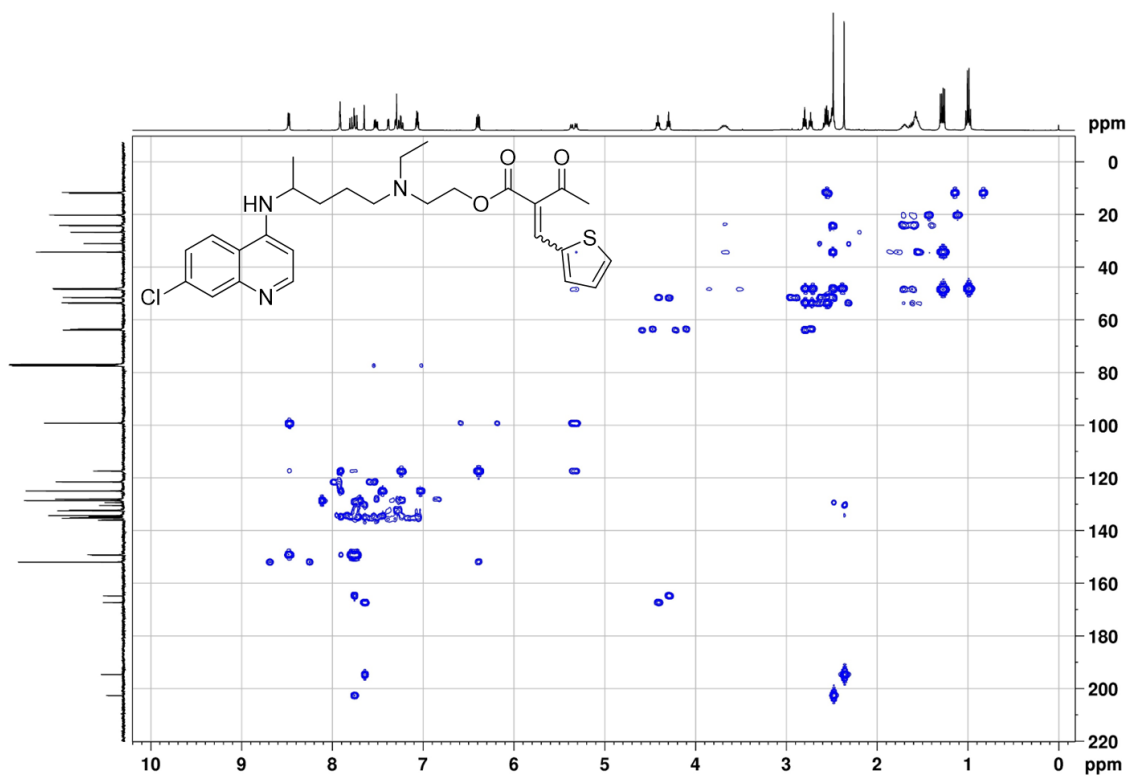


Figure S66. Heteronuclear correlation of a ^1H - ^{13}C bond (HMBC) in CDCl_3 of (*E/Z*)-**7o**.

*d*sel-HSQMBC-IPAP Spectra

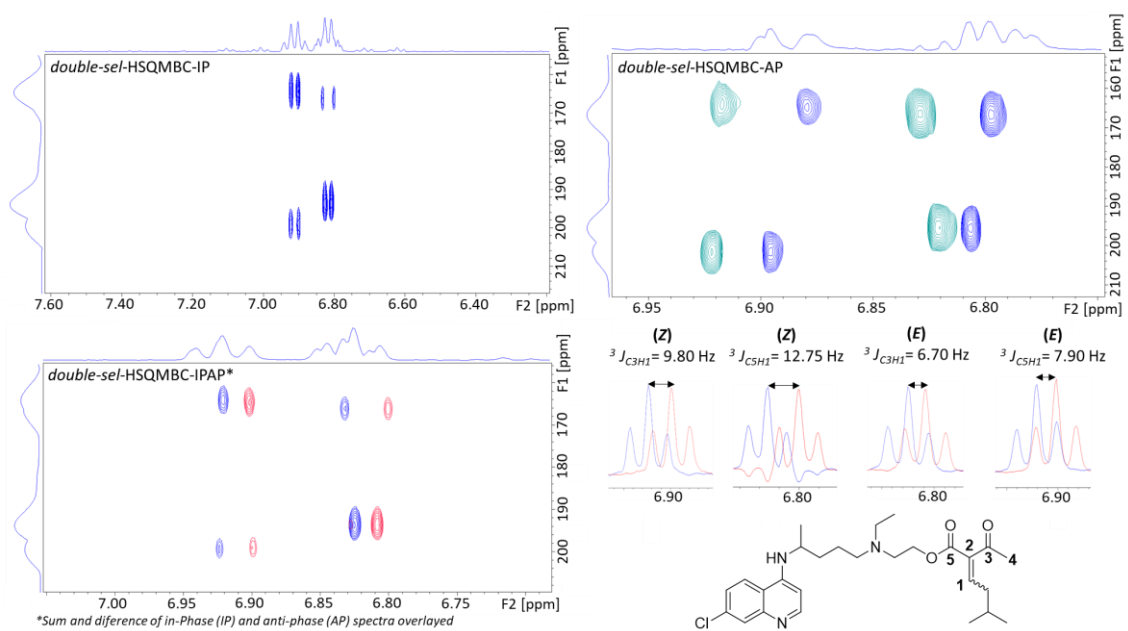


Figure S67. *d*sel-HSQMBC-IPAP spectra for the mixture of isomers (40:60, *E/Z*) from compound **7a**.

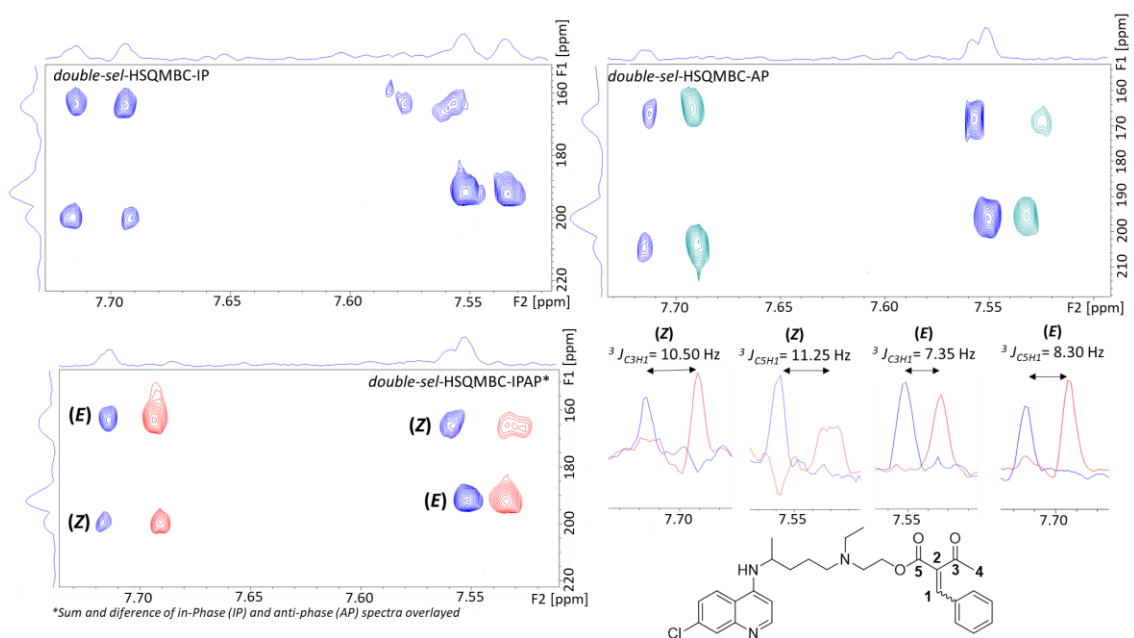


Figure S68. *d*sel-HSQMBC-IPAP spectra for the mixture of isomers (45:55, *E/Z*) from compound **7b**.

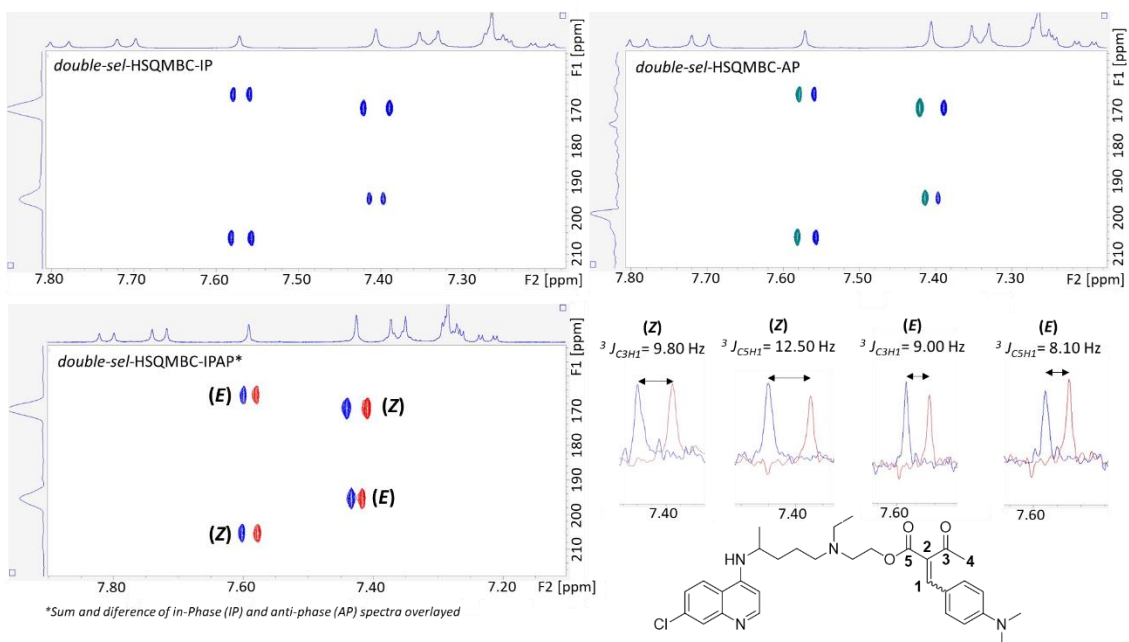


Figure S69. *dsel*-HSQMBC-IPAP spectra for the mixture of isomers (40:60, *E/Z*) from compound **7c**.

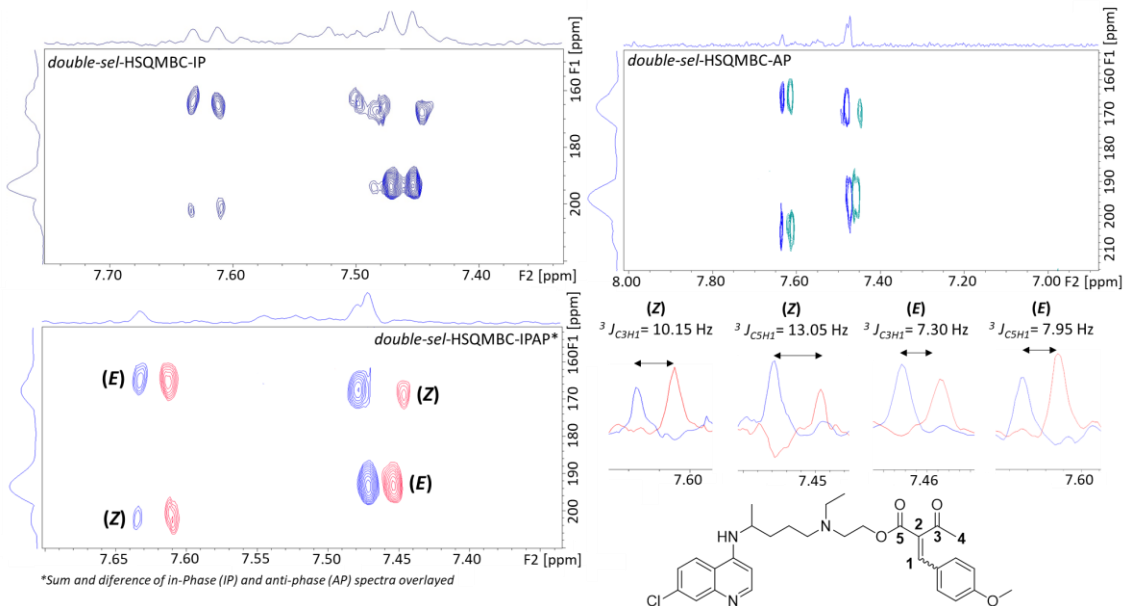


Figure S70. *dsel*-HSQMBC-IPAP spectra for the mixture of isomers (44:56, *E/Z*) from compound **7d**.

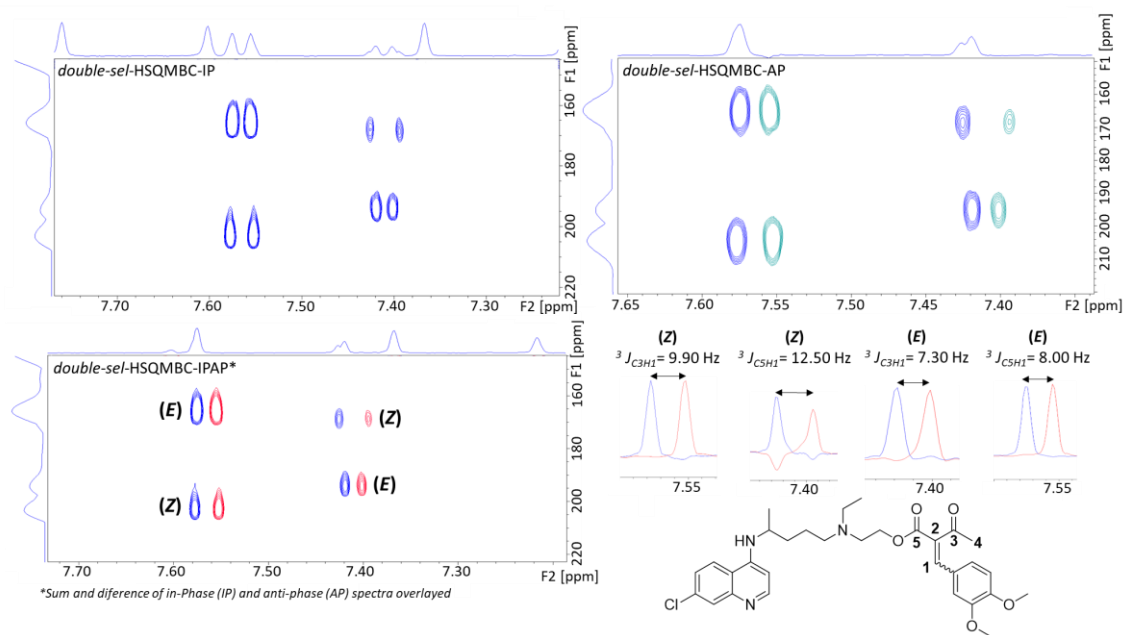


Figure S71. *dsel*-HSQMBC-IPAP spectra for the mixture of isomers (45:55, *E/Z*) from compound **7e**.

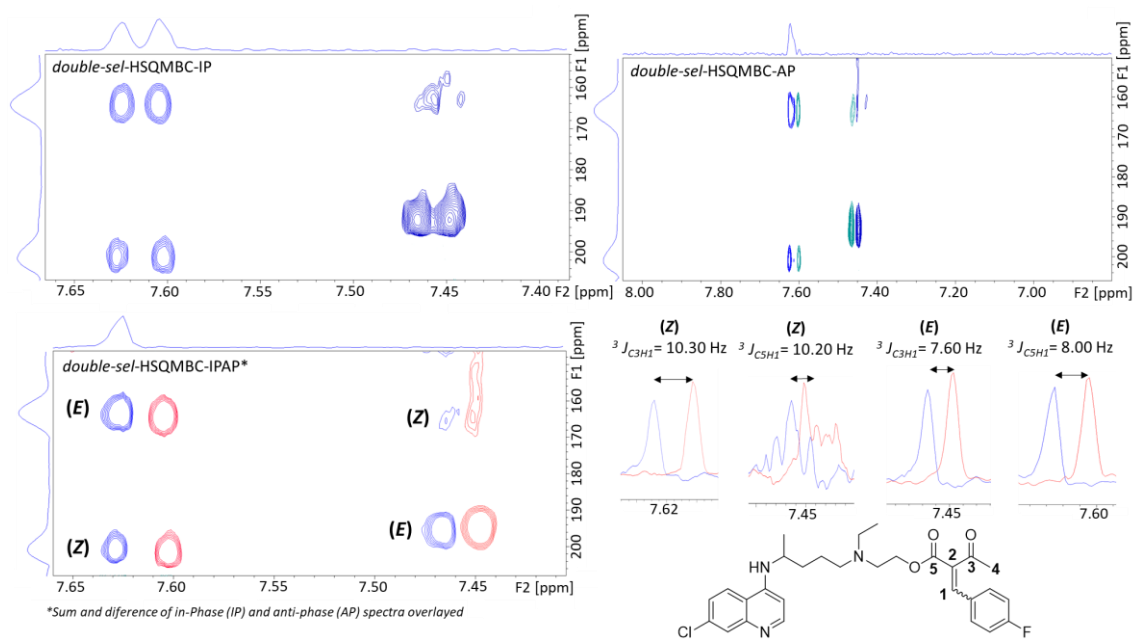


Figure S72. *dsel*-HSQMBC-IPAP spectra for the mixture of isomers (*E/Z* not determined due to overlap) from compound **7f**.

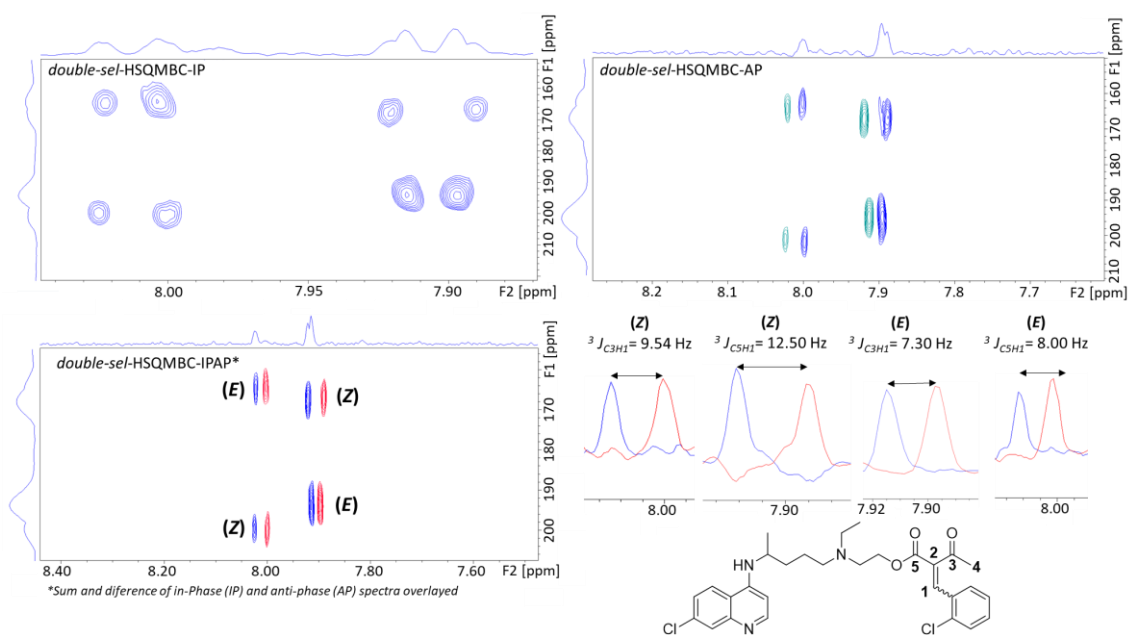


Figure S73. *dsel*-HSQMBC-IPAP spectra for the mixture of isomers (35:65, *E/Z*) from compound **7g**.

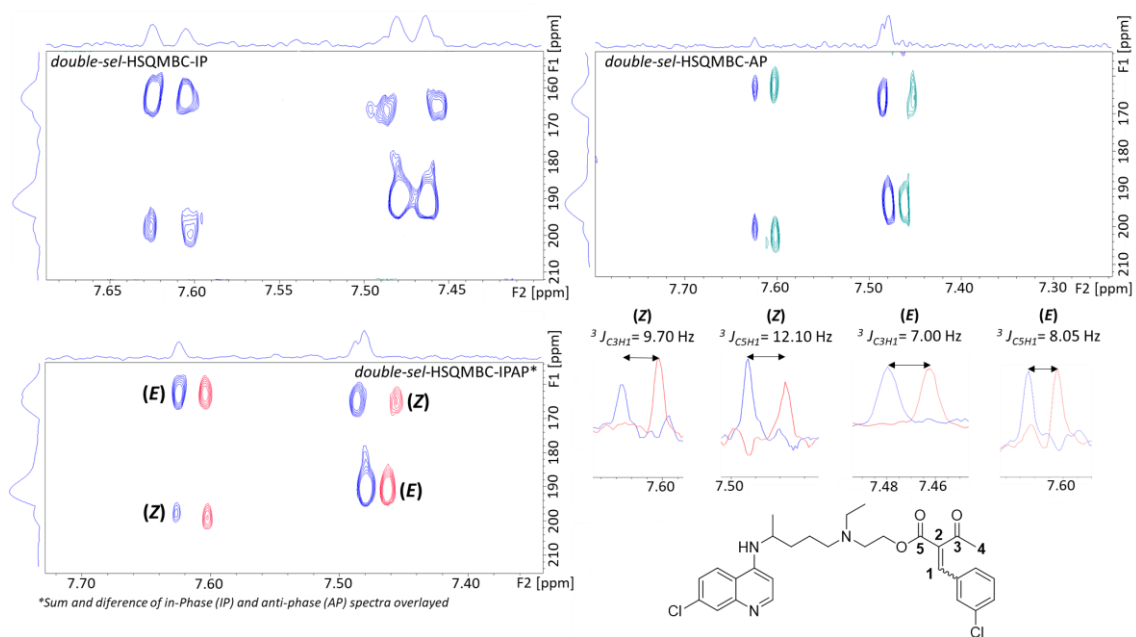


Figure S74. *dsel*-HSQMBC-IPAP spectra for the mixture of isomers (40:69, *E/Z*) from compound **7h**.

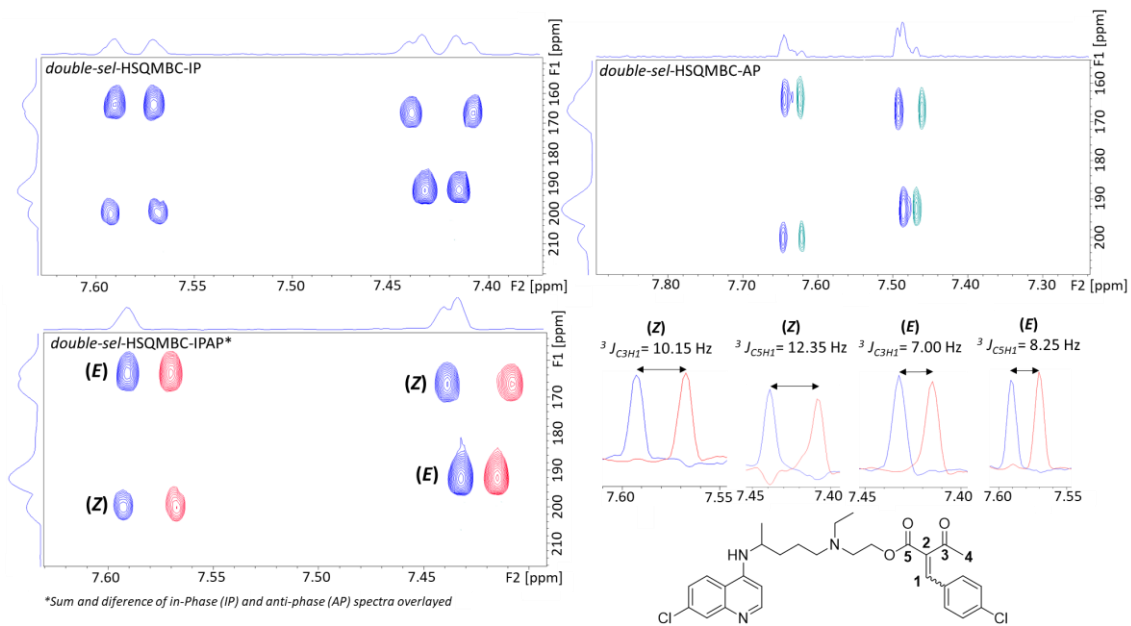


Figure S75. *dsel*-HSQMBC-IPAP spectra for the mixture of isomers (43:57, *E/Z*) from compound **7i**.

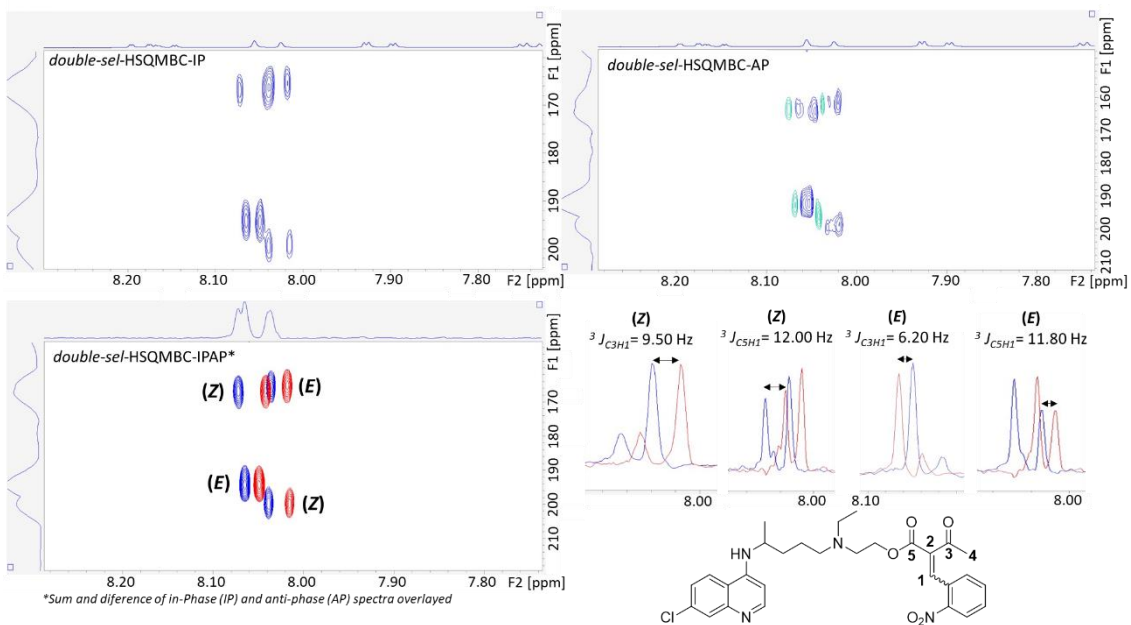


Figure S76. *dsel*-HSQMBC-IPAP spectra for the mixture of isomers (60:40, *E/Z*) from compound **7j**.

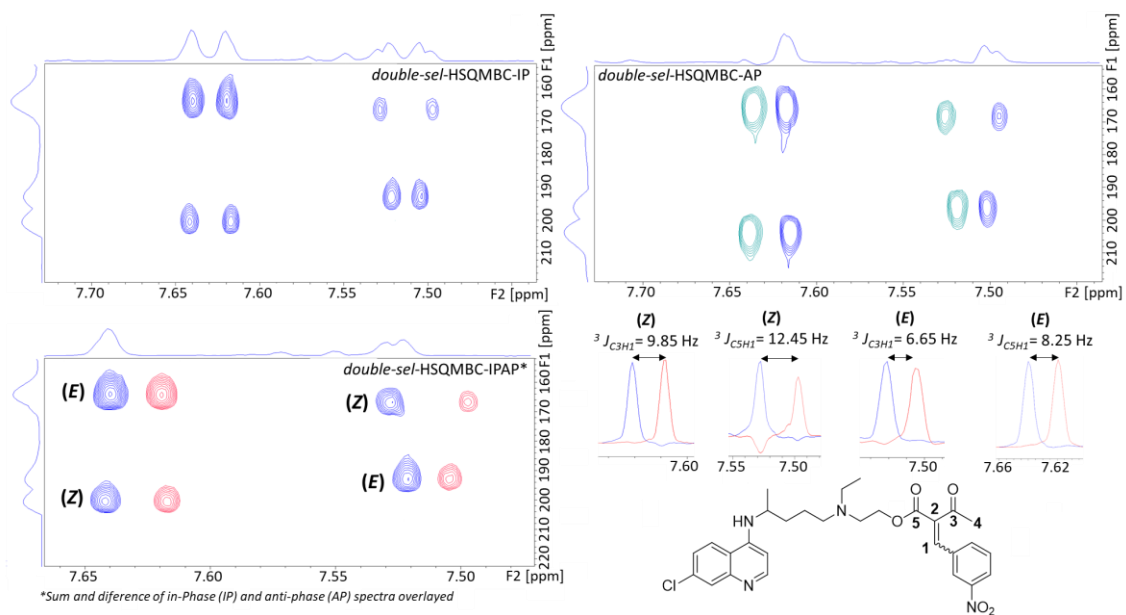


Figure S77. *dsel*-HSQMBC-IPAP spectra for the mixture of isomers (35:65, *E/Z*) from compound **7k**.

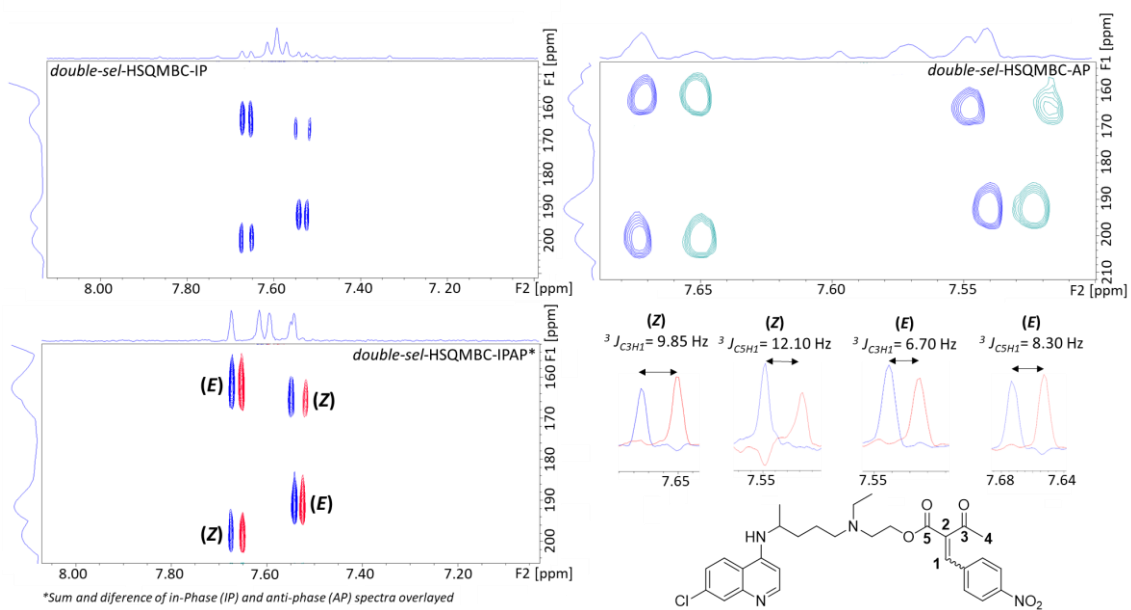


Figure S78. *dsel*-HSQMBC-IPAP spectra for the mixture of isomers (46:54, *E/Z*) from compound **7l**.

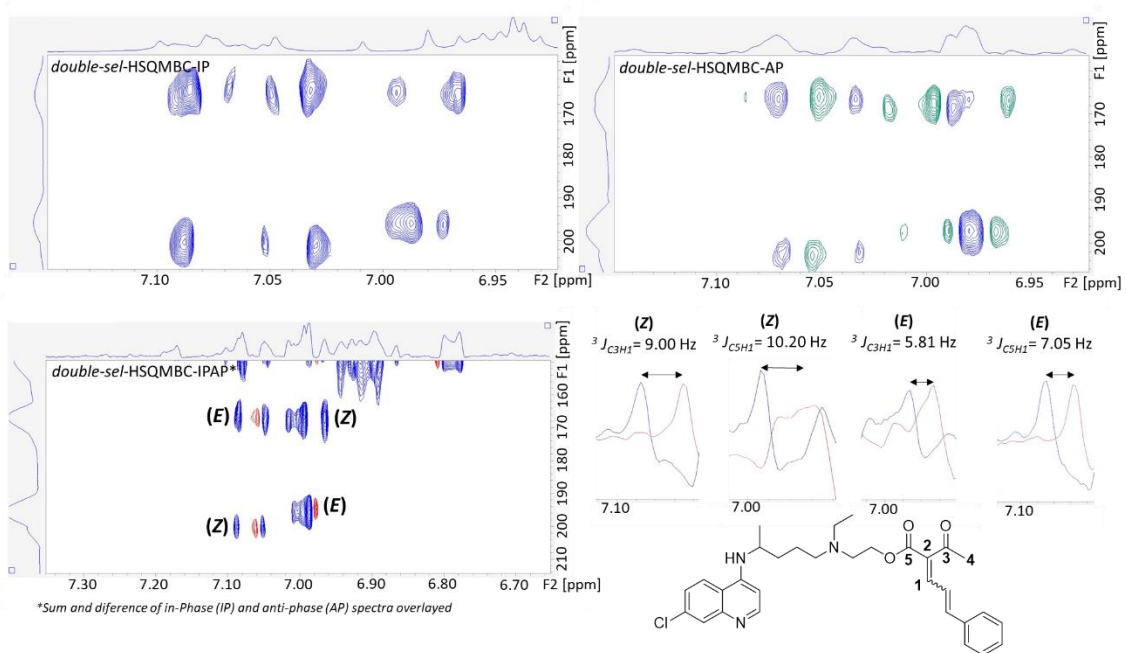


Figure S79. *dsel*-HSQMBC-IPAP spectra for the mixture of isomers (*E/Z* not determined due to overlap) from compound **7m**.

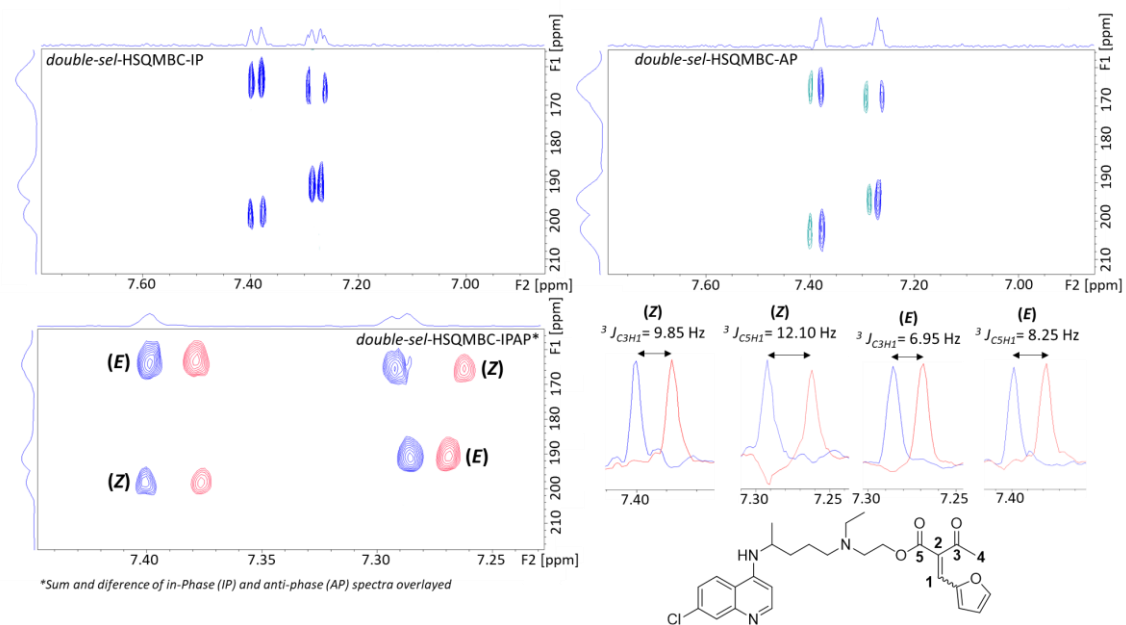


Figure S80. *dsel*-HSQMBC-IPAP spectra for the mixture of isomers (55:45, *E/Z*) from compound **7n**.

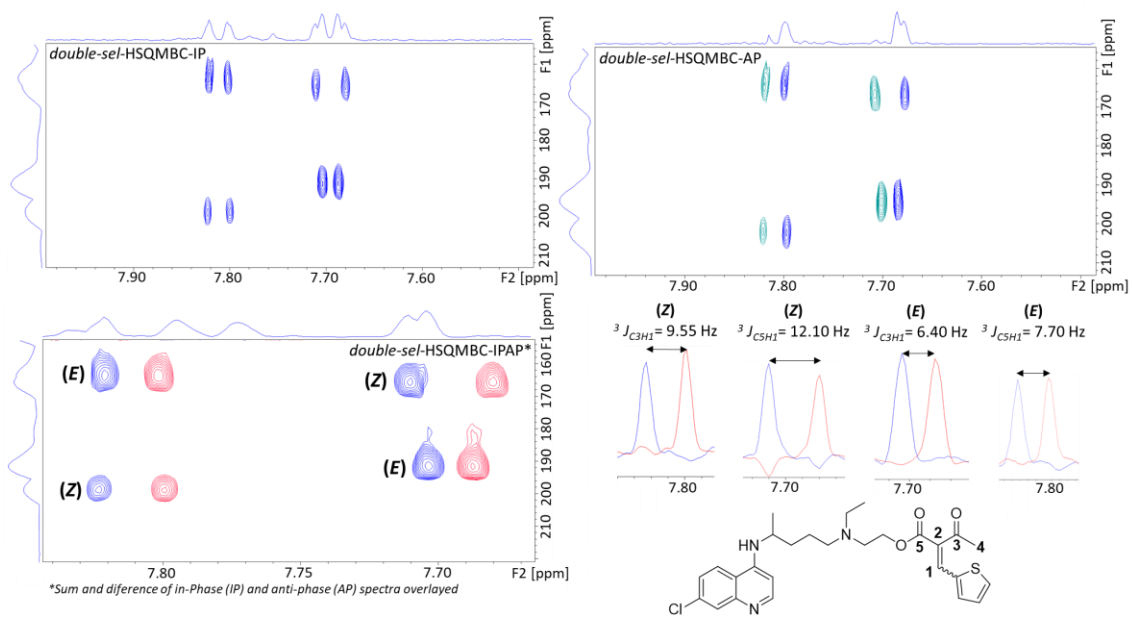


Figure S81. *dsel*-HSQMBC-IPAP spectra for the mixture of isomers (41:59, *E/Z*) from compound **7o**.

High-Resolution Mass Spectrometry (HRMS) spectra

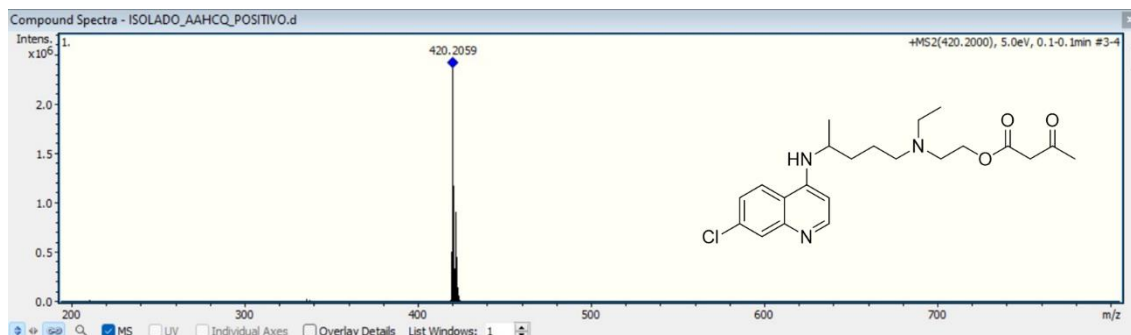


Figure S82. HRMS spectrum of **5**.

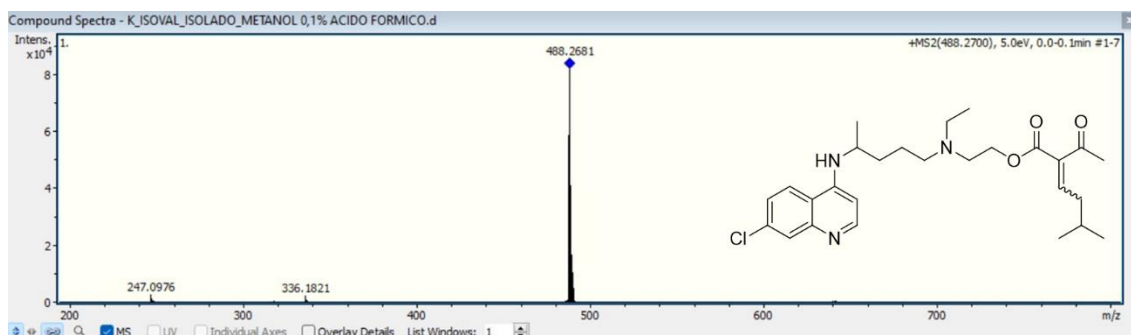


Figure S83. HRMS spectrum of (*E/Z*)-**7a**.

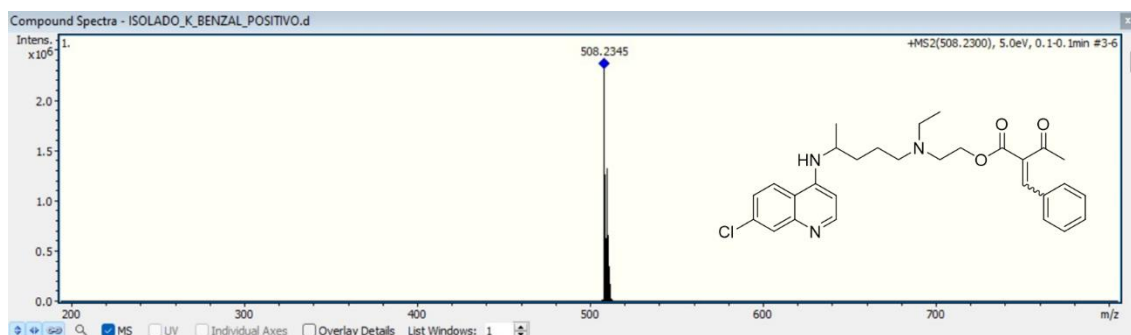


Figure S84. HRMS spectrum of (*E/Z*)-**7b**.

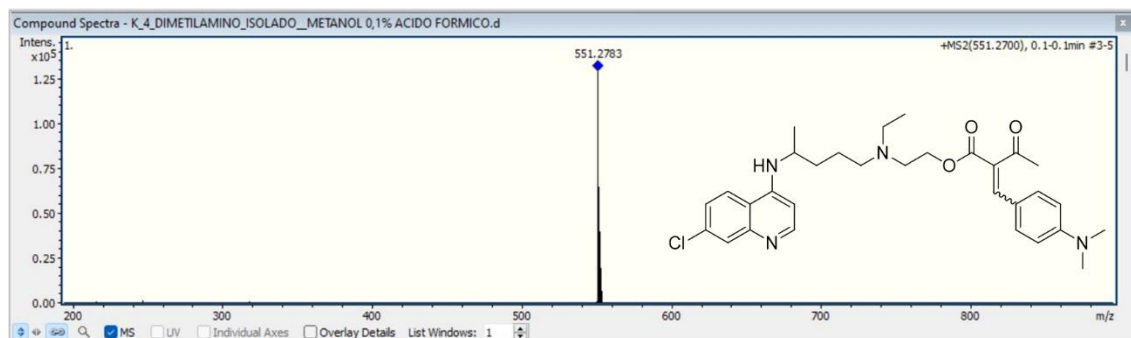


Figure S85. HRMS spectrum of (*E/Z*)-**7c**.

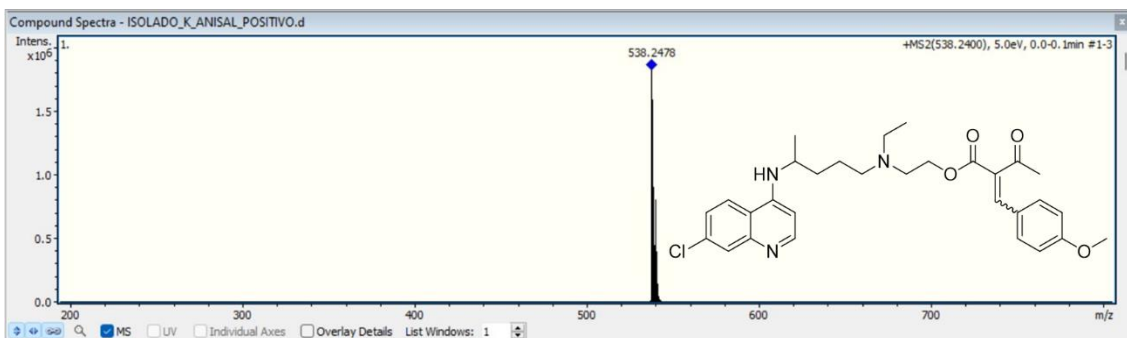


Figure S86. HRMS spectrum of (E/Z)-7d.

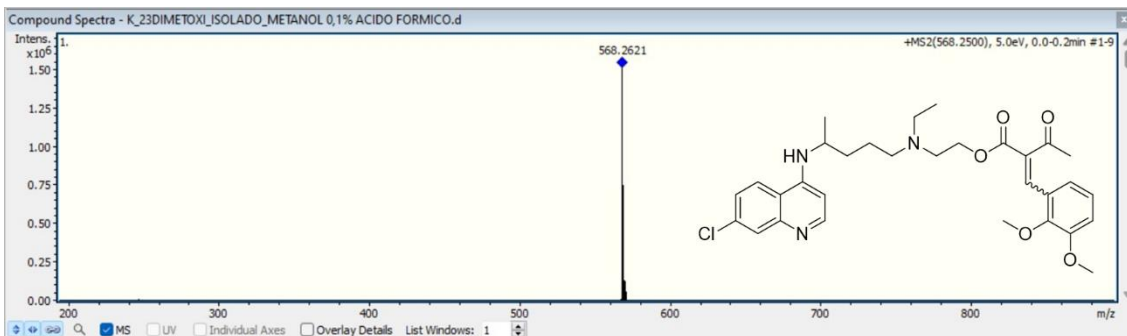


Figure S87. HRMS spectrum of (E/Z)-7e.

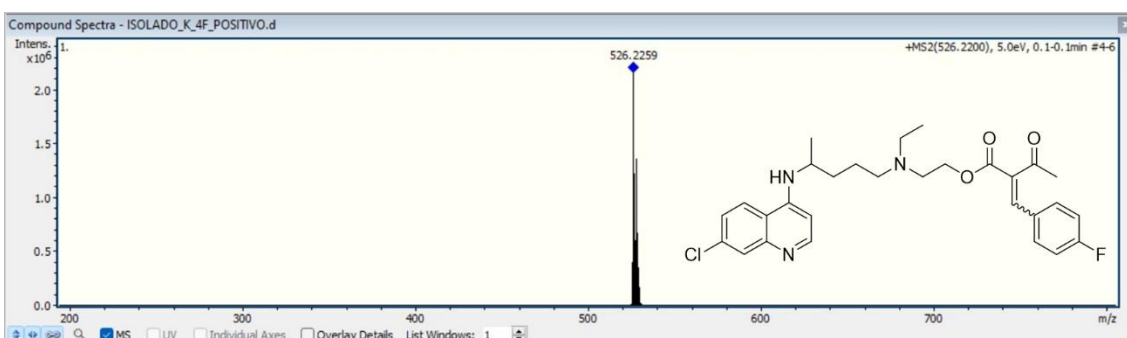


Figure S88. HRMS spectrum of (E/Z)-7f.

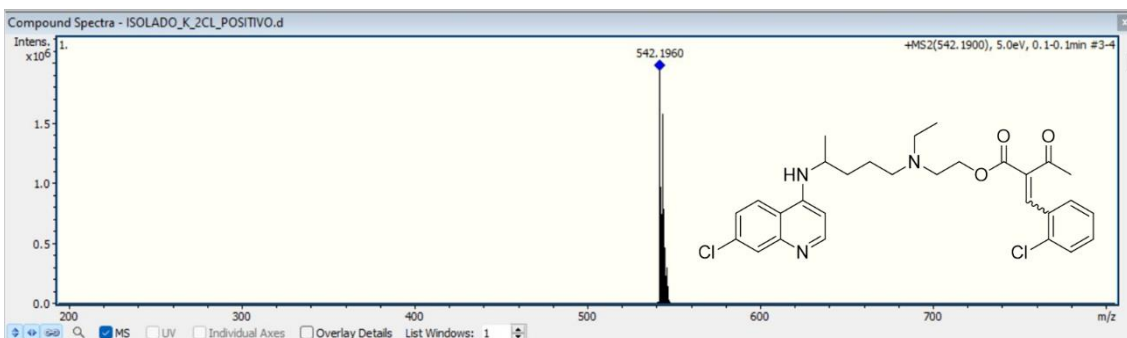


Figure S89. HRMS spectrum of (E/Z)-7g.

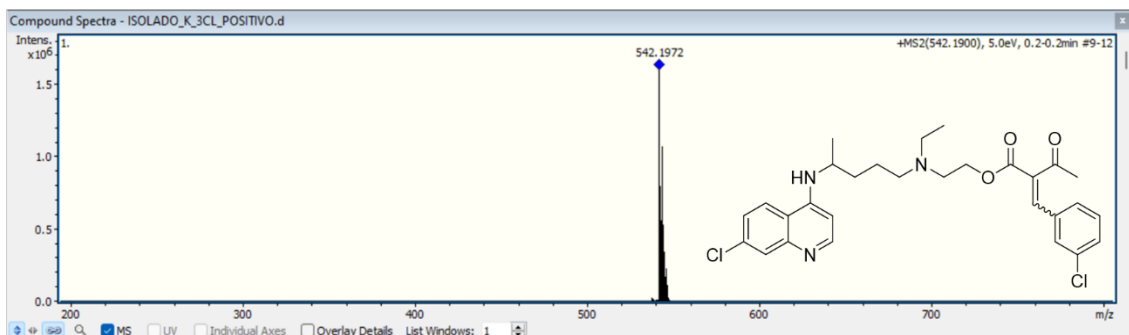


Figure S90. HRMS spectrum of (E/Z)-7h.

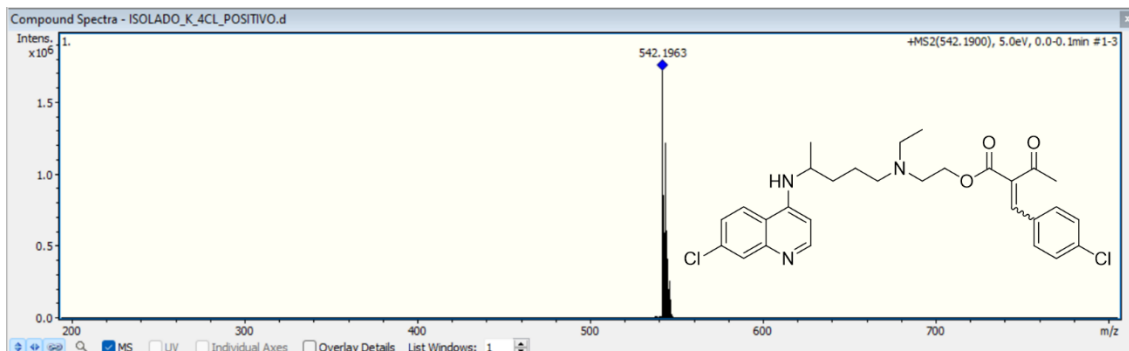


Figure S91. HRMS spectrum of (E/Z)-7i.

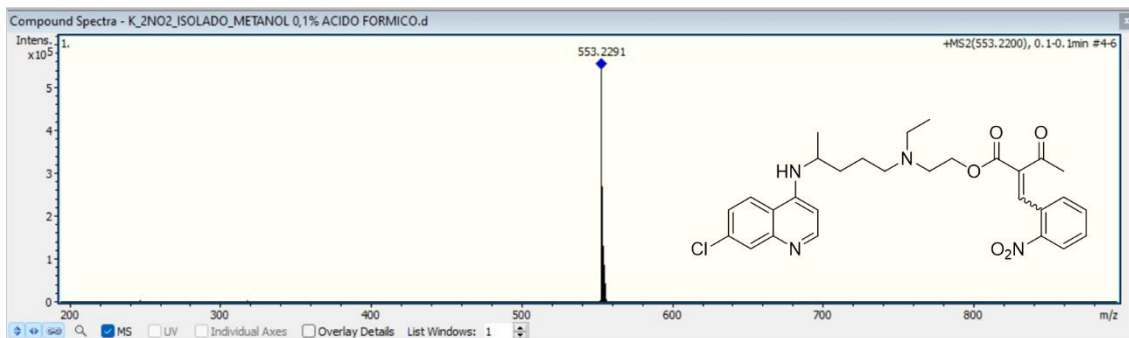


Figure S92. HRMS spectrum of (E/Z)-7j.

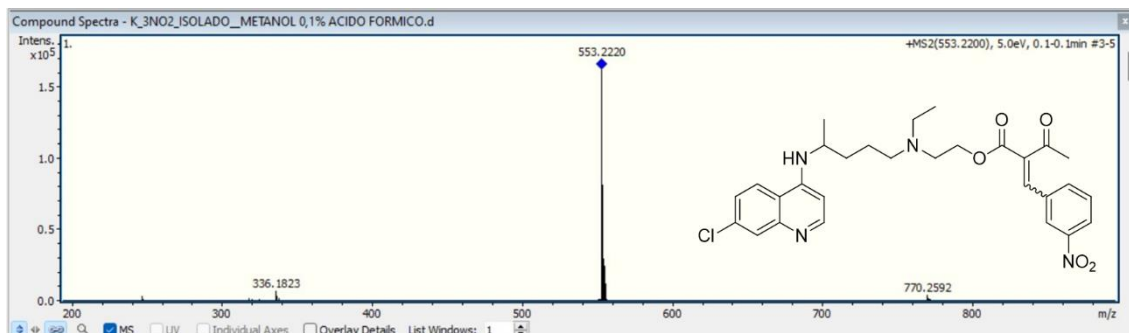


Figure S93. HRMS spectrum of (E/Z)-7k.

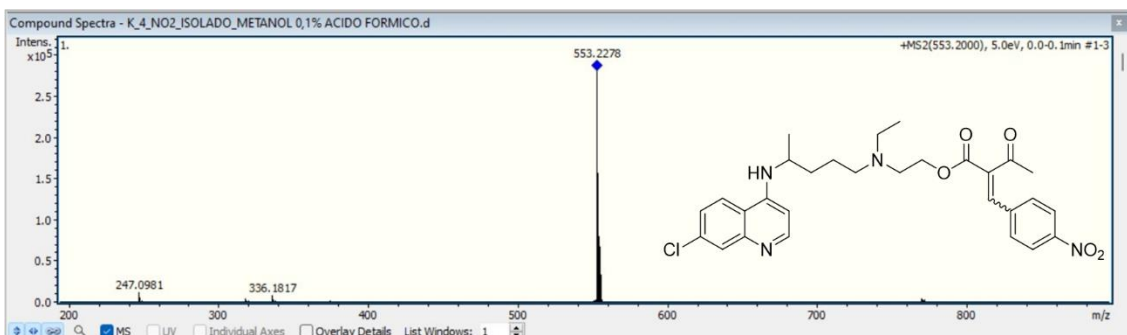


Figure S94. HRMS spectrum of (E/Z)-7l.

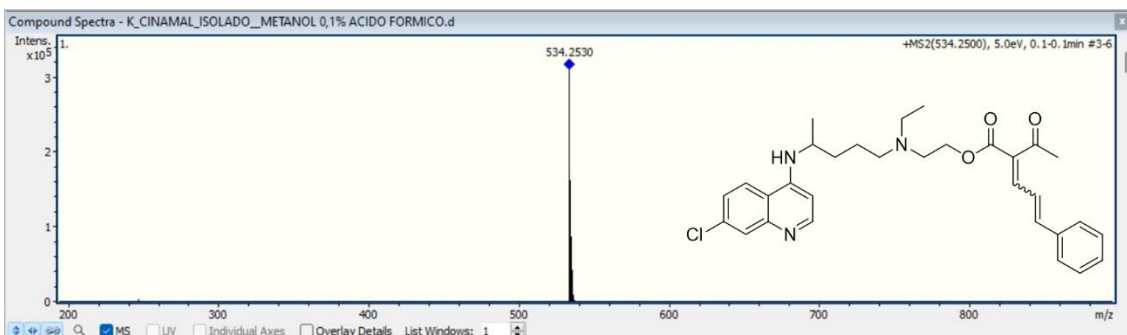


Figure S95. HRMS spectrum of (E/Z)-7m.

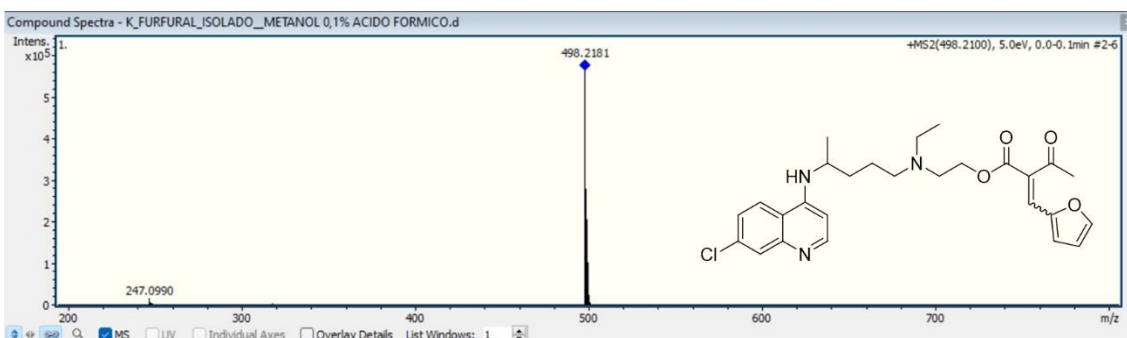


Figure S96. HRMS spectrum of (E/Z)-7n.

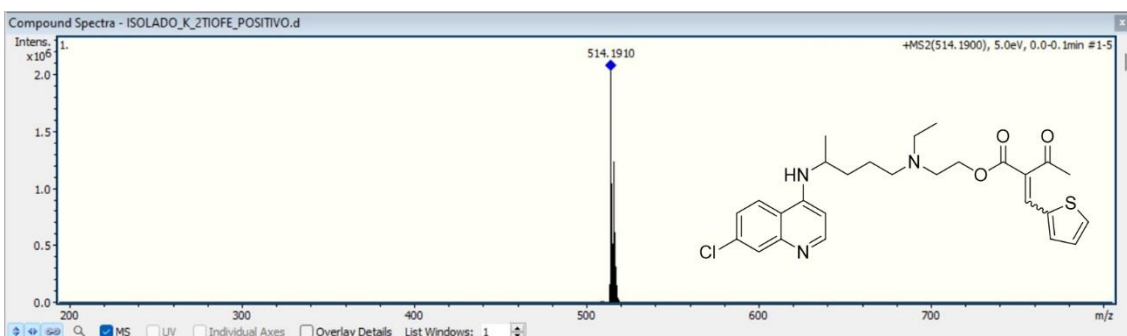


Figure S97. HRMS spectrum of (E/Z)-7o.

Fourier Transform Infrared Spectroscopy (FT-IR) spectra

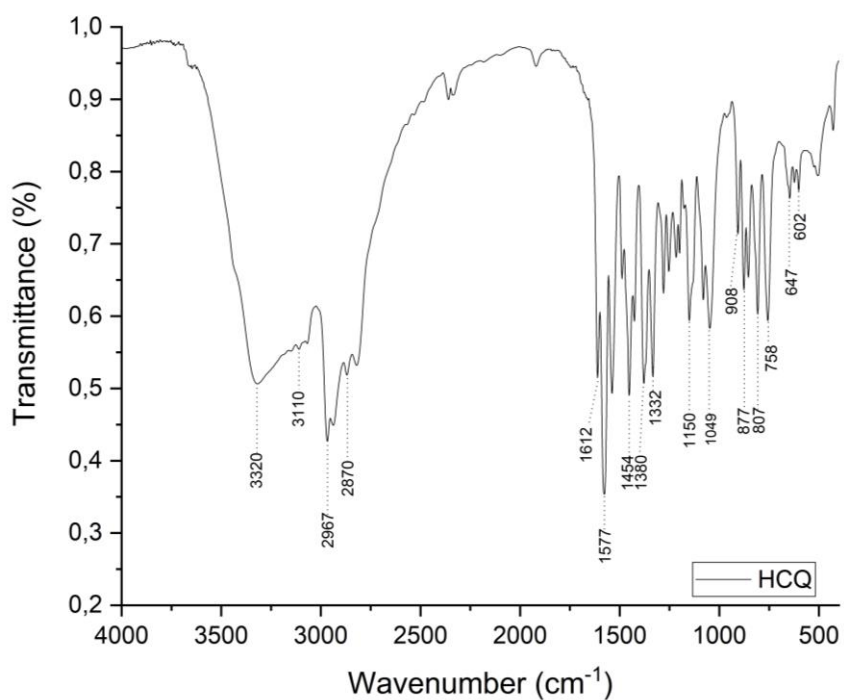


Figure S98. FT-IR spectrum of **4**.

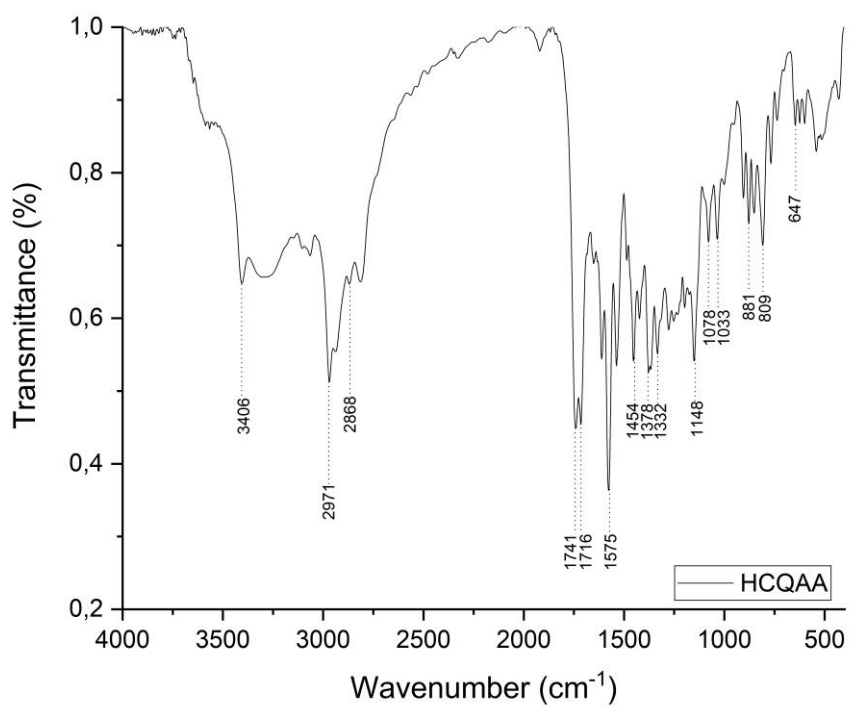


Figure S99. FT-IR spectrum of **5**.

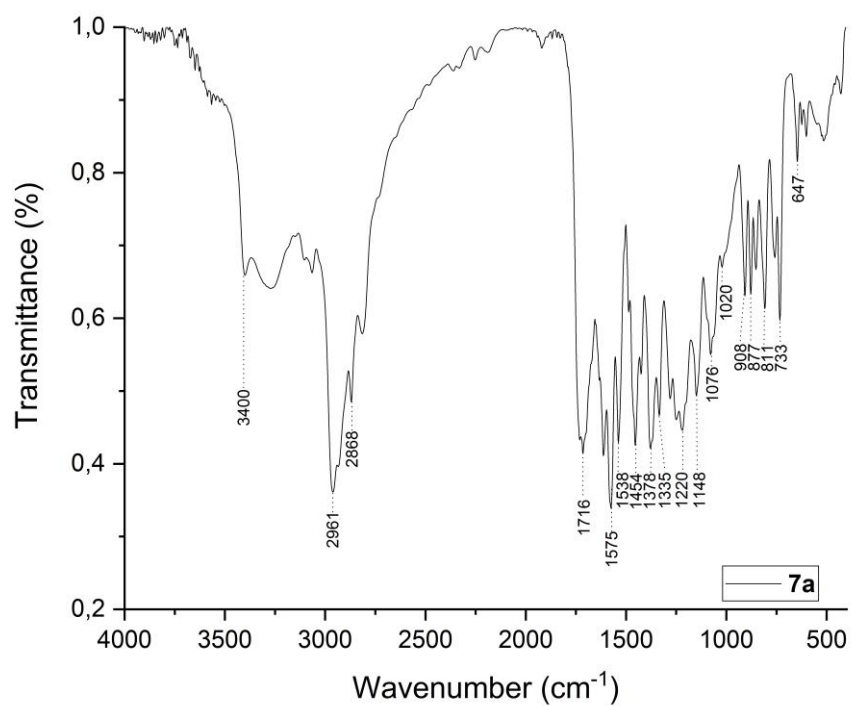


Figure S100. FT-IR spectrum of (E/Z)-7a.

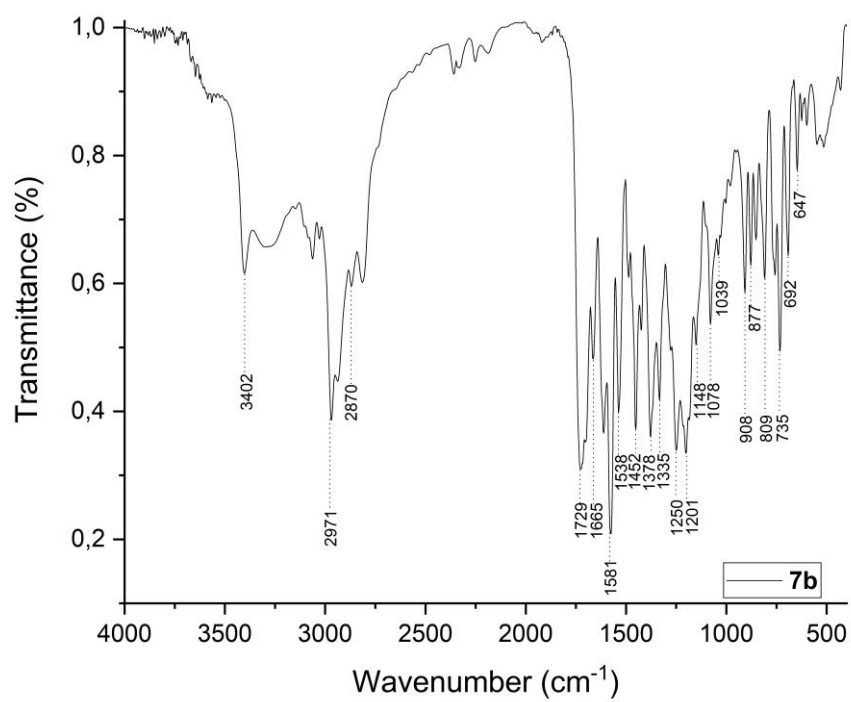


Figure S101. FT-IR spectrum of (E/Z)-7b.

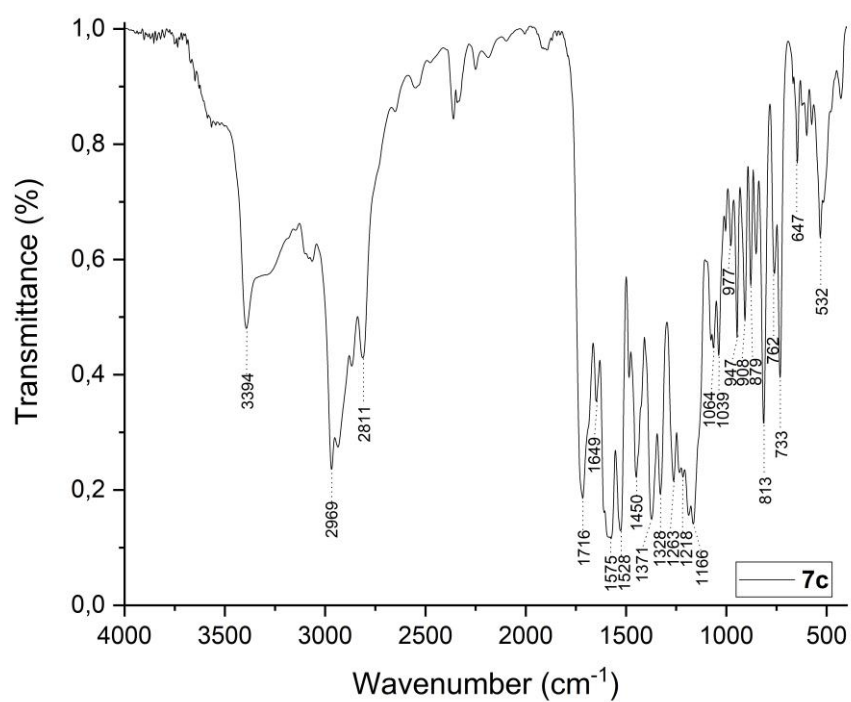


Figure S102. FT-IR spectrum of (*E/Z*)-**7c**.

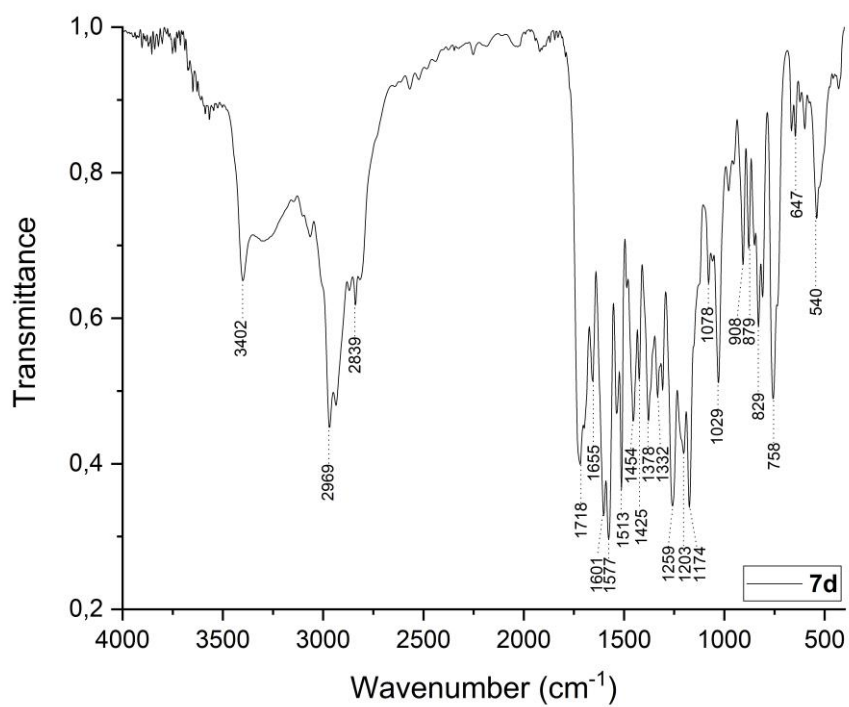


Figure S103. FT-IR spectrum of (*E/Z*)-**7d**.

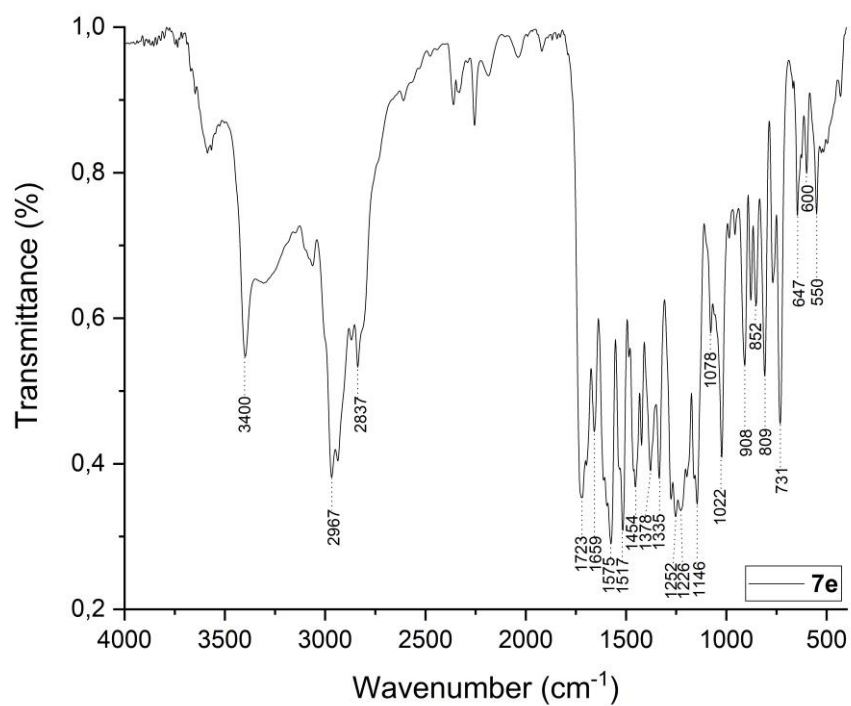


Figure S104. FT-IR spectrum of (*E/Z*)-**7e**.

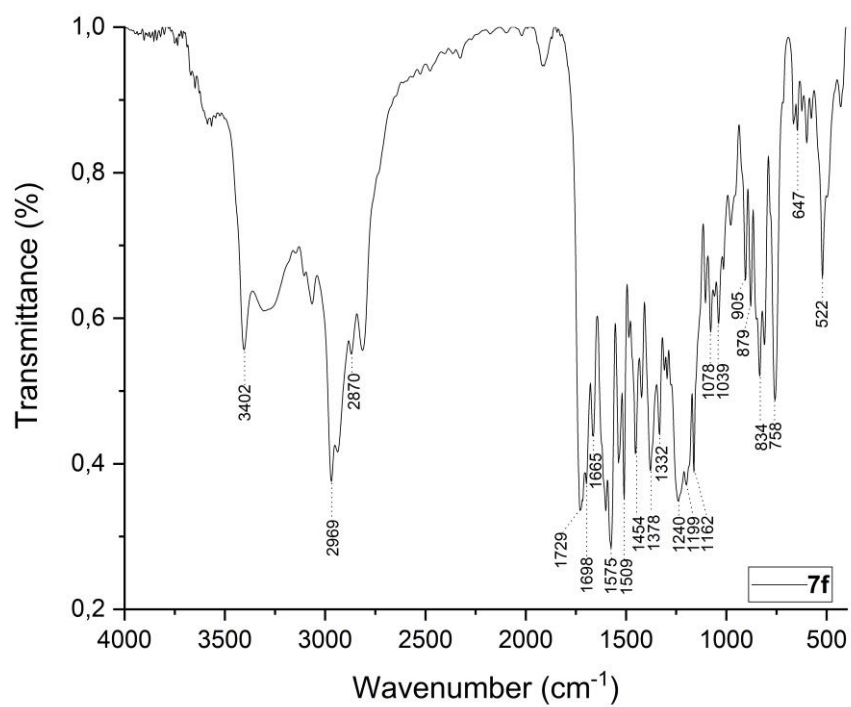


Figure S105. FT-IR spectrum of (*E/Z*)-**7f**.

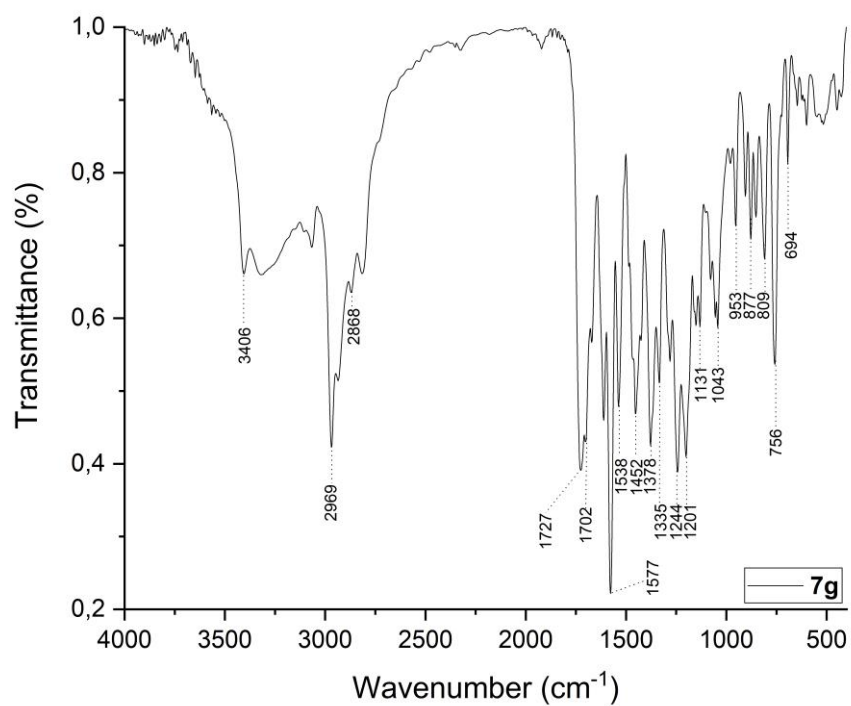


Figure S106. FT-IR spectrum of (E/Z)-7g.

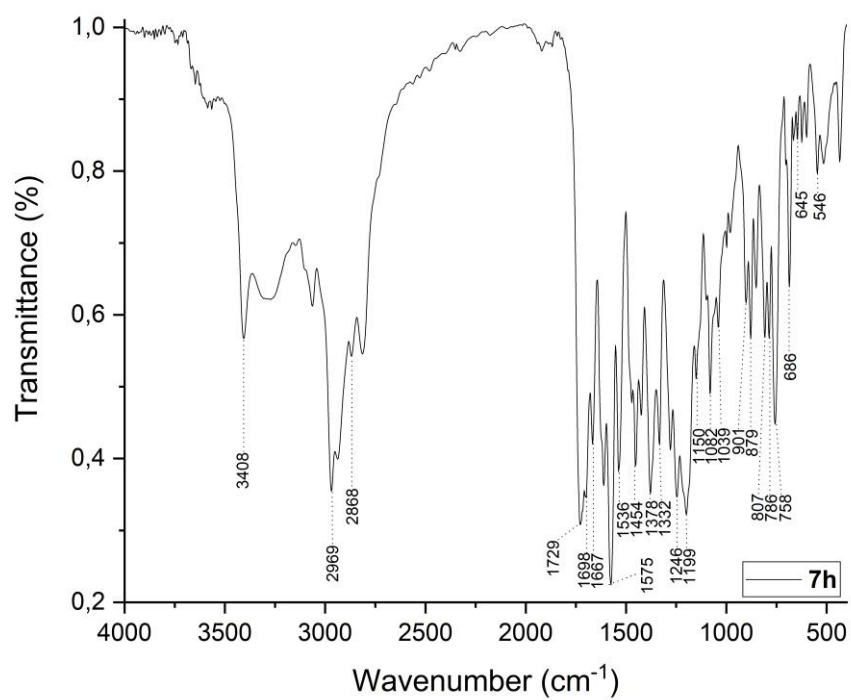


Figure S107. FT-IR spectrum of (E/Z)-7h.

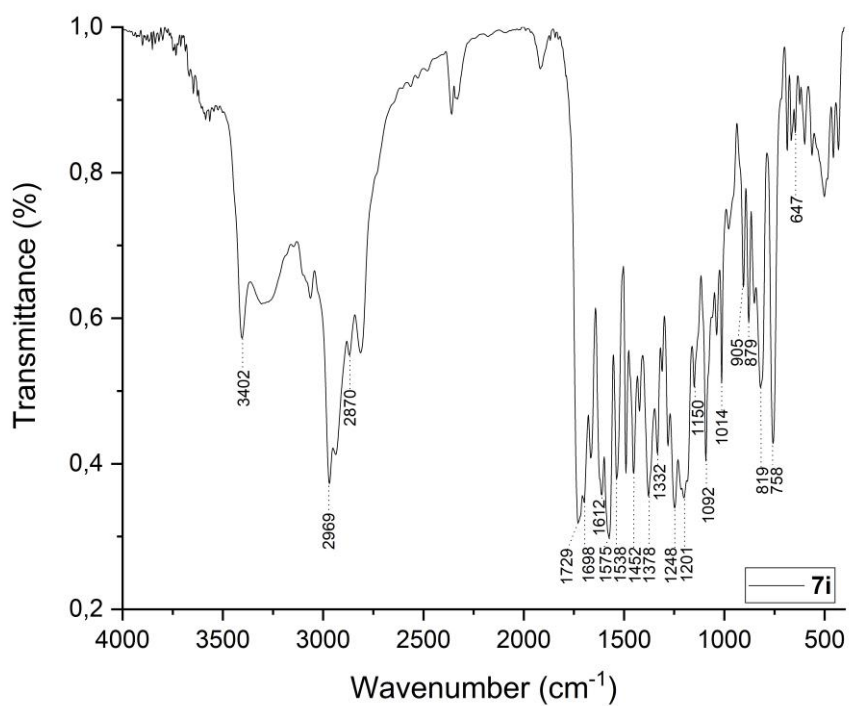


Figure S108. FT-IR spectrum of (*E/Z*)-**7i**.

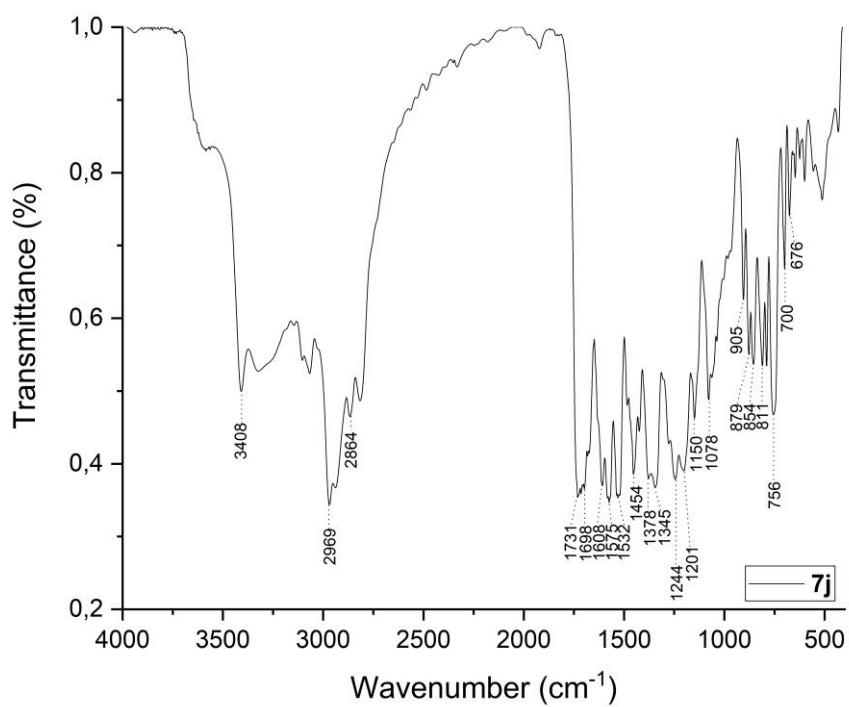


Figure S109. FT-IR spectrum of (*E/Z*)-**7j**.

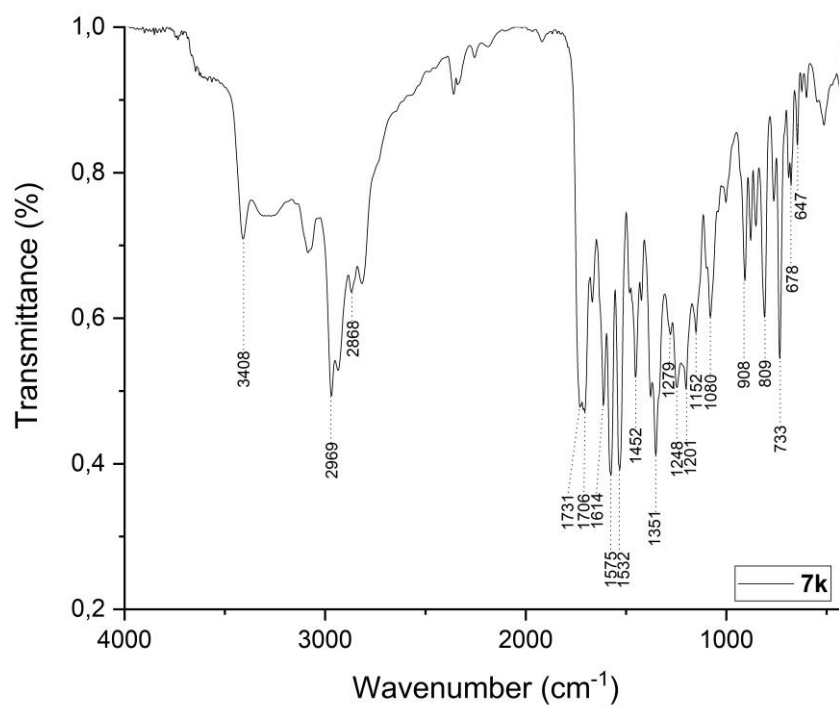


Figure S110. FT-IR spectrum of (*E/Z*)-**7k**.

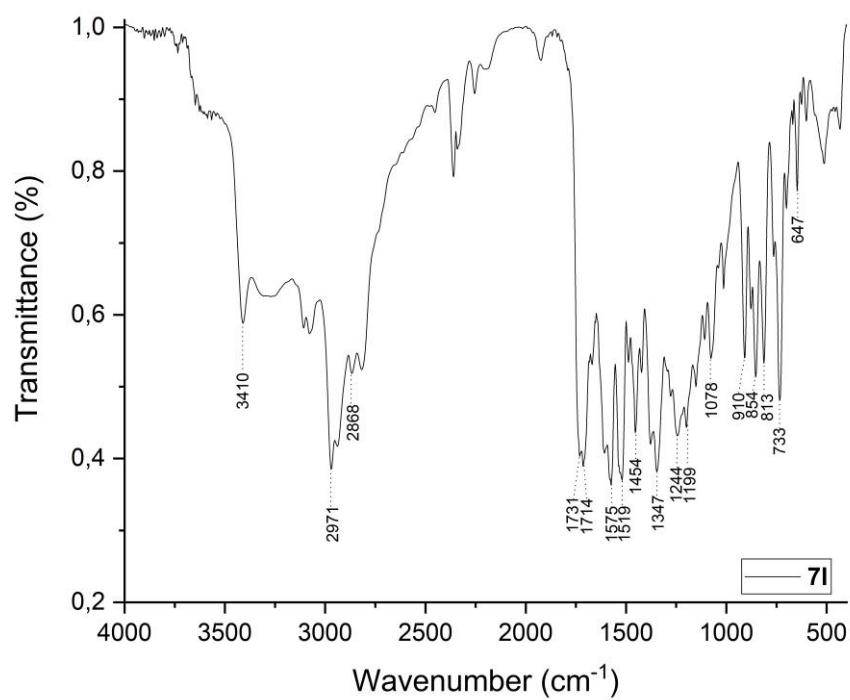


Figure S111. FT-IR spectrum of (*E/Z*)-**7l**.

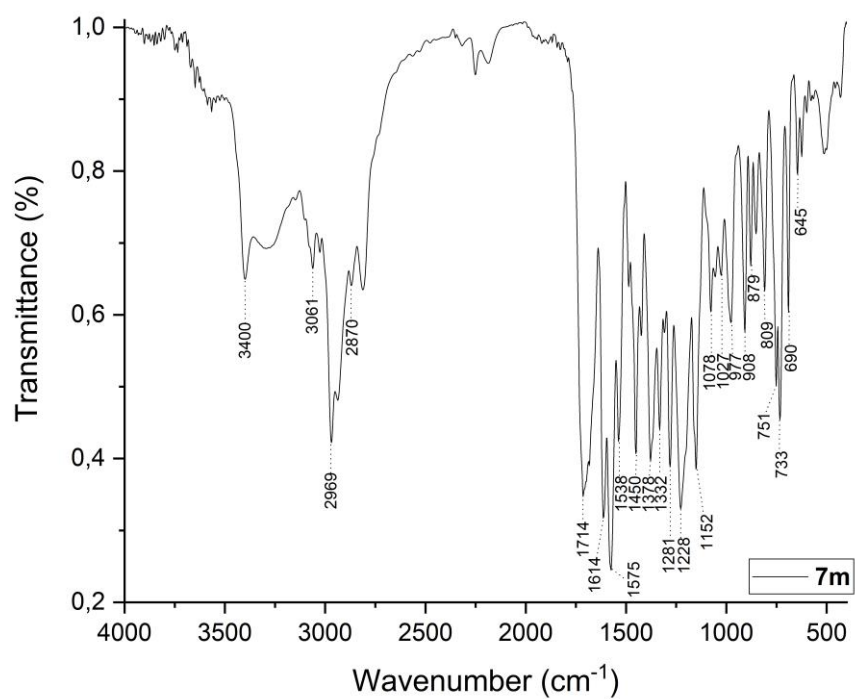


Figure S112. FT-IR spectrum of (*E/Z*)-**7m**.

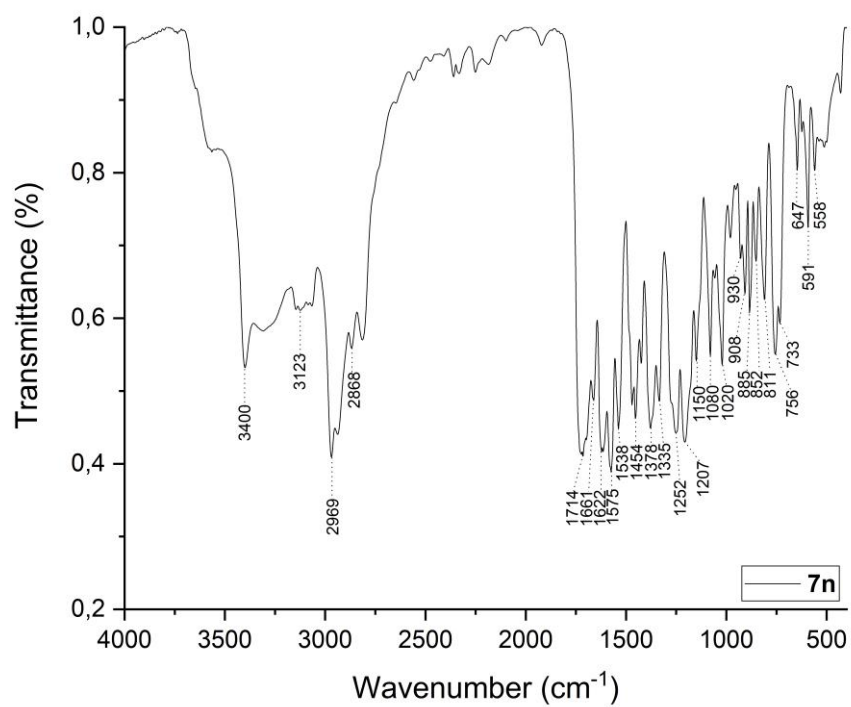


Figure S113. FT-IR spectrum of (*E/Z*)-**7n**.

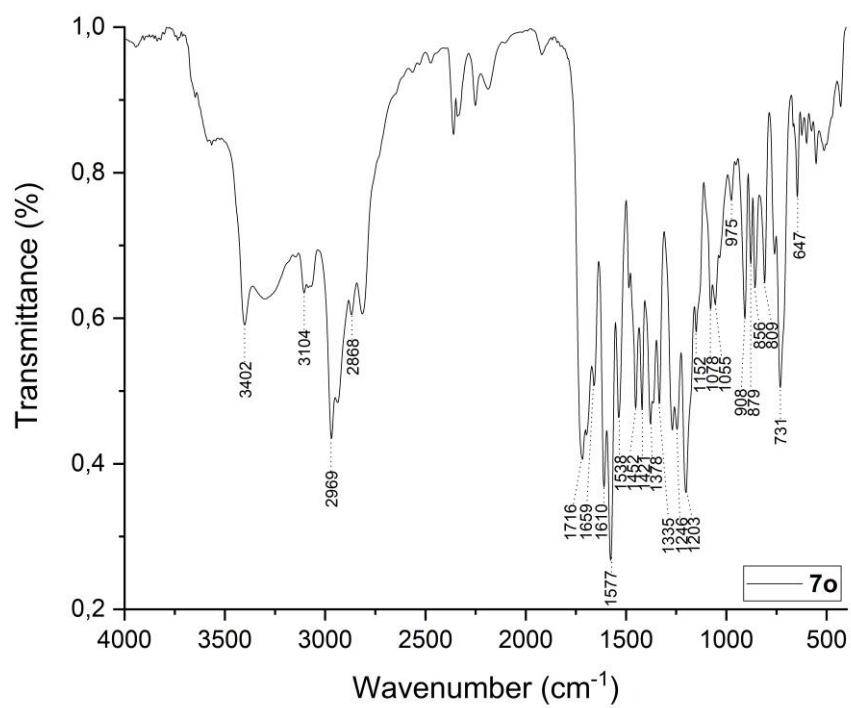


Figure S114. FT-IR spectrum of (E/Z)-7o.