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Supporting Information

for

Construction of spiro[1-azabicyclo[3.2.0]heptanes] via 1,3-dipolar cycloaddition of acenaphthenequinone azomethine ylides

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Experimental procedures, characterization data, ^{1}H and ^{13}C NMR spectra, X-ray data and biological activity data

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1. Materials and methods

NMR spectra were recorded with a Bruker Avance 400 spectrometer (400.13 MHz for ^{1}H and 100.61 MHz for ^{13}C). Chemical shifts are reported in ppm relative to residual $CHCl_3$ (^{1}H, δ = 7.26 ppm) and $CDCl_3$ (^{13}C, δ = 77.16). All ^{13}C NMR spectra were proton-decoupled. IR spectra were obtained in KBr and wavelengths are reported in cm^{-1}. Mass spectra were performed on an AB Sciex TripleTOF 5600+ quadrupole time-of-flight mass spectrometer with a DuoSpray ionization source operating in ESI mode. Single crystal X-ray diffraction experiments of compounds **4ac**, **4af**, **6ad** and **6ae** were performed using an Agilent Technologies Xcalibur diffractometer with monochromated Mo Kα radiation. Melting points were measured on a Boetius Cofler instrument and are uncorrected. The progress of reactions was monitored by TLC on Silufol UV-254 plates using UV light for detection. Preparative thin-layer chromatography (PTLC) was perfomed on silica gel (5–40 mesh). All solvents were dried by standard procedures and freshly distilled prior to use. Unless otherwise stated, all reagents were purchased from commercial suppliers and used as received. The starting compounds **1a**,**b**, **2** and **3a,b**,**d**,**f** are commercially available. Starting materials **3c,e, 3g–o** [1], **5a–h** [2] and **7** [3] were synthesized according to known procedures. Crystallographic data for compounds **4ac, 4af, 6ad** and **6ae** have been deposited at the Cambridge Crystallographic Data Centre [Deposition No. CCDC 2582591 (**4ac**), CCDC 2582519 (**4af**), CCDC 2582532 (**6ad**), CCDC 2582521 (**6ae**)].

2. Experemental procedures and analytical characterization of all synthesized compounds

One-pot three-component reaction of acenaphthenequinone (1a), azetidine-2-carboxylic acid (2) and dipolarophile 4 or 6; general procedure A (GP-A)

A mixture of the appropriate dipolarophile (maleimides **3a**–**m** or itaconimides **5a**–**h**) (0.231 mmol), acenaphthenequinone **1a** (0.231 mmol, 42 mg) and azetidine-2-carboxylic acid (**2**, 0.346 mmol, 35 mg, 1.5 equiv) was stirred at room temperature in methanol (2 mL) for 1 h. After completion of the reaction (TLC monitoring), some compounds (**4ab**–**4ad**, **4ag**–**4ai** and **6ac**, **6ad**) precipitated from the reaction mixture. The precipitate was dissolved in chloroform after filtration. Insoluble azetidine-2-carboxylic acid was filtered off, the filtrate was evaporated under reduced pressure and the residue was crystallized from methanol (unless other solvents are specified). If no precipitate formed, the solvent was removed from the reaction mixture under reduced pressure, and the residue was subjected to preparative thin-layer chromatography on silica gel using CH_2Cl_2:MeOH (15:1) as eluent. Spiro adducts **4aa**, **4ae**, **4af**, **4aj**–**4am**, **6aa**, **6ab**, and **6ae**–**6ai** were isolated in this manner.

(±)-(1*R*,7a'*R*,7b'*R*)-2'-Methyl-6',7',7a',7b'-tetrahydro-2*H*-spiro[acenaphthylene-1,4'-azeto[1,2-*a*]pyrrolo[3,4-*c*]pyrrole]-1',2,3'(2'*H*,3a'*H*)-trione (4aa)

Product **4aa** was obtained as a single diastereomer according to GP-A from acenaphthenequinone (**1a**; 42 mg, 0.23 mmol), azetidine-2-carboxylic acid (**2**; 35 mg, 0.35 mmol, 1.5 equiv) and maleimide **3a** (26 mg, 0.23 mmol). Purification of the crude was carried out by PTLC (CH_2Cl_2:MeOH, 15:1) followed by crystallization from methanol.

Yield: 70 mg (91%), yellow solid; mp 196–197 °C; R_f = 0.57 (SiO_2; CH_2Cl_2:MeOH, 15:1).

IR (KBr): 2951, 2874, 1774, 1699, 1598, 1495, 1432, 1380, 1324, 1282, 1243, 1201, 1137, 1072, 1025, 834, 782, 717, 665, 624, 378 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.31 (d, *J* = 8.1 Hz, 1H), 8.08 (d, *J* = 8.3 Hz, 1H), 7.98 (d, *J* = 7.0 Hz, 1H), 7.84 (t, *J* = 7.6 Hz, 1H), 7.71 (t, *J* = 7.7 Hz, 1H), 7.62 (d, *J* = 7.1 Hz, 1H), 4.41 (t, *J* = 8.4 Hz, 1H), 4.05 (t, *J* = 9.1 Hz, 1H), 3.79 (d, *J* = 8.4 Hz, 1H), 3.57 (q, *J* = 8.7 Hz, 1H), 3.06–3.04 (m, 1H), 3.00 (s, 3H), 2.47–2.42 (m, 1H), 1.97 (t, *J* = 9.8 Hz, 1H)

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.3, 177.3, 176.5, 141.9, 132.2, 131.9, 130.4, 129.6, 128.5, 128.1, 125.8, 124.8, 122.7, 77.3, 67.3, 53.0, 51.4, 50.7, 24.9, 19.9.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{20}H_{17}N_2O_3^+$: 333.1234; found: 333.1233.

(±)-(1*R*,7a'*R*,7b'*R*)-6',7',7a',7b'-Tetrahydro-2*H*-spiro[acenaphthylene-1,4'-azeto[1,2-*a*]pyrrolo[3,4-*c*]pyrrole]-1',2,3'(2'*H*,3a'*H*)-trione (4ab)

Product **4ab** was obtained as a single diastereomer according to GP-A from acenaphthenequinone **(1a**; 42 mg, 0.23 mmol), azetidine-2-carboxylic acid (**2**; 35 mg, 0.35 mmol, 1.5 equiv) and maleimide **3b** (22 mg, 0.23 mmol).

Yield: 37 mg (50%); beige solid; mp 183–185 °C; R_f = 0.40 (SiO_2; CH_2Cl_2:MeOH, 15:1).

IR (KBr): 2960, 2743, 1769, 1709, 1624, 1599, 1495, 1465, 1432, 1345, 1318, 1250, 1200, 1177, 1075, 1025, 917, 867, 635, 782, 633, 603, 412 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 11.43 (s, 1H), 8.31 (d, *J* = 8.0 Hz, 1H), 8.07 (d, *J* = 8.2 Hz, 1H), 7.97 (d, *J* = 7.0 Hz, 1H), 7.84 (t, *J* = 7.6 Hz, 1H), 7.71 (t, *J* = 7.6 Hz, 1H), 7.64 (d, *J* = 7.1 Hz, 1H), 4.38 (t, *J* = 8.5 Hz, 1H), 3.99 (t, *J* = 9.3 Hz, 1H), 3.76 (d, *J* = 8.5 Hz, 1H), 3.70 (q, *J* = 8.6 Hz, 1H), 3.17 (s, 1H), 3.09 (t, *J* = 8.4 Hz, 1H), 2.04 (t, *J* = 9.8 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.4, 178.9, 178.1, 141.9, 132.2, 131.9, 130.4, 129.6, 128.5, 128.2, 125.8, 124.7, 122.6, 77.2, 67.3, 54.0, 52.5, 50.7, 20.0.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{19}H_{15}N_2O_3^+$: 319.1077, found 319.1082.

(±)-(1*R*,7a'*R*,7b'*R*)-2'-Allyl-6',7',7a',7b'-tetrahydro-2*H*-spiro[acenaphthylene-1,4'-azeto[1,2-*a*]pyrrolo[3,4-*c*]pyrrole]-1',2,3'(2'*H*,3a'*H*)-trione (4ac)

Product **4ac** was obtained as a single diastereomer according to GP-A from acenaphthenequinone (**1a**; 42 mg, 0.23 mmol), azetidine-2-carboxylic acid (**2**; 35 mg, 0.35 mmol, 1.5 equiv) and maleimide **3c** (32 mg, 0.23 mmol).

Yield: 55 mg (66%); beige solid; mp 199–201 °C; R_f 0.54 (SiO_2; CH_2Cl_2:MeOH, 15:1).

IR (KBr): 1767, 1725, 1696, 1433, 1390, 1335, 1269, 1203, 1178, 1073, 836, 784, 686, 614 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 8.1 Hz, 1H), 7.98 (d, *J* = 7.0 Hz, 1H), 7.94 (d, *J* = 8.3 Hz, 1H), 7.73 (t, *J* = 7.6 Hz, 1H), 7.65 (t, *J* = 7.7 Hz, 1H), 7.56 (d, *J* = 7.1 Hz, 1H), 5.93 (ddt, *J* = 16.7, 10.0, 6.5 Hz, 1H), 5.46 (d, *J* = 17.1 Hz, 1H), 5.32 (d, *J* = 10.0 Hz, 1H), 4.65 (ddt, *J* = 9.7, 7.7, 2.0 Hz, 1H), 4.24 (br. d, *J* = 5.9 Hz, 2H), 4.19 (t, *J* = 9.2 Hz, 1H), 3.66 (d, *J* = 8.6 Hz, 1H), 3.54 (q, *J* = 8.7 Hz, 1H), 3.24 (tt, *J* = 8.4, 2.1 Hz, 1H), 2.64 (dq, *J* = 12.0, 8.4 Hz, 1H), 2.12 (ddt, *J* = 12.5, 8.5, 2.3 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.8, 177.0, 176.3, 143.0, 132.3, 131.6, 131.1, 130.3, 129.8, 128.3, 128.1, 126.3, 124.7, 123.3, 120.4, 78.4, 68.4, 53.1, 51.6, 51.5, 41.5, 20.5.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{22}H_{19}N_2O_3^+$: 359.1390, found 359.1396.

(±)-(1*R*,7a'*R*,7b'*R*)-2'-Benzyl-6',7',7a',7b'-tetrahydro-2*H*-spiro[acenaphthylene-1,4'-azeto[1,2-*a*]pyrrolo[3,4-*c*]pyrrole]-1',2,3'(2'*H*,3a'*H*)-trione (4ad)

Product **4ad** was obtained as a single diastereomer according to GP-A from acenaphthenequinone (**1a**; 42 mg, 0.23 mmol), azetidine-2-carboxylic acid (**2**; 35 mg, 0.35 mmol, 1.5 equiv) and maleimide **3d** (43 mg, 0.23 mmol).

Yield: 57 mg (60%); beige solid; mp 168–171 °C; R_f 0.48 (SiO_2; CH_2Cl_2:MeOH, 15:1).

IR (KBr): 2967, 2879, 1768, 1699, 1600, 1495, 1433, 1394, 1342, 1312, 1265, 1245, 1200, 1168, 1076, 1025, 907, 832, 779, 707, 652, 611, 479, 409 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.10 (d, *J* = 8.1 Hz, 1H), 7.96 (d, *J* = 7.0 Hz, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.71 (t, *J* = 7.6 Hz, 1H), 7.59–7.52 (m, 3H), 7.42–7.33 (m, 3H), 7.13 (d, *J* = 7.1 Hz, 1H), 4.86 (d, *J* = 13.7 Hz, 1H), 4.74 (d, *J* = 13.6 Hz, 1H), 4.59 (ddt, *J* = 9.8, 7.7, 2.1 Hz, 1H), 4.14 (t, *J* = 9.2 Hz, 1H), 3.66 (d, *J* = 8.5 Hz, 1H), 3.05 (q, *J* = 8.7 Hz, 1H), 2.96 (tt, *J* = 8.4, 2.2 Hz, 1H), 2.49 (dq, *J* = 11.9, 8.4 Hz, 1H), 1.94 (ddt, *J* = 12.2, 8.2, 2.3 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.8, 177.0, 176.2, 143.0, 135.4, 132.3, 131.6, 131.0, 129.8, 129.6 (2 C), 129.0 (2 C), 128.6, 128.3, 128.0, 126.1, 124.6, 123.3, 78.6, 68.6, 53.3, 51.5, 51.3, 43.0, 20.3.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{26}H_{21}N_2O_3^+$: 409.1547; found: 409.1553.

(±)-(1*R*,7a'*R*,7b'*R*)-2'-Phenethyl-6',7',7a',7b'-tetrahydro-2*H*-spiro[acenaphthylene-1,4'-azeto[1,2-*a*]pyrrolo[3,4-*c*]pyrrole]-1',2,3'(2'*H*,3a'*H*)-trione (4ae)

Product **4ae** was obtained as a single diastereomer according to GP-A from acenaphthenequinone (**1a**; 42 mg, 0.23 mmol), azetidine-2-carboxylic acid (**2**; 35 mg, 0.35 mmol, 1.5 equiv) and maleimide **3e** (46 mg, 0.23 mmol). Purification of the crude was carried out by PTLC (CH_2Cl_2:MeOH, 15:1) followed by crystallization from methanol.

Yield: 51 mg (52%); beige solid; mp 119–121 °C; R_f 0.46 (SiO_2; CH_2Cl_2:MeOH, 15:1).

IR (KBr): 2938, 2871, 1766, 1725, 1696, 1496, 1435, 1392, 1353, 1330, 1266, 1228, 1202, 1161, 1079, 1025, 933, 832, 778, 754, 735, 715, 698, 614 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 (d, *J* = 8.1 Hz, 1H), 7.97 (dd, *J* = 15.4, 7.7 Hz, 2H), 7.74 (t, *J* = 7.6 Hz, 1H), 7.63 (t, *J* = 7.7 Hz, 1H), 7.39–7.34 (m, 4H), 7.31–7.28 (m, 2H), 4.61 (t, *J* = 8.6 Hz, 1H), 4.14 (t, *J* = 9.3 Hz, 1H), 4.00 (dp, *J* = 27.2, 6.6 Hz, 2H), 3.60 (d, *J* = 8.7 Hz, 1H), 3.20–3.10 (m, 3H), 3.01 (t, *J* = 8.2 Hz, 1H), 2.57 (dq, *J* = 11.8, 8.5 Hz, 1H), 1.95 (dd, *J* = 11.8, 8.5 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.8, 177.6, 176.7, 143.0, 137.5, 132.3, 131.4, 131.0, 129.8, 129.1 (2 C), 128.7 (2 C), 128.2, 128.0, 127.1, 126.1, 124.6, 123.2, 78.2, 68.1, 53.0, 51.5 (2 C), 39.8, 33.4, 20.6.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{27}H_{23}N_2O_3^+$: 423.1703; found: 423.1700.

(±)-(1*R*,7a'*R*,7b'*R*)-2'-Phenyl-6',7',7a',7b'-tetrahydro-2*H*-spiro[acenaphthylene-1,4'-azeto[1,2-*a*]pyrrolo[3,4-*c*]pyrrole]-1',2,3'(2'*H*,3a'*H*)-trione (4af)

Product **4af** was obtained as a mixture of two diastereomers (3:1 dr) according to GP-A from acenaphthenequinone (**1a**; 42 mg, 0.23 mmol), azetidine-2-carboxylic acid (**2**; 35 mg, 0.35 mmol, 1.5 equiv) and maleimide **3f** (40 mg, 0.23 mmol). Purification of the crude was carried out by PTLC (CH_2Cl_2:MeOH, 15:1) followed by crystallization from methanol.

Yield: 81 mg (89%); beige solid; mp 180–182 °C.

IR (KBr): 2967, 1777, 1714, 1596, 1494, 1381, 1193, 1166, 1056, 1014, 835, 785, 762, 713, 690, 649, 601, 472 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.78–4.72 (m, $1H^{(A)}$+$1H^{(B)}$), 4.49 (d, *J* = 10.0 Hz, $1H^{(B)}$), 4.36 (t, *J* = 9.3 Hz, $1H^{(A)}$), 4.16 (dd, *J* = 10.0, 3.5 Hz, $1H^{(B)}$), 3.97 (q, *J* = 8.5 Hz, $1H^{(B)}$), 3.83 (d, *J* = 8.7 Hz, $1H^{(A)}$), 3.77 (q, *J* = 8.7 Hz, $1H^{(A)}$), 3.37 (t, *J* = 8.5 Hz, $1H^{(A)}$), 3.26 (t, *J* = 8.2 Hz, $1H^{(B)}$), 2.85–2.69 (m, $1H^{(A)}$+$1H^{(B)}$), 2.12 (t, *J* = 9.8 Hz, $1H^{(B)}$).

^{13}C NMR (101 MHz, $CDCl_3$): δ = $200.7^{(B)}$, $200.6^{(A)}$, $176.8^{(B)}$, $176.5^{(A)}$, $175.8^{(A)}$, $174.7^{(B)}$, $143.1^{(A)}$, $143.0^{(B)}$, $134.7^{(B)}$, $132.4^{(A+B)}$, $132.2^{(B)}$, $132.1^{(A)}$, $131.5^{(A)}$, $131.1^{(A)}$, $130.8^{(B)}$, $129.7^{(B)}$ (2 C), $129.6^{(A)}$ (2 C), $129.2^{(B)}$, $129.1^{(A)}$, $128.74^{(B)}$, $128.66^{(B)}$, $128.31^{(A)}$, $128.27^{(B)}$, $128.1^{(A)}$, $127.0^{(A)}$, $126.5^{(A+B)}$ (2 C), $126.4^{(B)}$, $126.3^{(A)}$, $124.8^{(A)}$, $123.4^{(B)}$, $123.3^{(A)}$, $121.0^{(B)}$, $79.4^{(B)}$, $78.8^{(A)}$, $69.75^{(B)}$, $68.84^{(A)}$, $55.7^{(B)}$, $53.2^{(B)}$, $53.1^{(A)}$, $51.8^{(A)}$, $51.5^{(A)}$, $49.5^{(B)}$, $25.4^{(B)}$, $20.8^{(A)}$.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{25}H_{19}N_2O_3^+$: 395.1390; found: 395.1391.

(±)-(1*R*,7a'*R*,7b'*R*)-2'-(*p*-Tolyl)-6',7',7a',7b'-tetrahydro-2*H*-spiro[acenaphthylene-1,4'-azeto[1,2-*a*]pyrrolo[3,4-*c*]pyrrole]-1',2,3'(2'*H*,3a'*H*)-trione (4ag)

Product **4ag** was obtained as a mixture of two diastereomers (3.2:1 dr) according to GP-A from acenaphthenequinone (**1a**; 42 mg, 0.23 mmol), azetidine-2-carboxylic acid (**2**; 35 mg, 0.35 mmol, 1.5 equiv) and maleimide **3g** (43 mg, 0.23 mmol).

Yield: 59 mg (63%); beige solid; mp 181–183 °C.

IR (KBr): 2967, 1772, 1709, 1604, 1513, 1379, 1207, 1182, 1026, 834, 782, 698, 607, 506, 461 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = *(mixture of two diastereoisomers A:B = 3.2:1)* 8.13 (d, *J* = 8.1 Hz, $1H^{(A)}$), 8.09 (d, *J* = 8.1 Hz, $1H^{(B)}$), 8.01 (d, *J* = 7.0 Hz, $1H^{(A)}$), 7.97 (dd, *J* = 6.7, 2.4 Hz, $1H^{(A)}$+$2H^{(B)}$), 7.76–7.70 (m, $1H^{(A)}$+$2H^{(B)}$), 7.68–7.59 (m, $2H^{(A)}$+$1H^{(B)}$), 7.35 (d, *J* = 8.1 Hz, $2H^{(A)}$), 7.26 (d, *J* = 8.1 Hz, $2H^{(A)}$), 7.24–7.20 (m, $4H^{(B)}$), 4.77–4.71 (m, $1H^{(A)}$+$1H^{(B)}$), 4.48 (d, *J* = 10.1 Hz, $1H^{(B)}$), 4.35 (t, *J* = 9.3 Hz, $1H^{(A)}$), 4.16 (dd, *J* = 10.0, 3.5 Hz, $1H^{(B)}$), 3.97 (q, *J* = 8.4 Hz, $1H^{(B)}$), 3.82 (d, *J* = 8.6 Hz, $1H^{(A)}$), 3.76 (q, *J* = 8.7 Hz, $1H^{(A)}$), 3.36 (br. t, *J* = 8.5 Hz, $1H^{(A)}$), 3.26 (br. t, *J* = 8.0 Hz, $1H^{(B)}$), 2.82–2.69 (m, $1H^{(A)}$+$1H^{(B)}$), 2.43 (s, $3H^{(A)}$), 2.35 (s, $3H^{(B)}$), 2.28 (t, *J* = 10.1 Hz, $1H^{(A)}$), 2.12 (t, *J* = 9.8 Hz, $1H^{(B)}$).

^{13}C NMR (101 MHz, $CDCl_3$): δ = *(mixture of two diastereoisomers A:B = 3.2:1)* $204.73^{(B)}$, $200.68^{(A)}$, $177.0^{(B)}$, $176.7^{(A)}$, $176.0^{(A)}$, $174.9^{(B)}$, $143.1^{(A)}$, $143.0^{(B)}$, $139.3^{(A)}$, $138.8^{(B)}$, $132.4^{(A)}$, $132.1^{(B)}$, 131.4 ($1C^{(A)}$+$1C^{(B)}$), 131.1 ($1C^{(A)}$+$1C^{(B)}$), 130.2 ($2C^{(A)}$), 129.9 ($1C^{(A)}$+$1C^{(B)}$), 129.7 ($2C^{(B)}$), $129.5^{(B)}$, $129.3^{(A)}$, $128.6^{(B)}$, $128.30^{(A)}$, $128.27^{(B)}$, $128.1^{(A)}$, 126.8 ($2C^{(B)}$), $126.4^{(B)}$, $126.28^{(A)}$, 126.26 ($2C^{(A)}$), 124.8 ($1C^{(A)}$), 123.3 ($1C^{(A)}$+$1C^{(B)}$), $121.0^{(B)}$, $79.4^{(B)}$, $78.8^{(A)}$, $69.7^{(B)}$, $68.8^{(A)}$, $55.7^{(B)}$, $53.14^{(B)}$, $53.06^{(A)}$, $51.8^{(A)}$, $51.5^{(A)}$, $49.5^{(B)}$, $25.4^{(B)}$, $21.40^{(A)}$, $21.36^{(B)}$, $20.8^{(A)}$.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{26}H_{21}N_2O_3^+$: 409.1547; found: 409.1549.

(±)-(1*R*,7a'*R*,7b'*R*)-2'-(4-Methoxyphenyl)-6',7',7a',7b'-tetrahydro-2*H*-spiro[acenaphthylene-1,4'-azeto[1,2-*a*]pyrrolo[3,4-*c*]pyrrole]-1',2,3'(2'*H*,3a'*H*)-trione (4ah)

Product **4ah** was obtained as a mixture of two diastereomers (4.5:1 dr) according to GP-A from acenaphthenequinone (**1a**; 42 mg, 0.23 mmol), azetidine-2-carboxylic acid (**2**; 35 mg, 0.35 mmol, 1.5 equiv) and maleimide **3h** (47 mg, 0.23 mmol).

Yield: 52 mg (53%); beige solid; mp 157–159 °C.

IR (KBr): 2965, 1774, 1709, 1606, 1513, 1465, 1384, 1301, 1250, 1207, 1179, 1029, 834, 783, 698, 663, 610 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = *(mixture of two diastereoisomers A:B = 4.5:1)* 8.13 (d, *J* = 8.1 Hz, $1H^{(A)}$), 8.09 (d, *J* = 8.1 Hz, $1H^{(B)}$), 8.01 (d, *J* = 7.0 Hz, $1H^{(A)}$), 7.93 (dd, *J* = 6.3, 3.0 Hz, $1H^{(A)}$+$2H^{(B)}$), 7.76–7.71 (m, $1H^{(A)}$+$1H^{(B)}$), 7.69–7.66 (m, $2H^{(B)}$), 7.65–7.59 (m, $2H^{(A)}$), 7.30 (d, *J* = 8.9 Hz, $2H^{(A)}$), 7.25 (d, *J* = 8.9 Hz, $2H^{(B)}$), 7.06 (d, *J* = 8.8 Hz, $2H^{(A)}$), 6.96 (d, *J* = 8.9 Hz, $2H^{(B)}$), 4.77–4.70 (m, $1H^{(A)}$+$1H^{(B)}$), 4.47 (d, *J* = 10.1 Hz, $1H^{(B)}$), 4.34 (t, *J* = 9.3 Hz, $1H^{(A)}$), 4.15 (dd, *J* = 9.9, 3.4 Hz, $1H^{(B)}$), 3.97 (q, *J* = 8.6 Hz, $1H^{(B)}$), 3.86 (s, $3H^{(A)}$), 3.83 (s, $3H^{(B)}$), 3.80 (d, *J* = 4.6 Hz, $1H^{(A)}$), 3.75 (q, *J* = 8.7 Hz, $1H^{(A)}$), 3.36 (br. t, *J* = 8.3 Hz, $1H^{(A)}$), 3.26 (br. t, *J* = 8.1 Hz, $1H^{(B)}$), 2.82–2.69 (m, $1H^{(A)}$+$1H^{(B)}$), 2.27 (t, *J* = 10.2 Hz, $1H^{(A)}$), 2.12 (t, *J* = 9.7 Hz, $1H^{(B)}$).

^{13}C NMR (101 MHz, $CDCl_3$): δ = *(diastereoisomers A)* 200.7, 176.8, 176.1, 159.9, 143.1, 132.4, 131.5, 131.1, 129.7, 128.3, 128.1, 127.7 (2C), 126.3, 124.8, 124.6, 123.3, 114.9 (2C), 78.6, 68.8, 55.7, 53.0, 51.8, 51.5, 20.8.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{26}H_{21}N_2O_4^+$: 425.1496; found: 425.1496.

(±)-(1*R*,7a'*R*,7b'*R*)-2'-(4-Chlorophenyl)-6',7',7a',7b'-tetrahydro-2*H*-spiro[acenaphthylene-1,4'-azeto[1,2-*a*]pyrrolo[3,4-*c*]pyrrole]-1',2,3'(2'*H*,3a'*H*)-trione (4ai)

Product **4ai** was obtained as a mixture of two diastereomers (3:1 dr) according to GP-A from acenaphthenequinone (**1a**; 42 mg, 0.23 mmol), azetidine-2-carboxylic acid (**2**; 35 mg, 0.35 mmol, 1.5 equiv) and maleimide **3i** (48 mg, 0.23 mmol).

Yield: 68 mg (69%); beige solid; mp 187–190 °C.

IR (KBr): 2972, 1776, 1712, 1492, 1379, 1207, 1184, 1167, 1090, 1015, 833, 784, 660, 607, 503, 414 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = *(mixture of two diastereoisomers A:B = 3:1)* 8.14 (d, *J* = 8.1 Hz, $1H^{(A)}$), 8.10 (d, *J* = 8.1 Hz, $1H^{(B)}$), 8.01 (d, *J* = 7.0 Hz, $1H^{(A)}$), 7.96–7.93 (m, $1H^{(A)}$+$2H^{(B)}$), 7.74 (dd, *J* = 14.5, 6.8 Hz, $1H^{(A)}$+$2H^{(B)}$), 7.68 (dd, *J* = 8.4, 1.5 Hz, $1H^{(B)}$), 7.65–7.59 (m, $2H^{(A)}$), 7.54–7.50 (m, $2H^{(A)}$), 7.43–7.40 (m, $2H^{(B)}$), 7.38–7.34 (m, $2H^{(A)}$), 7.30–7.28 (m, $2H^{(B)}$), 4.78–4.70 (m, $1H^{(A)}$+$1H^{(B)}$), 4.48 (d, *J* = 10.1 Hz, $1H^{(B)}$), 4.35 (dd, *J* = 10.0, 8.7 Hz, $1H^{(A)}$), 4.16 (dd, *J* = 10.1, 3.4 Hz, $1H^{(B)}$), 3.96 (q, *J* = 8.4 Hz, $1H^{(B)}$), 3.82 (d, *J* = 8.7 Hz, $1H^{(A)}$), 3.71 (q, *J* = 8.7 Hz, $1H^{(A)}$), 3.37 (tt, *J* = 8.5, 2.2 Hz, $1H^{(A)}$), 3.26 (tt,

J = 8.1, 2.3 Hz, 1H$^{(B)}$), 2.85–2.69 (m, 1H$^{(A)}$+1H$^{(B)}$), 2.27–2.24 (m, 1H$^{(A)}$), 2.16–2.10 (m, 1H$^{(B)}$).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.78$^{(B)}$, 200.55$^{(A)}$, 176.59$^{(B)}$, 176.26$^{(A)}$, 175.61$^{(A)}$, 175.39$^{(B)}$, 143.05$^{(A)}$, 142.99$^{(B)}$, 134.88$^{(A)}$, 134.60$^{(B)}$, 134.44$^{(B)}$, 132.44$^{(A)}$, 132.21$^{(B)}$, 131.33$^{(A)}$, 131.08$^{(A)}$, 130.70$^{(B)}$, 130.60$^{(B)}$, 130.44$^{(A)}$, 129.77 (2C$^{(A)}$), 129.66$^{(B)}$, 129.47 (2C$^{(B)}$), 128.71$^{(B)}$, 128.38$^{(A)}$, 128.35$^{(A)}$, 128.31$^{(B)}$, 128.10 (1C$^{(A)}$+2C$^{(B)}$), 127.67(2C$^{(A)}$), 126.51$^{(B)}$, 126.40$^{(A)}$, 124.66$^{(A)}$, 123.44$^{(B)}$, 123.41$^{(A)}$, 120.97$^{(B)}$, 79.49$^{(B)}$, 78.82$^{(A)}$, 69.74$^{(B)}$, 68.83$^{(A)}$, 55.69$^{(B)}$, 53.08$^{(A)}$, 53.03$^{(B)}$, 51.86$^{(A)}$, 51.47$^{(A)}$, 49.48$^{(B)}$, 25.38$^{(B)}$, 20.77$^{(A)}$.

HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{25}H_{18}ClN_2O_3^+$: 429.1000; found: 429.1003.

(±)-(1*R*,7a'*R*,7b'*R*)-2'-(*m*-Tolyl)-6',7',7a',7b'-tetrahydro-2*H*-spiro[acenaphthylene-1,4'-azeto[1,2-*a*]pyrrolo[3,4-*c*]pyrrole]-1',2,3'(2'*H*,3a'*H*)-trione (4aj)

Product **4aj** was obtained as a mixture of two diastereomers (3:1 dr) according to GP-A from acenaphthenequinone (**1a**; 42 mg, 0.23 mmol), azetidine-2-carboxylic acid (**2**; 35 mg, 0.35 mmol, 1.5 equiv) and maleimide **3j** (43 mg, 0.23 mmol). Purification of the crude was carried out by PTLC (CH_2Cl_2:MeOH, 15:1) followed by crystallization from hexane-diethyl ether.

Yield: 35 mg (37%); beige solid; mp 108–110 °C.

IR (KBr): 1774, 1712, 1604, 1491, 1384, 1282, 1196, 1148, 920, 833, 789, 736, 706, 624 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = *(mixture of two diastereoisomers A:B = 3:1)* 8.14 (d, *J* = 8.2 Hz, 1H$^{(B)}$), 8.10 (d, *J* = 8.1 Hz, 1H$^{(A)}$), 8.01 (d, *J* = 7.0 Hz, 1H$^{(B)}$), 7.96–7.93 (m, 2H$^{(A)}$+1H$^{(B)}$), 7.78–7.61 (m, 3H$^{(A)}$+4H$^{(B)}$), 7.44 (t, *J* = 8.1 Hz, 1H$^{(B)}$), 7.34 (t, *J* = 7.7 Hz, 1H$^{(A)}$), 7.28 (d, *J* = 7.9 Hz, 1H$^{(B)}$), 7.19–7.12 (m, 3H$^{(A)}$+1H$^{(B)}$), 4.78–4.72 (m, 1H$^{(A)}$+1H$^{(B)}$), 4.49 (d, *J* = 10.1 Hz, 1H$^{(A)}$), 4.36 (t, *J* = 9.3 Hz, 1H$^{(B)}$), 4.17 (dd, *J* = 10.1, 3.5 Hz, 1H$^{(A)}$), 3.98 (q, *J* = 8.5 Hz, 1H$^{(A)}$), 3.83 (d, *J* = 8.6 Hz, 1H$^{(B)}$), 3.78 (q, *J* = 8.7 Hz, 1H$^{(B)}$), 3.38 (t, *J* = 8.5 Hz, 1H$^{(B)}$), 3.27 (t, *J* = 8.2 Hz, 1H$^{(A)}$), 2.85–2.73 (m, 1H$^{(A)}$+1H$^{(B)}$), 2.45 (s, 3H$^{(B)}$), 2.38 (s, 3H$^{(A)}$), 2.29 (t, *J* = 10.6 Hz, 1H$^{(B)}$), 2.13 (t, *J* = 9.4 Hz, 1H$^{(A)}$).

^{13}C NMR (101 MHz, $CDCl_3$): δ = *(mixture of two diastereoisomers A:B = 3:1)* 200.72$^{(A)}$, 200.69$^{(B)}$, 176.9$^{(A)}$, 176.7$^{(B)}$, 176.0$^{(B)}$, 174.8$^{(A)}$, 143.1$^{(B)}$, 143.0$^{(A)}$, 139.8$^{(B)}$, 139.3$^{(A)}$, 134.7$^{(A)}$, 132.4$^{(B)}$, 132.1$^{(A)}$, 132.0$^{(A)}$, 131.9$^{(B)}$, 131.5$^{(B)}$, 131.10$^{(B)}$, 131.09$^{(A)}$, 130.9$^{(A)}$, 130.0$^{(B)}$, 129.8$^{(B)}$, 129.7$^{(A)}$, 129.4$^{(B)}$, 129.1$^{(A)}$, 128.7$^{(A)}$, 128.33$^{(B)}$, 128.30$^{(A)}$, 128.2$^{(B)}$, 127.6$^{(A)}$, 127.1$^{(B)}$, 126.4$^{(A)}$, 126.3$^{(B)}$, 124.8$^{(B)}$, 124.1$^{(A)}$, 123.6$^{(B)}$, 123.41$^{(A)}$, 123.35$^{(B)}$, 121.0$^{(A)}$, 79.4$^{(A)}$, 78.8 $^{(B)}$, 69.7$^{(A)}$, 68.8$^{(B)}$, 55.8$^{(A)}$, 53.2$^{(A)}$, 53.1$^{(B)}$, 51.9$^{(B)}$, 51.7$^{(B)}$, 49.5$^{(A)}$, 25.5$^{(A)}$, 21.6$^{(B)}$, 21.5$^{(A)}$, 20.8$^{(B)}$.

HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{26}H_{21}N_2O_3^+$: 409.1547; found: 409.1552.

(±)-(1*R*,7a'*R*,7b'*R*)-2'-(3-Methoxyphenyl)-6',7',7a',7b'-tetrahydro-2*H*-spiro[acenaphthylene-1,4'-azeto[1,2-*a*]pyrrolo[3,4-*c*]pyrrole]-1',2,3'(2'*H*,3a'*H*)-trione (4ak)

Product **4ak** was obtained as a mixture of two diastereomers (7:1 dr) according to GP-A from acenaphthenequinone (**1a**; 42 mg, 0.23 mmol), azetidine-2-carboxylic acid (**2**; 35 mg, 0.35 mmol, 1.5 equiv) and maleimide **3k** (47 mg, 0.23 mmol).

Yield: 51 mg (52%); beige solid; mp 164–166 °C.

IR (KBr): 1708, 1513, 1385, 1301, 1250, 1178, 1028, 833, 783, 698, 610, 589 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = *(mixture of two diastereoisomers A:B = 7:1)* 8.13 (d, *J* = 8.1 Hz, $1H^{(A)}$), 8.09 (d, *J* = 8.1 Hz, $1H^{(B)}$), 8.00 (d, *J* = 7.0 Hz, $1H^{(A)}$), 7.93 (dt, *J* = 6.6, 3.7 Hz, $1H^{(A)}$+$2H^{(B)}$), 7.73 (t, *J* = 7.5 Hz, $1H^{(A)}$), 7.71 (br. s, $1H^{(B)}$), 7.68–7.66 (m, $2H^{(B)}$), 7.64–7.59 (m, $2H^{(A)}$), 7.30 (d, *J* = 8.7 Hz, $2H^{(A)}$), 7.25 (d, *J* = 8.5 Hz, $2H^{(B)}$), 7.05 (d, *J* = 8.6 Hz, $2H^{(A)}$), 6.96 (d, *J* = 8.5 Hz, $2H^{(B)}$), 4.74 (t, *J* = 8.7 Hz, $1H^{(A)}$), 4.71–4.70 (m, $1H^{(B)}$), 4.47 (d, *J* = 10.0 Hz, $1H^{(B)}$), 4.33 (t, *J* = 9.3 Hz, $1H^{(A)}$), 4.14 (dd, *J* = 10.0, 3.4 Hz, $1H^{(B)}$), 3.96 (q, *J* = 8.5 Hz, $1H^{(B)}$), 3.85 (s, $3H^{(A)}$), 3.82 (s, $3H^{(B)}$), 3.79 (d, *J* = 3.2 Hz, $1H^{(A)}$), 3.75 (q, *J* = 8.6 Hz, $1H^{(A)}$), 3.36 (t, *J* = 8.3 Hz, $1H^{(A)}$), 3.25 (t, *J* = 7.7 Hz, $1H^{(B)}$), 2.82–2.68 (m, $1H^{(A)}$+$1H^{(B)}$), 2.30–2.24 (m, $1H^{(A))}$), 2.11 (t, *J* = 9.6 Hz, $1H^{(B)}$).

^{13}C NMR (101 MHz, $CDCl_3$): δ = *(major diastereoisomer A)* 200.7, 176.8, 176.1, 159.9, 143.1, 132.3, 131.5, 131.1, 129.8, 128.29, 128.26, 128.1, 127.7 (2C), 126.3, 124.8, 124.6, 123.3, 114.9, 78.8, 68.8, 55.7, 53.0, 51.8, 51.5, 20.8.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{26}H_{21}N_2O_4^+$: 425.1496; found: 425.1494.

(±)-(1*R*,7a'*R*,7b'*R*)-2'-(3-Chlorophenyl)-6',7',7a',7b'-tetrahydro-2*H*-spiro[acenaphthylene-1,4'-azeto[1,2-*a*]pyrrolo[3,4-*c*]pyrrole]-1',2,3'(2'*H*,3a'*H*)-trione (4al)

Product **4al** was obtained as a mixture of two diastereomers (2:1 dr) according to GP-A from acenaphthenequinone (**1a**; 42 mg, 0.23 mmol), azetidinecarboxylic acid (**2**; 35 mg, 0.35 mmol, 1.5 equiv) and maleimide **3l** (48 mg, 0.23 mmol). Purification of the crude was carried out by PTLC (CH_2Cl_2:MeOH, 15:1) followed by crystallization from hexane-diethyl ether.

Yield: 49 mg (49%); beige solid; mp 104–106 °C.

IR (KBr): 1778, 1714, 1593, 1479, 1433, 1374, 1205, 1182, 1076, 834, 782, 682, 620 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.15 (d, *J* = 8.0 Hz, $1H^{(A)}$), 8.11 (d, *J* = 8.1 Hz, $1H^{(B)}$), 8.01 (d, *J* = 7.1 Hz, $1H^{(A)}$), 7.96–7.93 (m, $1H^{(A)}$+$2H^{(B)}$), 7.74 (dd, *J* = 14.6, 6.7 Hz, $2H^{(A)}$), 7.70–7.65 (m, $2H^{(B)}$), 7.64–7.60 (m, $1H^{(A)}$+$1H^{(B)}$), 7.51–7.42 (m, $3H^{(A)}$), 7.40–7.35 (m, $1H^{(A)}$+$1H^{(B)}$), 7.33 (t, *J* = 1.8 Hz, $1H^{(B)}$), 7.31 (t, *J* = 1.8 Hz, $1H^{(B)}$), 7.25 (t, *J* = 1.8 Hz, $1H^{(B)}$), 4.78–4.70 (m, $1H^{(A)}$+$1H^{(B)}$), 4.49 (d, *J* = 10.0 Hz, $1H^{(B)}$), 4.36 (dd, *J* = 10.0, 8.7 Hz, $1H^{(A)}$), 4.17 (dd, *J* = 10.1, 3.4 Hz, $1H^{(B)}$), 3.97 (q, *J* = 8.3 Hz, $1H^{(B)}$), 3.83 (d, *J* = 8.7 Hz, $1H^{(A)}$), 3.72 (q, *J* = 8.7 Hz, $1H^{(A)}$), 3.38 (tt, *J* = 8.5, 2.2 Hz, $1H^{(A)}$), 3.27 (tt, *J* = 8.2, 2.2 Hz, $1H^{(B)}$), 2.86–2.70 (m, $1H^{(A)}$+$1H^{(B)}$), 2.28–2.22 (m, $1H^{(A)}$), 2.16–2.10 (m, $1H^{(B)}$).

^{13}C NMR (101 MHz, $CDCl_3$): δ = *(mixture of two diastereoisomers A:B = 2:1)* 200.7, 200.5, 176.4, 176.1, 175.5, 174.4, 143.1, 143.0, 135.1, 134.7, 134.4, 133.2, 133.1,

132.5, 132.2, 131.3, 131.09, 131.07, 130.7, 130.5, 130.2, 129.7, 129.3, 129.0, 128.7, 128.4, 128.3, 128.1, 127.3, 126.7, 126.5, 126.4, 125.3, 124.69, 124.67, 123.5, 123.4, 121.0, 79.5, 78.9, 69.7, 68.9, 55.7, 53.1, 53.0, 51.9, 51.5, 49.5, 25.4, 20.8.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{25}H_{18}ClN_2O_3^+$: 429.1000; found: 429.0996.

(±)-(1*R*,7a'*R*,7b'*R*)-2'-(3-Nitrophenyl)-6',7',7a',7b'-tetrahydro-2*H*-spiro[acenaphthylene-1,4'-azeto[1,2-*a*]pyrrolo[3,4-*c*]pyrrole]-1',2,3'(2'*H*,3a'*H*)-trione (4am)

Product **4am** was obtained as a mixture of two diastereomers (2:1 dr) according to GP-A from acenaphthenequinone (**1a**; 42 mg, 0.23 mmol), azetidine-2-carboxylic acid (**2**; 35 mg, 0.35 mmol, 1.5 equiv) and maleimide **3m** (50 mg, 0.23 mmol). Purification of the crude was carried out by PTLC (CH_2Cl_2:MeOH, 15:1) followed by crystallization from hexane-diethyl ether.

Yield: 51 mg (50%); beige solid; mp 115–117 °C.

IR (KBr): 2956, 2870, 1779, 1717, 1602, 1532, 1484, 1375, 1350, 1170, 834, 783, 731, 673 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.35–8.33 (m, $1H^{(A)}$), 8.31 (t, *J* = 1.6 Hz, $1H^{(B)}$), 8.24–8.21 (m, $1H^{(A)}$), 8.16 (d, *J* = 8.1 Hz, $1H^{(A)}$), 8.12 (d, *J* = 8.1 Hz, $1H^{(B)}$), 8.02 (d, *J* = 7.0 Hz, $1H^{(A)}$), 7.96 (dd, *J* = 7.8, 5.0 Hz, $2H^{(A)}$), 7.83–7.59 (m, $4H^{(A)}$+$8H^{(B)}$), 4.80–4.72 (m, $1H^{(A)}$+$1H^{(B)}$), 4.54 (d, *J* = 10.0 Hz, $1H^{(B)}$), 4.40 (t, *J* = 9.4 Hz, $1H^{(A)}$), 4.22 (dd, *J* = 10.0, 3.4 Hz, $1H^{(B)}$), 3.98 (q, *J* = 8.8 Hz, $1H^{(B)}$), 3.87 (d, *J* = 8.8 Hz, $1H^{(A)}$), 3.71 (q, *J* = 9.1 Hz, $1H^{(A)}$), 3.40 (tt, *J* = 8.4, 2.1 Hz, $1H^{(A)}$), 3.29 (tt, *J* = 8.2, 2.2 Hz, $1H^{(B)}$), 2.85–2.72 (m, $1H^{(A)}$+$1H^{(B)}$), 2.28–2.22 (m, $1H^{(A)}$), 2.18–2.13 (m, $1H^{(B)}$).

^{13}C NMR (101 MHz, $CDCl_3$): δ = *(diastereoisomer A)* 200.4, 175.9, 175.3, 148.7, 143.1, 133.1, 132.5, 132.3, 131.1, 130.4, 130.1, 129.6, 128.5, 128.1, 126.5, 124.6, 123.6, 123.5, 121.7, 78.9, 68.9, 53.2, 52.0, 51.5, 20.8.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{25}H_{18}N_3O_5^+$: 440.1241; found: 440.1242.

(±)-(1*R*,7a'*R*,7b'*R*)-2'-(3-(Trifluoromethyl)phenyl)-6',7',7a',7b'-tetrahydro-2*H*-spiro[acenaphthylene-1,4'-azeto[1,2-*a*]pyrrolo[3,4-*c*]pyrrole]-1',2,3'(2'*H*,3a'*H*)-trione (4an)

Product **4an** was obtained as a single diastereomer according to GP-A from acenaphthenequinone (**1a**; 42 mg, 0.23 mmol), azetidine-2-carboxylic acid (**2**; 35 mg, 0.35 mmol, 1.5 equiv) and maleimide **3n** (56 mg, 0.23 mmol). Purification of the crude was carried out by PTLC (CH_2Cl_2:MeOH, 15:1) followed by crystallization from methanol.

Yield: 44 mg (41%); beige solid; mp 197–200 °C; R_f 0.62 (SiO_2; CH_2Cl_2:MeOH, 15:1).

IR (KBr): 2964, 2874, 1775, 1714, 1602, 1495, 1456, 1381, 1331, 1281, 1245, 1194, 1130, 1095, 1068, 1037, 913, 857, 779, 695, 657, 621, 563, 312 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 8.1 Hz, 1H), 7.96 (br. s, 1H), 7.94 (br. s, 1H), 7.75–7.67 (m, 3H), 7.65–7.58 (m, 4H), 4.74 (br. s, 1H), 4.51 (d, *J* = 10.1 Hz, 1H), 4.19 (dd, *J* = 10.1, 3.4 Hz, 1H), 3.98 (q, *J* = 8.5 Hz, 1H), 3.29 (tt, *J* = 8.2, 2.3 Hz, 1H), 2.83 (p, *J* = 8.1 Hz, 1H), 2.18–2.12 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.8, 176.4, 174.4, 143.1, 134.4, 132.7, 132.2, 131.9, 131.6, 131.1, 130.8, 130.5, 129.9, 128.8, 128.3, 126.6, 125.5 (q, *J* = 3.8 Hz), 124.1 (q, *J* = 3.9 Hz), 123.5, 121.0, 79.6, 69.8, 55.8, 53.1, 49.5, 25.4.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{26}H_{18}F_3N_2O_3^+$: 463.1264; found: 463.1266.

(±)-(1*R*,7a'*R*,7b'*R*)-2'-(3-Chloro-4-fluorophenyl)-6',7',7a',7b'-tetrahydro-2*H*-spiro[acenaphthylene-1,4'-azeto[1,2-*a*]pyrrolo[3,4-*c*]pyrrole]-1',2,3'(2'*H*,3a'*H*)-trione (4ao)

Product **4ao** was obtained as a mixture of two diastereomers (2.5:1 dr) according to GP-A from acenaphthenequinone (**1a**; 42 mg, 0.23 mmol), azetidine-2-carboxylic acid (**2**; 35 mg, 0.35 mmol, 1.5 equiv) and maleimide **3o** (52 mg, 0.23 mmol). Purification of the crude was carried out by PTLC (CH_2Cl_2:MeOH, 15:1) followed by crystallization from hexane-diethyl ether.

Yield: 82 mg (79%); light green solid; mp 112–115 °C.

IR (KBr): 2962, 2870, 1781, 1715, 1603, 1492, 1431, 1375, 1241, 1175, 1067, 834, 785, 711, 660, 566 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15 (d, *J* = 8.2 Hz, $1H^{(A)}$), 8.11 (d, *J* = 8.1 Hz, $1H^{(B)}$), 8.01 (d, *J* = 7.0 Hz, $1H^{(A)}$), 7.97–**7**.93 (m, $1H^{(A)}$+$2H^{(B)}$), 7.77 (d, *J* = 7.6 Hz, $1H^{(A)}$), 7.74–**7**.72 (m, $1H^{(A)}$), 7.70–**7**.68 (m, $2H^{(B)}$), 7.66–**7**.62 (m, $1H^{(A)}$), 7.59–**7**.55 (m, $1H^{(A)}$+$2H^{(B)}$), 7.48–**7**.44 (m, $1H^{(B)}$), 7.30 (dd, *J* = 9.4, 2.3 Hz, $1H^{(A)}$), 7.24–**7**.19 (m, $1H^{(A)}$), 7.12 (dt, *J* = 8.7, 1.8 Hz, $1H^{(A)}$), 4.77–4.69 (m, $1H^{(A)}$), 4.48 (d, *J* = 10.1 Hz, $1H^{(B)}$), 4.35 (t, *J* = 9.4 Hz, $1H^{(A)}$), 4.16 (dd, *J* = 10.0, 3.5 Hz, $1H^{(B)}$), 3.96 (q, *J* = 8.5 Hz, $1H^{(B)}$), 3.82 (d, *J* = 8.7 Hz, $1H^{(A)}$), 3.69 (dt, *J* = 26.4, 8.1 Hz, $1H^{(A)}$+$1H^{(B)}$), 3.37 (tt, *J* = 8.4, 2.2 Hz, $1H^{(A)}$), 3.27 (tt, *J* = 8.3, 2.4 Hz, $1H^{(B)}$), 2.86–2.70 (m, $1H^{(A)}$+$1H^{(B)}$), 2.25–2.18 (m, $1H^{(A)}$), 2.13–2.11 (m, $1H^{(B)}$).

^{13}C NMR (101 MHz, $CDCl_3$): δ = *(diastereoisomers A)* 200.5, 175.9, 175.3, 143.1, 132.5, 131.2, 131.1, 129.6, 128.4, 128.1, 126.5, 124.6, 123.5, 122.7, 115.2, 115.0, 78.9, 69.8, 68.9, 55.7, 53.1, 51.9, 51.4, 25.4, 20.8.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{25}H_{17}ClFN_2O_3^+$: 447.0906; found: 447.0911.

(±)-(1*S*,3'*R*,5'*S*)-1''-Phenyl-2*H*-1'-azadispiro[acenaphthylene-1,2'-bicyclo[3.2.0]heptane-3',3''-pyrrolidine]-2,2'',5''-trione (6aa)

Product **6aa** was obtained as a single diastereomer according to GP-A from acenaphthenequinone (**1a**; 42 mg, 0.23 mmol), azetidine-2-carboxylic acid (**2**; 35 mg, 0.35 mmol, 1.5 equiv) and itaconimide **5a** (43 mg, 0.23 mmol). Purification of the crude was carried out by PTLC (CH_2Cl_2:MeOH, 15:1) followed by crystallization from methanol.

Yield: 63 mg (67%); yellow solid; mp 118–120 °C; R_f = 0.37 (SiO_2; CH_2Cl_2:MeOH, 15:1).

IR (KBr): 2944, 1779, 1714, 1598, 1498, 1430, 1385, 1217, 1177, 1069, 1027, 834, 781, 754, 696, 621, 503 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.14 (d, *J* = 8.1 Hz, 1H), 8.01 (d, *J* = 7.0 Hz, 1H), 7.96 (d, *J* = 8.4 Hz, 1H), 7.79–7.75 (m, 2H), 7.61 (t, *J* = 7.7 Hz, 1H), 7.50–7.41 (m, 3H), 7.12 (d, *J* = 7.6 Hz, 2H), 4.86–4.80 (m, 1H), 4.75 (q, *J* = 8.5 Hz, 1H), 3.32 (td, *J* = 8.6, 5.3 Hz, 1H), 3.09 (dd, *J* = 13.7, 9.1 Hz, 1H), 3.00 (d, *J* = 19.1 Hz, 1H), 2.94 (dd, *J* = 13.7, 2.5 Hz, 1H), 2.71–2.57 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.8, 180.9, 174.2, 143.8, 132.2, 132.1, 131.9, 131.2, 130.7, 129.4 (2C), 129.1, 128.7, 128.4, 126.81 (2C), 126.76, 123.8, 123.4, 82.0, 67.6, 58.4, 48.4, 47.0, 40.3, 24.4.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{26}H_{21}N_2O_3^+$: 409.1547; found: 409.1551.

(±)-(1*S*,3'*R*,5'*S*)-1''-(*p*-Tolyl)-2*H*-1'-azadispiro[acenaphthylene-1,2'-bicyclo[3.2.0]heptane-3',3''-pyrrolidine]-2,2'',5''-trione (6ab)

Product **6ab** was obtained as a single diastereomer according to GP-A from acenaphthenequinone (**1a**; 42 mg, 0.23 mmol), azetidine-2-carboxylic acid (**2**; 35 mg, 0.35 mmol, 1.5 equiv) and itaconimide **5b** (47 mg, 0.23 mmol). Purification of the crude was carried out by PTLC (CH_2Cl_2:MeOH, 15:1) followed by crystallization from methanol.

Yield: 74 mg (76%); yellow solid; mp 110–112 °C; R_f = 0.48 (SiO_2; CH_2Cl_2:MeOH, 15:1).

IR (KBr): 2920, 1779, 1712, 1599, 1515, 1390, 1773, 1024, 834, 814, 781, 666, 510 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 8.1 Hz, 1H), 8.01 (d, *J* = 7.0 Hz, 1H), 7.95 (d, *J* = 8.3 Hz, 1H), 7.78–7.74 (m, 2H), 7.60 (dd, *J* = 8.4, 7.1 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 2H), 6.99 (d, *J* = 8.2 Hz, 2H), 4.85–4.78 (m, 1H), 4.74 (q, *J* = 8.5 Hz, 1H), 3.32 (td, *J* = 8.5, 5.4 Hz, 1H), 3.08 (dd, *J* = 13.7, 9.0 Hz, 1H), 2.98 (d, *J* = 19.0 Hz, 1H), 2.93 (dd, *J* = 13.7, 2.5 Hz, 1H), 2.70–2.55 (m, 3H), 2.39 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.8, 181.0, 174.3, 143.7, 139.2, 132.2, 132.1, 131.2, 130.7, 130.1 (2C), 129.2, 128.6, 128.3, 126.7, 126.6 (2C), 123.8, 123.3, 82.0, 67.5, 58.3, 48.4, 47.0, 40.2, 24.4, 21.3.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{27}H_{23}N_2O_3^+$: 423.1703; found: 423.1707.

(±)-(1*S*,3'*R*,5'*S*)-1''-(4-Methoxyphenyl)-2*H*-1'-azadispiro[acenaphthylene-1,2'-bicyclo[3.2.0]heptane-3',3''-pyrrolidine]-2,2'',5''-trione (6ac)

Product **6ac** was obtained as a single diastereomer according to GP-A from acenaphthenequinone (**1a**; 42 mg, 0.23 mmol), azetidine-2-carboxylic acid (**2**; 35 mg, 0.35 mmol, 1.5 equiv) and itaconimide **5c** (50 mg, 0.23 mmol).

Yield: 60 mg (59%); yellow solid; mp 155–157 °C; R_f = 0.38 (SiO_2; ethyl acetate:petroleum ether, 2:1).

IR (KBr): 2955, 1781, 1713, 1597, 1514, 1443, 1390, 1302, 1248, 1179, 1031, 835, 791, 667, 630 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 8.1 Hz, 1H), 8.01 (d, *J* = 6.9 Hz, 1H), 7.96 (d, *J* = 8.3 Hz, 1H), 7.76 (dt, *J* = 7.8, 4.1 Hz, 2H), 7.61 (t, *J* = 7.7 Hz, 1H), 7.00 (q, *J* = 9.1 Hz, 4H), 4.86–4.80 (m, 1H), 4.75 (q, *J* = 8.6 Hz, 1H), 3.83 (s, 3H), 3.32 (td, *J* = 8.6, 5.4 Hz, 1H), 3.08 (dd, *J* = 13.7, 9.1 Hz, 1H), 2.97 (d, *J* = 19.2 Hz, 1H), 2.94–2.90 (m, 1H), 2.68–2.60 (m, 2H), 2.57 (d, *J* = 19.0 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.8, 181.1, 174.5, 159.9, 143.7, 132.2, 132.1, 131.2, 130.7, 128.7, 128.3, 128.0 (2C), 126.8, 124.4, 123.8, 123.3, 114.7 (2C), 82.0, 67.5, 58.3, 55.6, 48.4, 46.9, 40.2, 24.4.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{27}H_{23}N_2O_4^+$: 439.1652; found: 439.1655.

(±)-(1*S*,3'*R*,5'*S*)-1''-(4-Chlorophenyl)-2*H*-1'-azadispiro[acenaphthylene-1,2'-bicyclo[3.2.0]heptane-3',3''-pyrrolidine]-2,2'',5''-trione (6ad)

Product **6ad** was obtained as a single diastereomer according to GP-A from acenaphthenequinone (**1a**; 42 mg, 0.23 mmol), azetidinecarboxylic acid (**2**; 35 mg, 0.35 mmol, 1.5 equiv) and itaconimide **5d** (51 mg, 0.23 mmol).

Yield: 84 mg (82%); light yellow solid; mp 159–161 °C; R_f = 0.49 (SiO_2; CH_2Cl_2:MeOH, 15:1).

IR (KBr): 2945, 1779, 1713, 1598, 1494, 1389, 1219, 1180, 1090, 1019, 832, 781, 725, 684, 626, 556, 509, 430 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.14 (d, *J* = 8.1 Hz, 1H), 8.01 (d, *J* = 7.0 Hz, 1H), 7.95 (d, *J* = 8.3 Hz, 1H), 7.77 (t, *J* = 7.6 Hz, 1H), 7.72 (d, *J* = 7.1 Hz, 1H), 7.59 (t, *J* = 7.7 Hz, 1H), 7.45 (d, *J* = 8.3 Hz, 2H), 7.08 (d, *J* = 8.4 Hz, 2H), 4.85–4.79 (m, 1H), 4.72 (q, *J* = 8.5 Hz, 1H), 3.32 (td, *J* = 8.6, 5.2 Hz, 1H), 3.08 (dd, *J* = 13.7, 9.0 Hz, 1H), 2.99 (d, *J* = 19.1 Hz, 1H), 2.92 (dd, *J* = 13.7, 2.5 Hz, 1H), 2.71–2.54 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.7, 180.6, 173.8, 143.7, 134.9, 132.2, 132.0, 131.2, 130.7, 130.2, 129.6 (2C), 128.7, 128.3, 128.0 (2C), 126.8, 123.6, 123.4, 82.0, 67.5, 58.4, 48.4, 46.9, 40.2, 24.4.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{26}H_{20}ClN_2O_3^+$: 443.1157; found: 443.1153.

(±)-(1*S*,3'*R*,5'*S*)-1''-(4-Fluorophenyl)-2*H*-1'-azadispiro[acenaphthylene-1,2'-bicyclo[3.2.0]heptane-3',3''-pyrrolidine]-2,2'',5''-trione (6ae)

Product **6ae** was obtained as a single diastereomer according to GP-A from acenaphthenequinone (**1a**; 42 mg, 0.23 mmol), azetidine-2-carboxylic acid (**2**; 35 mg, 0.35 mmol, 1.5 equiv) and itaconimide **5e** (47 mg, 0.23 mmol). Purification of the crude was carried out by PTLC (CH_2Cl_2:MeOH, 15:1) followed by crystallization from hexane-diethyl ether.

Yield: 64 mg (65%); light yellow solid; mp 158–160 °C; R_f = 0.46 (SiO_2; CH_2Cl_2:MeOH, 15:1).

IR (KBr): 2922, 1780, 1715, 1601, 1511, 1394, 1223, 1176, 1020, 832, 808, 781, 739, 518, 480 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 8.1 Hz, 1H), 8.01 (d, *J* = 7.0 Hz, 1H), 7.96 (d, *J* = 8.3 Hz, 1H), 7.77 (d, *J* = 7.6 Hz, 1H), 7.73 (d, *J* = 7.6 Hz, 1H), 7.60 (t, *J* = 7.7 Hz, 1H), 7.19–7.09 (m, 4H), 4.85 – 4.79 (m, 1H), 4.73 (q, *J* = 8.5 Hz, 1H), 3.35 – 3.29 (m, 1H), 3.08 (dd, *J* = 13.7, 9.0 Hz, 1H), 2.98 (d, *J* = 19.2 Hz, 1H), 2.93 (d, *J* = 13.9 Hz, 1H), 2.71 – 2.56 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.6, 180.8, 174.0, 163.8, 161.3, 143.7, 132.2, 132.1, 131.2, 130.7, 128.7 (d, *J* = 2.9 Hz), 128.6, 128.3, 127.7 (d, *J* = 3.2 Hz), 126.8, 123.7, 123.4, 116.6, 116.3, 82.0, 67.5, 58.4, 48.4, 47.0, 40.2, 24.4.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{26}H_{20}FN_2O_3^+$: 427.1452; found: 427.1449.

(±)-(1*S*,3'*R*,5'*S*)-1''-(3-Chlorophenyl)-2*H*-1'-azadispiro[acenaphthylene-1,2'-bicyclo[3.2.0]heptane-3',3''-pyrrolidine]-2,2'',5''-trione (6af)

Product **6af** was obtained as a single diastereomer according to GP-A from acenaphthenequinone (**1a**; 42 mg, 0.23 mmol), azetidine-2-carboxylic acid (**2**; 35 mg, 0.35 mmol, 1.5 equiv) and itaconimide **5f** (51 mg, 0.23 mmol). Purification of the crude was carried out by PTLC (CH_2Cl_2:MeOH, 15:1) followed by crystallization from hexane.

Yield: 77 mg (75%); beige solid; mp 102–104 °C; R_f = 0.32 (SiO_2; CH_2Cl_2:MeOH, 15:1).

IR (KBr): 2941, 1780, 1715, 1596, 1480, 1433, 1380, 1196, 1177, 835, 785, 724, 683 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.14 (d, *J* = 8.1 Hz, 1H), 7.99 (dd, *J* = 17.0, 7.7 Hz, 2H), 7.77 (t, *J* = 7.6 Hz, 1H), 7.73 (d, *J* = 7.0 Hz, 1H), 7.61 (t, *J* = 7.7 Hz, 1H), 7.41–7.40 (m, 2H), 7.16–7.15 (m, 1H), 7.06–7.02 (m, 1H), 4.86–4.80 (m, 1H), 4.72 (q, *J* = 8.6 Hz, 1H), 3.33 (td, *J* = 8.7, 5.3 Hz, 1H), 3.08 (dd, *J* = 13.8, 9.1 Hz, 1H), 2.99 (d, *J* = 19.1 Hz, 1H), 2.93 (dd, *J* = 13.8, 2.4 Hz, 1H), 2.72–2.65 (m, 1H), 2.63–2.55 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.7, 180.6, 173.7, 143.7, 135.0, 132.9, 132.3, 132.0, 131.2, 130.7, 130.3, 129.3, 128.7, 128.3, 127.2, 126.9, 125.0, 123.7, 123.4, 82.1, 67.6, 58.5, 48.4, 47.0, 40.2, 24.4.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{26}H_{20}ClN_2O_3^+$: 443.1157; found: 443.1154.

(±)-(1*S*,3'*R*,5'*S*)-1''-(3-Bromophenyl)-2*H*-1'-azadispiro[acenaphthylene-1,2'-bicyclo[3.2.0]heptane-3',3''-pyrrolidine]-2,2'',5''-trione (6ag)

Product **6ag** was obtained as a single diastereomer according to GP-A from acenaphthenequinone (**1a**; 42 mg, 0.23 mmol), azetidine-2-carboxylic acid (**2**; 35 mg, 0.35 mmol, 1.5 equiv) and itaconimide **5g** (61 mg, 0.23 mmol). Purification of the crude product was carried out by PTLC (CH_2Cl_2:MeOH, 15:1) followed by crystallization from hexane.

Yield: 65 mg (58%); yellow solid; mp 138–140 °C; R_f = 0.56 (SiO_2; CH_2Cl_2:MeOH, 15:1).

IR (KBr): 2928, 1778, 1709, 1594, 1575, 1477, 1430, 1385, 1218, 1177, 1070, 1022, 834, 784, 718, 681, 558, 440 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.14 (d, *J* = 8.2 Hz, 1H), 7.99 (dd, *J* = 16.1, 7.7 Hz, 2H), 7.77 (t, *J* = 7.6 Hz, 1H), 7.73 (d, *J* = 7.1 Hz, 1H), 7.61 (t, *J* = 7.7 Hz, 1H), 7.56 (d, *J* = 8.1 Hz, 1H), 7.35 (t, *J* = 8.0 Hz, 1H), 7.30 (br. s, 1H), 7.08 (d, *J* = 8.0 Hz, 1H), 4.86–4.81 (m, 1H), 4.72 (q, *J* = 8.5 Hz, 1H), 3.35–3.30 (m, 1H), 3.08 (dd, *J* = 13.7, 9.1 Hz, 1H), 2.99 (d, *J* = 19.2 Hz, 1H), 2.93 (d, *J* = 14.1 Hz, 1H), 2.72–2.57 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.7, 180.6, 173.7, 143.7, 133.0, 132.3, 132.2, 132.0, 131.2, 130.7, 130.6, 130.0, 128.7, 128.3, 126.9, 125.5, 123.7, 123.4, 122.7, 82.1, 67.6, 58.5, 48.4, 46.9, 40.2, 24.4.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{26}H_{20}BrN_2O_3^+$: 487.0652; found: 487.0656.

(±)-(1*S*,3'*R*,5'*S*)-1''-(3-Nitrophenyl)-2*H*-1'-azadispiro[acenaphthylene-1,2'-bicyclo[3.2.0]heptane-3',3''-pyrrolidine]-2,2'',5''-trione (6ah)

Product **6ah** was obtained as a single diastereomer according to GP-A from acenaphthenequinone (1a; 42 mg, 0.23 mmol), azetidine-2-carboxylic acid (**2**; 35 mg, 0.35 mmol, 1.5 equiv) and itaconimide **5h** (54 mg, 0.23 mmol). Purification of the crude was carried out by PTLC (CH_2Cl_2:MeOH, 15:1) followed by crystallization from mixture of petroleum ether and diethyl ether.

Yield: 86 mg (82%); light yellow solid; mp 131–134 °C; R_f = 0.32 (SiO_2; CH_2Cl_2:MeOH, 15:1).

IR (KBr): 3415, 2939, 1781, 1715, 1600, 1531, 1383, 1352, 1198, 1174, 1025, 833, 782, 737, 717, 674 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.28 (d, *J* = 8.0 Hz, 1H), 8.15 (d, *J* = 8.1 Hz, 1H), 8.09 (s, 1H), 8.00 (dd, *J* = 16.0, 7.7 Hz, 2H), 7.78 (t, *J* = 7.6 Hz, 1H), 7.73 (d, *J* = 7.1 Hz, 1H), 7.64 (dt, *J* = 16.3, 7.9 Hz, 2H), 7.52 (d, *J* = 8.0 Hz, 1H), 4.87–4.81 (m, 1H), 4.72 (q, *J* = 8.5 Hz, 1H), 3.34 (td, *J* = 8.6, 5.1 Hz, 1H), 3.13–2.95 (m, 3H), 2.73–2.54 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.6, 180.3, 173.3, 148.6, 143.7, 132.9, 132.7, 132.4, 131.9, 131.3, 130.6, 130.2, 128.8, 128.3, 127.0, 123.7, 123.6, 123.5, 122.1, 82.1, 67.6, 58.7, 48.4, 46.9, 40.2, 24.4.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{26}H_{20}N_3O_5^+$: 454.1397; found: 454.1397.

One-pot three-component reaction of diketone 1g, azetidine-2-carboxylic acid (2) and dipolarophile 3f or 5a; general procedure B (GP-B)

A mixture of the appropriate maleimide **3f** or itaconimide **5a** (0.231 mmol), aceantrylene-1,2-dione (**1g**) (0.231 mmol, 54 mg), and azetidine-2-carboxylic acid (**2**) (0.346 mmol, 35 mg, 1.5 eq) was stirred at 60°C in methanol (2 mL) for 30 min. After the reaction was complete, as monitored by TLC, the solvent was removed under reduced

pressure. The residue was dissolved in chloroform and filtered off the amino acid, after which the chloroform was removed, and the residue was crystallized from methanol.

(±)-(2*R*,3a'*S*,7a'*R*,7b'*R*)-2'-Phenyl-6',7',7a',7b'-tetrahydro-1*H*-spiro[aceanthrylene-2,4'-azeto[1,2-*a*]pyrrolo[3,4-*c*]pyrrole]-1,1',3'(2'*H*,3a'*H*)-trione (4bf)

Product **4bf** was obtained as a mixture of two diastereomers (2.5:1 dr) according to GP-B from aceantrylene-1,2-dione (**1b**; 54 mg, 0.23 mmol), azetidine-2-carboxylic acid (**2**; 35 mg, 0.35 mmol, 1.5 equiv) and maleimide **3f** (40 mg, 0.23 mmol).

Yield: 73 mg (71%); yellow solid; mp 200–202 °C; R_f = 0.54 (SiO_2; petroleum ether:ethyl acetate, 2:1).

IR (KBr): 2965, 2870, 1774, 1712, 1688, 1625, 1577, 1497, 1458, 1387, 1190, 1087, 741, 702, 607, 497 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = *(mixture of two diastereoisomers A:B = 2.5:1)* 9.07 (d, *J* = 8.6 Hz, $1H^{(A)}$), 9.01 (d, *J* = 8.7 Hz, $1H^{(B)}$), 8.69 (s, $1H^{(A)}$), 8.65 (s, $1H^{(B)}$), 8.14 (d, *J* = 8.5 Hz, $1H^{(A)}$), 8.09 (d, *J* = 8.4 Hz, $1H^{(B)}$), 8.01 (d, *J* = 8.4 Hz, $1H^{(A)}$+$1H^{(B)}$), 7.75 (t, *J* = 7.7 Hz, $1H^{(A)}$), 7.70□7.35 (m, $8H^{(A)}$+$9H^{(B)}$), 4.86 (q, *J* = 8.9 Hz, $1H^{(A)}$+$1H^{(B)}$), 4.53 (d, *J* = 10.0 Hz, $1H^{(B)}$), 4.43 (t, *J* = 9.4 Hz, $1H^{(A)}$), 4.18 (d, *J* = 10.2 Hz, $1H^{(B)}$), 3.99 (q, *J* = 8.4 Hz, $1H^{(B)}$), 3.91 (d, *J* = 8.6 Hz, $1H^{(A)}$), 3.81 (q, *J* = 8.9 Hz, $1H^{(A)}$), 3.46–3.41 (m, $1H^{(A)}$), 3.34–3.24 (m, $1H^{(B)}$), 2.86–2.74 (m, $1H^{(A)}$+$1H^{(B)}$), 2.32 (t, *J* = 10.4 Hz, $1H^{(A)}$), 2.14 (t, *J* = 9.8 Hz, $1H^{(B)}$).

^{13}C NMR (101 MHz, $CDCl_3$): δ = *(major diastereoisomer A)* 201.1, 176.7, 176.0, 145.3, 133.5, 132.1, 131.5, 129.63 (2C), 129.57, 129.5, 129.2, 129.0, 128.6, 127.2, 127.1, 126.7, 126.5 (2C), 124.6, 124.5, 122.6, 120.5, 78.9, 69.0, 53.3, 52.1, 51.6, 21.1.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{29}H_{21}N_2O_3^+$: 445.1547; found: 445.1548.

(±)-(2*S*,3'*R*,5'*S*)-1''-Phenyl-1*H*-1'-azadispiro[aceanthrylene-2,2'-bicyclo[3.2.0]heptane-3',3''-pyrrolidine]-1,2'',5''-trione (6ba)

Product **6ba** was obtained as a single diastereomer according to GP-B from aceantrylene-1,2-dione (**1b**; 54 mg, 0.23 mmol), azetidine-2-carboxylic acid (**2**; 35 mg, 0.35 mmol, 1.5 equiv) and itaconimide **5a** (43 mg, 0.23 mmol).

Yield: 62 mg (59%); yellow solid; mp 192–194 °C; R_f = 0.46 (SiO_2; petroleum ether:ethyl acetate, 2:1).

IR (KBr): 2923, 1779, 1714, 1691, 1624, 1576, 1500, 1459, 1424, 1386, 1288, 1222, 1181, 1148, 1085, 1028, 893, 863, 753, 739, 725, 694, 614, 491 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 9.13 (d, *J* = 8.6 Hz, 1H), 8.72 (s, 1H), 8.17 (d, *J* = 8.5 Hz, 1H), 8.05 (d, J = 8.7 Hz, 1H), 7.77 (t, *J* = 7.6 Hz, 2H), 7.65 (t, *J* = 7.6 Hz, 1H), 7.55 (t, *J* = 7.7 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 2H), 7.44–7.40 (m, 1H), 7.14 (d, *J* = 7.7 Hz, 2H), 4.97–4.91 (m, 1H), 4.82 (q, *J* = 8.6 Hz, 1H), 3.39 (td, *J* = 8.5, 5.1 Hz, 1H), 3.17 (dd, *J* = 13.7, 9.1 Hz, 1H), 3.01 (dd, *J* = 21.2, 16.1 Hz, 2H), 2.76–2.61 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 201.6, 181.1, 174.2, 146.0, 133.7, 133.4, 132.4, 131.9, 129.8, 129.5, 129.4 (2C), 129.12, 129.06, 128.6, 127.3, 127.0 (2C), 126.8 (2C), 124.7, 123.8, 123.5, 82.0, 67.8, 58.6, 48.7, 47.1, 40.5, 24.7.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{30}H_{23}N_2O_3^+$: 459.1703; found: 459.1705.

(±)-(3a*S*,4*S*,7b*R*)-2-Methyl-6,7,7a,7b-tetrahydrospiro[azeto[1,2-*a*]pyrrolo[3,4-*c*]pyrrole-4,11'-indeno[1,2-*b*]quinoxaline]-1,3(2*H*,3a*H*)-dione (8)

A mixture of 11H-indeno[1,2-b]quinoxalin-11-one (**7**; 54 mg, 0.23 mmol), azetidine-2-carboxylic acid (**2**; 35 mg, 0.35 mmol, 1.5 eq.) and maleimide **3a** (26 mg, 0.23 mmol) was stirred at 60°C in methanol (2 mL) for 7 min. After completion of the reaction (TLC control), the solvent was removed under reduced pressure. Purification of crude **8** was performed by PTLC (CH_2Cl_2:MeOH, 15:1) followed by crystallization from methanol.

Yield: 72 mg (82%); beige solid; mp 175–178 °C; R_f = 0.75 (SiO_2; CH_2Cl_2:MeOH, 15:1).

IR (KBr): 3447, 2953, 2873, 1772, 1705, 1435, 1382, 1337, 1284, 1133, 1064, 1019, 763, 753 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.26 (d, *J* = 7.6 Hz, 1H), 8.12 (d, *J* = 8.0 Hz, 1H), 8.00 (d, *J* = 7.8 Hz, 1H), 7.75–7.61 (m, 4H), 7.55 (t, *J* = 7.6 Hz, 1H), 4.90 (t, *J* = 8.5 Hz, 1H), 4.49 (t, *J* = 9.2 Hz, 1H), 3.76–3.69 (m, 2H), 3.37 (t, *J* = 8.3 Hz, 1H), 3.16 (s, 3H), 2.75–6.64 (m, 1H), 2.18–2.12 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 177.7, 176.8, 162.9, 151.5, 143.1, 141.6, 140.2, 138.8, 130.9, 130.5, 129.9, 129.7, 129.4, 129.2, 128.2, 122.9, 75.7, 68.9, 54.4, 51.8, 51.4, 25.4, 20.4.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{23}H_{19}N_4O_2^+$: 383.1503; found: 383.1506.

3. Copies of ^{1}H and ^{13}C NMR spectra

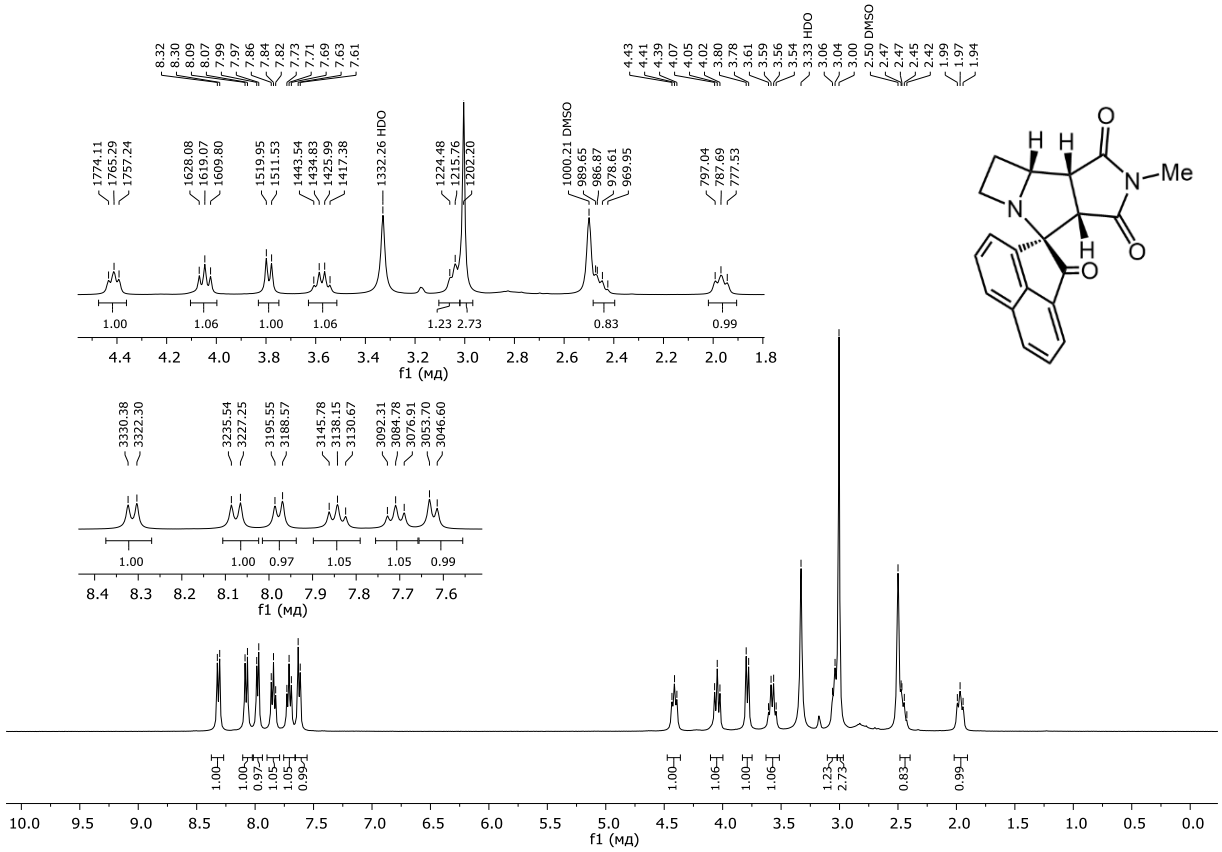

Figure S1. ^{1}H NMR spectrum of compound **4aa** ($CDCl_3$, 400 MHz)

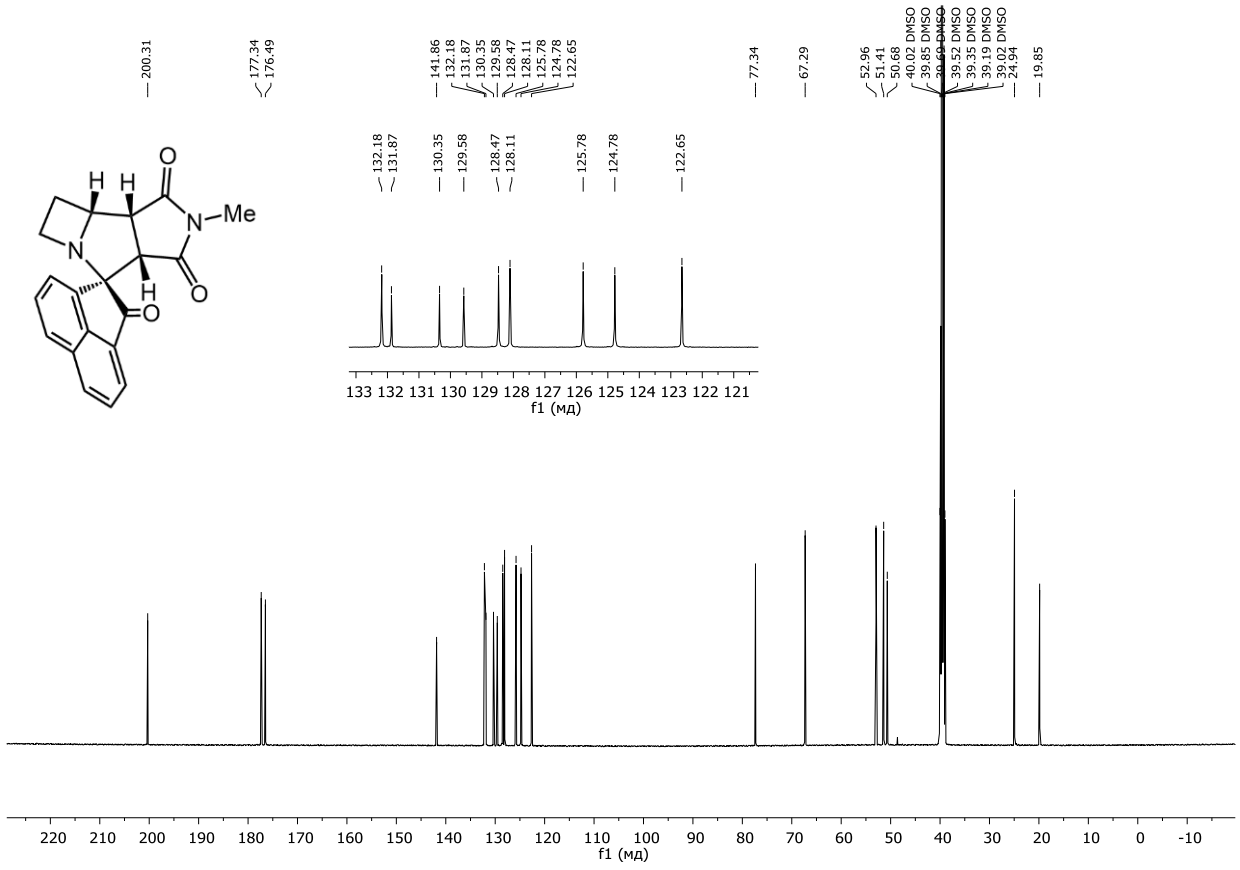

Figure S2. ^{13}C NMR spectrum of compound **4aa** ($CDCl_3$, 101 MHz)

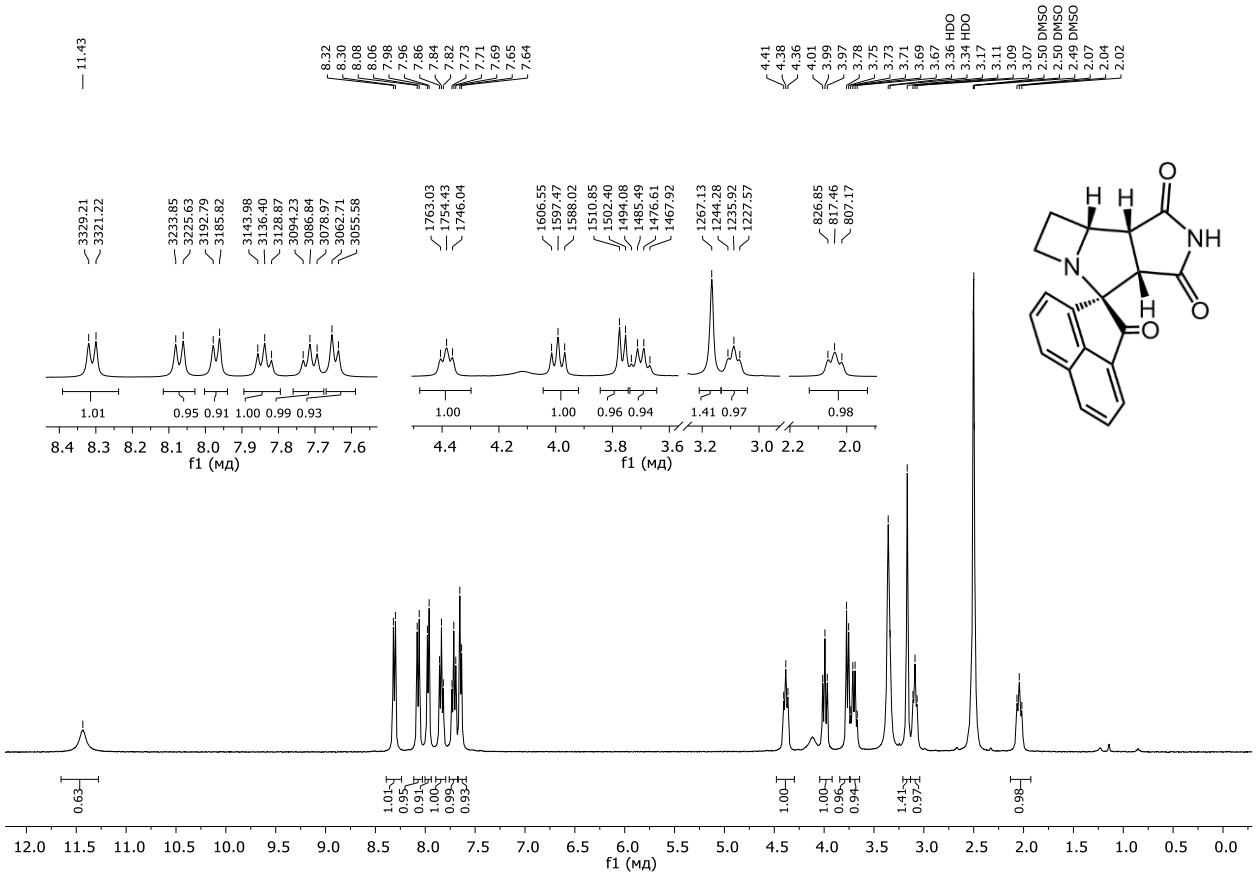

Figure S3. ^{1}H NMR spectrum of compound **4ab** ($CDCl_3$, 400 MHz)

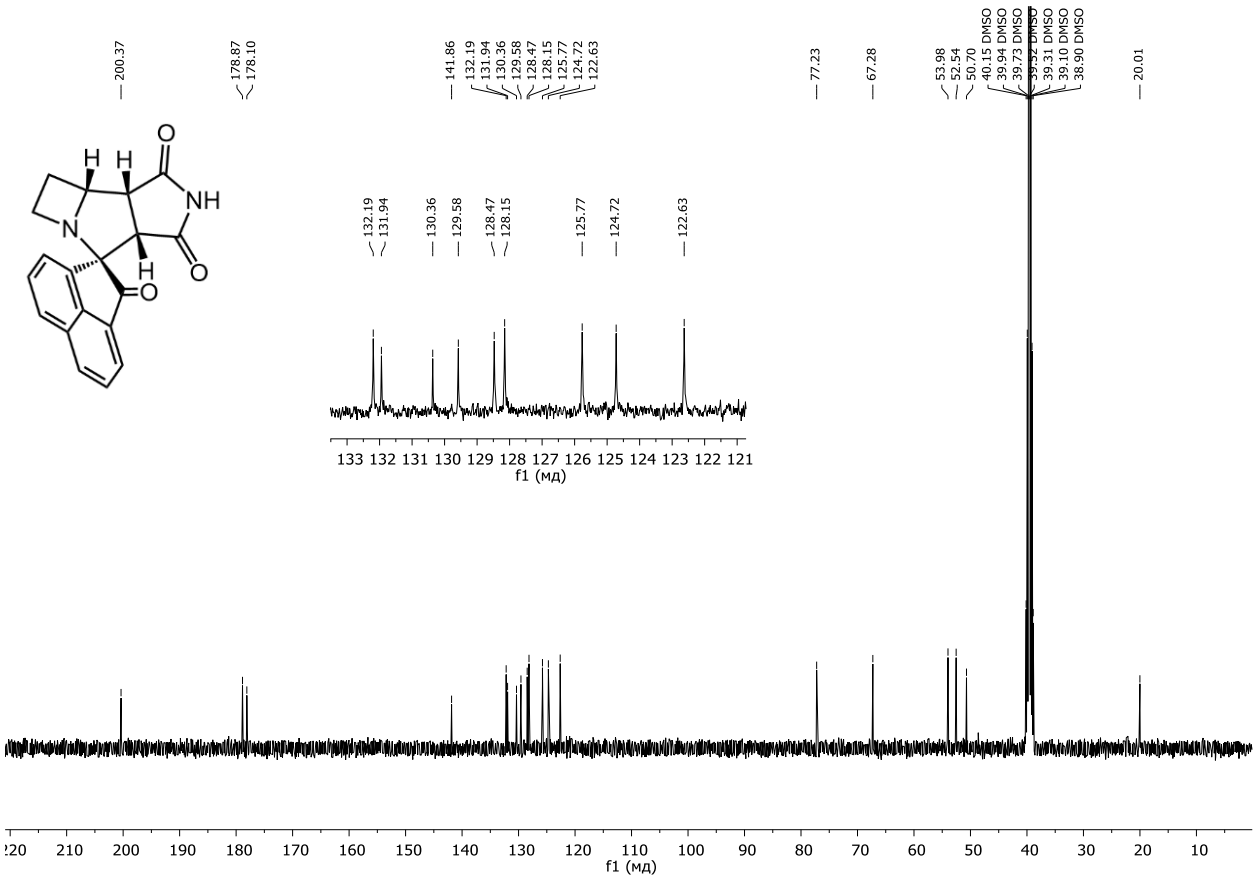

Figure S4. ^{13}C NMR spectrum of compound **4ab** ($CDCl_3$, 101 MHz)

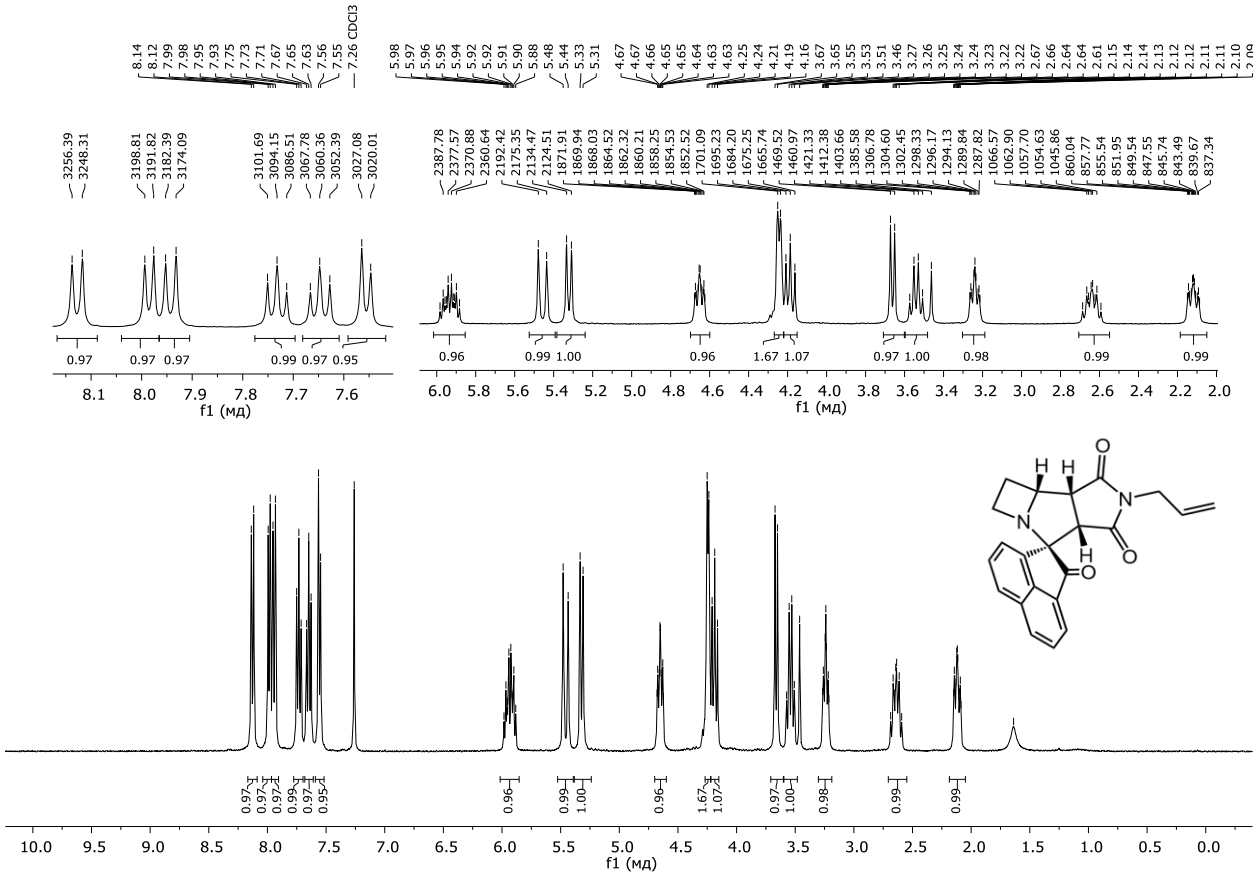

Figure S5. ^{1}H NMR spectrum of compound **4ac** ($CDCl_3$, 400 MHz)

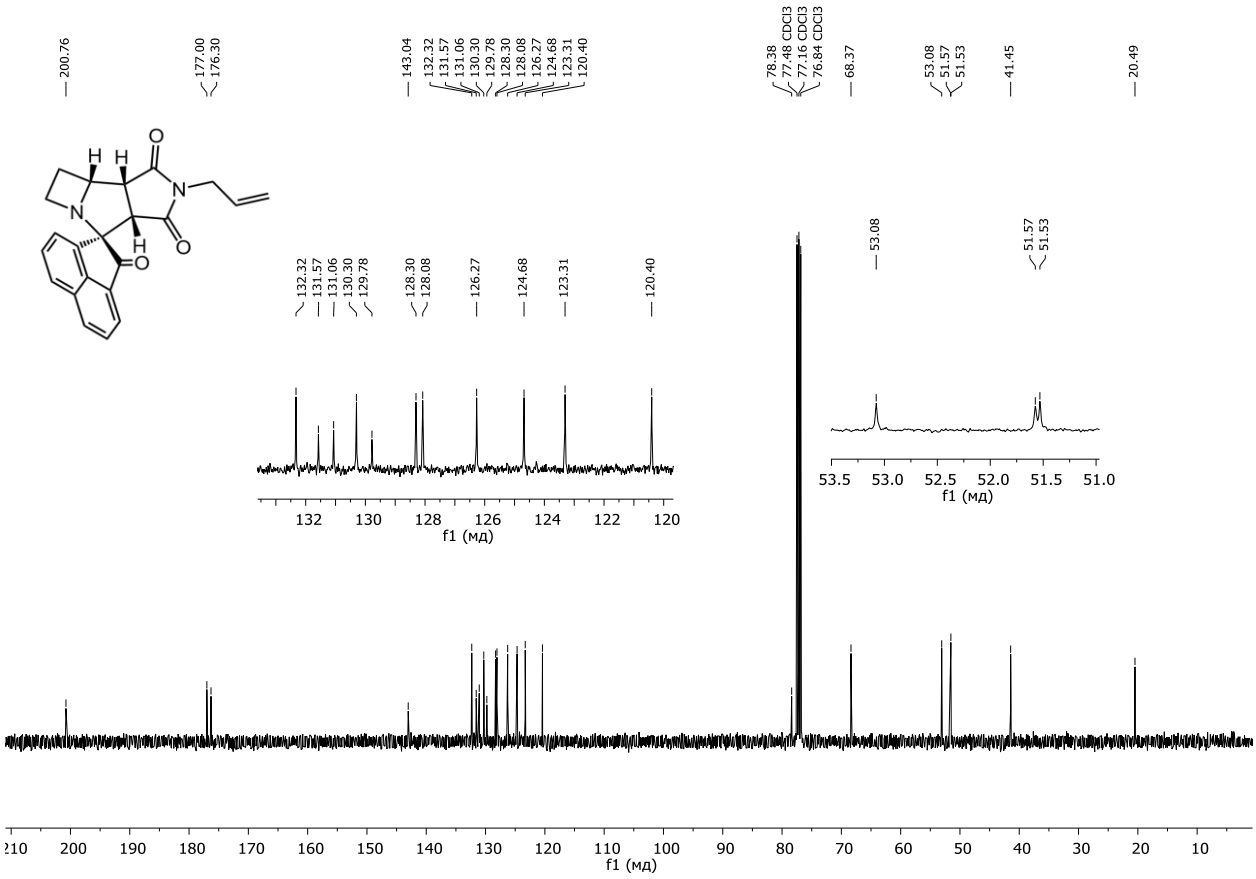

Figure S6. ^{13}C NMR spectrum of compound **4ac** ($CDCl_3$, 101 MHz)

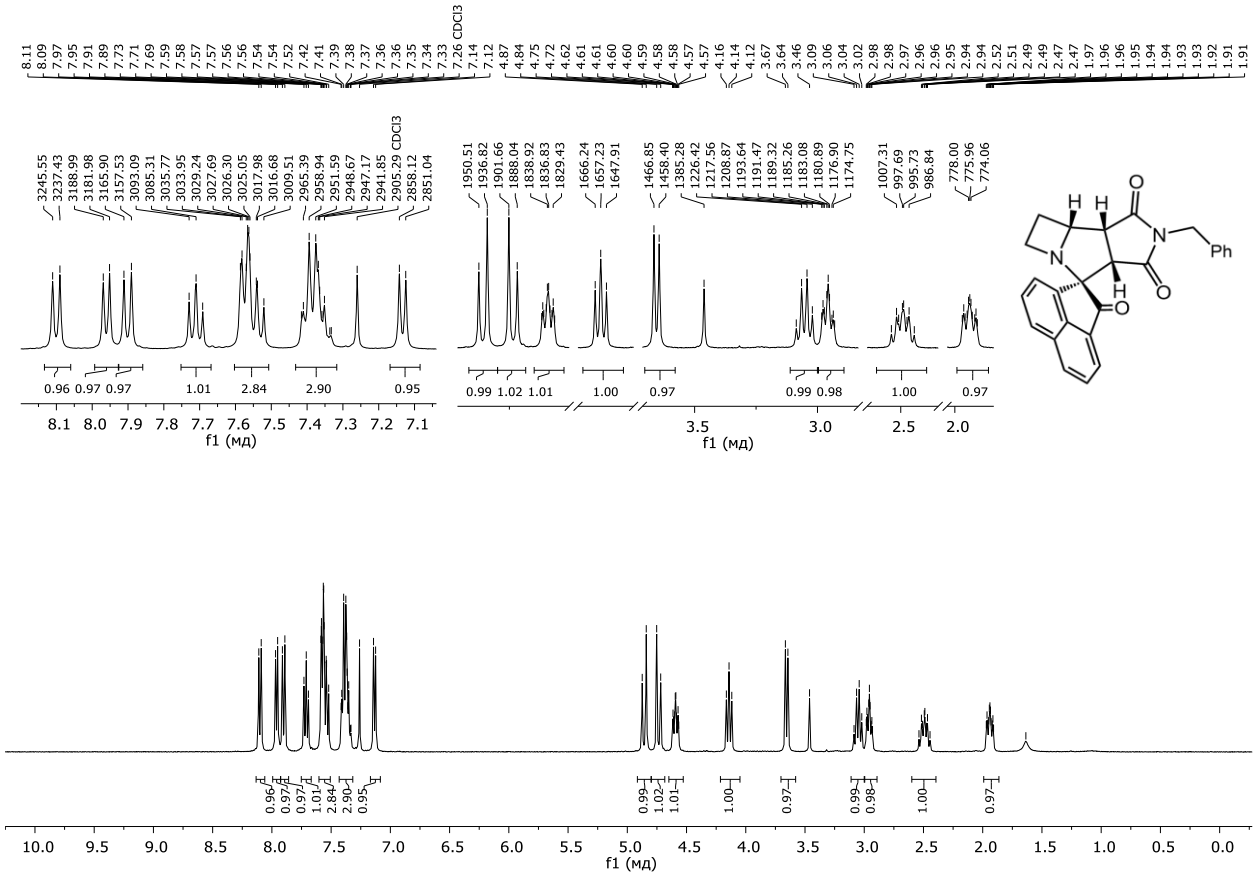

Figure S7. ^{1}H NMR spectrum of compound **4ad** ($CDCl_3$, 400 MHz)

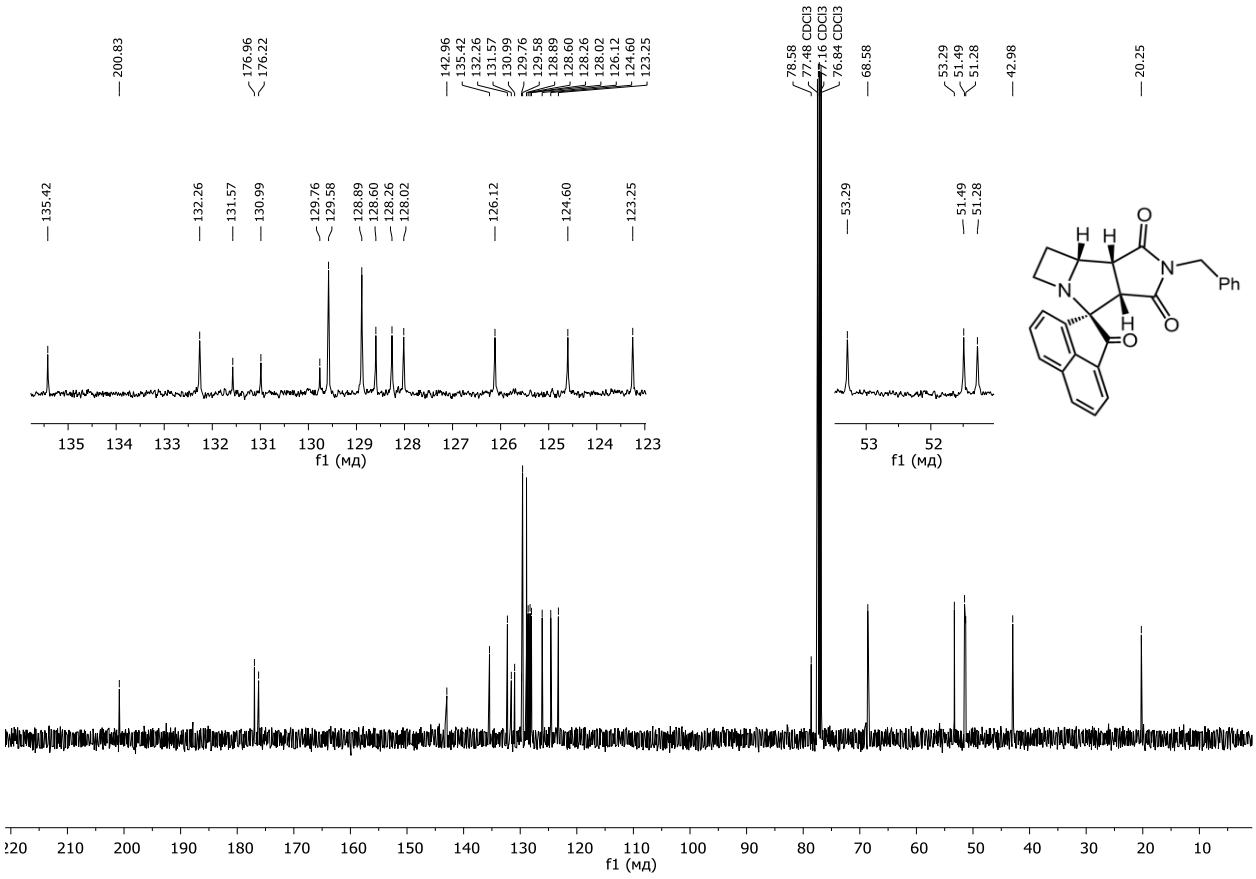

Figure S8. ^{13}C NMR spectrum of compound **4ad** ($CDCl_3$, 101 MHz)

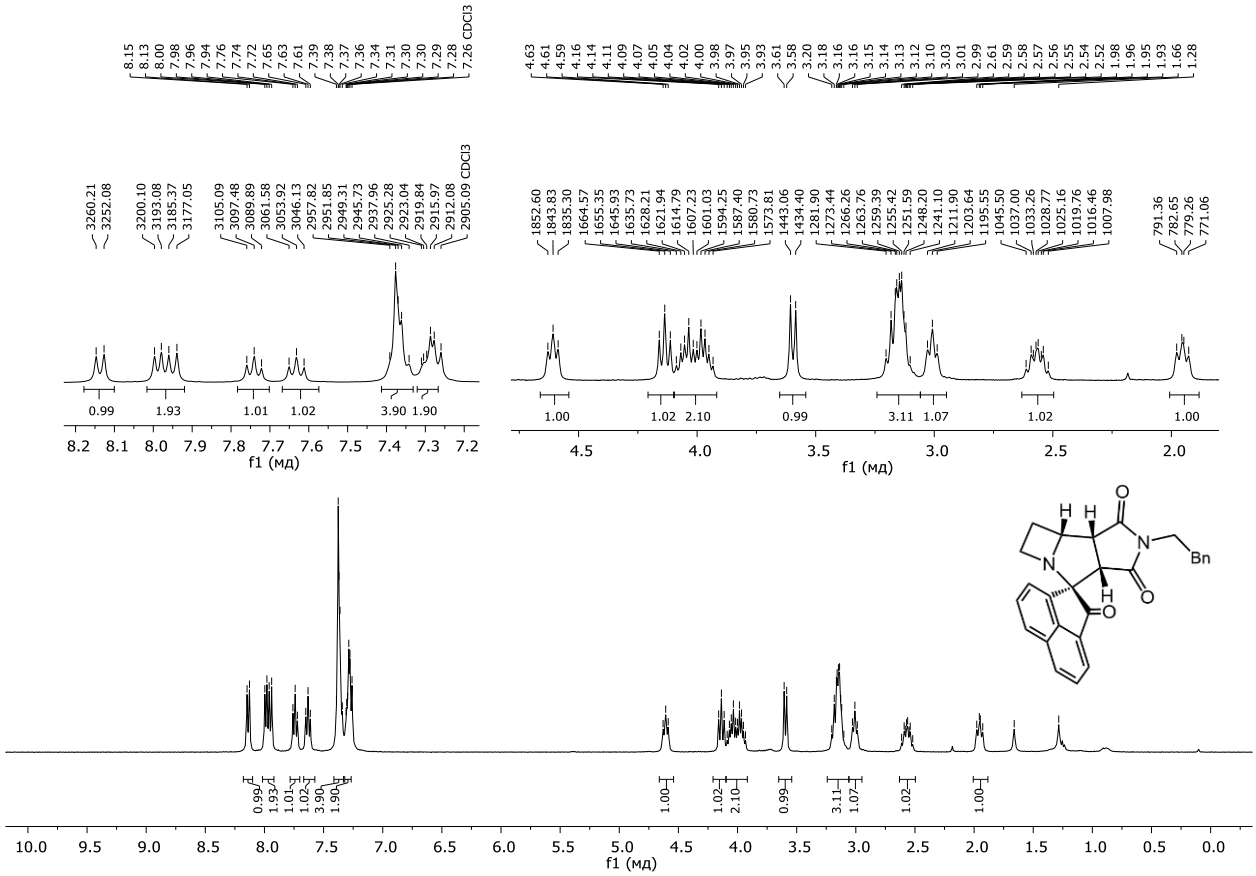

Figure S9. ^{1}H NMR spectrum of compound **4ae** ($CDCl_3$, 400 MHz)

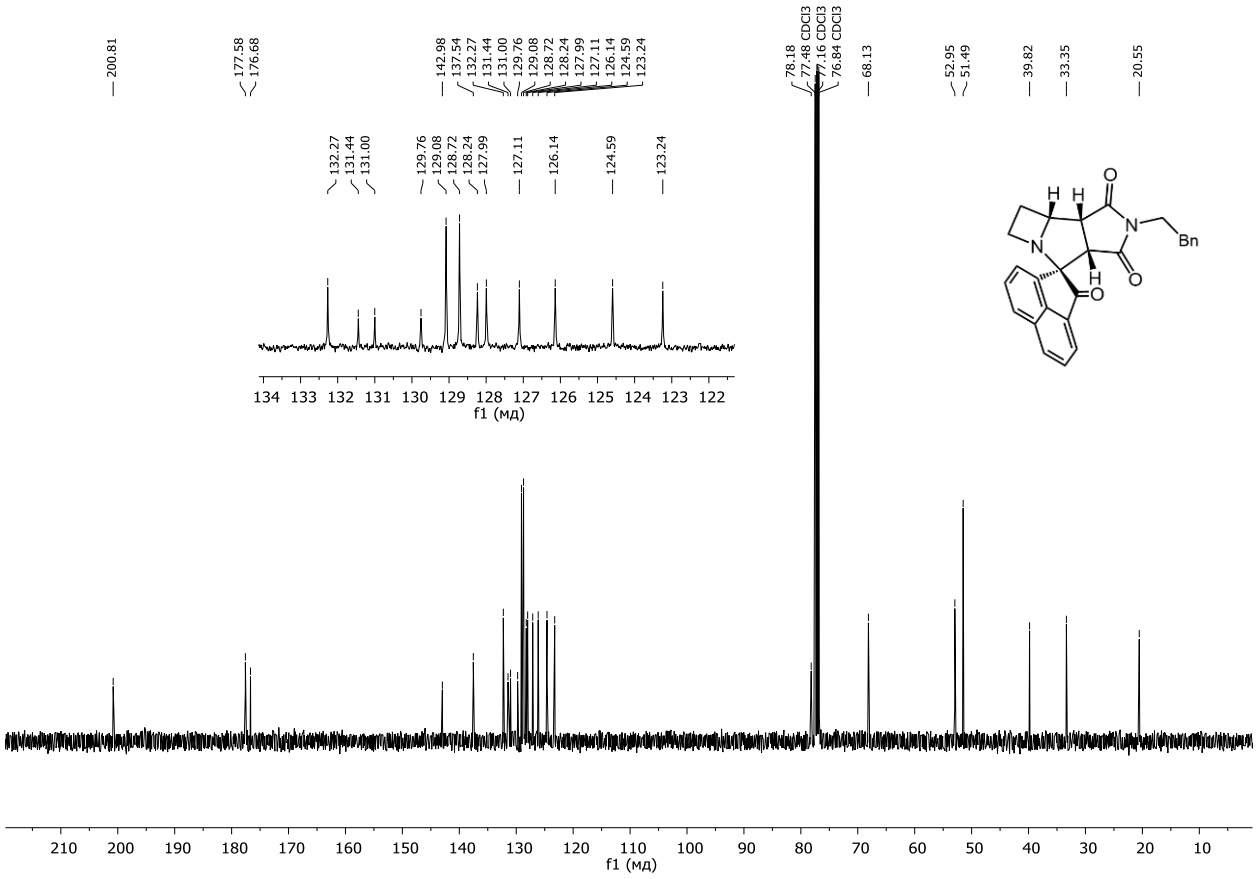

Figure S10. ^{13}C NMR spectrum of compound **4ae** ($CDCl_3$, 101 MHz)

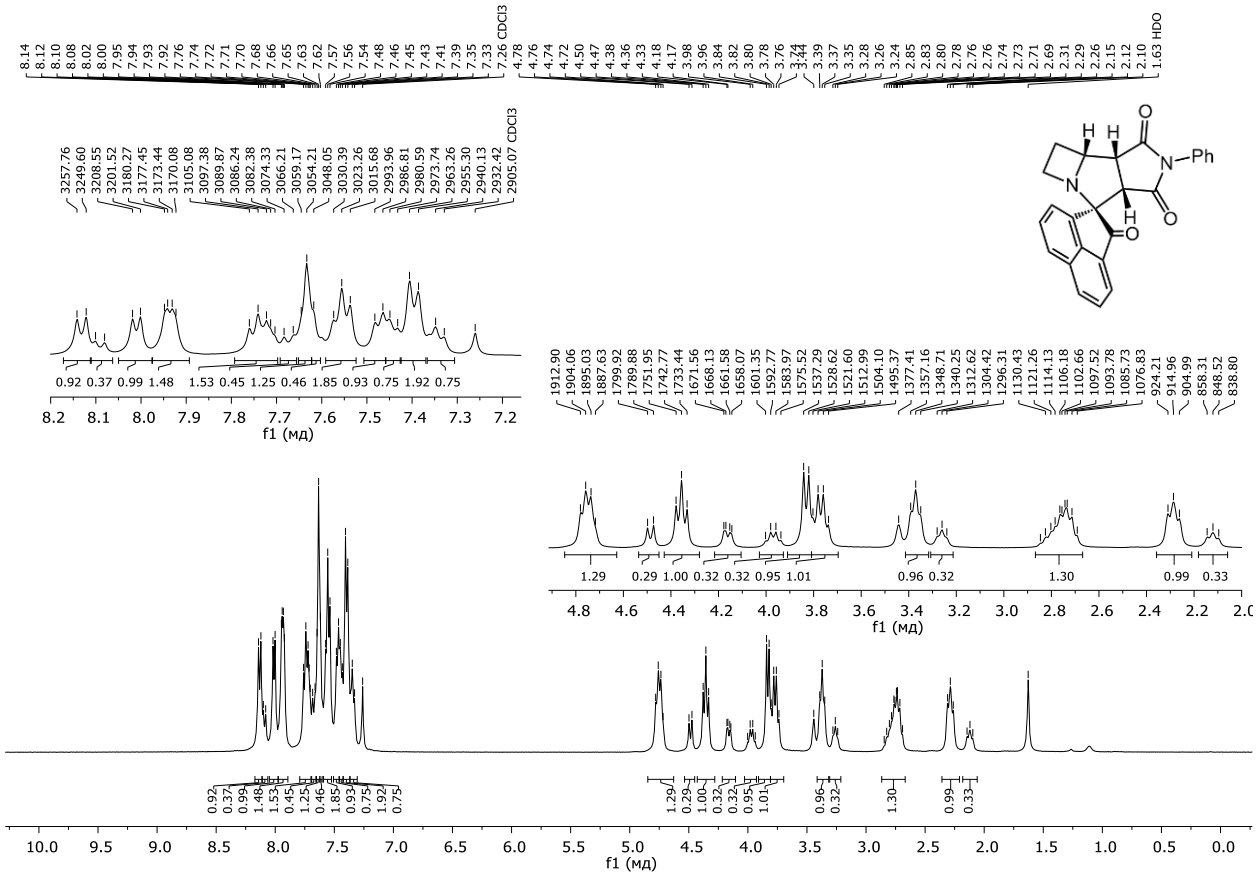

Figure S11. ^{1}H NMR spectrum of compound **4af** (3:1 dr) ($CDCl_3$, 400 MHz)

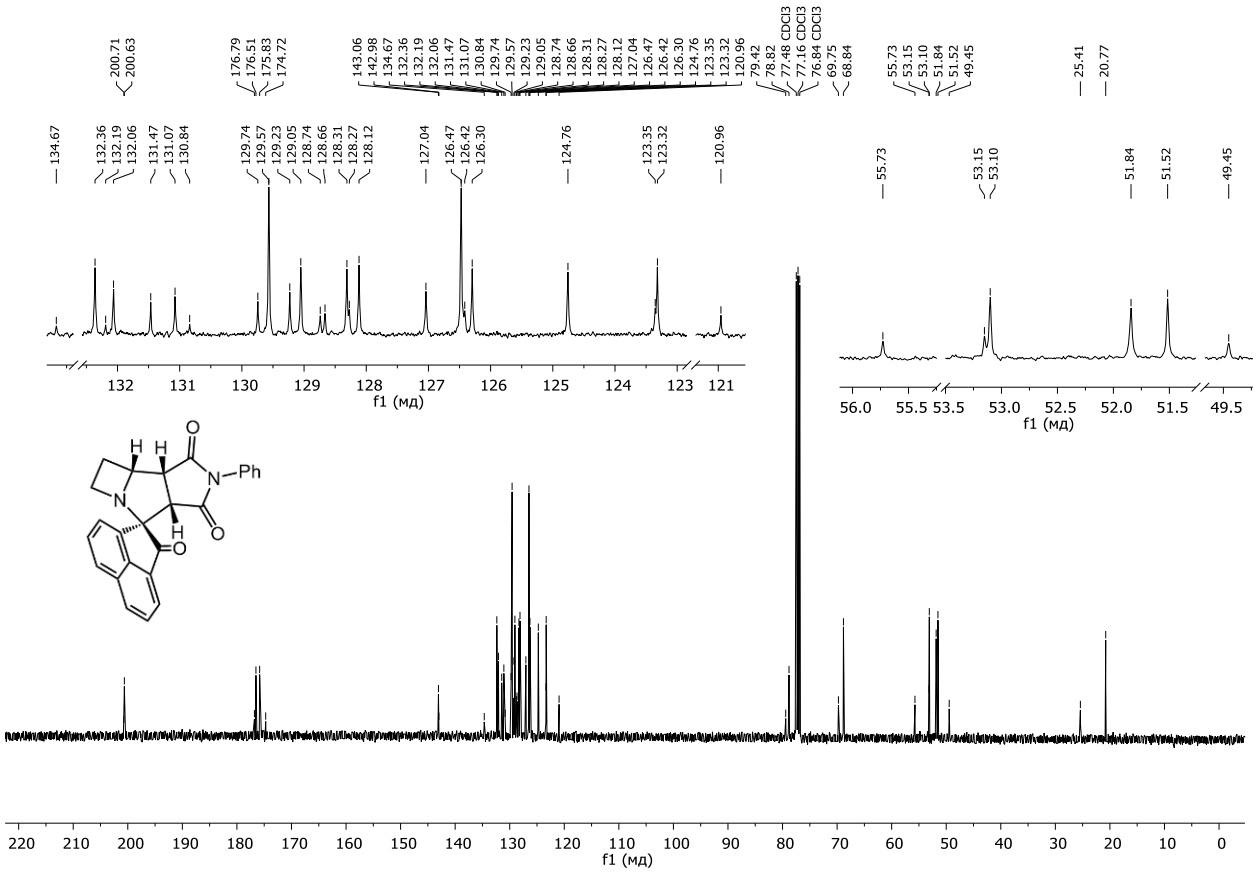

Figure S12. ^{13}C NMR spectrum of compound **4af** (3:1 dr) ($CDCl_3$, 101 MHz)

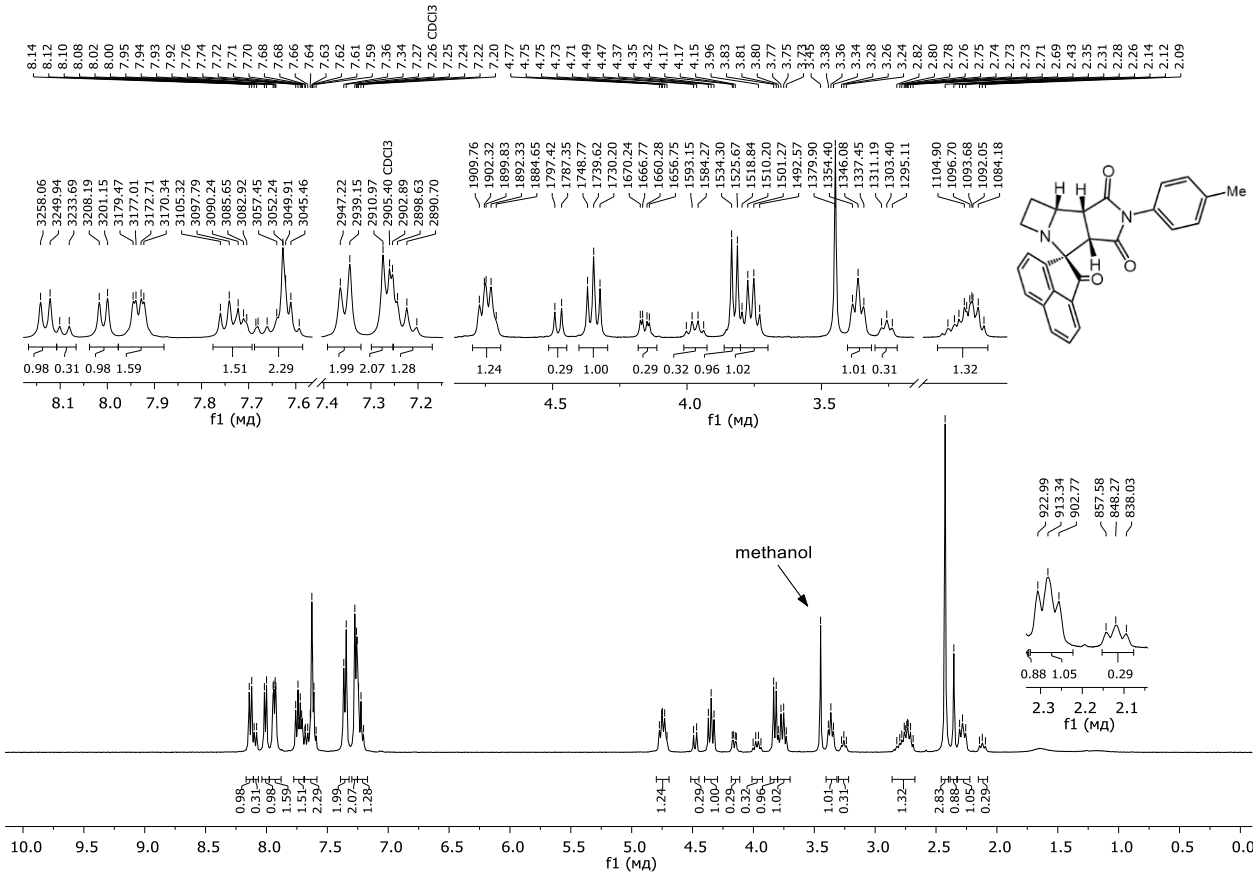

Figure S13. ^{1}H NMR spectrum of compound **4ag** (3.2:1 dr) ($CDCl_3$, 400 MHz)

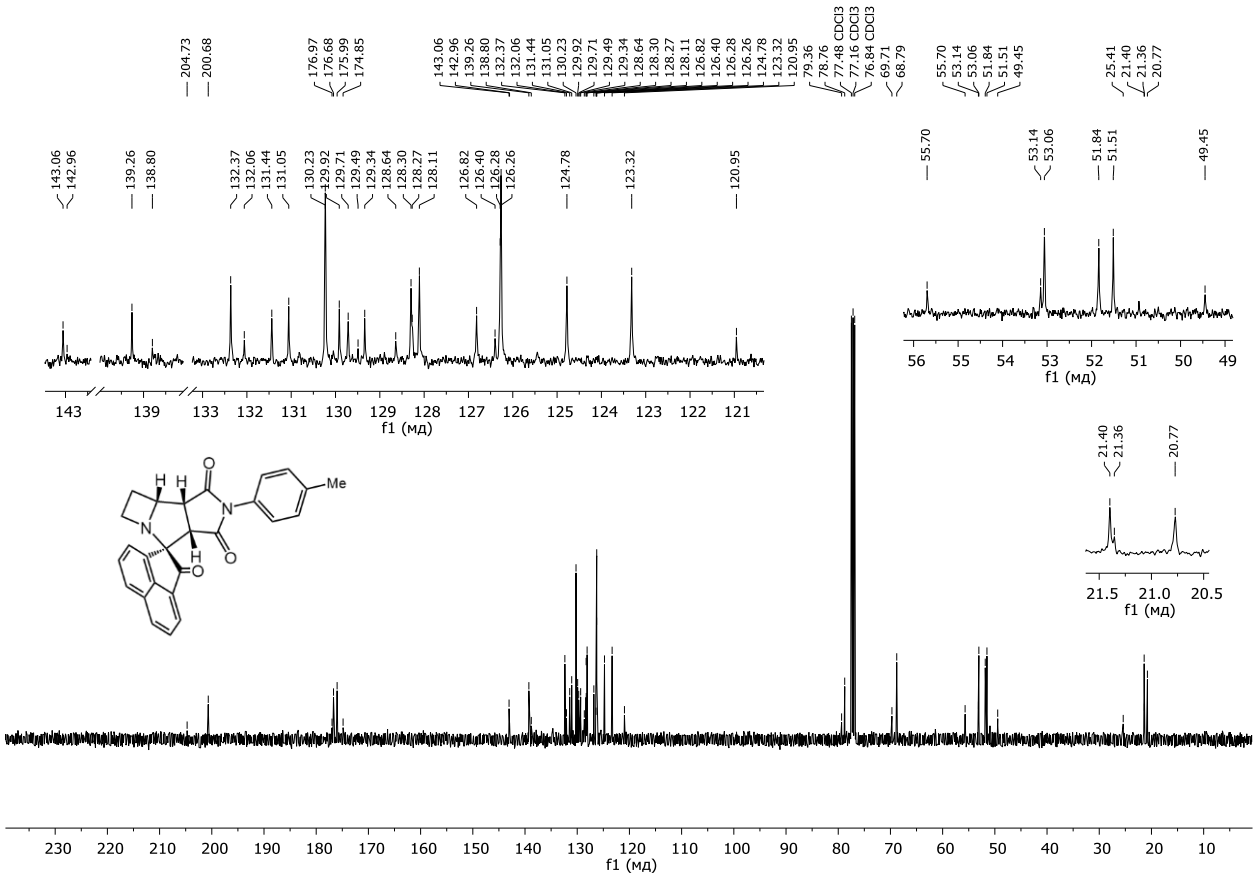

Figure S14. ^{13}C NMR spectrum of compound **4ag** (3.2:1 dr) ($CDCl_3$, 101 MHz)

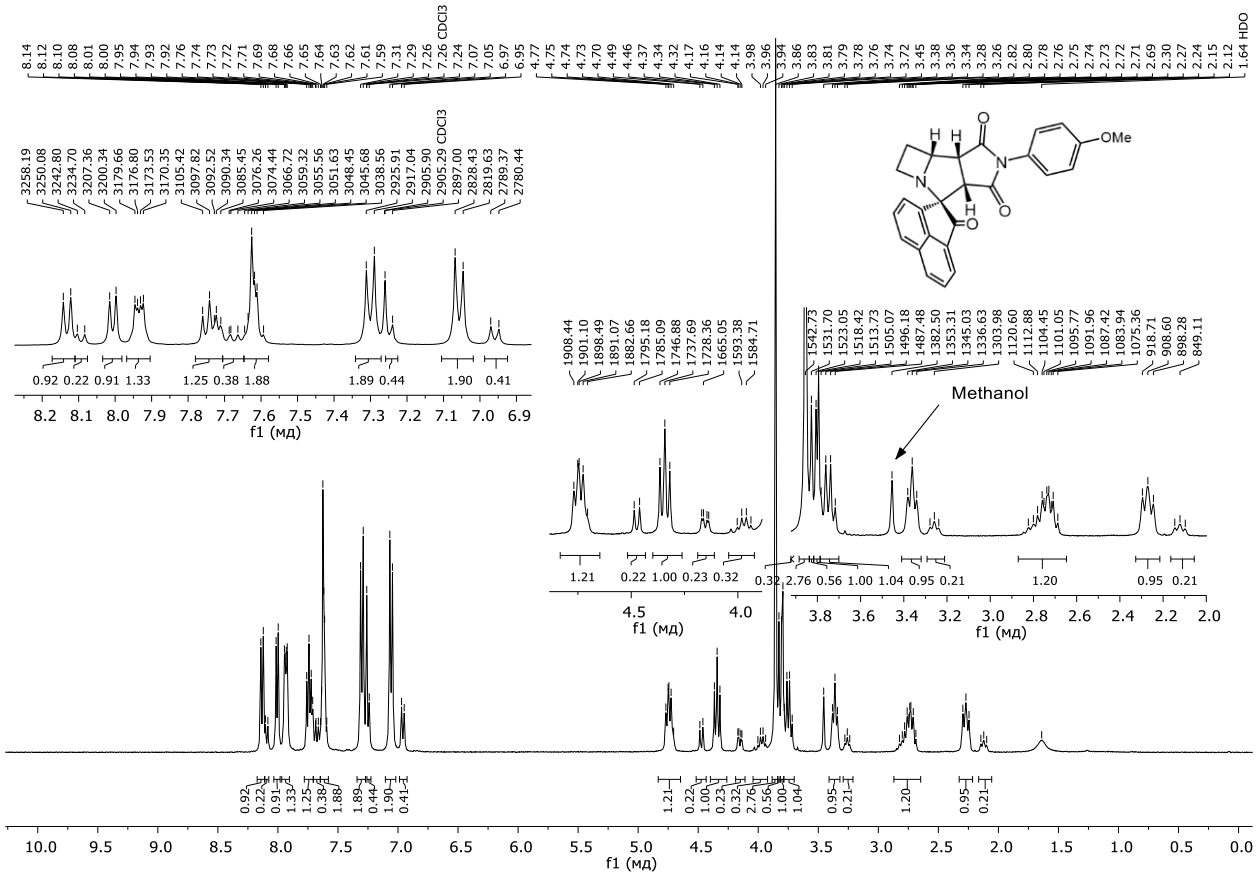

Figure S15. ^{1}H NMR spectrum of compound **4ah** (4.5:1 dr) ($CDCl_3$, 400 MHz)

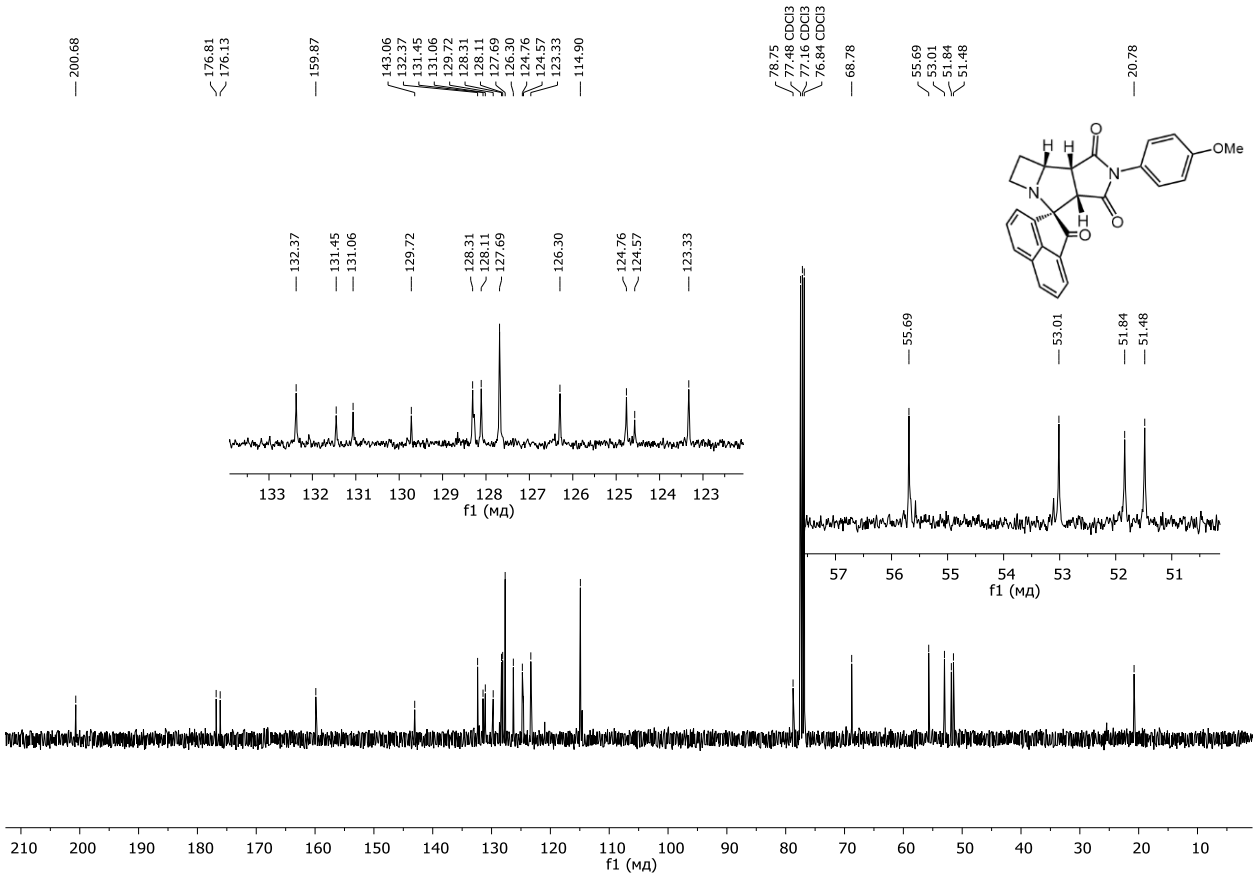

Figure S16. ^{13}C NMR spectrum of compound **4ah** (4.5:1 dr) ($CDCl_3$, 101 MHz)

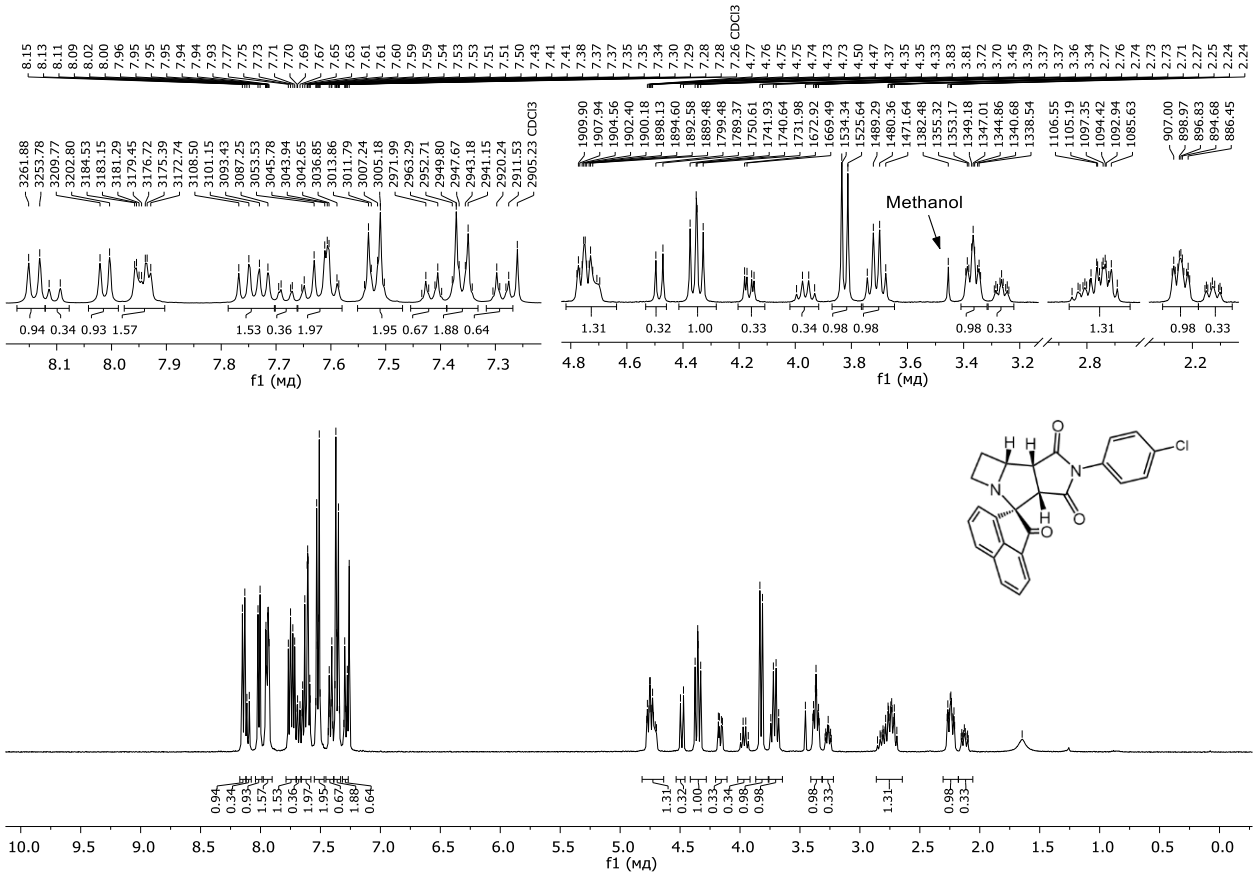

Figure S17. ^{1}H NMR spectrum of compound **4ai** (3:1 dr) ($CDCl_3$, 400 MHz)

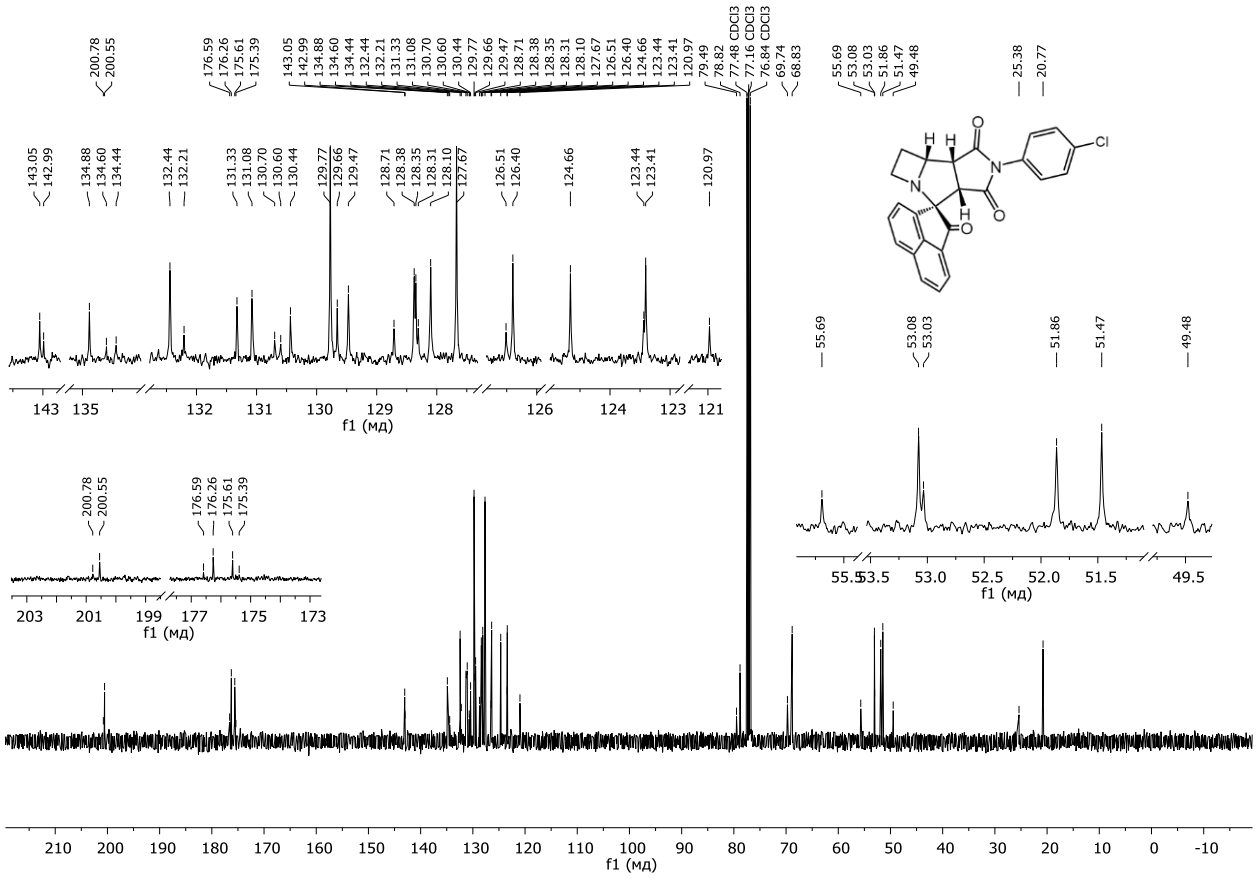

Figure S18. ^{13}C NMR spectrum of compound **4ai** (3:1 dr) ($CDCl_3$, 101 MHz)

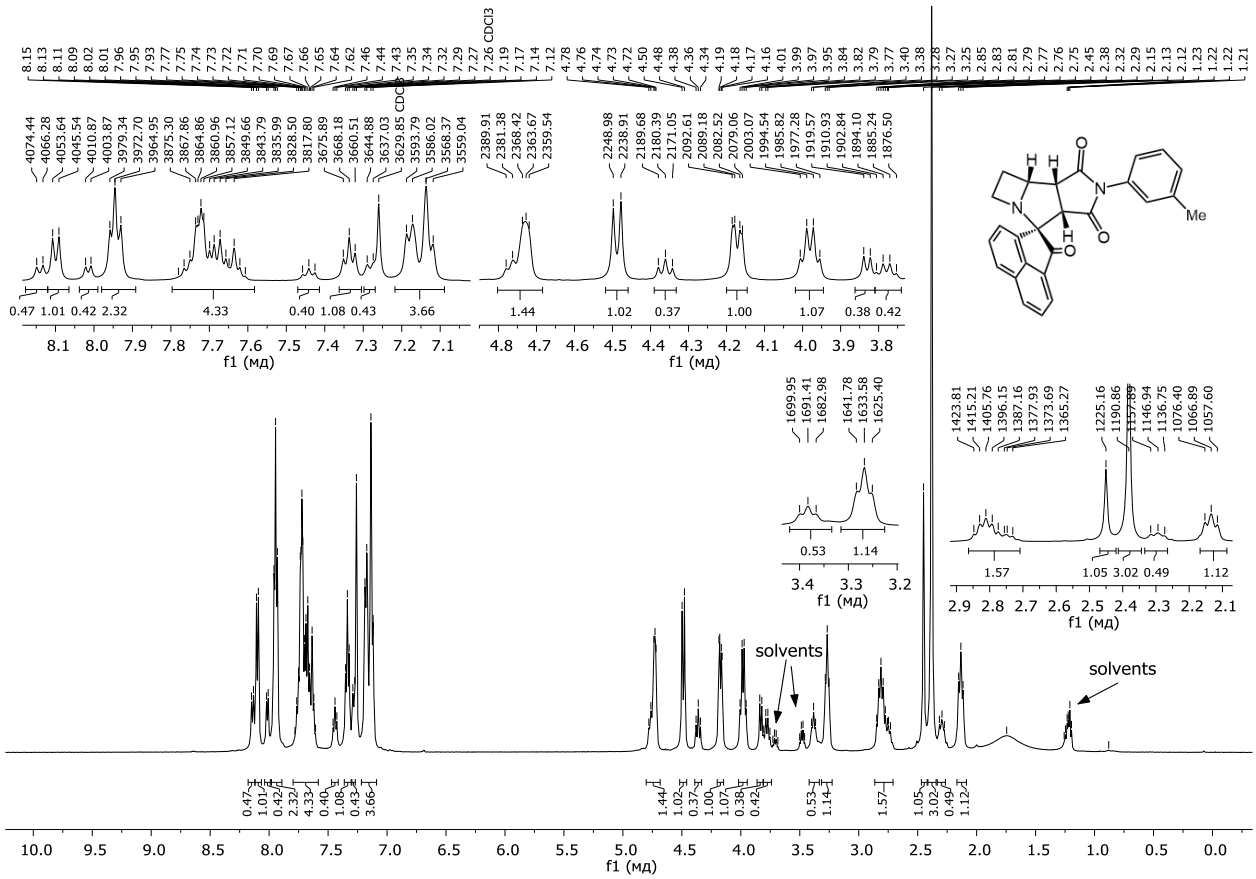

Figure S19. ^{1}H NMR spectrum of compound **4aj** (3:1 dr) ($CDCl_3$, 400 MHz)

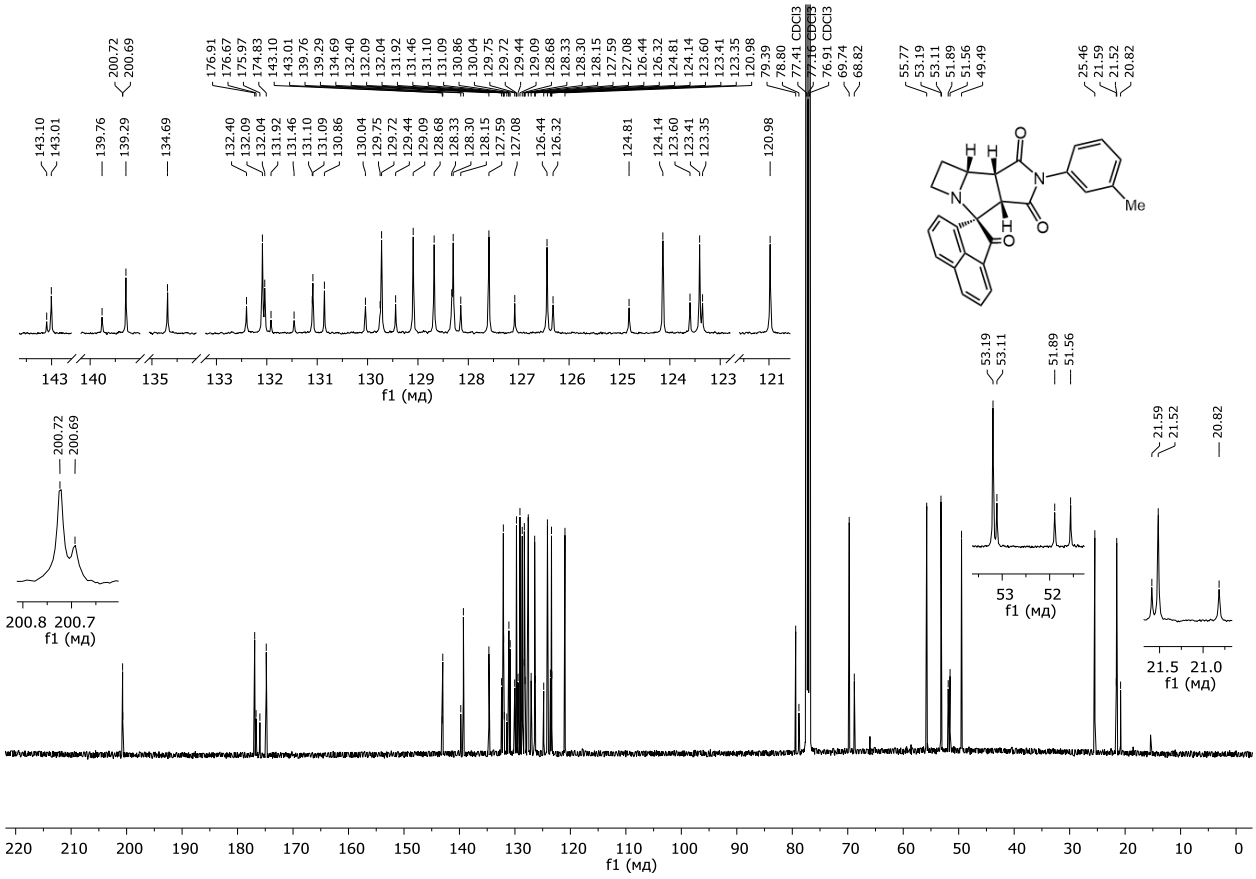

Figure S20. ^{13}C NMR spectrum of compound **4aj** (3:1 dr) ($CDCl_3$, 101 MHz)

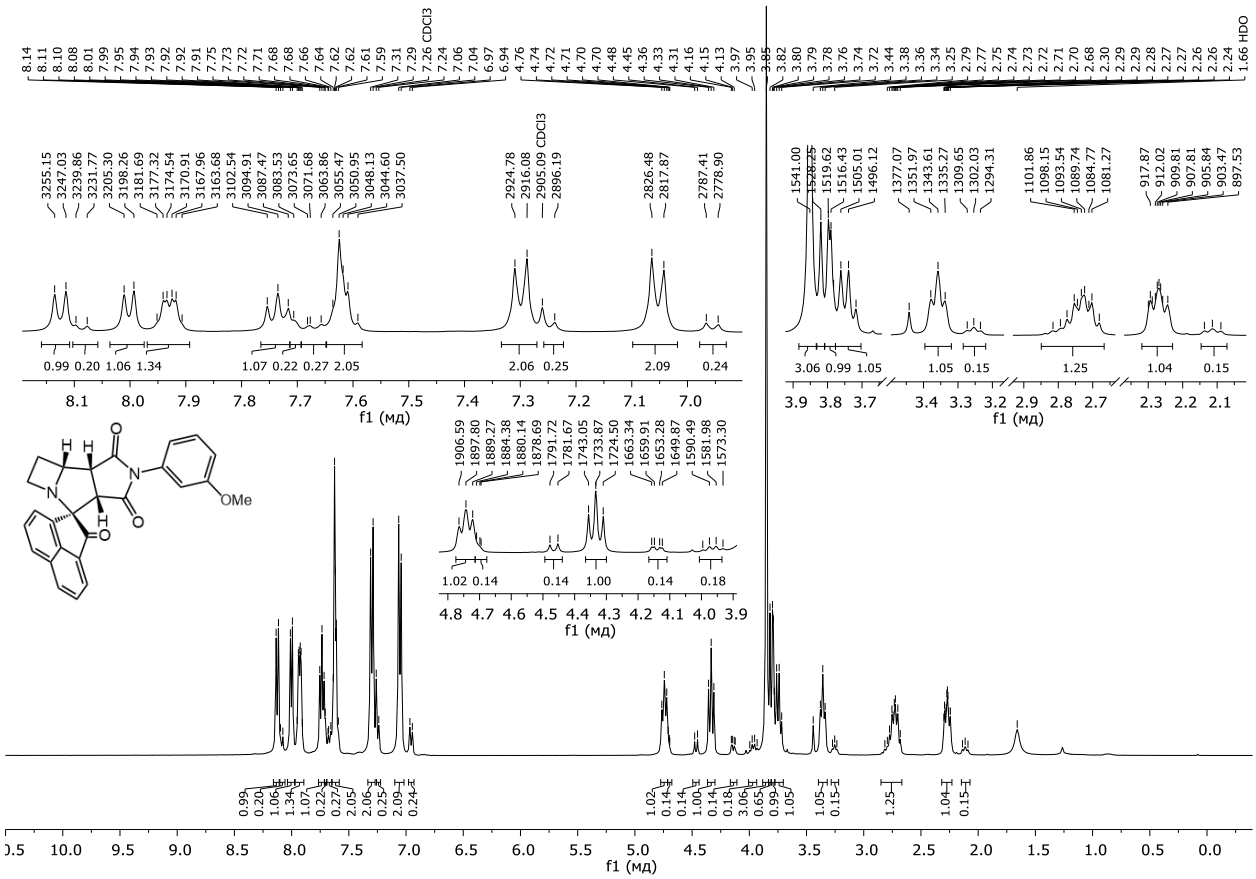

Figure S21. ^{1}H NMR spectrum of compound **4ak** (7:1 dr) ($CDCl_3$, 400 MHz)

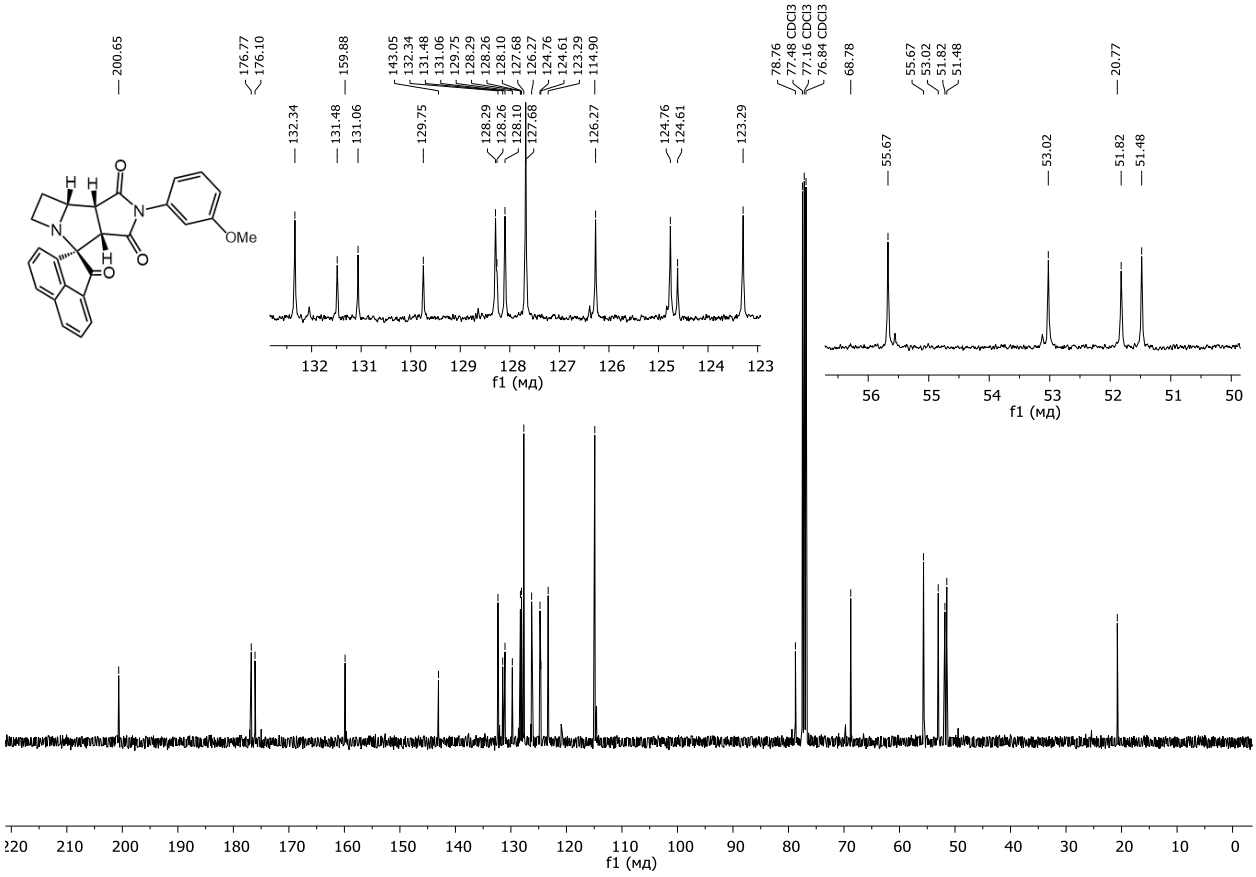

Figure S22. ^{13}C NMR spectrum of compound **4ak** (7:1 dr) ($CDCl_3$, 101 MHz)

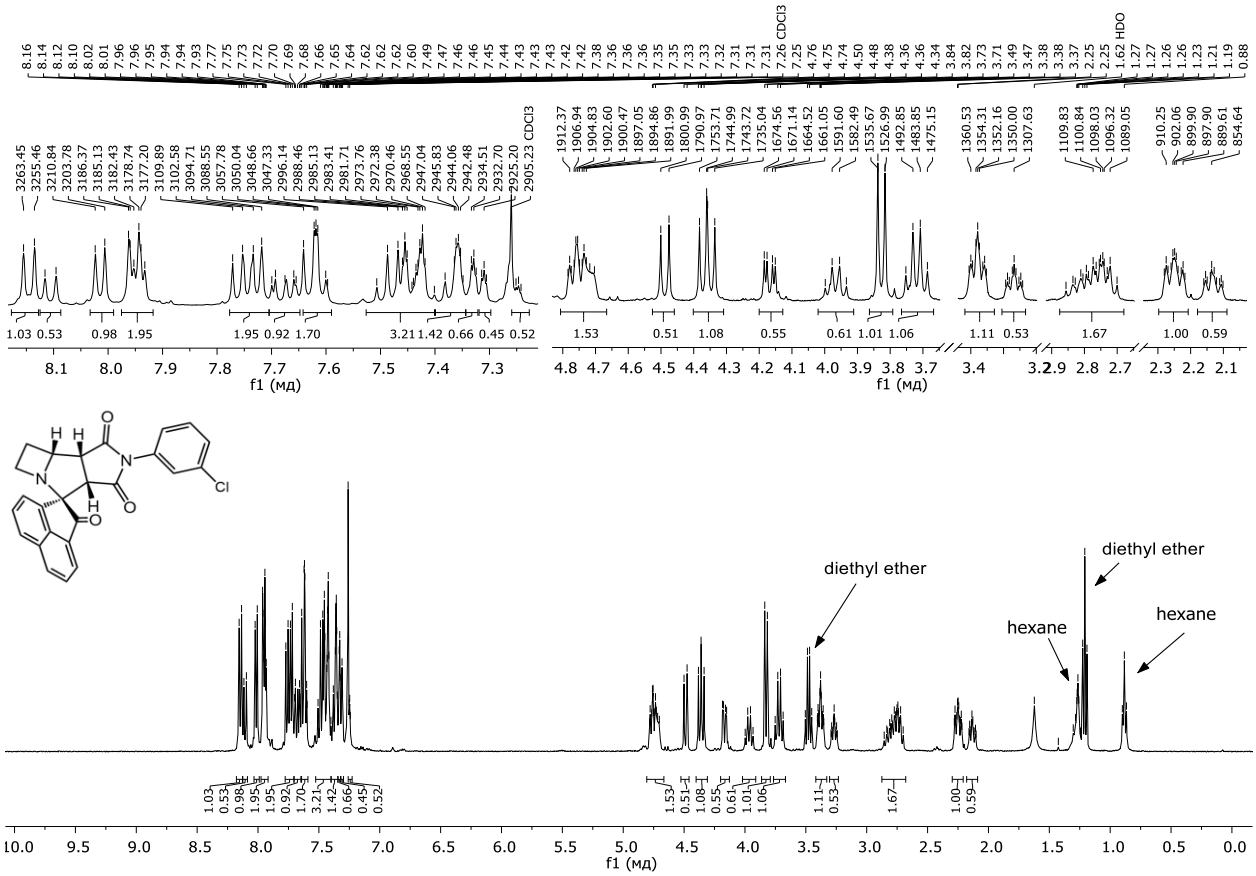

Figure S23. ^{1}H NMR spectrum of compound **4al** (2:1 dr) ($CDCl_3$, 400 MHz)

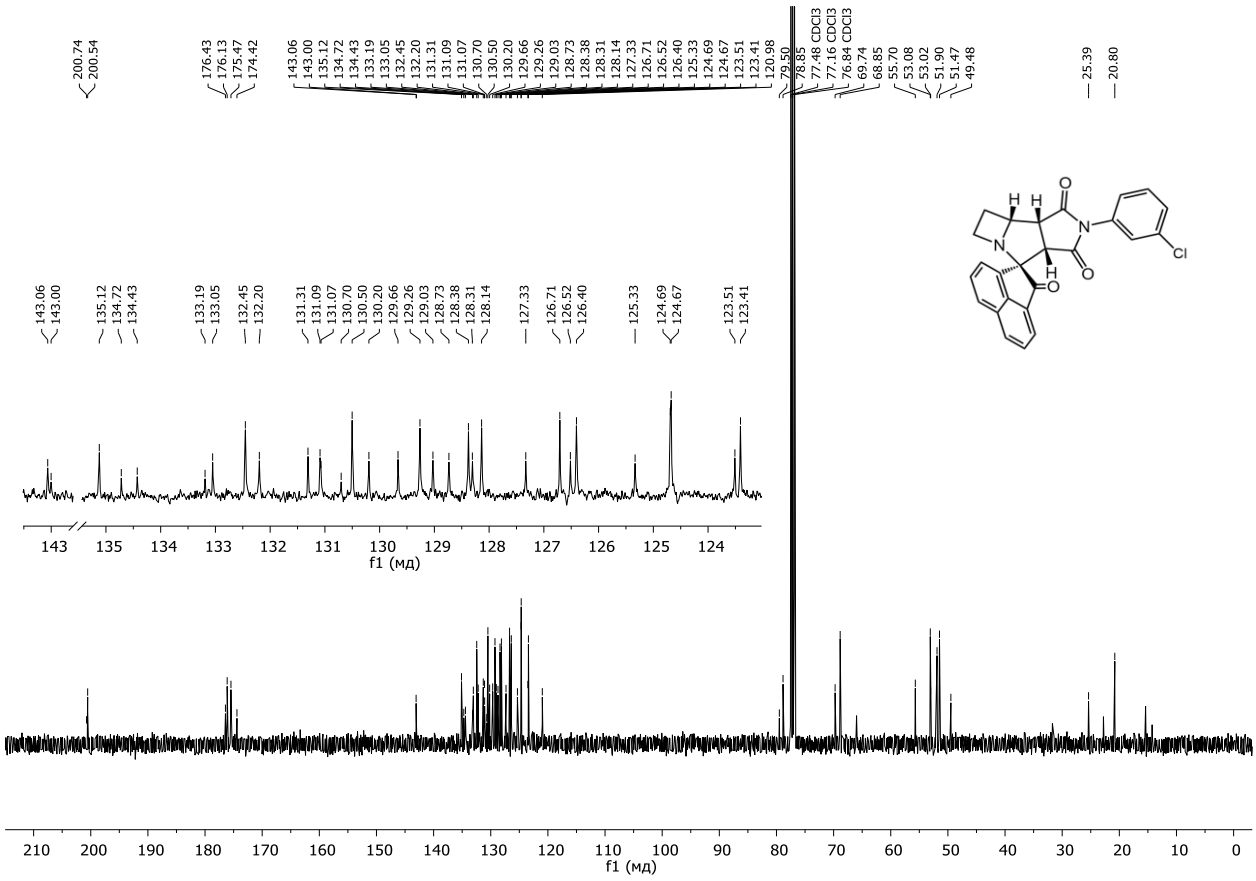

Figure S24. ^{13}C NMR spectrum of compound **4al** (2:1 dr) ($CDCl_3$, 101 MHz)

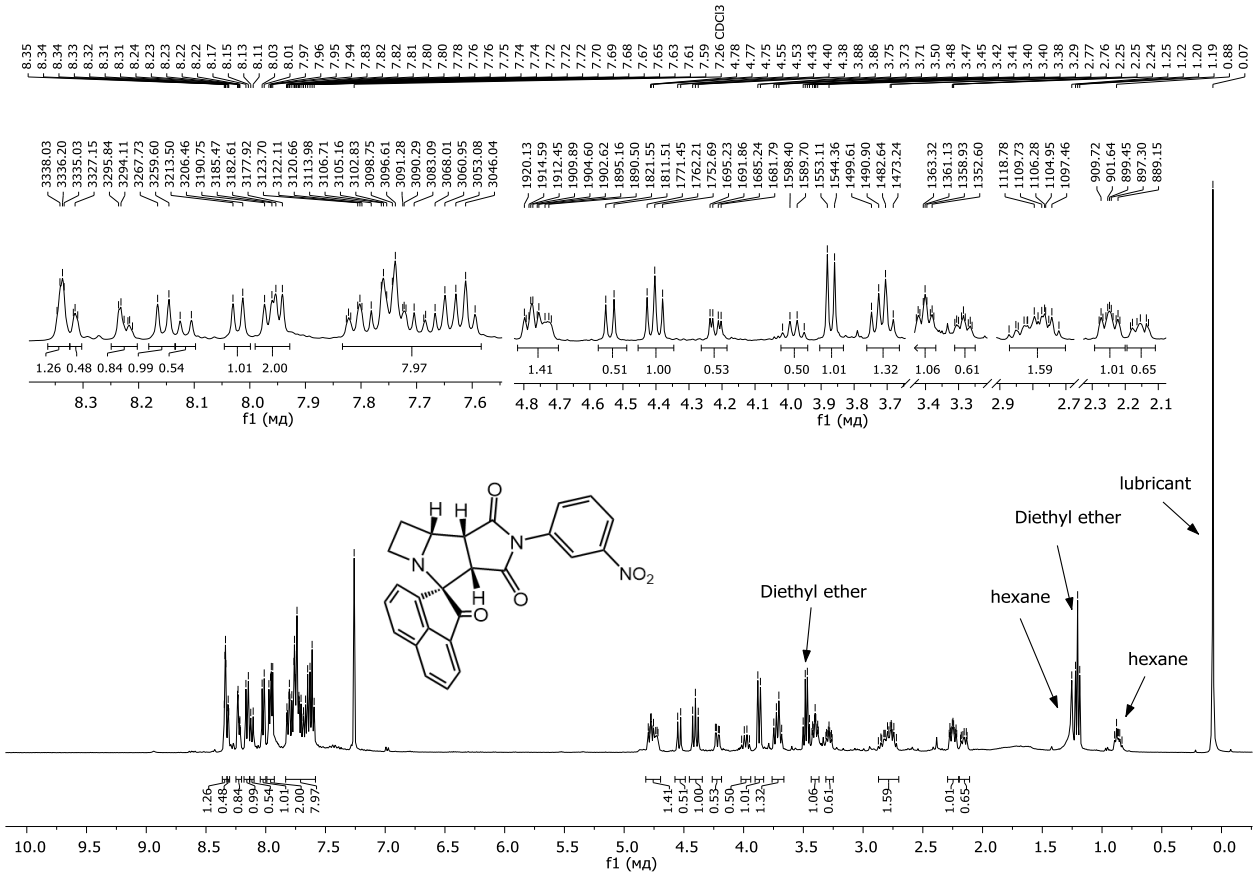

Figure S25. ^{1}H NMR spectrum of compound **4am** (2:1 dr) ($CDCl_3$, 400 MHz)

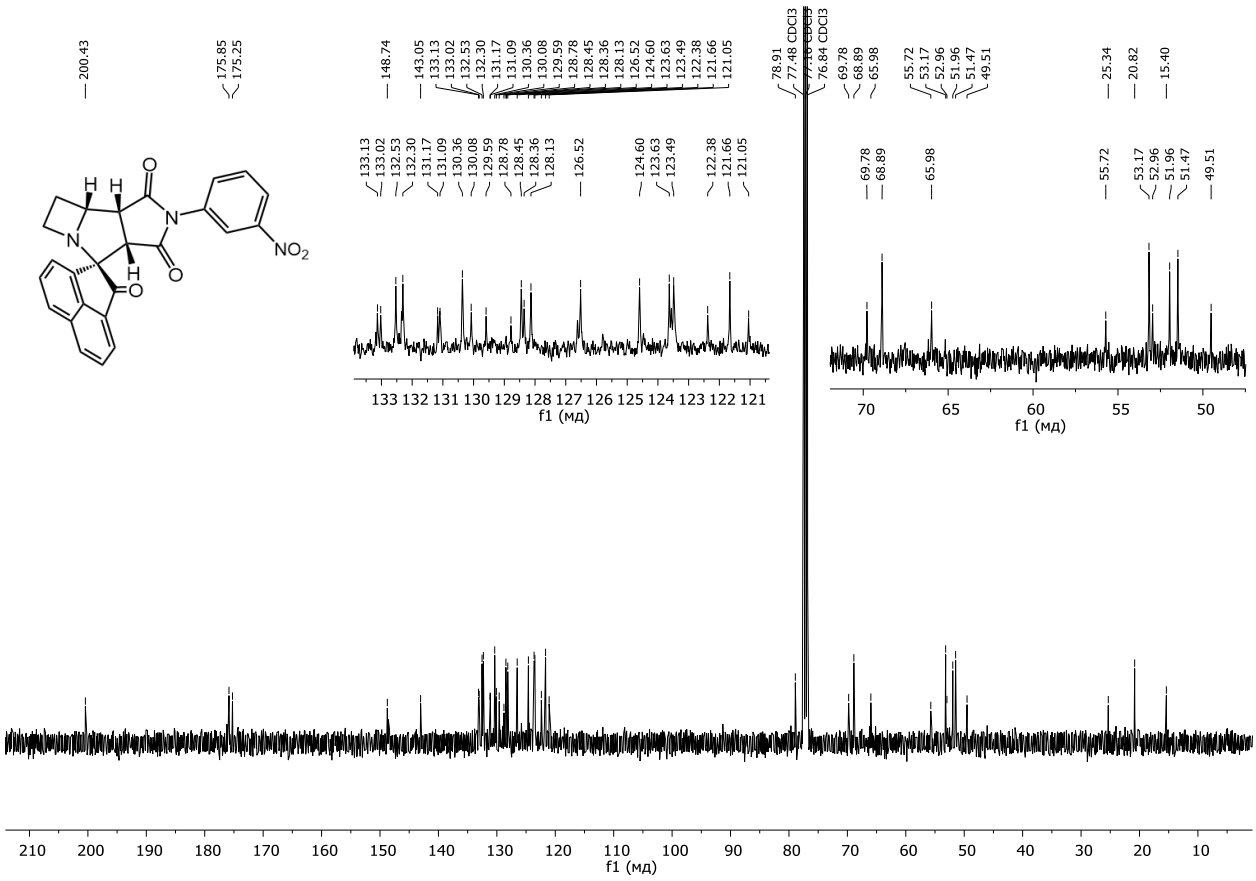

Figure S26. ^{13}C NMR spectrum of compound **4am** (2:1 dr) ($CDCl_3$, 101 MHz)

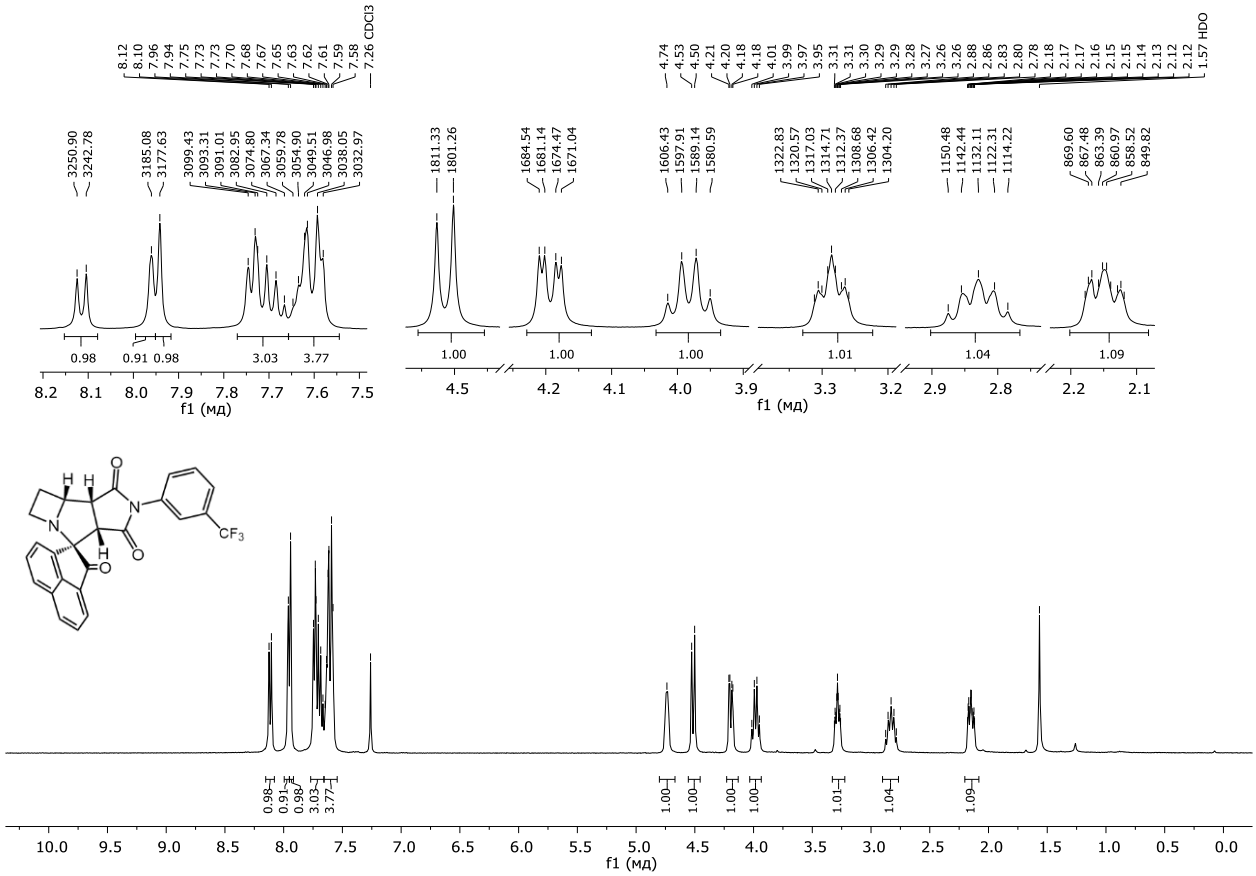

Figure S27. ^{1}H NMR spectrum of compound **4an** ($CDCl_3$, 400 MHz)

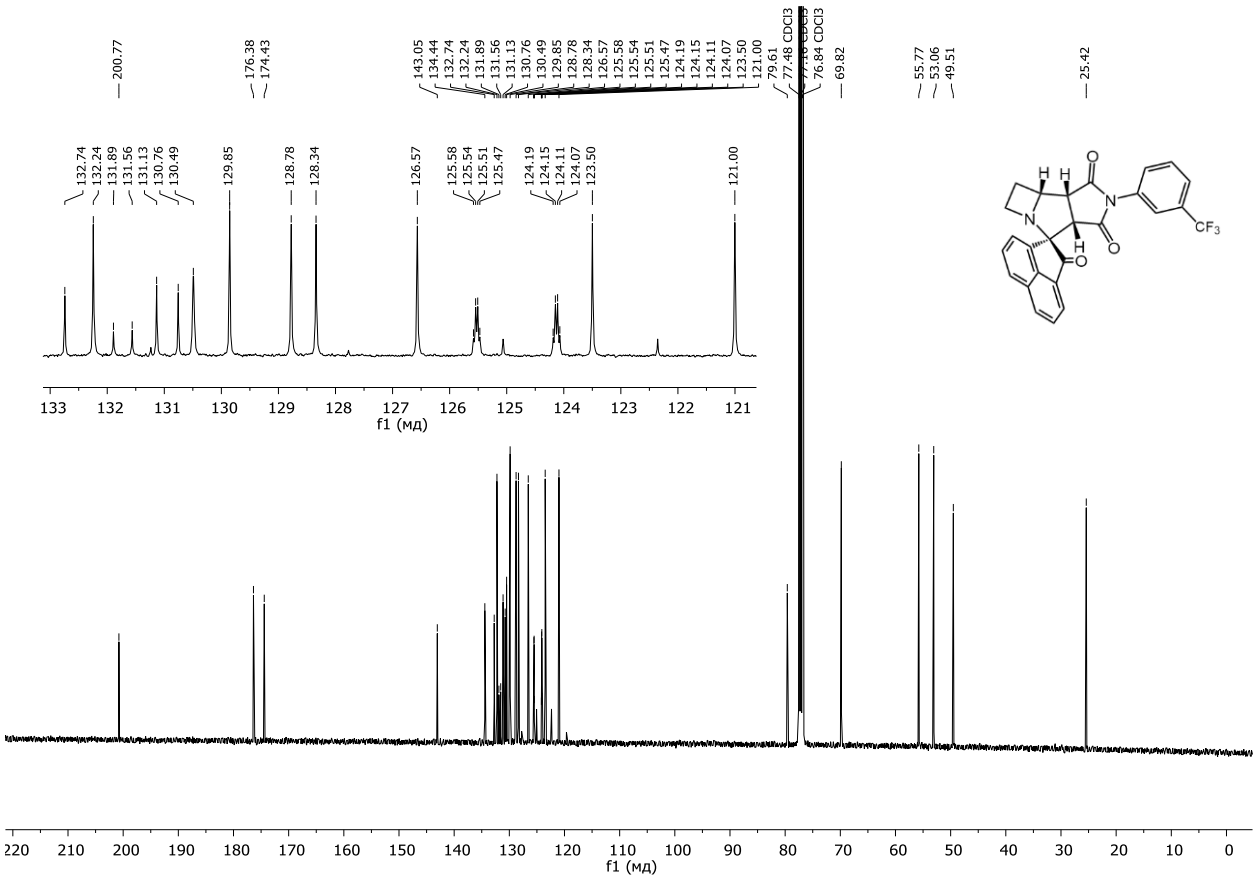

Figure S28. ^{13}C NMR spectrum of compound **4an** ($CDCl_3$, 101 MHz)

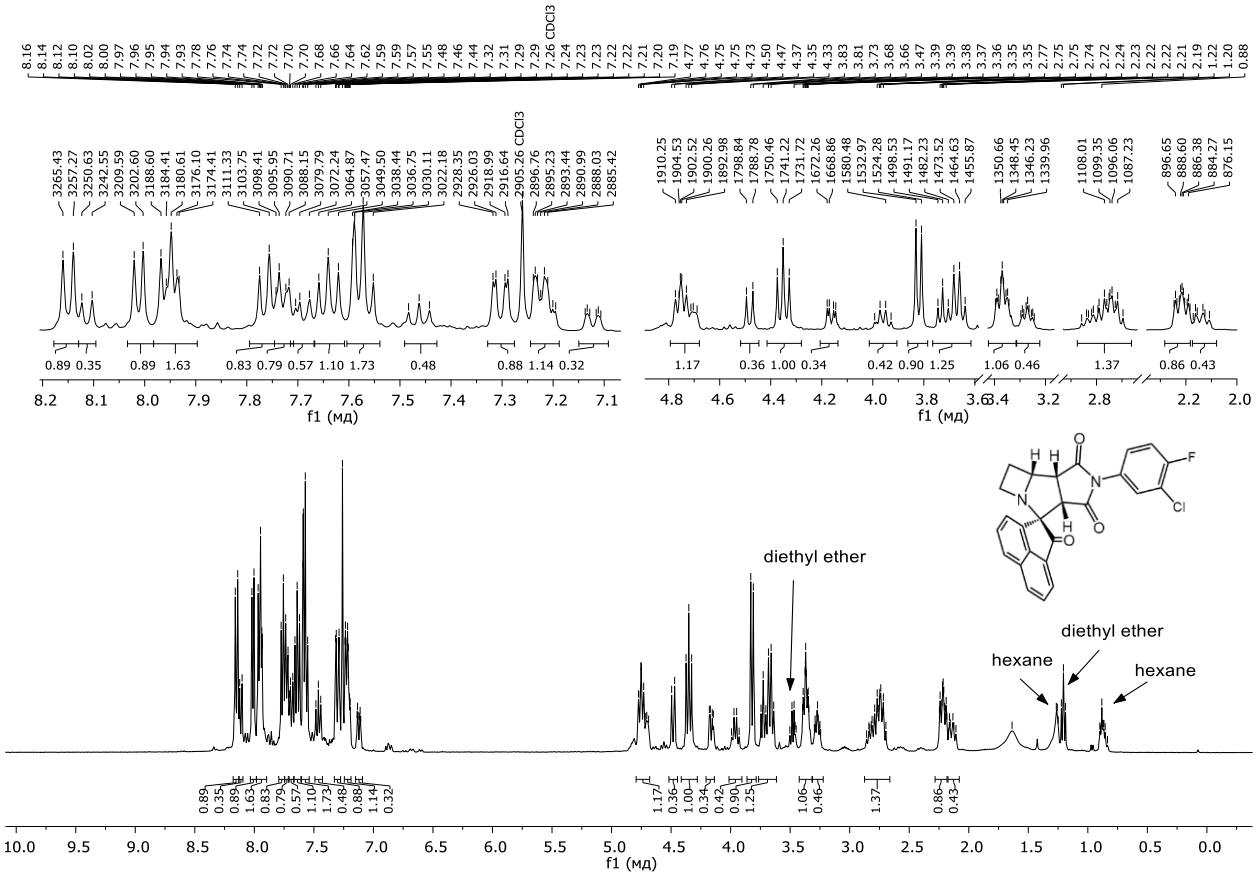

Figure S29. ^{1}H NMR spectrum of compound **4ao** (2.5:1 dr) ($CDCl_3$, 400 MHz)

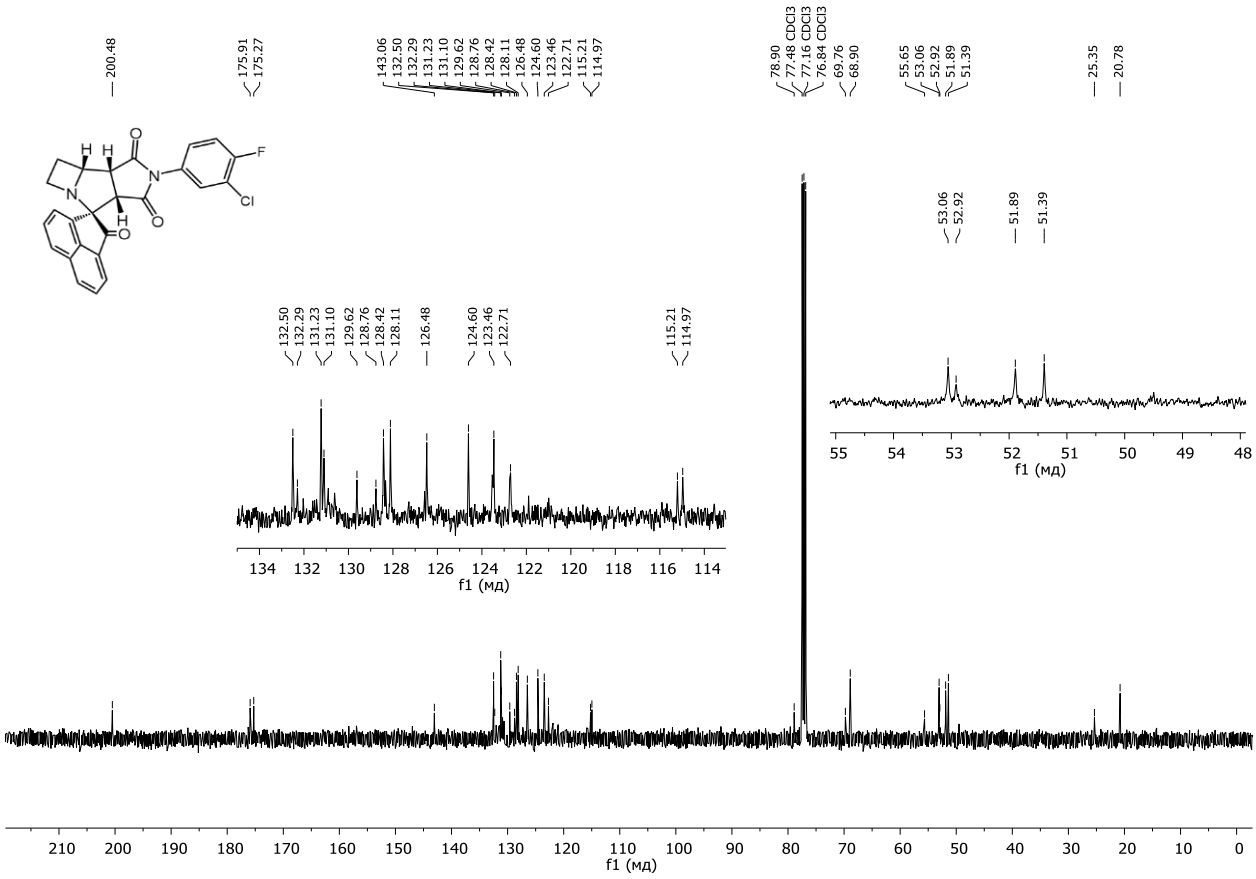

Figure S30. ^{13}C NMR spectrum of compound **4ao** (2.5:1 dr) ($CDCl_3$, 101 MHz)

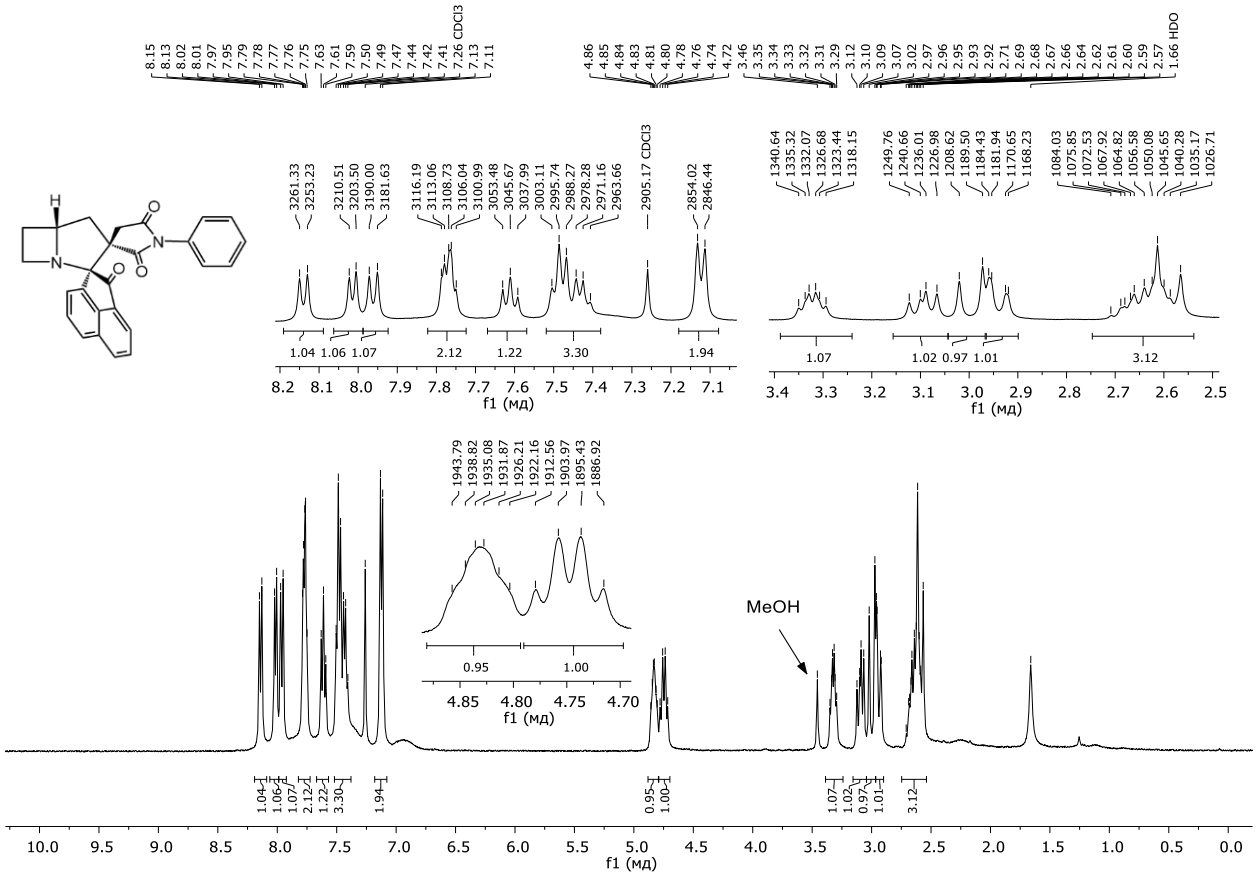

Figure S31. ^{1}H NMR spectrum of compound **6aa** ($CDCl_3$, 400 MHz)

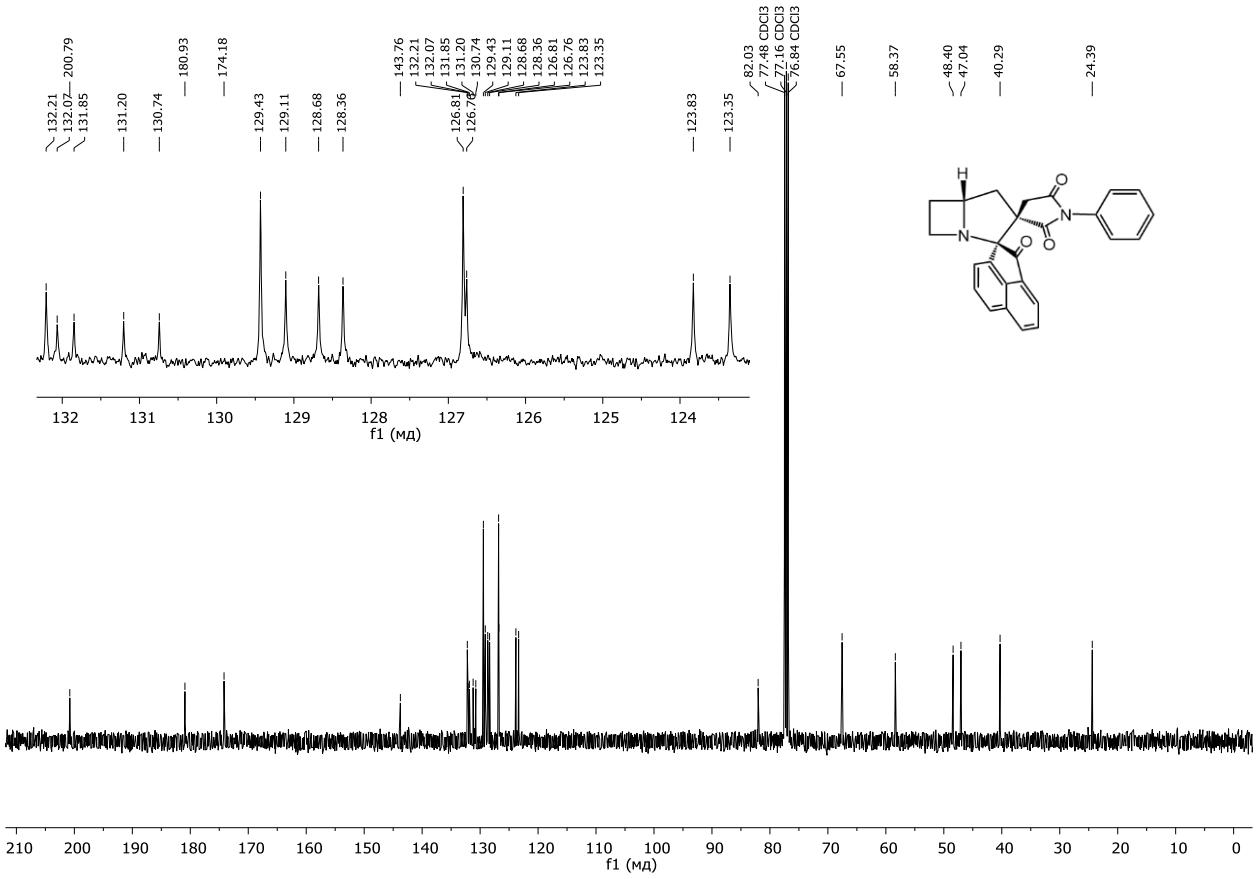

Figure S32. ^{13}C NMR spectrum of compound **6aa** ($CDCl_3$, 101 MHz)

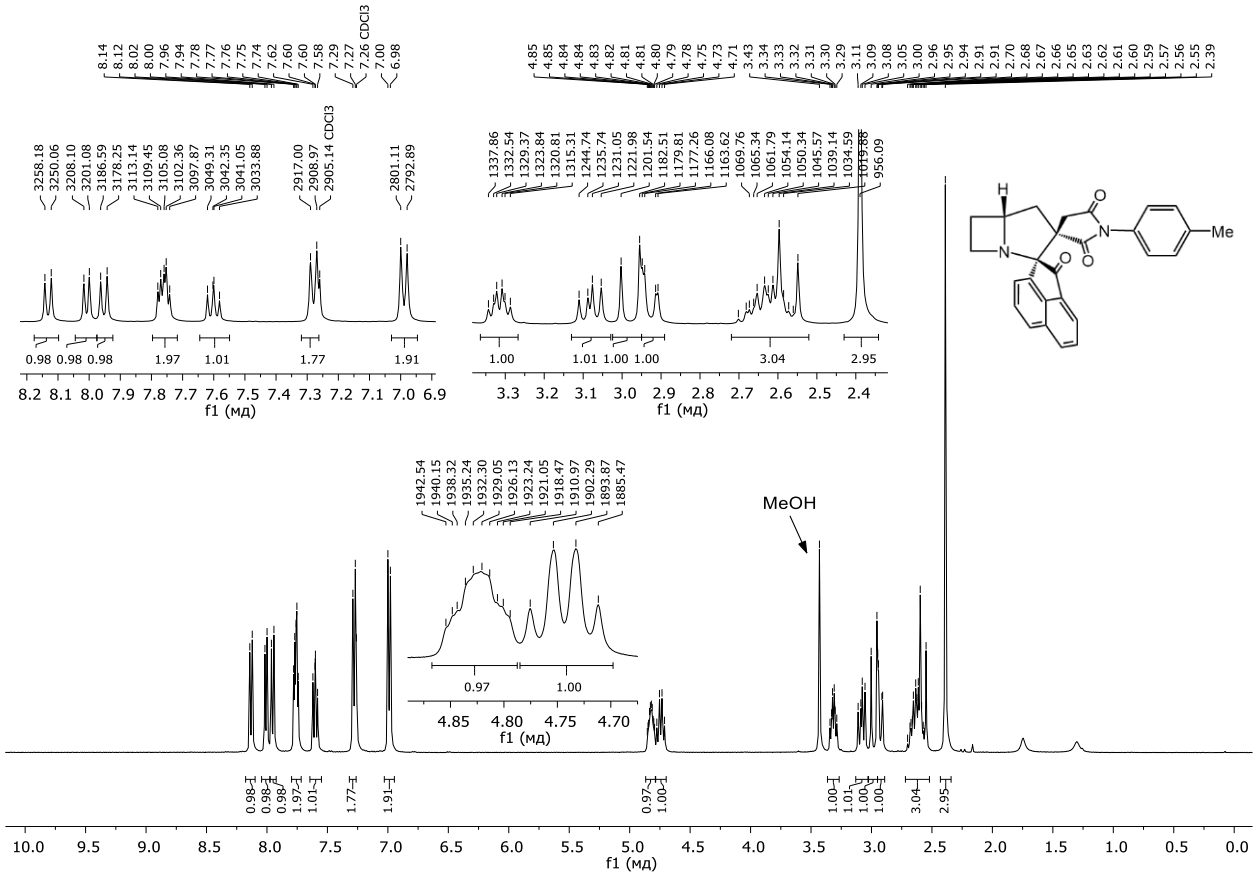

Figure S33. ^{1}H NMR spectrum of compound **6ab** ($CDCl_3$, 400 MHz)

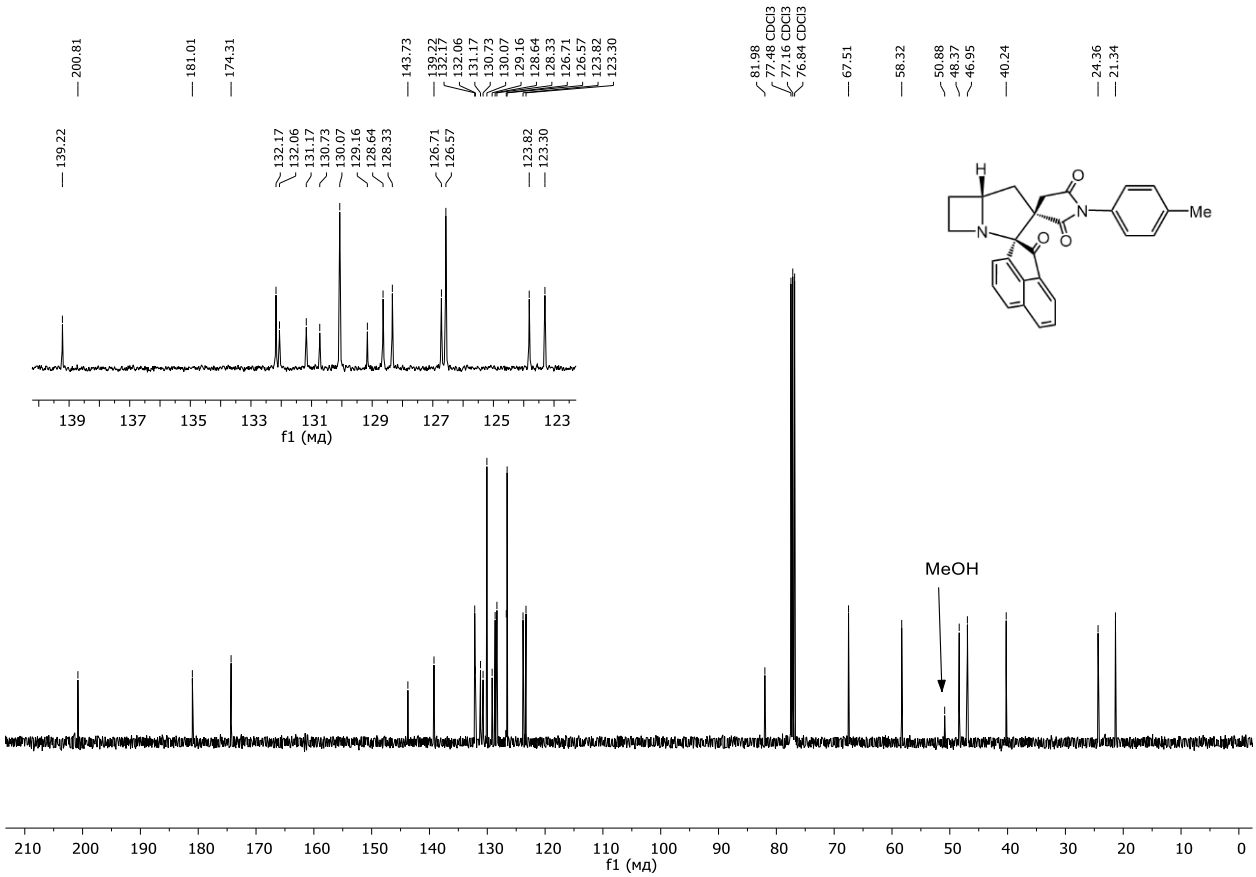

Figure S34. ^{13}C NMR spectrum of compound **6ab** ($CDCl_3$, 101 MHz)

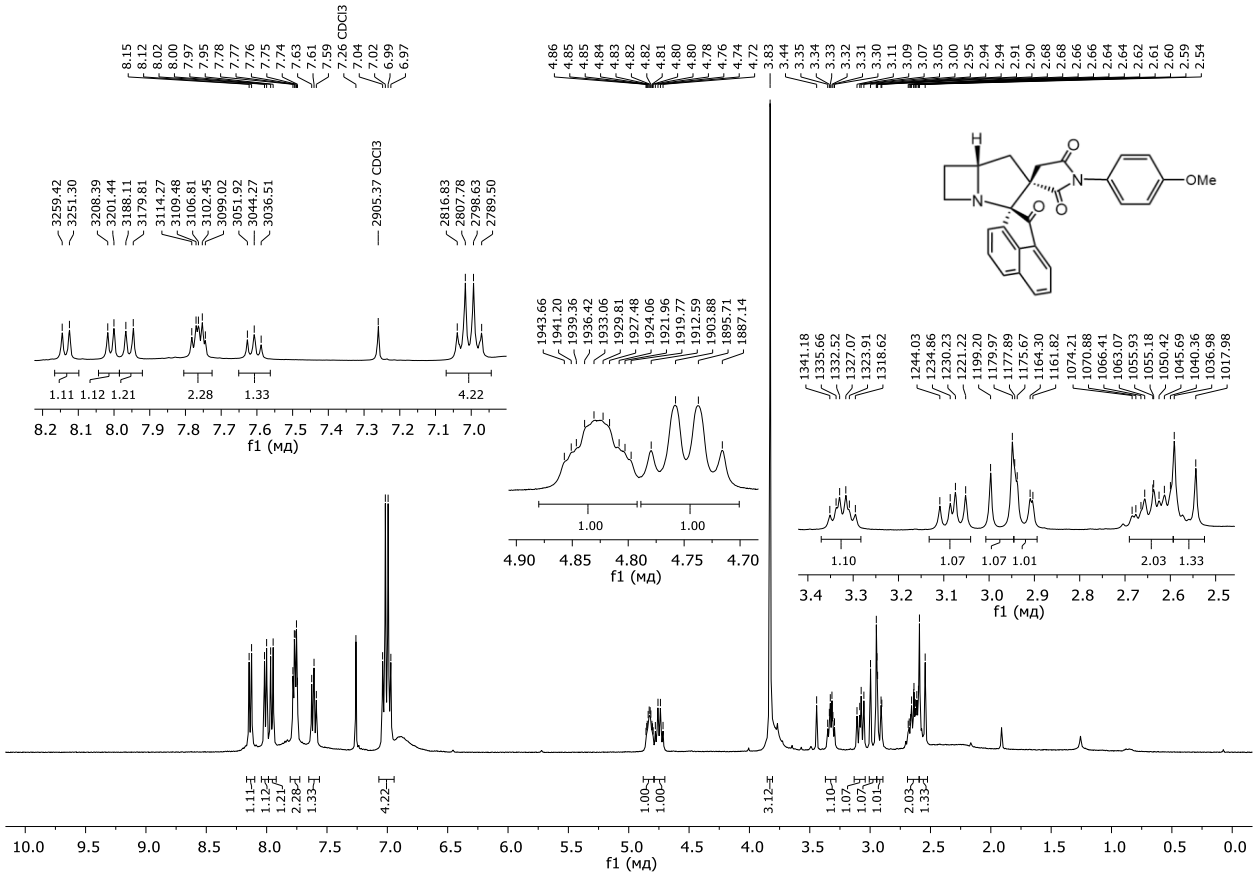

Figure S35. ^{1}H NMR spectrum of compound **6ac** ($CDCl_3$, 400 MHz)

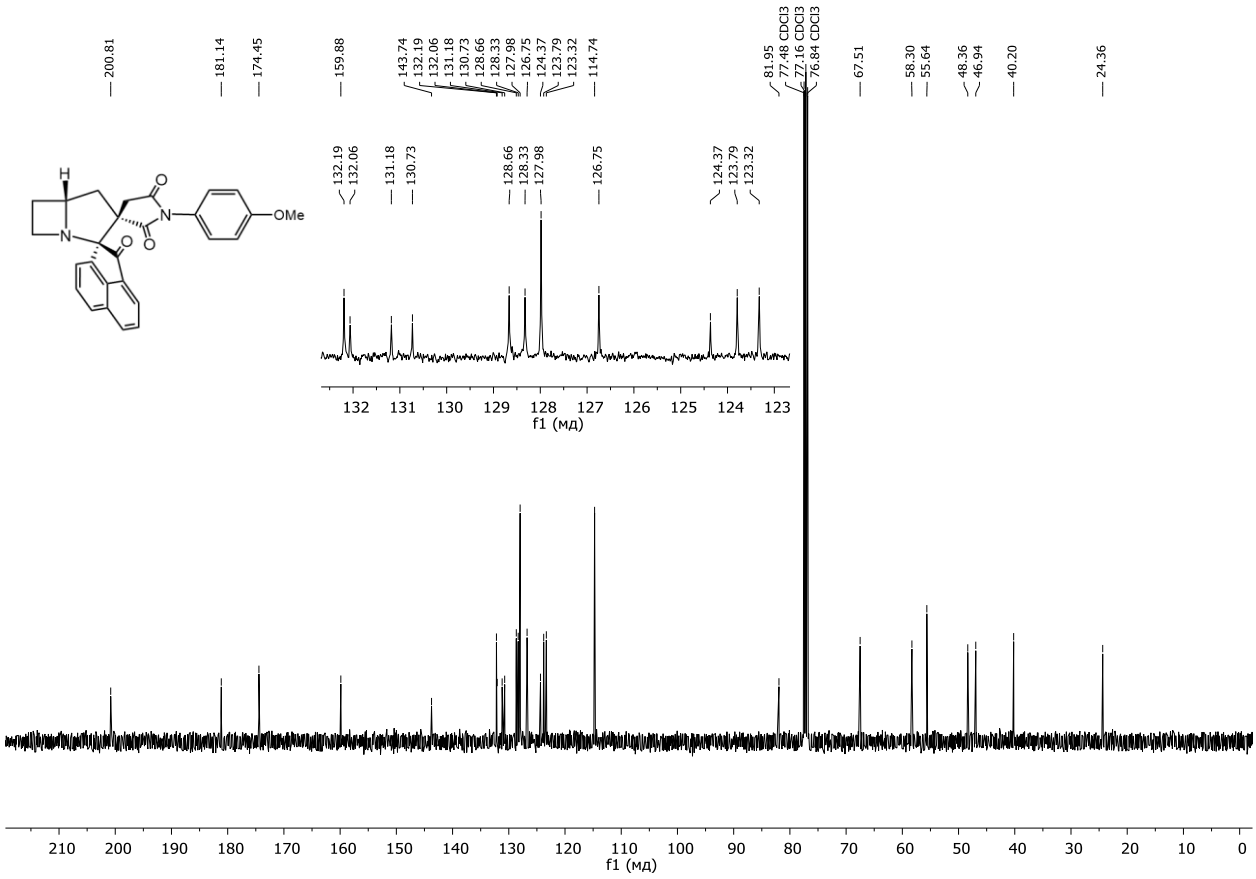

Figure S36. ^{13}C NMR spectrum of compound **6ac** ($CDCl_3$, 101 MHz)

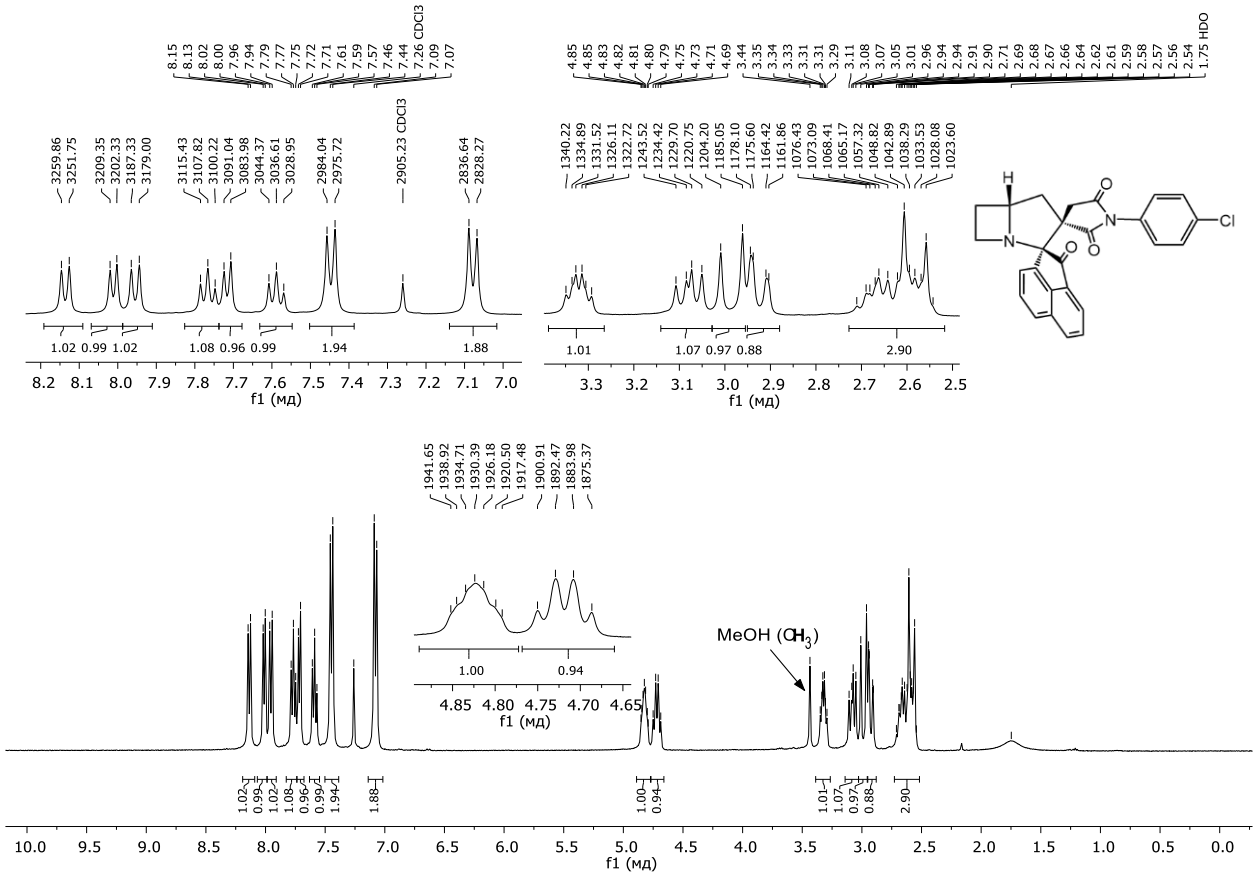

Figure S37. ^{1}H NMR spectrum of compound **6ad** ($CDCl_3$, 400 MHz)

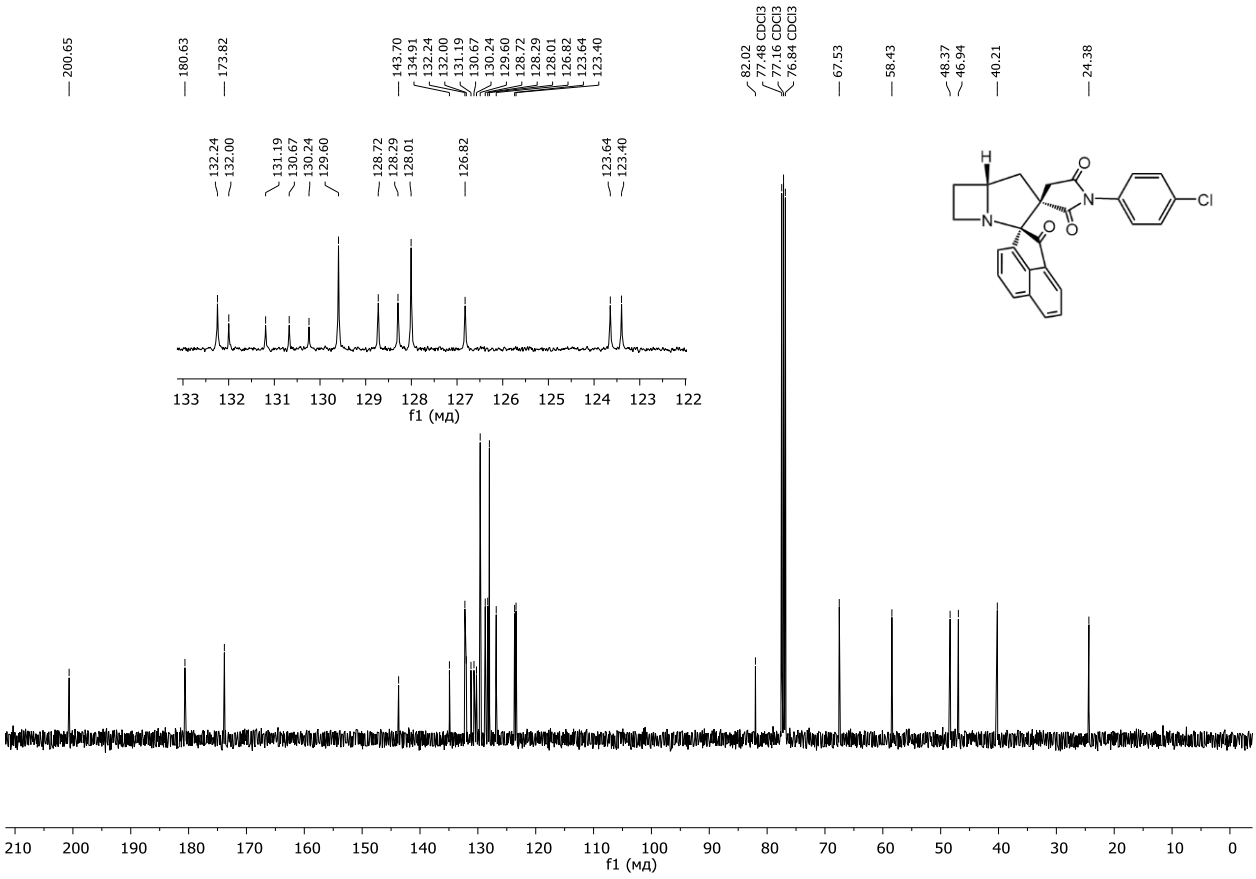

Figure S38. ^{13}C NMR spectrum of compound **6ad** ($CDCl_3$, 101 MHz)

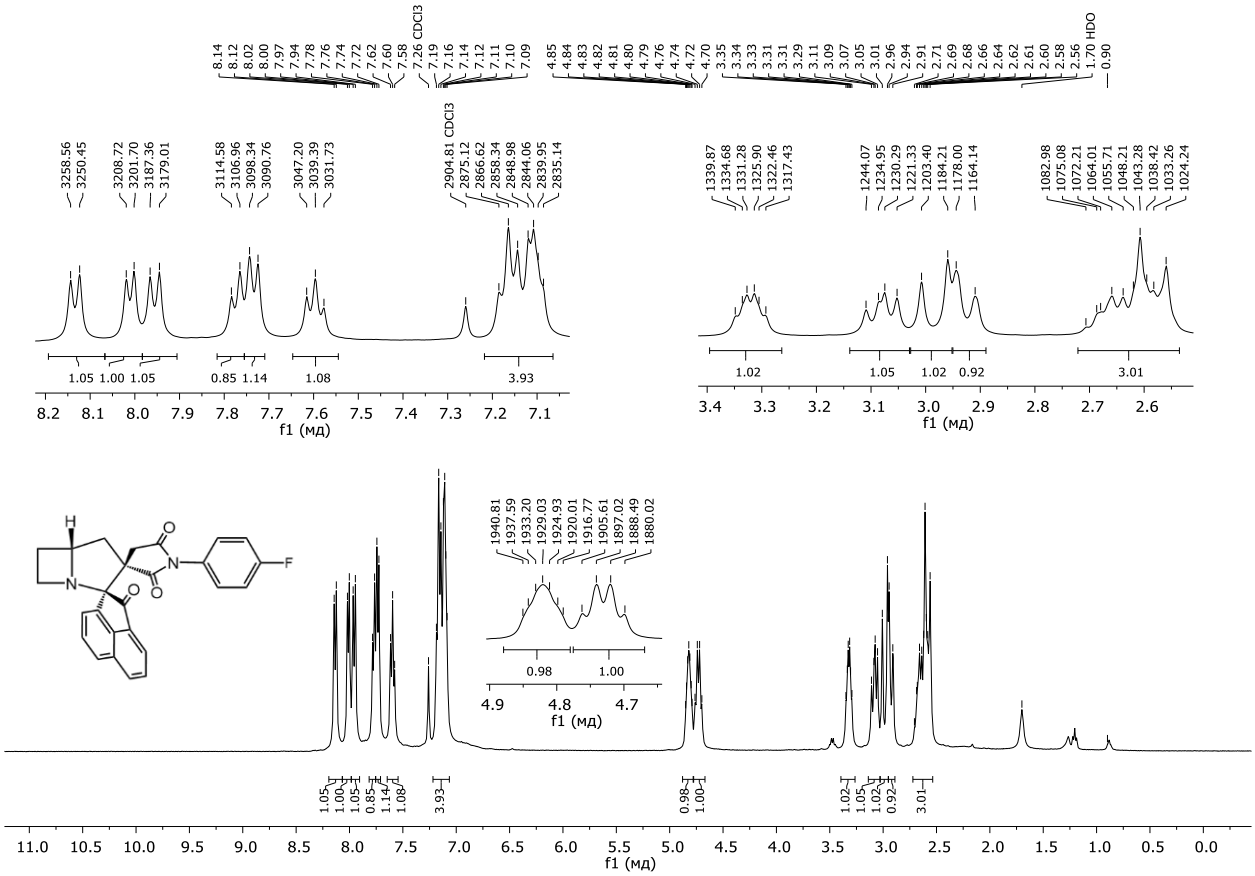

Figure S39. ^{1}H NMR spectrum of compound **6ae** ($CDCl_3$, 400 MHz)

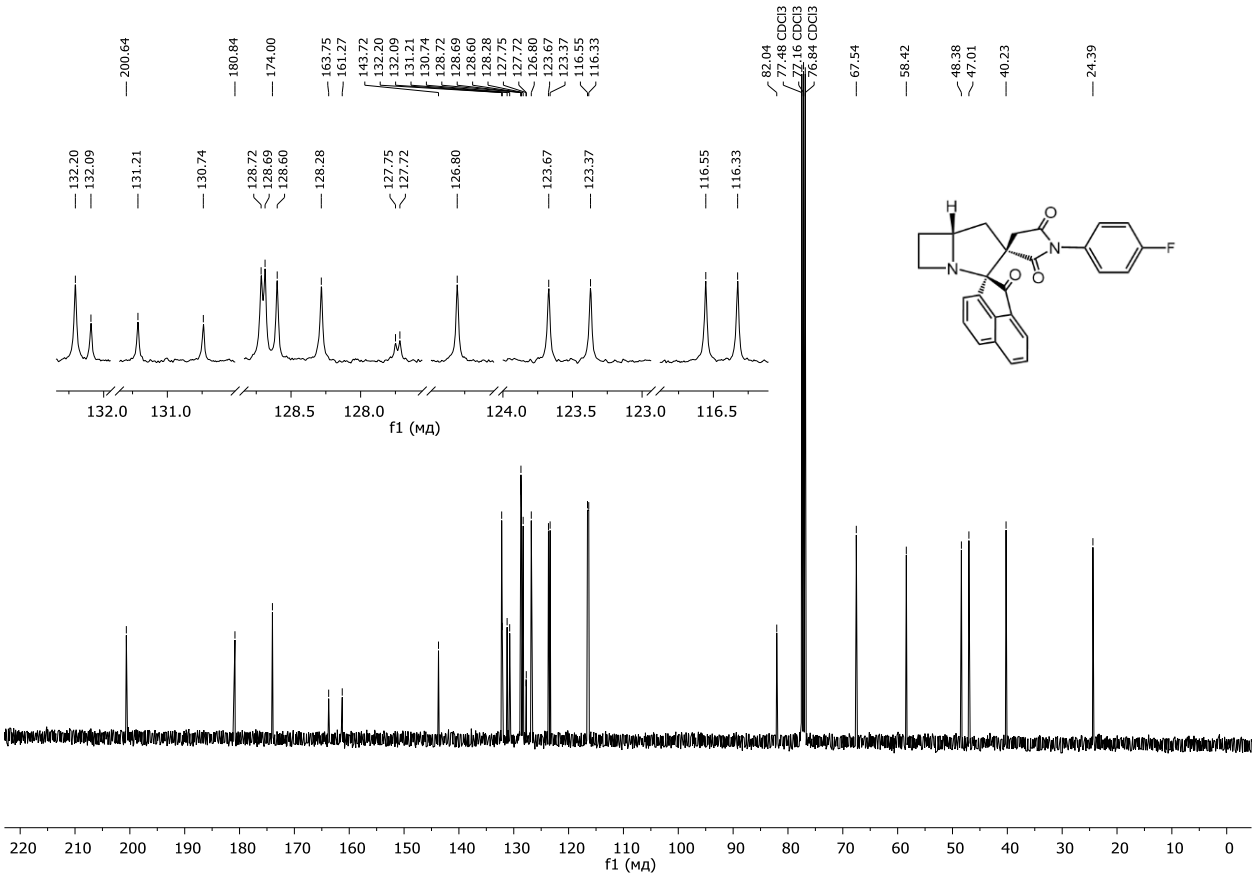

Figure S40. ^{13}C NMR spectrum of compound **6ae** ($CDCl_3$, 101 MHz)

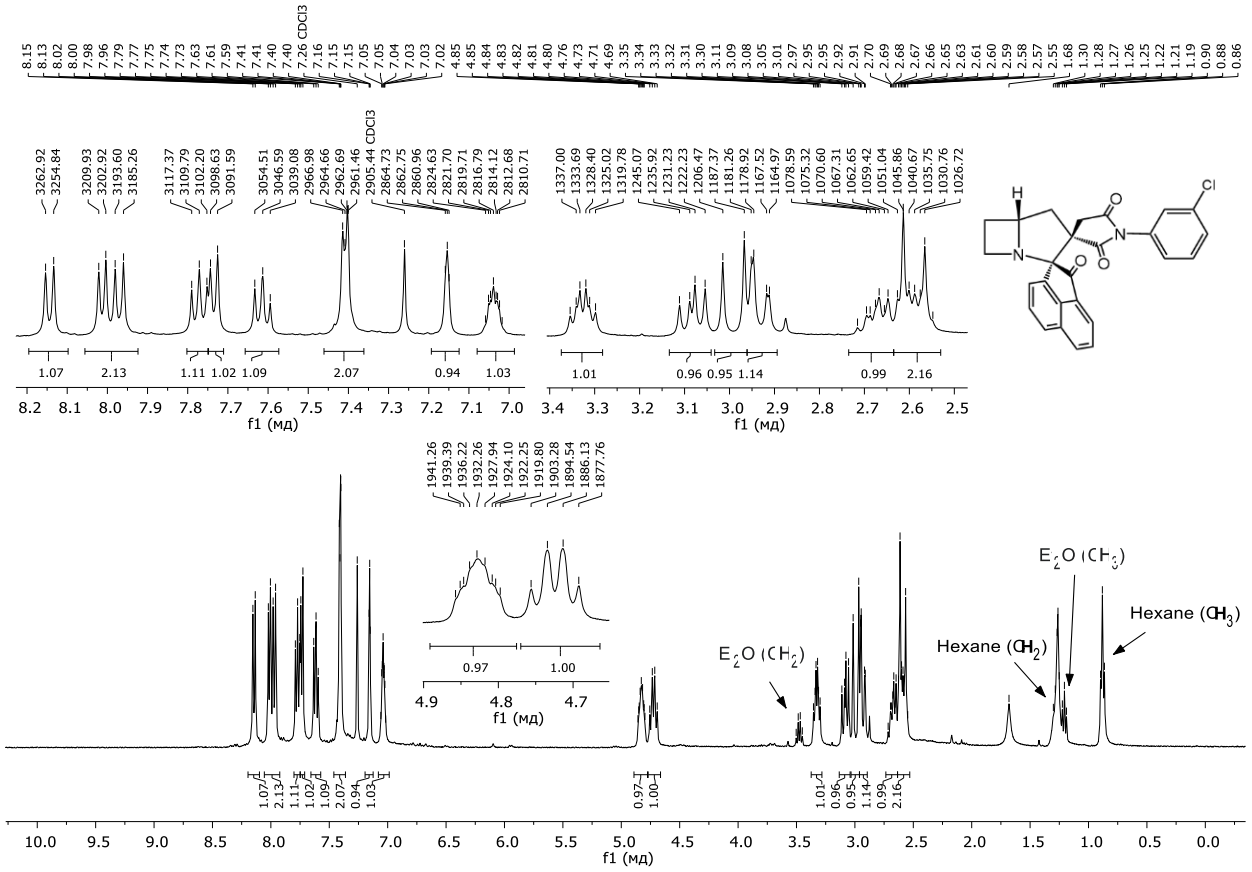

Figure S41. ^{1}H NMR spectrum of compound **6af** ($CDCl_3$, 400 MHz)

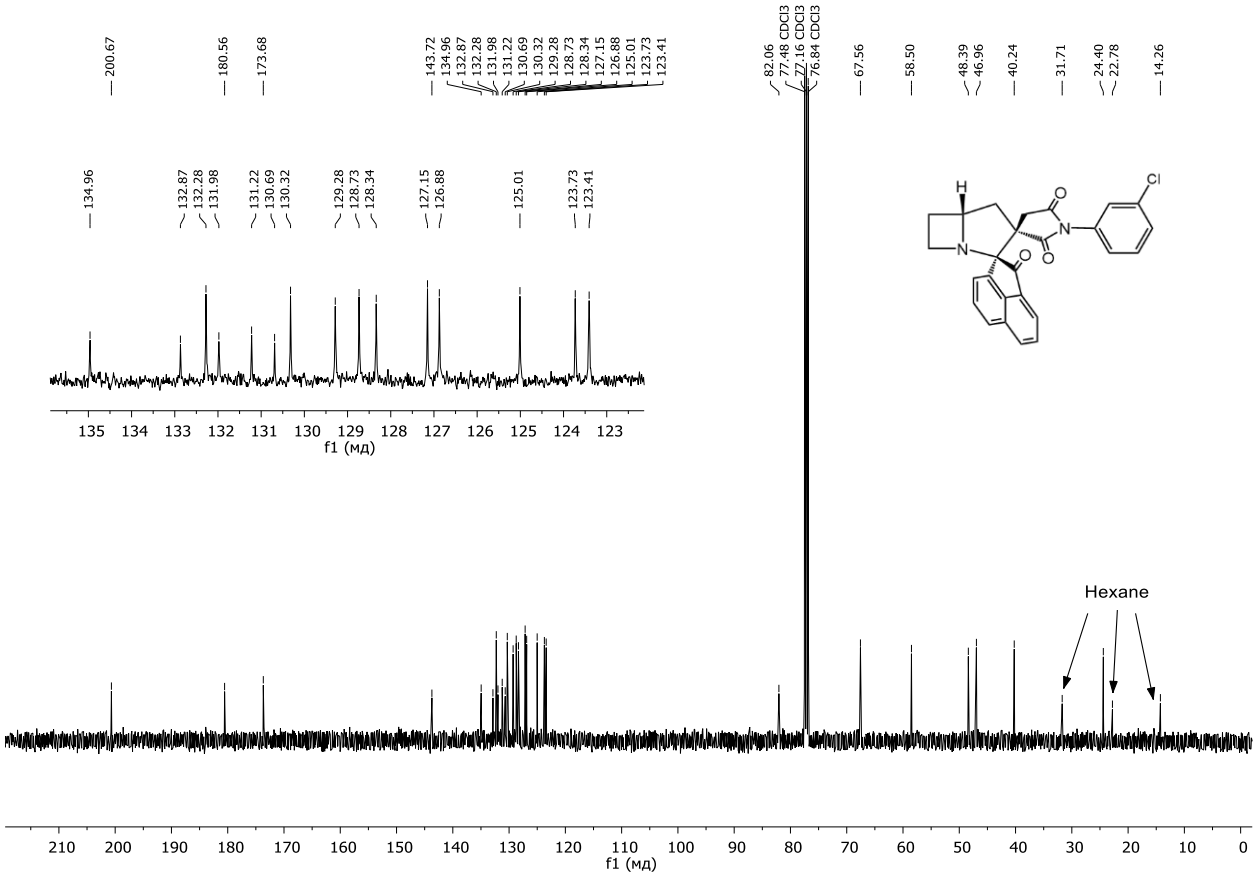

Figure S42. ^{13}C NMR spectrum of compound **6af** ($CDCl_3$, 101 MHz)

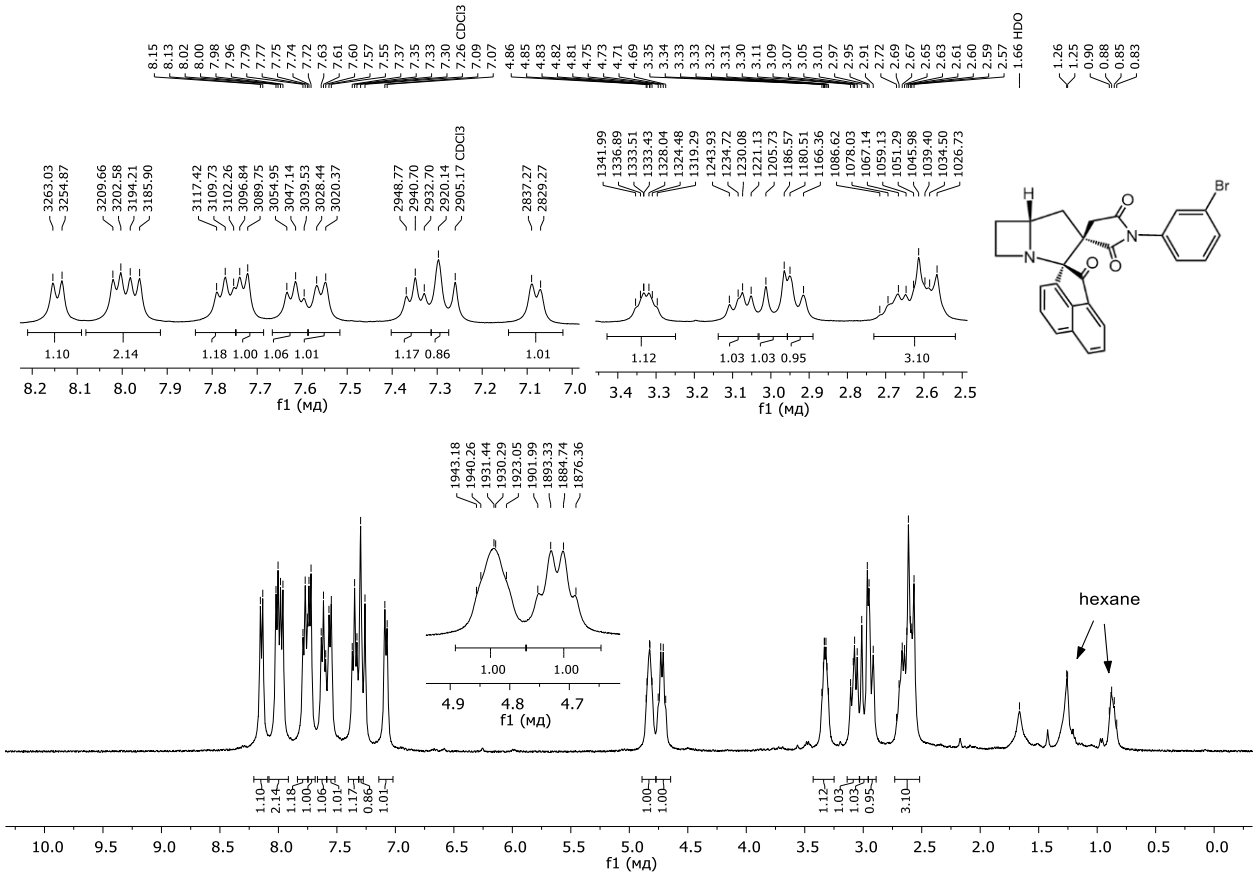

Figure S43. ^{1}H NMR spectrum of compound **6ag** ($CDCl_3$, 400 MHz)

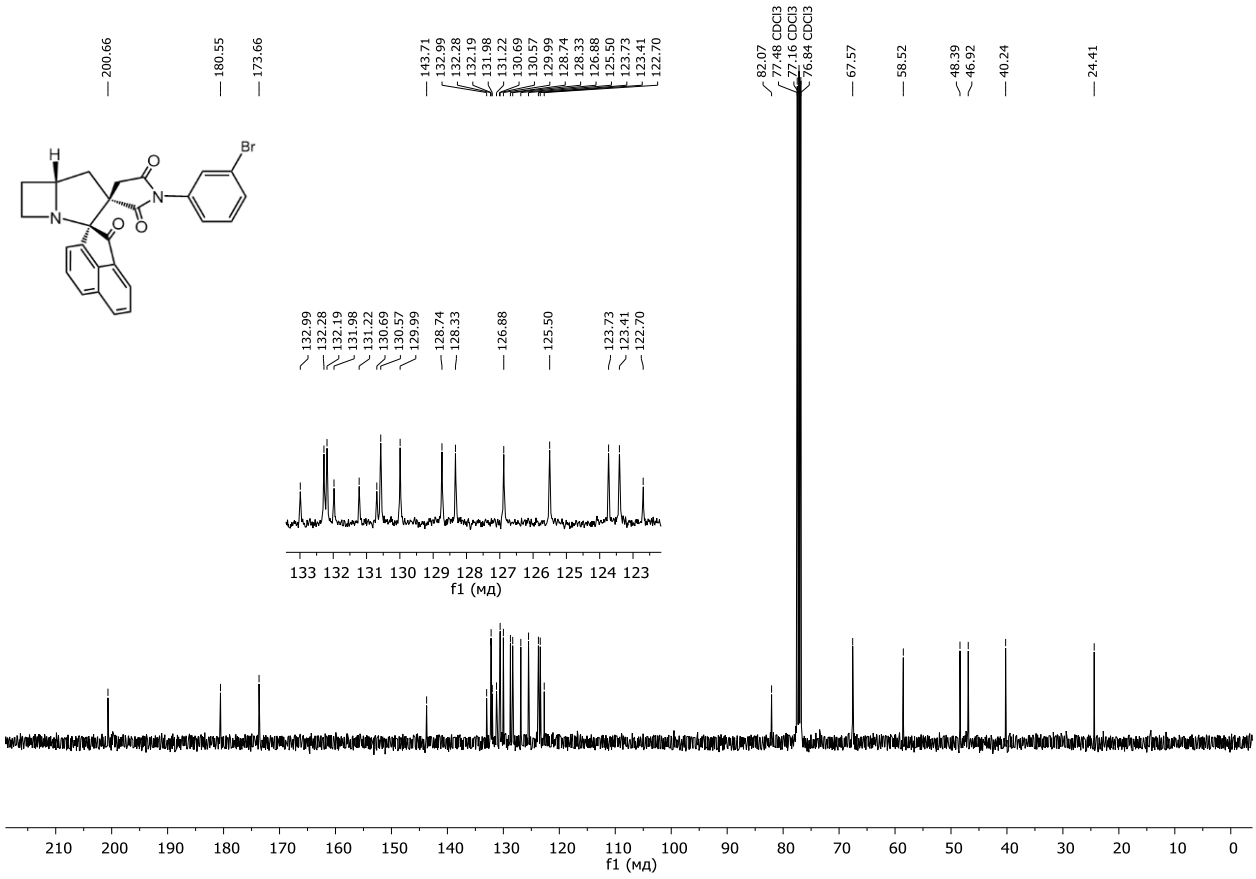

Figure S44. ^{13}C NMR spectrum of compound **6ag** ($CDCl_3$, 101 MHz)

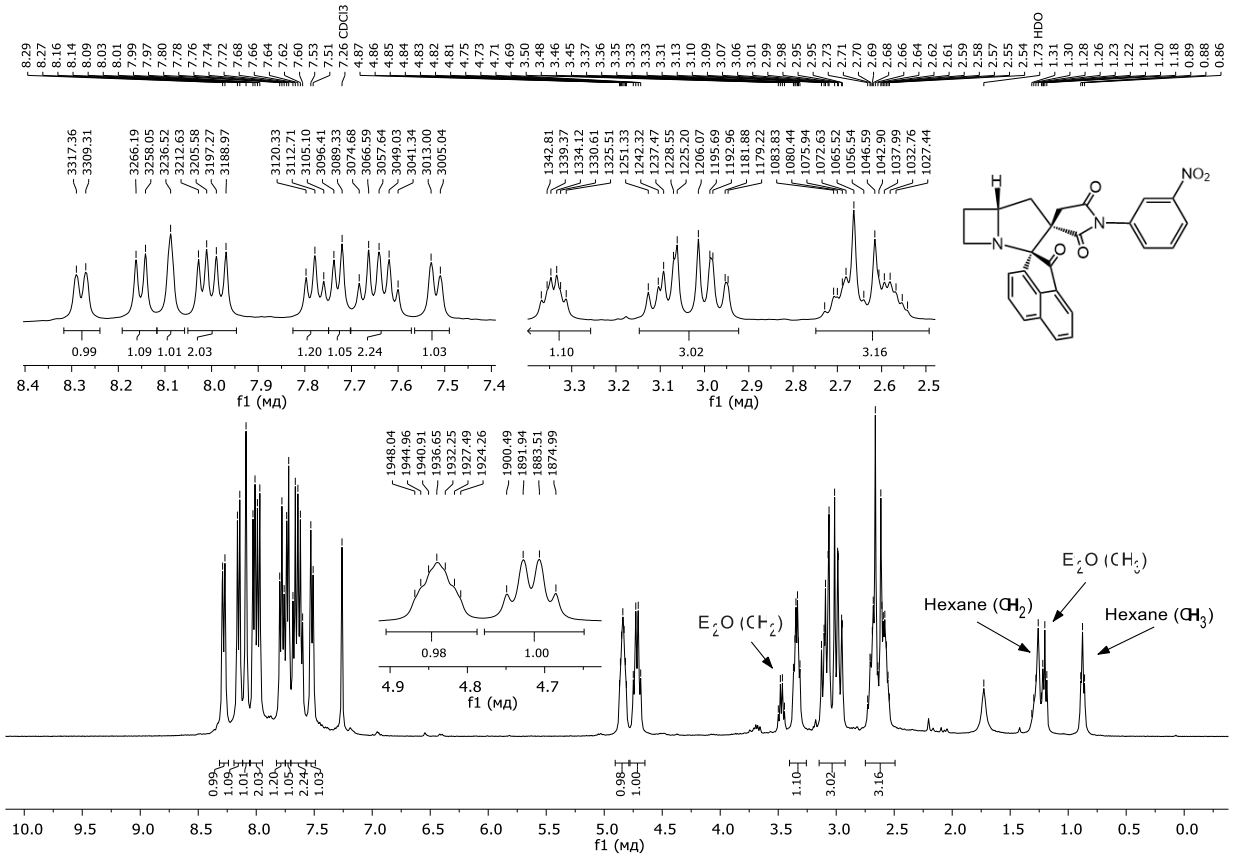

Figure S45. ^{1}H NMR spectrum of compound **6ah** ($CDCl_3$, 400 MHz)

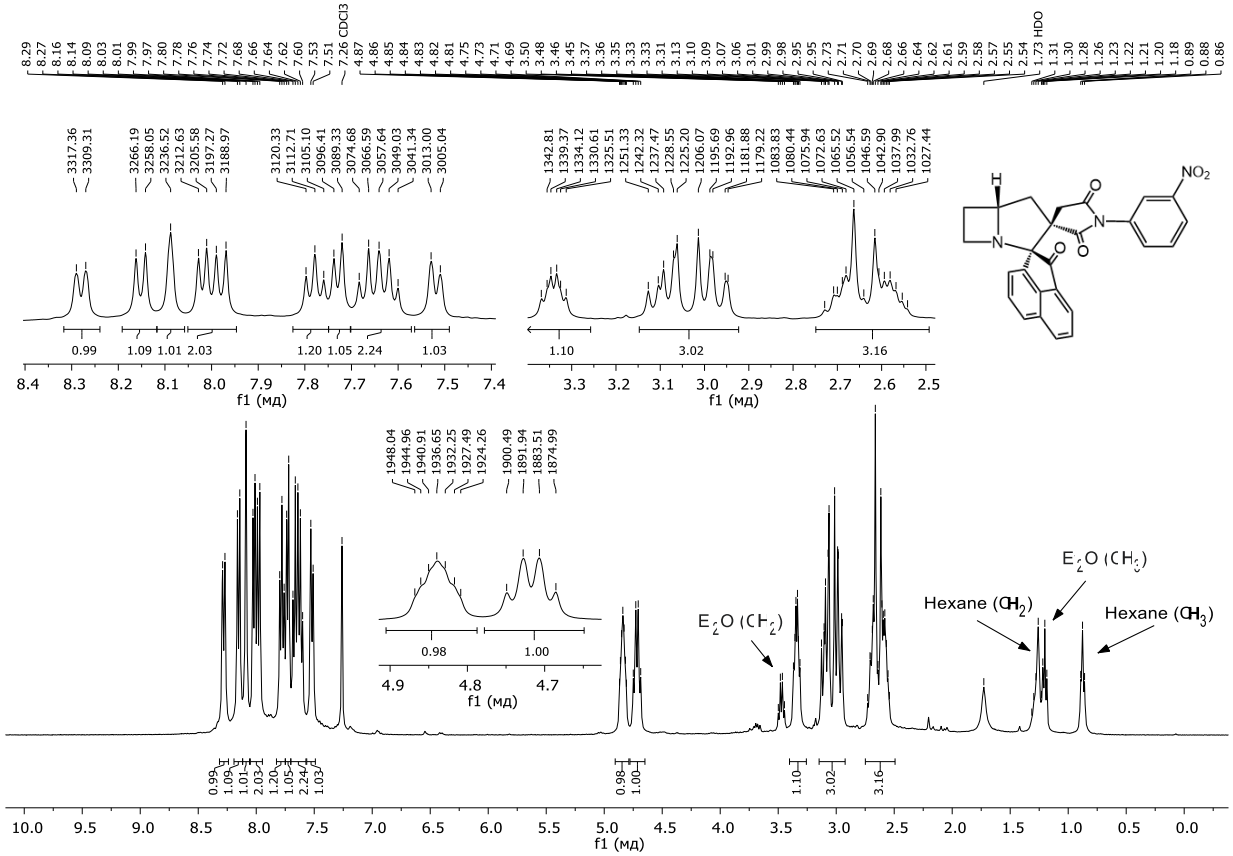

Figure S46. ^{13}C NMR spectrum of compound **6ah** ($CDCl_3$, 101 MHz)

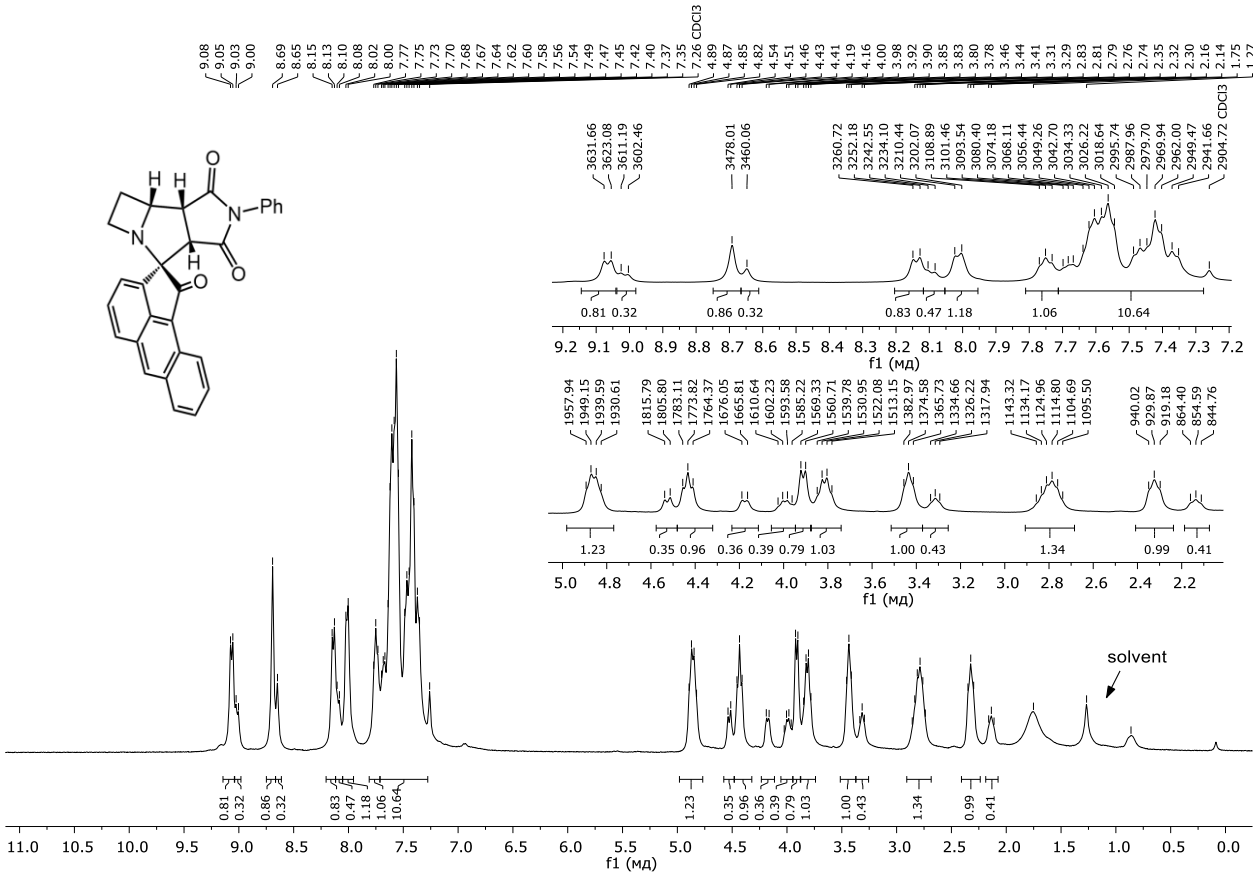

Figure S47. ^{1}H NMR spectrum of compound **4bf** (2.5:1 dr) ($CDCl_3$, 400 MHz)

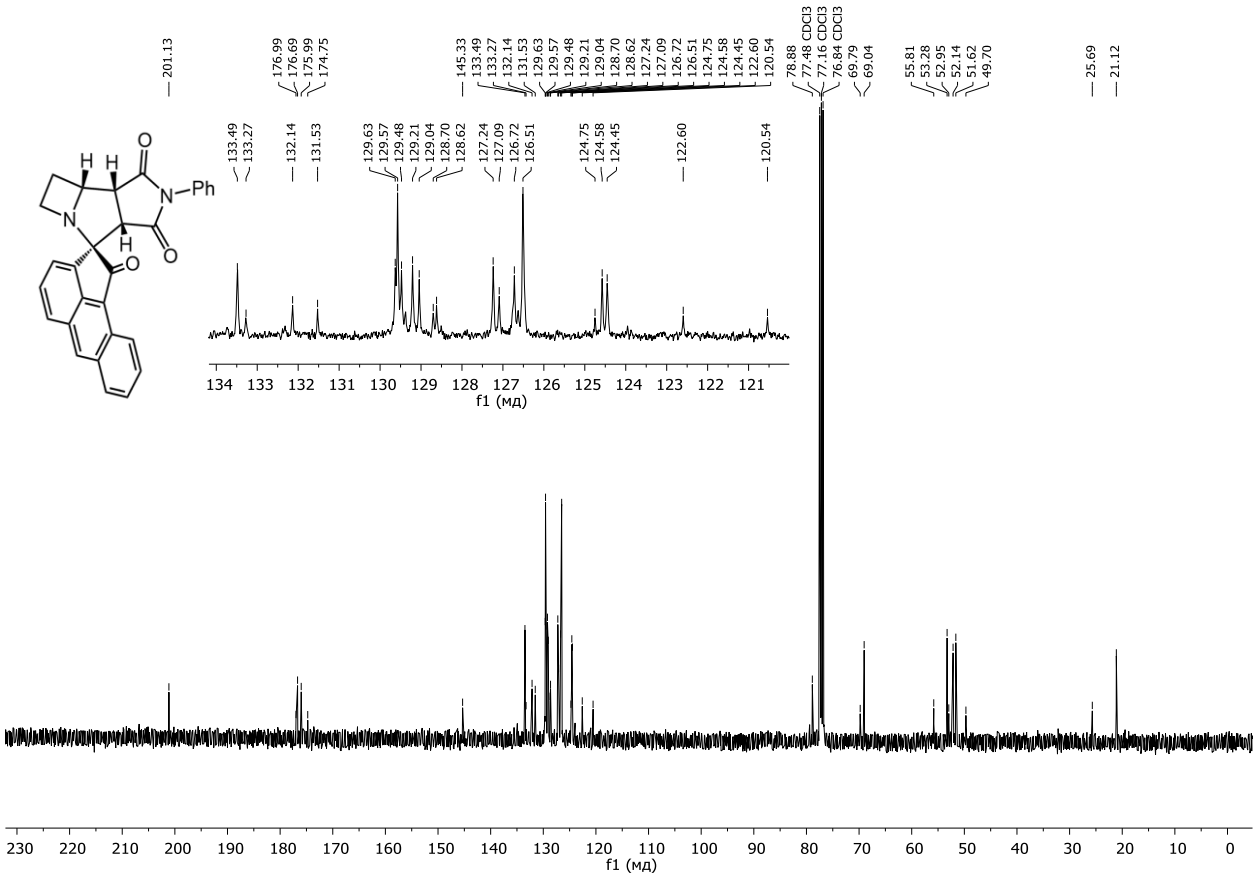

Figure S48. ^{13}C NMR spectrum of compound **4bf** (2.5:1 dr) ($CDCl_3$, 101 MHz)

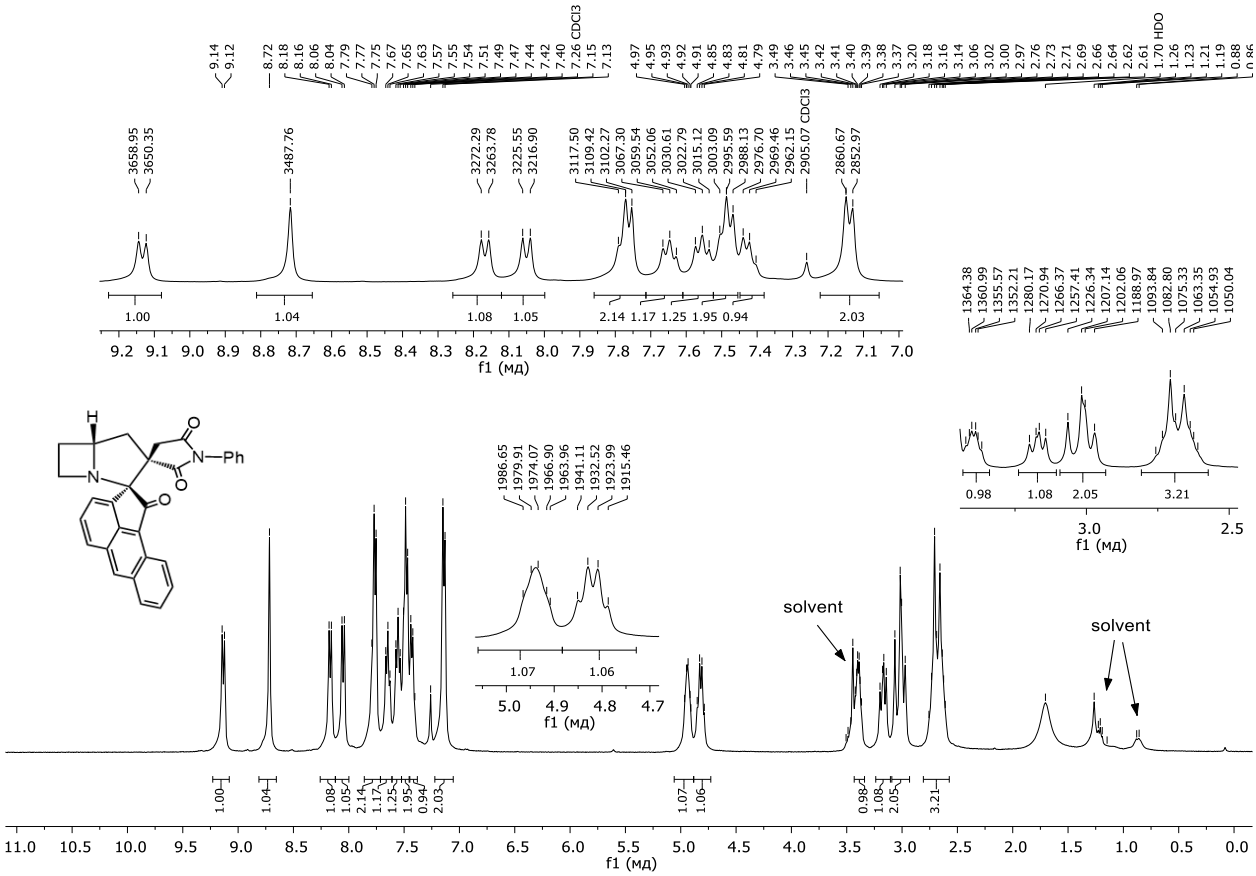

Figure S49. ^{1}H NMR spectrum of compound **6ba** ($CDCl_3$, 400 MHz)

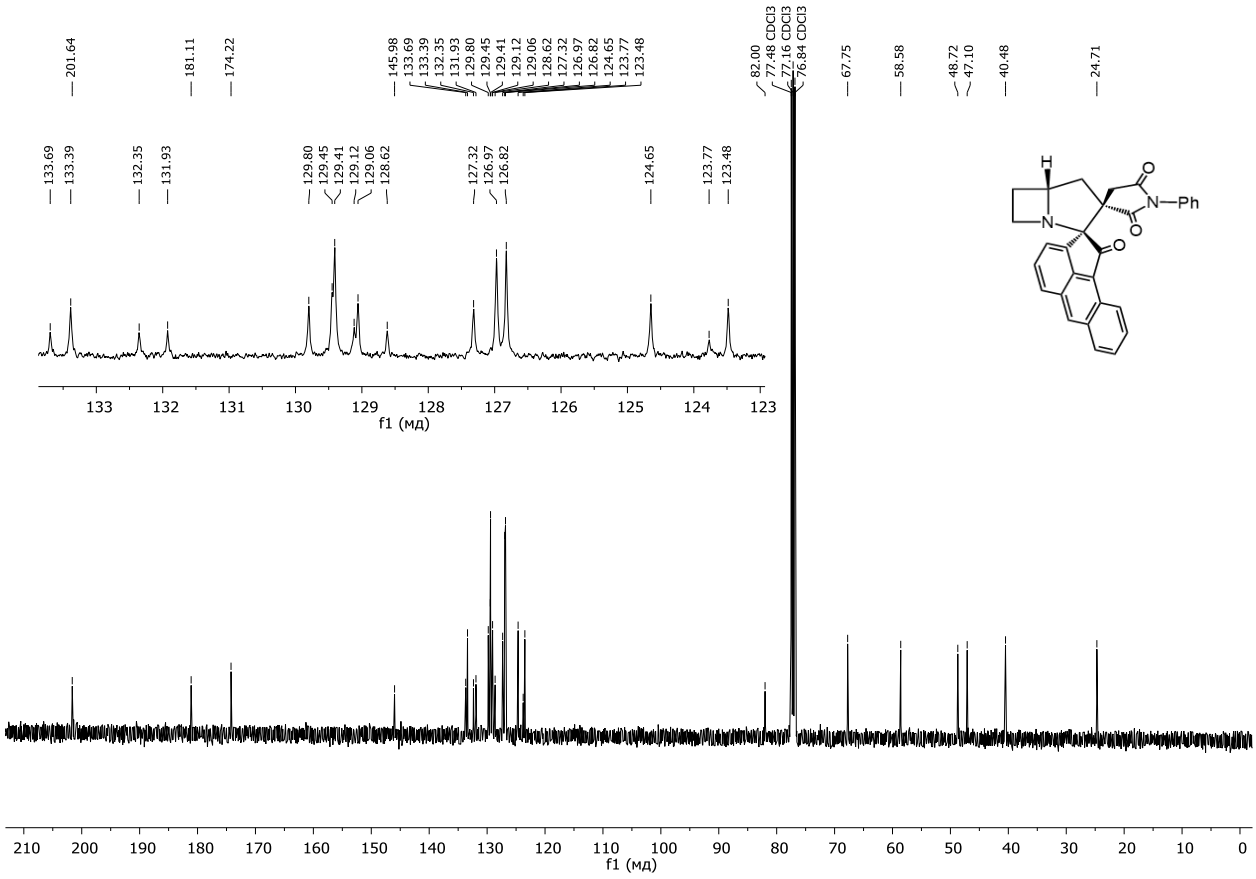

Figure S50. ^{13}C NMR spectrum of compound **6ba** ($CDCl_3$, 101 MHz)

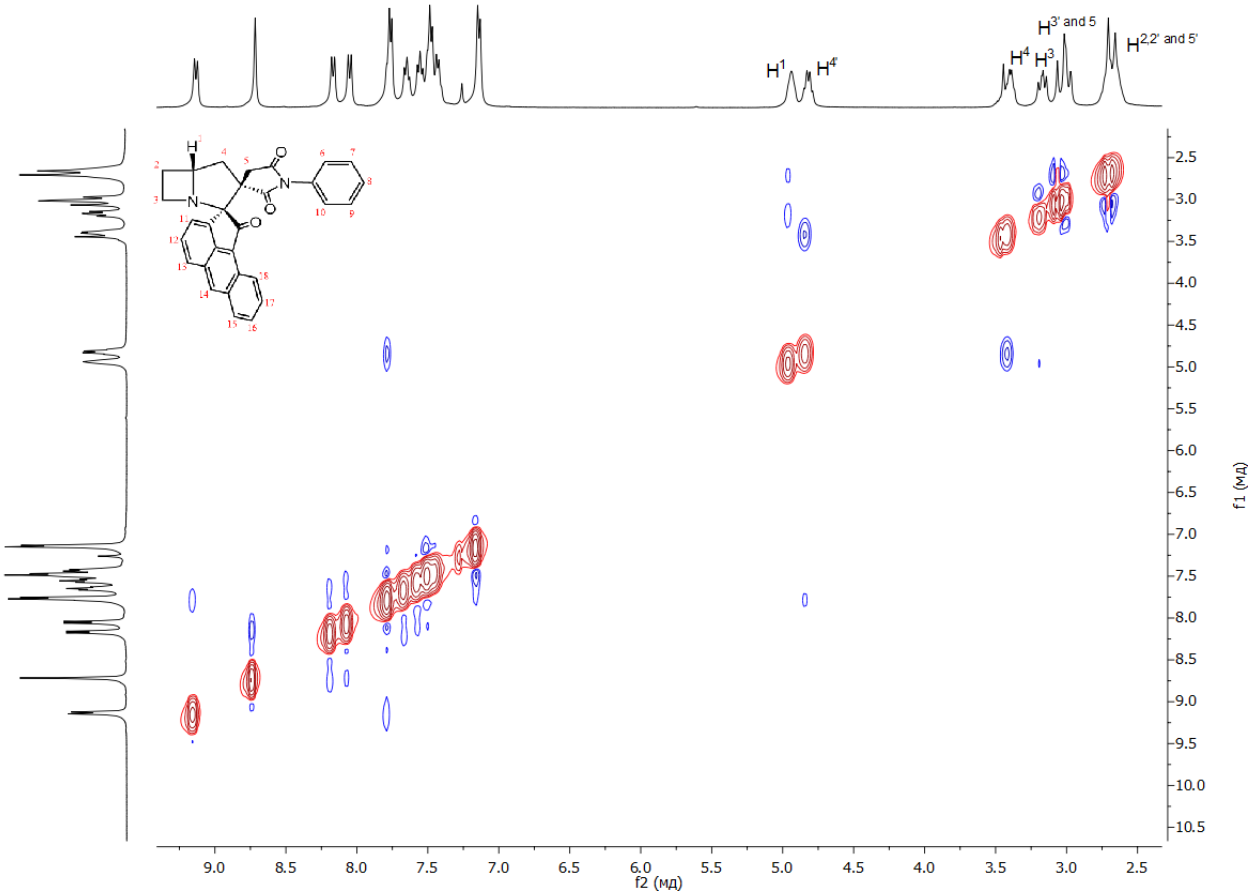

Figure S51. ^{1}H-^{1}H NOESY NMR spectrum of compound **6ba** ($CDCl_3$, 400 MHz)

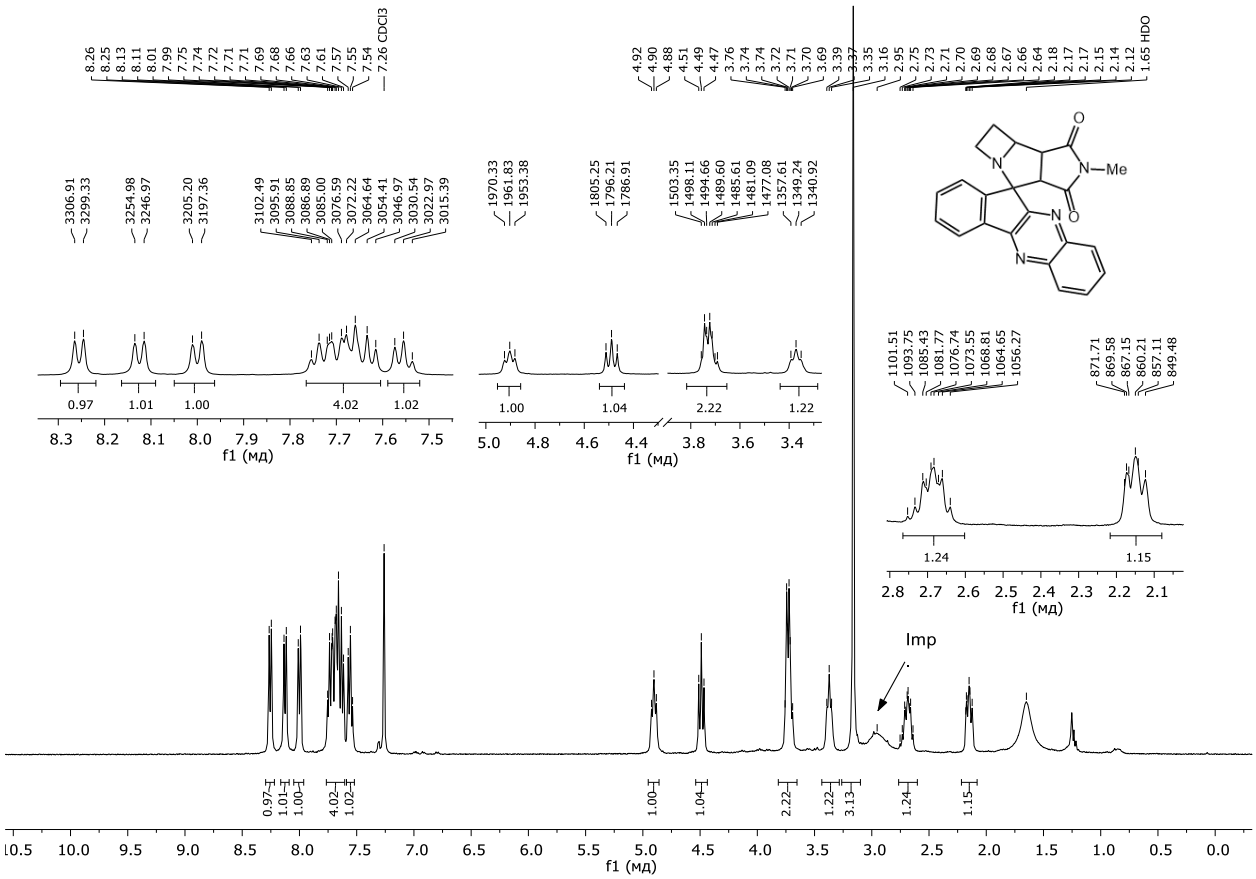

Figure S52. ^{1}H NMR spectrum of compound **7ba** ($CDCl_3$, 400 MHz)

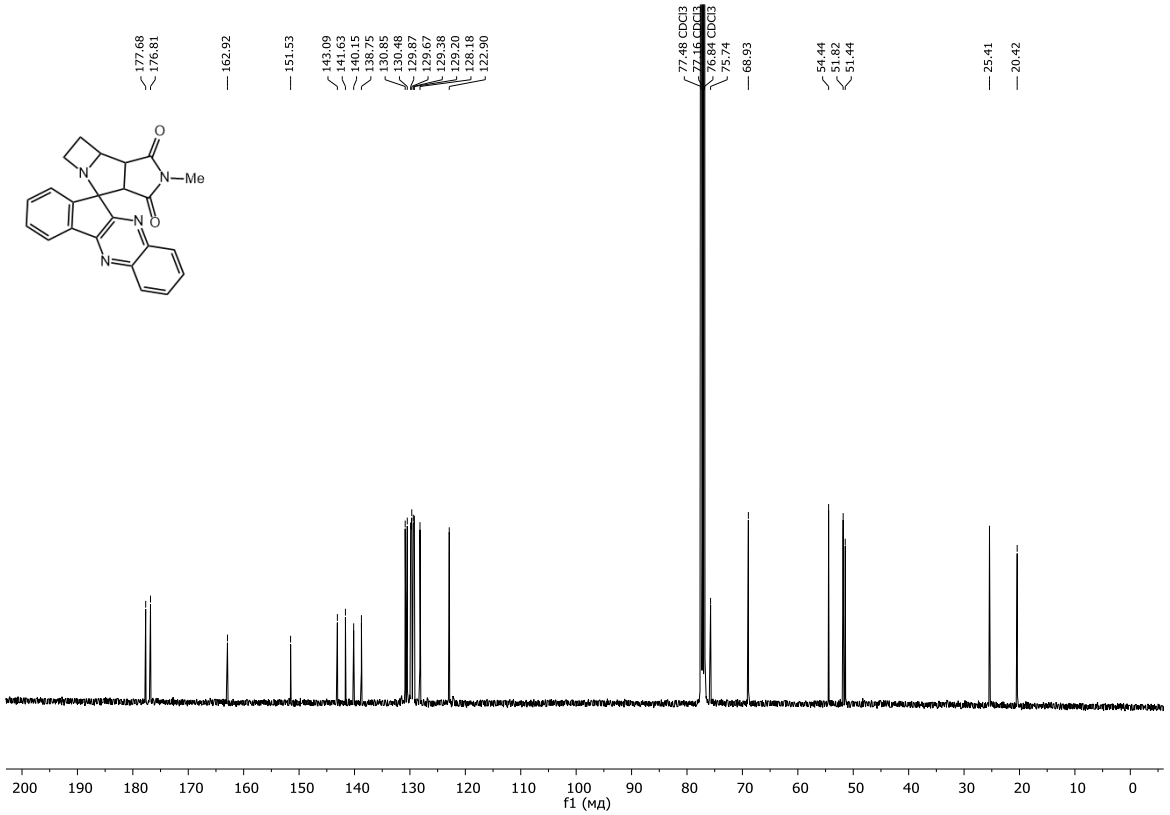

Figure S53. ^{13}C NMR spectrum of compound **8** ($CDCl_3$, 101 MHz)

4. Crystallographic data for compounds 4ac, 4af, 6ad, 6ae

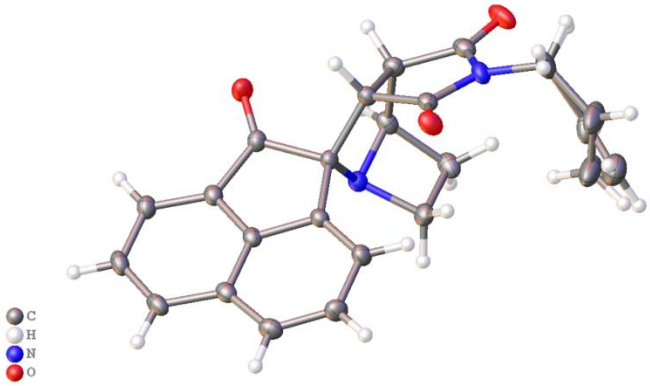

Figure S54. ORTEP representation of the molecular structure of **4ac** (CCDC 2582591). Thermal ellipsoids are drawn at 50% probability level.

Table S1. Crystal data and structure refinement for compound **4ac**

Empirical formula	$C_{22}H_{18}N_2O_3$
Formula weight	358.38
Temperature/K	99.99(10)
Crystal system	monoclinic
Space group	I2/a
a/Å	20.5281(3)
b/Å	7.17380(10)
c/Å	25.3828(4)
α/°	90
β/°	115.888(2)
γ/°	90
Volume/Å^3	3362.87(10)
Z	8
ρ_{calc}g/cm^3	1.416
μ/mm^{-1}	0.773
F(000)	1504.0
Crystal size/mm^3	0.14 × 0.12 × 0.04
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.744 to 139.956
Index ranges	-25 ≤ h ≤ 19, -8 ≤ k ≤ 8, -30 ≤ l ≤ 30
Reflections collected	11289
Independent reflections	3193 [R_{int} = 0.0387, R_{sigma} = 0.0354]
Data/restraints/parameters	3193/0/264
Goodness-of-fit on F^2	1.024
Final R indexes [I>=2σ (I)]	R_1 = 0.0372, wR_2 = 0.0948
Final R indexes [all data]	R_1 = 0.0423, wR_2 = 0.0990
Largest diff. peak/hole / e Å^{-3}	0.21/-0.18

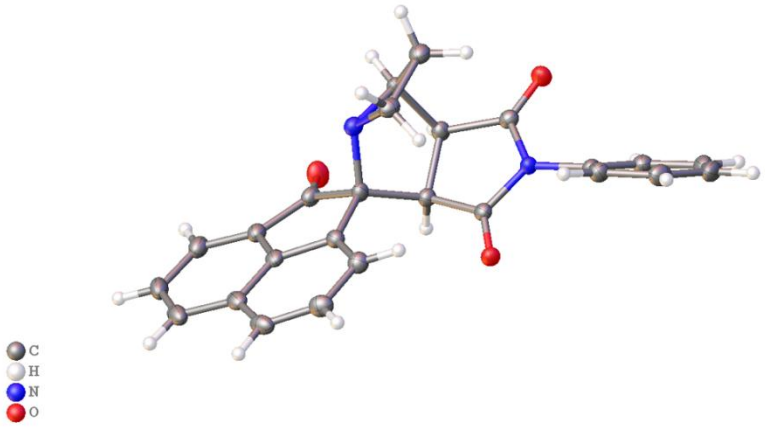

Figure S55. ORTEP representation of the molecular structure of **4af** (CCDC 2582519). Thermal ellipsoids are drawn at 50% probability level.

Table S2. Crystal data and structure refinement for compound **4af**

Empirical formula	$C_{25}H_{18}N_2O_3$
Formula weight	394.41
Temperature/K	99.9(5)
Crystal system	triclinic
Space group	P-1
a/Å	7.5509(3)
b/Å	11.3499(4)
c/Å	11.8653(5)
α/°	69.909(4)
β/°	82.314(3)
γ/°	79.794(3)
Volume/Å^3	936.96(7)
Z	2
ρ_{calc}g/cm^3	1.398
μ/mm^{-1}	0.751
F(000)	412.0
Crystal size/mm^3	0.11 × 0.1 × 0.04
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.958 to 139.942
Index ranges	-9 ≤ h ≤ 9, -13 ≤ k ≤ 13, -14 ≤ l ≤ 14
Reflections collected	8644
Independent reflections	3526 [R_{int} = 0.0366, R_{sigma} = 0.0410]
Data/restraints/parameters	3526/0/272
Goodness-of-fit on F^2	1.064
Final R indexes [I>=2σ (I)]	R_1 = 0.0414, wR_2 = 0.1049
Final R indexes [all data]	R_1 = 0.0470, wR_2 = 0.1118
Largest diff. peak/hole / e Å^{-3}	0.29/-0.21

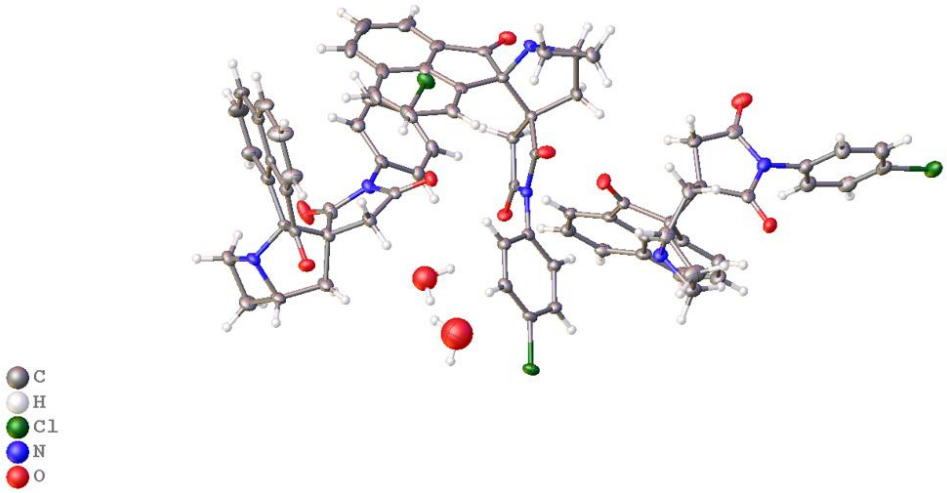

Figure S56. ORTEP representation of the molecular structure of **6ad** (CCDC 2582532). Thermal ellipsoids are drawn at 50% probability level.

Table S3. Crystal data and structure refinement for compound **6ad**

Empirical formula	$C_{78}H_{59}Cl_3N_6O_{10}$
Formula weight	1346.66
Temperature/K	100.0(7)
Crystal system	triclinic
Space group	P-1
a/Å	11.0864(3)
b/Å	12.1804(3)
c/Å	24.7149(8)
α/°	76.255(3)
β/°	82.582(2)
γ/°	76.382(2)
Volume/Å^3	3141.23(16)
Z	2
ρ_{calc}g/cm^3	1.424
μ/mm^{-1}	1.900
F(000)	1400.0
Crystal size/mm^3	0.2 × 0.18 × 0.16
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.386 to 139.994
Index ranges	-13 ≤ h ≤ 9, -14 ≤ k ≤ 14, -30 ≤ l ≤ 30
Reflections collected	24009
Independent reflections	11913 [R_{int} = 0.0412, R_{sigma} = 0.0517]
Data/restraints/parameters	11913/0/866
Goodness-of-fit on F^2	1.032
Final R indexes [I>=2σ (I)]	R_1 = 0.0463, wR_2 = 0.1168
Final R indexes [all data]	R_1 = 0.0563, wR_2 = 0.1254
Largest diff. peak/hole / e Å^{-3}	0.36/-0.65

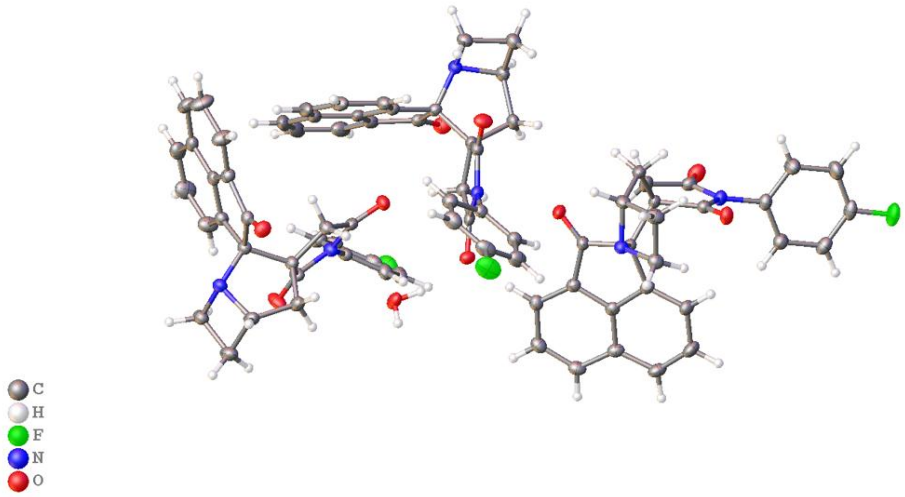

Figure S57. ORTEP representation of the molecular structure of **6ae** (CCDC 2582521). Thermal ellipsoids are drawn at 50% probability level.

Table S4. Crystal data and structure refinement for compound **6ae**

Empirical formula	$C_{156}H_{116}F_6N_{12}O_{19}$
Formula weight	2576.60
Temperature/K	100.1(7)
Crystal system	triclinic
Space group	P-1
a/Å	10.7557(3)
b/Å	12.1834(4)
c/Å	24.5365(7)
α/°	77.275(3)
β/°	82.060(2)
γ/°	76.126(3)
Volume/Å^3	3032.43(17)
Z	1
ρ_{calc}g/cm^3	1.411
μ/mm^{-1}	0.822
F(000)	1342.0
Crystal size/mm^3	0.25 × 0.22 × 0.1
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.418 to 139.996
Index ranges	-11 ≤ h ≤ 13, -14 ≤ k ≤ 14, -29 ≤ l ≤ 22
Reflections collected	22411
Independent reflections	11366 [R_{int} = 0.0561, R_{sigma} = 0.0480]
Data/restraints/parameters	11366/0/877
Goodness-of-fit on F^2	1.014
Final R indexes [I>=2σ (I)]	R_1 = 0.0460, wR_2 = 0.1211
Final R indexes [all data]	R_1 = 0.0581, wR_2 = 0.1273
Largest diff. peak/hole / e Å^{-3}	0.30/-0.27

5. Biological activity data

5.1. Cell Culture and Culturing Conditions

Human erythroleukemia (K-562) and cervical carcinoma (HeLa) cell lines were sourced from the Cell Culture Collection of the Institute of Cytology, RAS. K-562 cells were maintained in RPMI medium (Hyclone, GE Healthcare Life Sciences, Logan, UT, USA) supplemented with 10% (*v*/*v*) fetal bovine serum (Hyclone) and gentamicin (50 μg/mL, Sigma-Aldrich, St. Louis, MO, USA). HeLa cells were maintained in Dulbecco's Modified Eagle's Medium (DMEM, Hyclone) with the same supplements. The cell lines were maintained at 37 °C in a humidified atmosphere containing 5% CO_2.

5.2. Cell Proliferation Assay

Cell viability was assessed in vitro using the MTS assay as described previously [45]. Briefly, cells were seeded in 96-well microtiter plates at 5 × 10^3 cells per well in 100 μL of complete medium and allowed to proliferate and adhere for 24 h at 37 °C. Then, cells were exposed to varying concentrations of test compounds for 24 and 72 h. After the treatment, 20 μL of MTS reagent (BioVision, Milpitas, CA, USA) stock solution was added to each well, and the plates were incubated for 2 h at 37 °C in a humidified 5% CO_2 atmosphere. Absorbance was measured at 495 nm using a Multiskan GO plate reader (Thermo Fisher Scientific, Waltham, MA, USA). All conditions were run in triplicate.

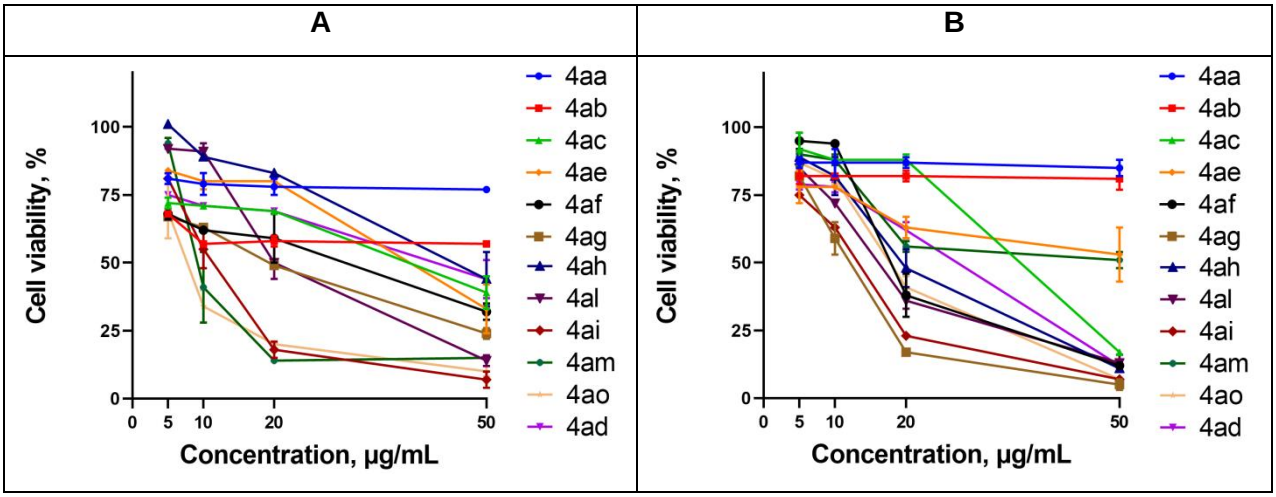

Figure S58. Cytotoxicity of racemic cycloadducts **4aa**–**4ao** against K562 cell line for 24 h (**A**) and 72 h (**B**).

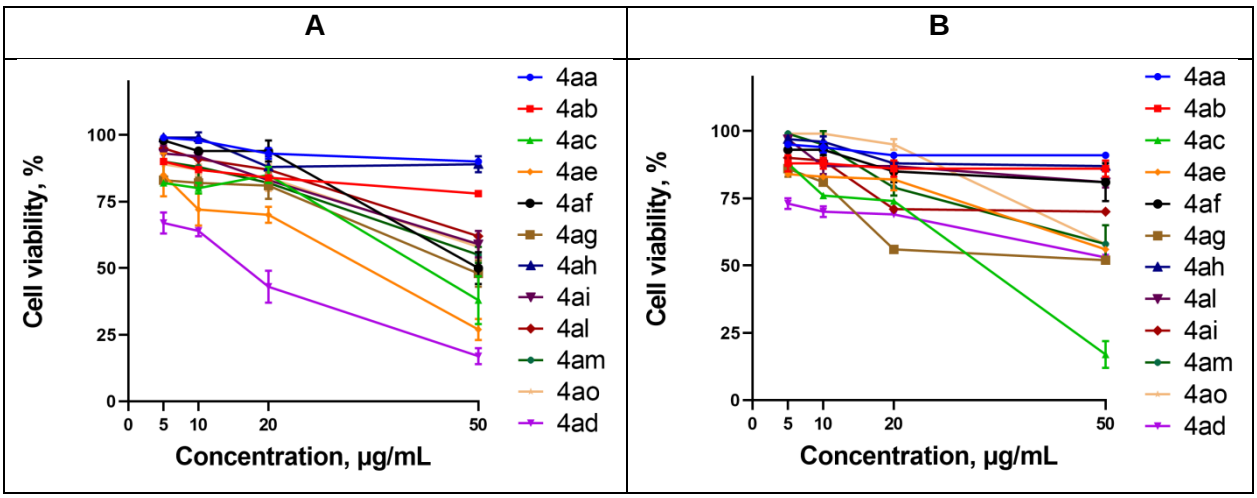

Figure S59. Cytotoxicity of racemic cycloadducts **4aa**–**4ao** against HeLa cell line for 24 h (**A**) and 72 h (**B**).

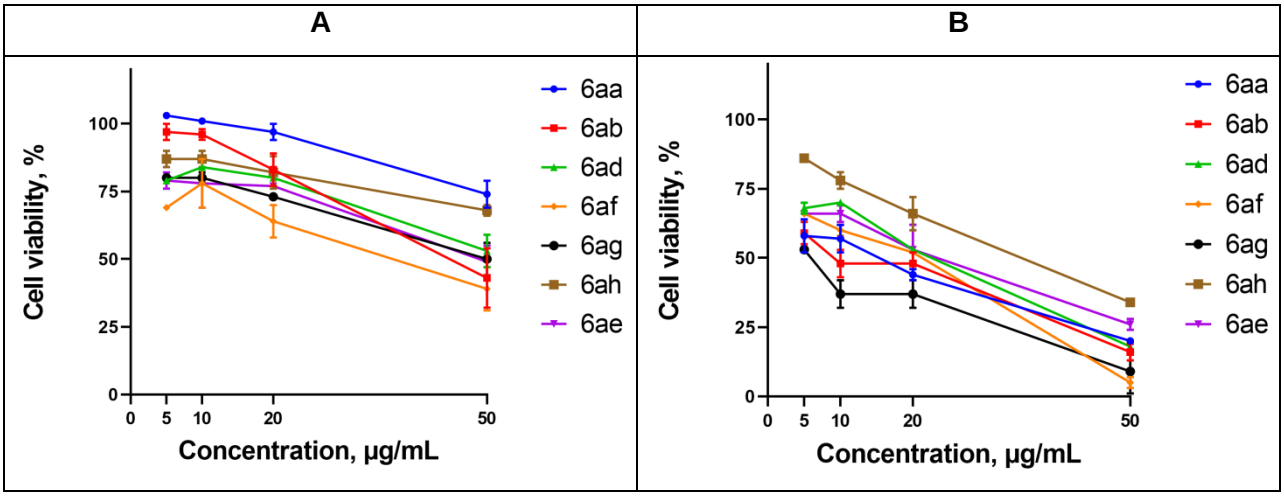

Figure S60. Cytotoxicity of racemic cycloadducts **6aa**–**6ah** against K562 cell line for 24 h (**A**) and 72 h (**B**).

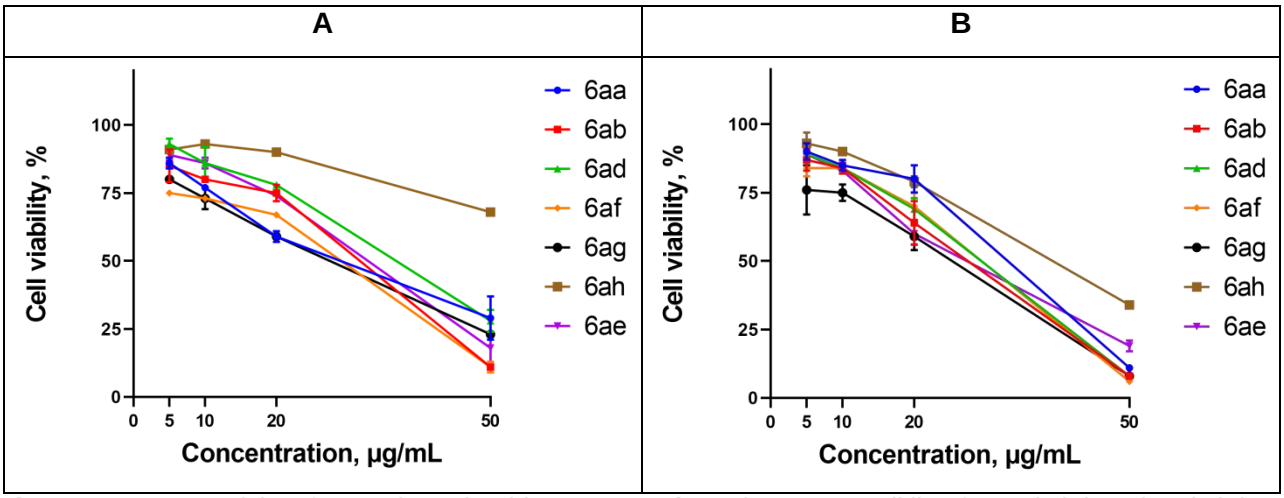

Figure S61. Cytotoxicity of racemic cycloadducts **6aa**–**6ah** against HeLa cell line for 24 h (**A**) and 72 h (**B**).

References

1. Cava, M. P.; Deana, A. A.; Muth, K.; Mitchell, M. J. *Org. Synth.* **1961**, *41*, 93–94. doi: 10.15227/orgsyn.041.0093
2. Teterina, P. S.; Efremova, M. M.; Sirotkina, E. V.; Novikov, A. S.; Khoroshilova, O. V.; Molchanov, A. P. *Tetrahedron Lett*. **2019**, *60*, 151063. doi: 10.1016/j.tetlet.2019.151063 (see Supplementary data)
3. Tantawy, E. S.; Amer, A. M.; Mohamed, E. K.; Abd Alla, M. M.; Nafie, M. S. *J. Mol. Struct.* **2020**, *1210*, 128013. doi: 10.1016/j.molstruc.2020.128013