Supplementary Information

Stereoselective assembly of 3,4-epoxypyrrolines via nucleophilic addition induced domino cyclization of 6-halo-1-oxa-4-azahexatrienes

Ilia A. Smetanin,[a] Anastasiya V. Agafonova,[a] Nikolai V. Rostovskii,[a] Alexander F. Khlebnikov,[a] Dmitry S. Yufit[b] and Mikhail S. Novikov*[a]

[a] St. Petersburg State University, Institute of Chemistry, 7/9 Universitetskaya nab., St. Petersburg, 199034, Russia.

[b] University of Durham, Department of Chemistry, South Road, Durham DH1 3LE, U.K.

Email: m.novikov@spbu.ru

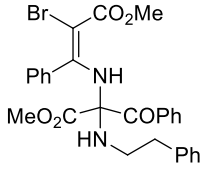
Table of Contents

1. General experimental details

All solvents were distilled and dried prior to use. 1,2-Dichloroethane (DCE) and dichloromethane were washed with concentrated H_2SO_4, water, then distilled from P_2O_5 and stored over anhydrous K_2CO_3. Melting points were determined on a hot stage microscope and are uncorrected. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded on a Bruker AVANCE 400 spectrometer in solvent indicated below. Chemical shifts (δ) are reported in ppm downfield from tetramethylsilane. IR spectra were recorded on a Shimadzu IR Affinity-1 spectrophotometer in KBr. Crystallographic data for the structures **5c** (CCDC 1936159), **6b** (CCDC 1936158), **13** (CCDC 1936916) have been deposited with the Cambridge Crystallographic Data Centre. Photochemical experiments were carried out with a mercury lamp Tungsram HGOK 400 (main radiation bands 310, 360, 365 nm). Column chromatography was performed on silica gel 60 M (0.04–0.063 mm). Thin-layer chromatography (TLC) was conducted on aluminum sheets precoated with SiO_2 ALUGRAM SIL G/UV254. 2*H*-Azirines **1a**–**d**,**f**,[1] **1e**,[2] **1g**,[3] **1h**,[4] **1i**[5] diazo compounds **2a**,[6] **2b**,**c**,**e**,**f**,**i**,[7] **2d**,[8] **2g**,[9] **2h**[10] and oxazatrienes **3a**–**e**,**zb**,**zc** [4] were prepared by the reported procedures.

2. Synthesis of aminal 4a

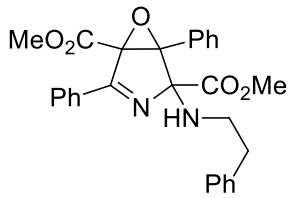
Methyl (*E*)-2-bromo-3-{[1-methoxy-1,3-dioxo-2-(phenethylamino)-3-phenylpropan-2-yl]-amino}-3-phenylacrylate (4a)



To a solution of oxazatriene **3a** (129 mg, 0.3 mmol) in anhydrous CH_2Cl_2 (2 mL) a solution of 2-phenylethan-1-amine (40 mg, 0.33 mmol) in CH_2Cl_2 (1 mL) was added dropwise under stirring. The mixture was stirred at room temperature for 30 min, the solvent was removed under reduced pressure, and the residue was purified by column chromatography (hexane/EtOAc, 5:1) to give **4a** (147 mg, 89%) as a colorless solid. M.p. 88–89 °C (Et_2O–hexane). ^{1}H NMR (300 MHz, C_6D_6) δ 2.50–2.66 (m, 2H), 2.89–3.07 (m, 5H), 3.63 (s, 3H), 6.61 (d, 2H, *J* 7.3 Hz), 6.84–6.96 (br. s, 1H), 6.99–7.24 (m, 12H), 8.33–8.36 (m, 2H), 11.68 (s, 1H). ^{13}C NMR (75 MHz, C_6D_6) δ 36.4, 43.1, 52.0, 52.6, 80.4, 85.0, 126.5, 128.5, 128.8, 129.1, 129.4, 129.9, 130.1, 133.4, 134.0, 135.8, 139.9 (signal of one carbon is overlapped), 160.6, 167.8, 169.4, 189.2. HRMS–ESI: $[M + H]^+$ calcd for $C_{28}H_{28}{}^{79}BrN_2O_5^+$ $[M+H]^+$: 551.1176; found 551.1178.

3. Synthesis of epoxypyrrolines 5

3.1. Synthesis of dimethyl 2,5-diphenyl-4-(2-phenylethyl)-6-oxa-3-azabicyclo[3.1.0]hex-2-ene-1,4-dicarboxylate (5a)



To a solution of oxazatriene **3a** (129 mg, 0.3 mmol) in anhydrous CH_2Cl_2 (2 mL) a solution of 2-phenylethan-1-amine (40 mg, 0.33 mmol) in CH_2Cl_2 (1 mL) was added dropwise under stirring. The mixture was stirred at room temperature for 30 min and the solvent was removed under reduced pressure. The residue was dissolved in anhydrous acetonitrile (5 mL) and dry K_2CO_3 (124 mg, 0.9 mmol) was added. The resulting mixture was refluxed for 1 h under stirring. The reaction mixture was washed with water (10 mL) and the aqueous layer was extracted with CH_2Cl_2 (2×5 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (hexane/EtOAc, from 10:1 to 4:1) to give **5a** (89 mg, 63%) as a colorless oil (unseparated mixture of diastereomers 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.18 (br. s, 1H), 2.52 (br. s, 1H), 2.70–2.98 (m, 2H), 3.05–3.35 (m, 2H), 3.57 (s, 3H), 3.67 and 3.69 (2 s, 6H), 3.80 (s, 3H), 7.10–7.64 (m, 13H), 7.82 (d, 2H, *J* 7.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 36.7, 37.1, 45.1, 45.5, 52.6, 52.7, 52.82, 52.83, 67.8, 69.8, 75.2, 78.7, 91.4, 92.9, 126.0, 126.1, 127.9, 128.0, 128.1, 128.16, 128.23, 128.3, 128.5, 128.67, 128.7, 128.8, 128.9, 129.2, 129.4, 129.5, 131.6, 131.75, 131.8, 139.2, 139.7 (signals of three carbons are overlapped), 164.3, 164.9, 168.0, 169.7, 172.3, 172,4. HRMS–ESI: $[M + H]^+$ calcd for $C_{28}H_{27}N_2O_5^+$ $[M+H]^+$: 471.1914; found 471.1905.

3.2. General procedures for the preparation of epoxypyrrolines 5b–5zb

Procedure A (from oxazatrienes 3)

To a solution of oxazatrienes **3a–e** (0.3 mmol) in anhydrous CH_2Cl_2 (2 mL) a solution of nucleophile (quantities are indicated below) in CH_2Cl_2 (1 mL) was added dropwise under stirring. The mixture was stirred at room temperature for 24 h, the solvent was removed under reduced pressure and the residue was purified by column chromatography to give pure epoxypyrroline **5b**–**g**,**j**–**z**. In the case of compounds **5h**,**i**,**5za** the reaction mixture was washed with water (2×1 mL), the organic layer was dried over Na_2SO_4, the solvent was removed under reduced pressure and the residue was crystallized from hexane/Et_2O/CH_2Cl_2 mixture to give pure **5h**,**i**,**5za**.

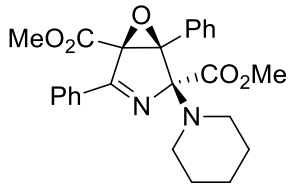
Procedure B (from azirines 1)

To a solution of diazo compound **2a–h** (quantities are indicated below) and azirine **1a–i** (0.5 mmol) in anhydrous 1,2-dichloroethane (1.5 mL) at reflux under argon $Rh_2(OAc)_4$ (2 mol %) was added. The stirred mixture was heated under reflux until nitrogen evolution stopped. The resulting mixture was evaporated under reduced pressure, and the residue was filtered through a pad of silica gel using toluene/EtOAc 30:1 mixture as eluent. The filtrate was concentrated under reduced pressure, and the residue was dissolved in anhydrous CH_2Cl_2 (5 mL). A solution of nucleophile (quantities are indicated below) in CH_2Cl_2 (1.5 mL) was added dropwise to the resulting mixture under stirring. The mixture was stirred at room temperature for 24 h, the solvent was removed under reduced pressure and the residue was purified by column chromatography to give epoxypyrroline **5b–5za**.

Procedure C (from halohydrins 6)

To a solution of halohydrin **6a**–**d** (0.3 mmol) in anhydrous CH_2Cl_2 (3 mL) under stirring 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (91 mg, 0.6 mmol) was added. The reaction mixture was stirred at room temperature for 12 h, then washed with water (2×1 mL), the organic layer was dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was crystallized from Et_2O/hexane mixture to give epoxypyrroline **5b**,**d**,**z**,**zb**.

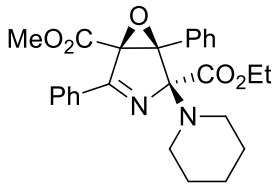
Dimethyl *rac*-(1*R*,4*R*,5*S*)-5-methyl-2-phenyl-4-(piperidin-1-yl)-6-oxa-3-azabicyclo-[3.1.0]hex-2-ene-1,4-dicarboxylate (5b)



Compound **5b** (124 mg, 95%) was obtained as a colorless solid according to procedure A from oxazatriene **3a** (129 mg, 0.3 mmol) and piperidine (77 mg, 0.9 mmol) using hexane/EtOAc mixture (from 5:1 to 2:1) as eluent for chromatography. Compound **5b** (174 mg, 80%) was also obtained according to procedure B from azirine **1a** (127 mg, 0.5 mmol), diazo compound **2a** (714 mg, 3.5 mmol) and piperidine (128 mg, 1.5 mmol) using hexane/EtOAc mixture (from 10:1 to 2:1) as eluent for chromatography. Compound **5b** (126 mg, 95%) was also obtained according to the procedure C from chlorohydrin **6a** (141 mg, 0.3 mmol). M.p. 141–142 °C (Et_2O/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.42–1.52 (m, 2H), 1.58–1.71 (m, 4H), 2.70–2.84 (m, 2H), 3.02–3.15 (m, 2H), 3.59 (s, 3H), 3.69 (s, 3H), 7.33–7.43 (m, 5H), 7.44–7.57 (m, 3H), 7.79–7.86 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.4, 26.3, 50.2, 52.6, 52.7, 68.1, 73.4, 98.1, 128.1 (2C),

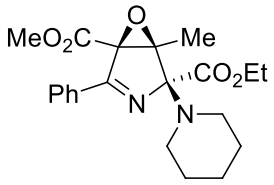
128.4, 128.7, 129.2, 130.8, 131.6, 132.0, 164.7, 169.0, 171.8. HRMS–ESI: $[M+H]^+$ calcd for $C_{25}H_{27}N_2O_5^+$ $[M+H]^+$ 435.1914; found 435.1921. $\nu_{max/cm^{-1}}$ 1756 (C=O), 1613 (C=N).

4-Ethyl 1-methyl *rac*-(1*R*,4*R*,5*S*)-5-methyl-2-phenyl-4-(piperidin-1-yl)-6-oxa-3-azabicyclo-[3.1.0]hex-2-ene-1,4-dicarboxylate (5c)



Compound **5c** (118 mg, 88%) was obtained as a colorless solid according to procedure A from oxazatriene **3b** (133 mg, 0.3 mmol) or **3zc** (120 mg, 0.3 mmol) and piperidine (77 mg, 0.9 mmol) using hexane/EtOAc mixture (from 5:1 to 2:1) as eluent for chromatography. Compound **5c** (173 mg, 77%) was also obtained according to procedure B from azirine **1a** (127 mg, 0.5 mmol), diazo compound **2b** (1.31 g, 6 mmol) and piperidine (128 mg, 1.5 mmol) using hexane/EtOAc mixture (from 10:1 to 2:1) as eluent for chromatography. M.p. 141–142 °C (Et_2O/hexane). ^1H NMR (300 MHz, $CDCl_3$) δ 1.17 (t, 3H, *J* 7.3 Hz), 1.40–1.53 (m, 2H), 1.56–1.70 (m, 4H), 2.69–2.86 (m, 2H), 2.98–3.16 (m, 2H), 3.59 (s, 3H), 4.02–4.24 (m, 2H), 7.30–7.59 (m, 8H), 7.75–7.87 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 24.5, 26.3, 50.2, 52.7, 61.9, 68.2, 73.2, 98.0, 128.0, 128.1, 128.3, 128.7, 129.2, 130.8, 131.5, 132.1, 164.8, 168.3, 171.9. HRMS–ESI: $[M+H]^+$ calcd for $C_{26}H_{29}N_2O_5^+$ $[M+H]^+$ 449.2071; found 449.2064. $\nu_{max/cm^{-1}}$ 1757 (C=O), 1749 (C=O), 1613 (C=N).

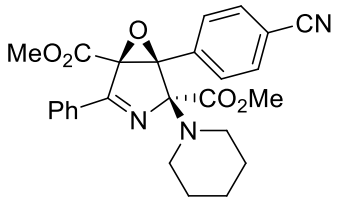
4-Ethyl 1-methyl *rac*-(1*R*,4*R*,5*S*)-5-methyl-2-phenyl-4-(piperidin-1-yl)-6-oxa-3-azabicyclo-[3.1.0]hex-2-ene-1,4-dicarboxylate (5d)



Compound **5d** (44 mg, 38%) was obtained as a colorless solid according to procedure A from oxazatriene **3c** (115 mg, 0.3 mmol) using hexane/EtOAc mixture (from 5:1 to 2:1) as eluent for chromatography. Compound **5d** (66 mg, 34%) was also obtained according to procedure B from azirine **1a** (127 mg, 0.5 mmol), diazo compound **2c** (234 mg, 1.5 mmol) and piperidine (128 mg, 1.5 mmol) using hexane/EtOAc mixture (from 10:1 to 2:1) as eluent for chromatography. Compound **5d** (112 mg, 97%) was also obtained according to procedure C from chlorohydrin **6b** (127 mg, 0.3 mmol). M.p. 135–136 °C (Et_2O–hexane). ^1H NMR (300 MHz, $CDCl_3$) δ 1.28 (t,

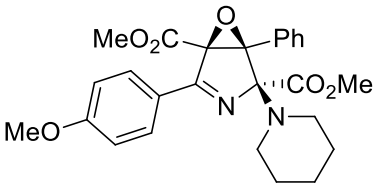
3H, *J* 7.1 Hz), 1.41–1.55 (m, 2H), 1.59–1.72 (m, 7H), 2.67–2.86 (m, 2H), 2.87–3.05 (m, 2H), 3.78 (m, 3H), 4.27 (q, 2H, *J* 7.1 Hz), 7.38–7.57 (m, 3H), 7.68–7.80 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.5, 14.0, 24.5, 26.4, 49.7, 52.8, 62.0, 67.5, 70.0, 96.4, 128.0, 128.6, 131.5, 132.2, 165.5, 168.7, 172.3. HRMS–ESI: $[M+Na]^+$ calcd for $C_{21}H_{26}N_2NaO_5^+$ $[M+Na]^+$ 409.1734; found 409.1733. $\nu_{max/cm^{-1}}$ 1750 (C=O), 1599 (C=N).

Dimethyl *rac*-(1*R*,4*R*,5*S*)-5-(4-cyanophenyl)-2-phenyl-4-(piperidin-1-yl)-6-oxa-3-azabicyclo-[3.1.0]hex-2-ene-1,4-dicarboxylate (5e)



Compound **5e** (111 mg, 80%) was obtained as a colorless solid according to procedure A from oxazatriene **3d** (137 mg, 0.3 mmol) and piperidine (77 mg, 0.9 mmol) using hexane/EtOAc mixture (from 5:1 to 2:1) as eluent for chromatography. Compound **5e** (138 mg, 60%) was also obtained according to procedure B from azirine **1a** (127 mg, 0.5 mmol), diazo compound **2d** (229 mg, 1.0 mmol) and piperidine (128 mg, 1.5 mmol) using hexane/EtOAc mixture (from 10:1 to 2:1) as eluent for chromatography. M.p. 174–175 °C (Et_2O/hexane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.39–1.53 (m, 2H), 1.54–1.76 (m, 4H), 2.61–2.81 (m, 2H), 2.89–3.10 (m, 2H), 3.60 (s, 3H), 3.73 (s, 3H), 7.42–7.62 (m, 5H), 7.66–7.70 (m, 2H), 7.75–7.81 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.3, 26.3, 50.3, 52.9, 53.0, 68.4, 72.6, 98.1, 113.3, 118.0, 128.1, 128.8, 129.1, 131.6, 131.9, 132.1, 136.1, 164.1, 168.9, 171.6. HRMS–ESI: $[M+Na]^+$ calcd for $C_{26}H_{25}N_3NaO_5^+$ $[M+Na]^+$ 482.1686; found 482.1668. $\nu_{max/cm^{-1}}$ 2229 (C≡N), 1757 (C=O), 1741 (C=O), 1604 (C=N).

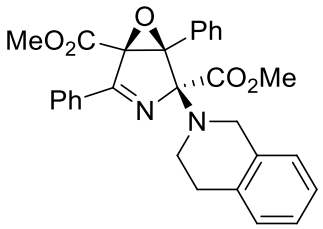
Dimethyl *rac*-(1*R*,4*R*,5*S*)-2-(4-methoxyphenyl)-5-phenyl-4-(piperidin-1-yl)-6-oxa-3-azabicyclo[3.1.0]hex-2-ene-1,4-dicarboxylate (5f)



Compound **5f** (113 mg, 81%) was obtained as a colorless solid according to procedure A from oxazatriene **3e** (138 mg, 0.3 mmol) and piperidine (77 mg, 0.9 mmol) using hexane/EtOAc mixture (from 5:1 to 2:1) as eluent for chromatography. Compound **5f** (144 mg, 62%) was also

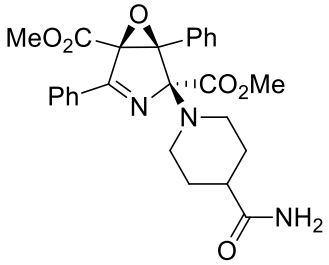
obtained according to procedure B from azirine **1b** (142 mg, 0.5 mmol), diazo compound **2a** (714 mg, 3.5 mmol) and piperidine (128 mg, 1.5 mmol) using hexane/EtOAc mixture (from 10:1 to 2:1) as eluent for chromatography. M.p. 160–162 °C (Et_2O/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40–1.52 (m, 2H), 1.57–1.68 (m, 4H), 2.67–2.84 (m, 2H), 2.98–3.13 (m, 2H), 3.60 (s, 3H), 3.68 (s, 3H), 3.88 (s, 3H), 6.91–7.03 (m, 2H), 7.31–7.45 (m, 5H), 7.71–7.83 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.4, 26.3, 50.2, 52.6, 52.7, 55.4, 68.0, 73.5, 97.9, 114.1, 124.7, 128.1, 128.3, 129.1, 129.9, 130.9, 162.4, 164.9, 169.3, 170.8. HRMS–ESI: $[M+H]^+$ calcd for $C_{26}H_{29}N_2O_6^+$ $[M+H]^+$ 465.2020; found 465.2029.

Dimethyl *rac*-(1*R*,4*R*,5*S*)-4-(3,4-dihydroisoquinolin-2(1*H*)-yl)-2,5-diphenyl-6-oxa-3-azabicyclo[3.1.0]hex-2-ene-1,4-dicarboxylate (5g)



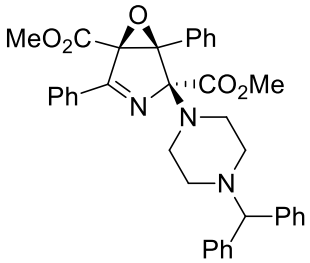
Compound **5g** (179 mg, 74%) was obtained as a colorless oil according procedure B from azirine **1a** (127 mg, 0.5 mmol), diazo compound **2a** (714 mg, 3.5 mmol) and 1,2,3,4-tetrahydroisoquinoline (200 mg, 1.5 mmol) using hexane/EtOAc mixture (from 10:1 to 2:1) as eluent for chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.85–3.08 (m, 2H), 3.17–3.36 (m, 2H), 3.65 (s, 3H), 3.70 (s, 3H), 4.02 and 4.40 (AB-q, 2H, *J* 15 Hz), 7.00–7.07 (m, 1H), 7.07–7.17 (m, 3H), 7.33–7.46 (m, 5H), 7.47–7.61 (m, 3H), 7.81–7.90 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.8, 47.5, 51.3, 52.8, 52.9, 68.2, 73.6, 97.5, 125.4, 125.8, 126.6, 128.0, 128.1, 128.5, 128.6, 128.7, 129.4, 130.3, 131.8, 131.9, 134.5, 135.0, 164.7, 168.7, 172.5. HRMS–ESI: $[M+H]^+$ calcd for $C_{29}H_{27}N_2O_5^+$ $[M+H]^+$ 483.1914; found 483.1919. $\nu_{max/cm^{-1}}$ 1756 (C=O), 1740 (C=O), 1609 (C=N).

Dimethyl *rac*-(1*R*,4*R*,5*S*)-4-(4-carbamoylpiperidin-1-yl)-2,5-diphenyl-6-oxa-3-azabicyclo-[3.1.0]hex-2-ene-1,4-dicarboxylate (5h)



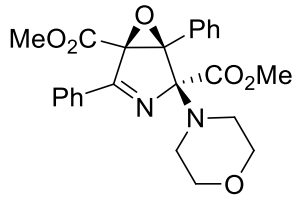
Compound **5h** (125 mg, 87%) was obtained as a colorless solid according to procedure A from oxazatriene **3a** (129 mg, 0.3 mmol) and piperidine-4-carboxamide (115 mg, 0.9 mmol). Compound **5h** (177 mg, 74%) was also obtained according to procedure B from azirine **1a** (127 mg, 0.5 mmol), diazo compound **2a** (714 mg, 3.5 mmol) and piperidine-4-carboxamide (192 mg, 1.5 mmol) using EtOAc as eluent for chromatography. M.p. 115–117 °C (hexane/Et_2O/CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.71–2.00 (m, 4H), 2.09–2.23 (m, 1H), 2.43 (td, 1H, *J* 11.4 Hz, *J* 2.6 Hz), 2.79 (td, 1H, *J* 11.4 Hz, *J* 2.6 Hz), 3.23 (d, 1H, *J* 11.5 Hz), 3.49 (d, 1H, *J* 11.5 Hz), 3.59 (s, 3H), 3.65 (s, 3H), 5.72 (br. d, 2H, *J* 57.8 Hz), 7.30–7.42 (m, 5H), 7.43–7.60 (m, 3H), 7.75–7.81 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.2 (2C), 42.8, 48.3, 49.4, 52.7, 52.8, 68.0, 73.2, 97.6, 127.9, 128.0, 128.5, 128.7, 129.4, 130.2, 131.8, (signal of one carbon is overlapped), 164.6, 168.7, 172.3, 177.5. HRMS–ESI: $[M+H]^+$ calcd for $C_{26}H_{28}N_3O_6^+$ $[M+H]^+$ 478.1973; found 478.1969. $\nu_{max/cm^{-1}}$ 1745 (C=O), 1687 (C=O), 1609 (C=N).

Dimethyl *rac*-(1*R*,4*R*,5*S*)-4-(4-benzhydrylpiperazin-1-yl)-2,5-diphenyl-6-oxa-3-azabicyclo-[3.1.0]hex-2-ene-1,4-dicarboxylate (5i)



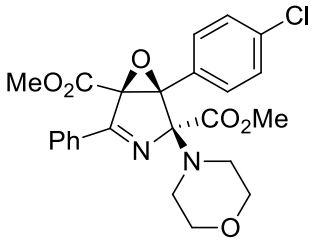
Compound **5i** (157 mg, 87%) was obtained as a colorless solid according to procedure A from oxazatriene **3a** (129 mg, 0.3 mmol) and 1-benzhydrylpiperazine (227 mg, 0.9 mmol). Compound **5i** (225 mg, 75%) was also obtained according to procedure B from azirine **1a** (127 mg, 0.5 mmol), diazo compound **2a** (714 mg, 3.5 mmol) and 1-benzhydrylpiperazine (378 mg, 1.5 mmol) using EtOAc as eluent for chromatography. M.p. 222–226 °C (dec., hexane/Et_2O/CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.51 (br. s, 4H), 2.80–2.95 (m, 2H), 3.14–3.27 (m, 2H), 3.61 (s, 3H), 3.66 (s, 3H), 4.25 (s, 1H), 7.14–7.20 (m, 2H), 7.24–7.28 (m, 2H), 7.31–7.46 (m, 9H), 7.46–7.60 (m, 3H), 7.78–7.88 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 49.2, 52.1, 52.6, 52.8, 68.0, 73.4, 76.1, 97.3, 126.8, 126.81, 127.91, 127.93, 127.95, 128.1, 128.36, 128.37, 128.5, 128.7, 129.4, 130.3, 131.7, 131.9, 142.8 (signal of one carbon is overlapped), 164.7, 168.5, 172.2. HRMS–ESI: $[M+H]^+$ calcd for $C_{37}H_{36}N_3O_5^+$ $[M+H]^+$ 602.2649; found 602.2641. $\nu_{max/cm^{-1}}$ 1762 (C=O), 1743 (C=O), 1609 (C=N).

Dimethyl *rac*-(1*R*,4*R*,5*S*)-4-(morpholin-4-yl)-2,5-phenyl-6-oxa-3-azabicyclo[3.1.0]hex-2-ene-1,4-dicarboxylate (5j)



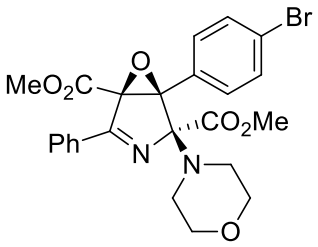
Compound **5j** (174 mg, 80%) was obtained as a colorless solid according to procedure B from azirine **1a** (127 mg, 0.5 mmol), diazo compound **2a** (714 mg, 3.5 mmol) and morpholine (131 mg, 1.5 mmol) using hexane/EtOAc mixture (from 10:1 to 2:1) as eluent for chromatography. M.p. 154–155 °C (Et_2O/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.79–2.94 (m, 2H), 3.09–3.23 (m, 2H), 3.60 (s, 3H), 3.69 (s, 3H), 3.75–3.80 (m, 4H), 7.32–7.43 (m, 5H), 7.44–7.60 (m, 3H), 7.76–7.89 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 49.4, 52.7, 52.8, 67.1, 68.0, 73.2, 97.0, 127.8, 128.0, 128.5, 128.7, 129.4, 130.2, 131.7, 131.8, 164.5, 168.2, 172.4. HRMS–ESI: $[M+H]^+$ calcd for $C_{24}H_{25}N_2O_6^+$ $[M+H]^+$ 437.1707; found 437.1701.

Dimethyl *rac*-(1*R*,4*R*,5*S*)-5-(4-chlorophenyl)-4-(morpholin-4-yl)-2-phenyl-6-oxa-3-azabicyclo[3.1.0]hex-2-ene-1,4-dicarboxylate (5k)



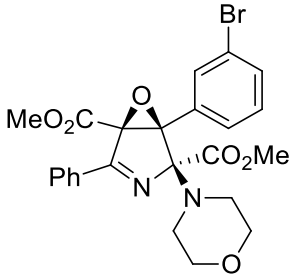
Compound **5k** (188 mg, 80%) was obtained as a colorless solid according to procedure B from azirine **1a** (127 mg, 0.5 mmol), diazo compound **2e** (835 mg, 3.5 mmol) and morpholine (131 mg, 1.5 mmol) using hexane/EtOAc mixture (from 10:1 to 2:1) as eluent for chromatography. M.p. 184–186 °C (Et_2O/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.84 (dt, 2H, *J* 10 Hz, *J* 4.6 Hz), 3.11 (dt, 2H, *J* 10 Hz, *J* 4.6 Hz), 3.63 (s, 3H), 3.72 (s, 3H), 3.76 (t, 4H, *J* 4.6 Hz), 7.30–7.40 (m, 4H), 7.45–7.52 (m, 2H), 7.52–7.60 (m, 1H), 7.77–7.84 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 49.5, 52.9, 53.0, 67.1, 68.2, 72.6, 96.9, 128.0, 128.75, 128.81, 128.9, 129.3, 131.6, 132.0, 135.7, 164.3, 168.2, 172.4. HRMS–ESI: $[M+H]^+$ calcd for $C_{24}H_{24}{}^{35}ClN_2O_6^+$ $[M+H]^+$ 471.1317; found 471.1321. $\nu_{max/cm^{-1}}$ 1743 (C=O), 1610 (C=N).

Dimethyl *rac*-(1*R*,4*R*,5*S*)-5-(4-bromophenyl)-4-(morpholin-4-yl)-2-phenyl-6-oxa-3-azabicyclo[3.1.0]hex-2-ene-1,4-dicarboxylate (5l)



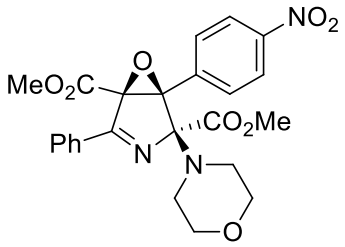
Compound **5l** (201 mg, 78%) was obtained as a colorless solid according to procedure B from azirine **1a** (127 mg, 0.5 mmol), diazo compound **2f** (991 mg, 3.5 mmol) and morpholine (131 mg, 1.5 mmol) using hexane/EtOAc mixture (from 10:1 to 2:1) as eluent for chromatography. M.p. 198–199 °C (Et_2O/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.83 (dt, 2H, *J* 9.8 Hz, *J* 4.6 Hz), 3.11 (dt, 2H, *J* 9.8 Hz, *J* 4.6 Hz), 3.64 (s, 3H), 3.72 (s, 3H), 3.77 (t, 4H, *J* 4.6 Hz), 7.24–7.30 (m, 2H), 7.45–7.60 (m, 5H), 7.77–7.84 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 49.5, 52.9, 53.0, 67.1, 68.2, 72.6, 96.9, 124.0, 128.1, 128.8, 129.3, 129.6, 131.6, 131.8, 132.0, 164.3, 168.2, 172.4. HRMS–ESI: $[M+H]^+$ calcd for $C_{24}H_{24}{}^{79}BrN_2O_6{}^+$ $[M+H]^+$ 515.0812; found 515.0808. $\nu_{max/cm^{-1}}$ 1741 (C=O), 1608 (C=N).

Dimethyl *rac*-(1*R*,4*R*,5*S*)-5-(3-bromophenyl)-4-(morpholin-4-yl)-2-phenyl-6-oxa-3-azabicyclo[3.1.0]hex-2-ene-1,4-dicarboxylate (5m)



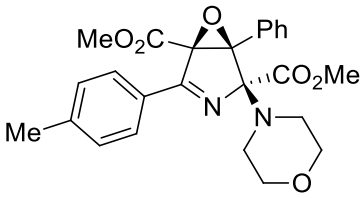
Compound **5m** (193 mg, 75%) was obtained as a colorless solid according to procedure B from azirine **1a** (127 mg, 0.5 mmol), diazo compound **2g** (991 mg, 3.5 mmol) and morpholine (131 mg, 1.5 mmol) using hexane/EtOAc mixture (from 10:1 to 2:1) as eluent for chromatography. M.p. 128–129 °C (Et_2O/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.77–2.90 (m, 2H), 3.06–3.18 (m, 2H), 3.64 (s, 3H), 3.74 (s, 3H), 3.77 (t, 4H, *J* 4.7 Hz), 7.23–7.31 (m, 1H), 7.31–7.38 (m, 1H), 7.45–7.61 (m, 5H), 7.76–7.86 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 49.5, 52.9, 53.0, 67.1, 68.1, 72.4, 97.0, 122.5, 126.7, 128.1, 128.8, 130.1, 131.0, 131.6, 132.0, 132.5, 132.7, 164.2, 168.1, 172.3. HRMS–ESI: $[M+H]^+$ calcd for $C_{24}H_{24}{}^{79}BrN_2O_6{}^+$ $[M+H]^+$ 515.0812; found 515.0805. $\nu_{max/cm^{-1}}$ 1756 (C=O), 1735 (C=O), 1606 (C=N).

Dimethyl *rac*-(1*R*,4*R*,5*S*)-4-(morpholin-4-yl)-5-(4-nitrophenyl)-2-phenyl-6-oxa-3-azabicyclo[3.1.0]hex-2-ene-1,4-dicarboxylate (5n)



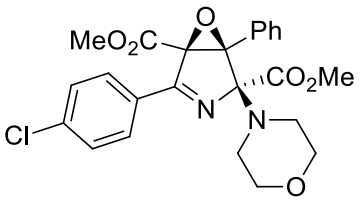
Compound **5n** (180 mg, 75%) was obtained as a colorless solid according to procedure B from azirine **1a** (127 mg, 0.5 mmol), diazo compound **2h** (299 mg, 1.2 mmol) and morpholine (131 mg, 1.5 mmol) using hexane/EtOAc mixture (from 10:1 to 2:1) as eluent for chromatography. M.p. 205–207 °C (Et_2O/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.76–2.88 (m, 2H), 3.04–3.16 (m, 2H), 3.63 (s, 3H), 3.70–3.81 (m, 7H), 7.47–7.52 (m, 2H), 7.54–7.66 (m, 3H), 7.78–7.83 (m, 2H), 8.23–8.28 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 49.5, 53.1, 53.2, 67.1, 68.5, 72.3, 97.0, 123.7, 128.1, 128.8, 129.2, 131.3, 132.2, 137.4, 148.4, 163.9, 168.1, 172.2. HRMS–ESI: $[M+H]^+$ calcd for $C_{24}H_{24}N_3O_8^+$ $[M+H]^+$ 482.1558; found 482.1550.

Dimethyl *rac*-(1*R*,4*R*,5*S*)-4-(morpholin-4-yl)-5-phenyl-2-(4-methylphenyl)-6-oxa-3-azabicyclo[3.1.0]hex-2-ene-1,4-dicarboxylate (5o)



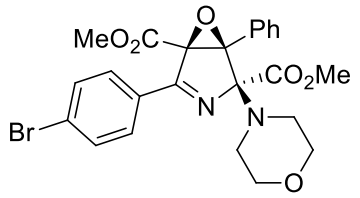
Compound **5o** (153 mg, 68%) was obtained as a colorless solid according to procedure B from azirine **1c** (134 mg, 0.5 mmol), diazo compound **2a** (714 mg, 3.5 mmol) and morpholine (131 mg, 1.5 mmol) using hexane/EtOAc mixture (from 10:1 to 2:1) as eluent for chromatography. M.p. 73–75 °C (Et_2O/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.44 (s, 3H), 2.80–2.92 (m, 2H), 3.10–3.21 (m, 2H), 3.61 (s, 3H), 3.69 (s, 3H), 3.77 (t, 4H, *J* 4.7 Hz), 7.28–7.30 (m, 2H), 7.31–7.42 (m, 5H), 7.68–7.73 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 49.5, 52.7, 52.8, 67.2, 68.1, 73.2, 96.9, 127.9, 128.1, 128.5, 129.0, 129.41, 129.43, 130.3, 142.5, 164.6, 168.3, 172.2. HRMS–ESI: $[M+H]^+$ calcd for $C_{25}H_{27}N_2O_6^+$ $[M+H]^+$ 451.1864; found 451.1857. $\nu_{max/cm^{-1}}$ 1750 (C=O), 1735 (C=O), 1605 (C=N).

Dimethyl *rac*-(1*R*,4*R*,5*S*)-2-(4-chlorophenyl)-4-(morpholin-4-yl)-5-phenyl-6-oxa-3-azabicyclo[3.1.0]hex-2-ene-1,4-dicarboxylate (5p)



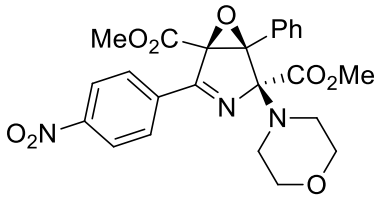
Compound **5p** (195 mg, 83%) was obtained as a colorless solid according to procedure B from azirine **1d** (144 mg, 0.5 mmol), diazo compound **2a** (714 mg, 3.5 mmol) and morpholine (131 mg, 1.5 mmol) using hexane/EtOAc mixture (from 10:1 to 2:1) as eluent for chromatography. M.p. 126–127 °C (Et_2O/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.77–2.91 (m, 2H), 3.07–3.21 (m, 2H), 3.61 (s, 3H), 3.69 (s, 3H), 3.77 (t, 4H, *J* 4.6 Hz), 7.31–7.43 (m, 5H), 7.44–7.49 (m, 2H), 7.72–7.76 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 49.4, 52.8, 52.9, 67.1, 67.8, 73.4, 97.1, 127.9, 128.6, 129.1, 129.4, 129.6, 130.0, 130.2, 138.2, 164.4, 168.1, 171.5. HRMS–ESI: $[M+H]^+$ calcd for $C_{24}H_{24}{}^{35}ClN_2O_6^+$ $[M+H]^+$ 471.1317; found 471.1317. $\nu_{max/cm^{-1}}$ 1741 (C=O), 1621 (C=N).

Dimethyl *rac*-(1*R*,4*R*,5*S*)-2-(4-bromophenyl)-4-(morpholin-4-yl)-5-phenyl-6-oxa-3-azabicyclo[3.1.0]hex-2-ene-1,4-dicarboxylate (5q)



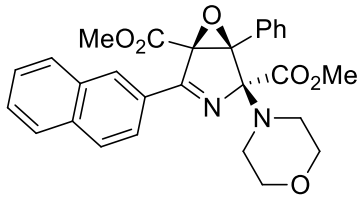
Compound **5q** (207 mg, 80%) was obtained as a colorless solid according to procedure B from azirine **1e** (167 mg, 0.5 mmol), diazo compound **2a** (714 mg, 3.5 mmol) and morpholine (131 mg, 1.5 mmol) using hexane/EtOAc mixture (from 10:1 to 2:1) as eluent for chromatography. M.p. 138–140 °C (Et_2O/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.78–2.90 (m, 2H), 3.09–3.19 (m, 2H), 3.62 (s, 3H), 3.69 (s, 3H), 3.78 (t, 4H, *J* 4.7 Hz), 7.31–7.44 (m, 5H), 7.59–7.73 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 49.5, 52.8, 53.0, 67.2, 67.8, 73.5, 97.1, 126.7, 127.9, 128.6, 129.56, 129.58, 130.0, 130.6, 132.1, 164.4, 168.1, 171.6. HRMS–ESI: $[M+H]^+$ calcd for $C_{24}H_{24}{}^{79}BrN_2O_6^+$ $[M+H]^+$ 515.0812; found 515.0819.

Dimethyl *rac*-(1*R*,4*R*,5*S*)-4-(morpholin-4-yl)-2-(4-nitrophenyl)-5-phenyl-6-oxa-3-azabicyclo[3.1.0]hex-2-ene-1,4-dicarboxylate (5r)



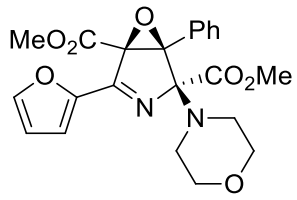
Compound **5r** (195 mg, 81%) was obtained as a colorless solid according to procedure B from azirine **1f** (150 mg, 0.5 mmol), diazo compound **2a** (714 mg, 3.5 mmol) and morpholine (131 mg, 1.5 mmol) using hexane/EtOAc mixture (from 10:1 to 2:1) as eluent for chromatography. M.p. 165–167 °C (Et_2O/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.78–2.91 (m, 2H), 3.08–3.21 (m, 2H), 3.61 (s, 3H), 3.69 (s, 3H), 3.77 (t, 4H, *J* 4.7 Hz), 7.29–7.46 (m, 5H), 7.92–8.04 (m, 2H), 8.30–8.40 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 49.4, 52.9, 53.0, 67.1, 67.6, 73.7, 97.4, 123.9, 127.8, 128.6, 129.1, 129.6, 129.7, 137.2, 149.6, 164.1, 167.7, 171.1. HRMS–ESI: $[M+H]^+$ calcd for $C_{24}H_{24}N_3O_8^+$ $[M+H]^+$ 482.1558; found 482.1560. $\nu_{max/cm^{-1}}$ 1740 (C=O), 1603 (C=N).

Dimethyl *rac*-(1*R*,4*R*,5*S*)-4-(morpholin-4-yl)-2-(naphthalen-2-yl)-5-phenyl-6-oxa-3-azabicyclo[3.1.0]hex-2-ene-1,4-dicarboxylate (5s)



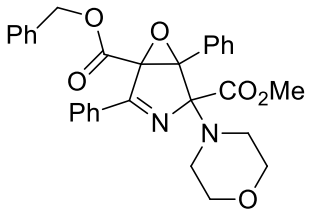
Compound **5s** (187 mg, 77%) was obtained as a colorless solid according to procedure B from azirine **1g** (152 mg, 0.5 mmol), diazo compound **2a** (714 mg, 3.5 mmol) and morpholine (131 mg, 1.5 mmol) using hexane/EtOAc mixture (from 10:1 to 2:1) as eluent for chromatography. M.p. 167–169 °C (Et_2O/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.84–2.97 (m, 2H), 3.15–3.27 (m, 2H), 3.63 (s, 3H), 3.72 (s, 3H), 3.80 (t, 4H, *J* 4.7 Hz), 7.36–7.47 (m, 5H), 7.52–7.65 (m, 2H), 7.86–8.01 (m, 4H), 8.26 (br. s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 49.5, 52.8, 52.9, 67.2, 68.2, 73.4, 97.1, 124.4, 126.8, 127.8, 127.9, 128.55, 128.61, 128.9, 129.0, 129.2, 129.5, 130.2, 132.8, 134.9, 164.6, 168.3, 172.5. HRMS–ESI: $[M+H]^+$ calcd for $C_{28}H_{27}N_2O_6^+$ $[M+H]^+$ 487.1864; found 487.1856. $\nu_{max/cm^{-1}}$ 1756 (C=O), 1604 (C=N).

Dimethyl *rac*-(1*R*,4*R*,5*S*)-2-(furan-2-yl)-4-(morpholin-4-yl)-5-phenyl-6-oxa-3-azabicyclo-[3.1.0]hex-2-ene-1,4-dicarboxylate (5t)



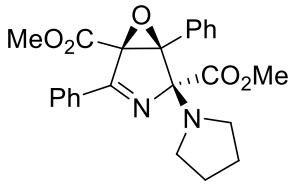
Compound **5t** (149 mg, 77%) was obtained as a colorless solid according to procedure B from azirine **1h** (122 mg, 0.5 mmol), diazo compound **2a** (714 mg, 3.5 mmol) and morpholine (131 mg, 1.5 mmol) using hexane/EtOAc mixture (from 10:1 to 2:1) as eluent for chromatography. M.p. 153–155 °C (Et_2O/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.79–2.92 (m, 2H), 3.07–3.20 (m, 2H), 3.66 (s, 3H), 3.70 (s, 3H), 3.77 (t, 4H, *J* 4.6 Hz), 6.60 (dd, 1H, *J* 3.5 Hz, 1.7 Hz), 7.08 (d, 1H, *J* 3.5 Hz), 7.31–7.44 (m, 5H), 7.65 (d, 1H, *J* 1.7 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 49.4, 52.8, 52.9, 67.1, 67.7, 73.1, 96.9, 112.5, 115.9, 127.8, 128.5, 129.5, 129.8, 146.2, 147.1, 162.3, 163.9, 168.0. HRMS–ESI: $[M+H]^+$ calcd for $C_{22}H_{23}N_2O_7^+$ $[M+H]^+$ 427.1500; found 427.1504. $\nu_{max/cm^{-1}}$ 1758 (C=O), 1616 (C=N).

1-Benzyl 4-methyl 4-(morpholin-4-yl)-2,5-diphenyl-6-oxa-3-azabicyclo[3.1.0]hex-2-ene-1,4-dicarboxylate (5u)



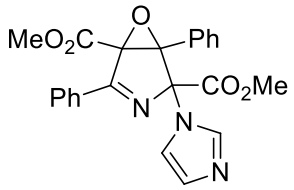
Compound **5u** (197 mg, 77%) (unseparated mixture of diastereomers, 10:1) was obtained as a colorless oil according to procedure B from azirine **1i** (165 mg, 0.5 mmol), diazo compound **2a** (714 mg, 3.5 mmol) and morpholine (131 mg, 1.5 mmol) using hexane/EtOAc mixture (from 10:1 to 2:1) as eluent for chromatography. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.79–2.94 (m, 2H), 3.07–3.23 (m, 2H), 3.64 and 3.72 (2s, 3H), 3.77 (t, 4H, *J* 4.6 Hz), 5.00 and 5.13 (AB-q, 2H, *J* 12 Hz), 6.99–7.03 (m, 2H), 7.18–7.60 (m, 11H), 7.76–7.85 (2m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 49.4, 52.60, 52.64, 67.2, 67.6, 68.1, 73.3, 97.0, 127.9, 128.0, 128.10, 128.14, 128.39, 128.42, 128.47, 128.5, 128.6, 129.4, 130.1, 131.67, 131.69, 134.3, 163.8, 163.9, 168.0, 168.2, 172.7 (other signals are overlapped). HRMS–ESI: $[M+H]^+$ calcd for $C_{30}H_{29}N_2O_6^+$ $[M+H]^+$ 513.2020; found 513.2027.

Dimethyl *rac*-(1*R*,4*R*,5*S*)-2,5-diphenyl-4-(pyrrolidin-1-yl)-6-oxa-3-azabicyclo[3.1.0]hex-2-ene-1,4-dicarboxylate (5v)



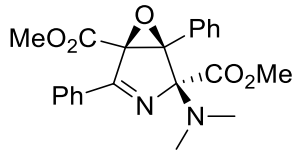
Compound **5v** (158 mg, 75%) was obtained as a colorless solid according to procedure B from azirine **1a** (127 mg, 0.5 mmol), diazo compound **2a** (714 mg, 3.5 mmol) and pyrrolidine (107 mg, 1.5 mmol) using hexane/EtOAc mixture (from 10:1 to 2:1) as eluent for chromatography. M.p. 169–170 °C (Et_2O/hexane).^{1}H NMR (400 MHz, $CDCl_3$) δ 1.71–1.92 (m, 4H), 2.88–3.05 (m, 2H), 3.10–3.29 (m, 2H), 3.62 (s, 3H), 3.66 (s, 3H), 7.31–7.43 (m, 5H), 7.44–7.66 (m, 3H), 7.79–7.85 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.2, 49.4, 52.7, 52.8, 67.5, 73.9, 96.1, 127.8, 128.0, 128.6, 128.7, 129.4, 129.9, 131.6, 132.0, 164.8, 168.4, 172.2. HRMS–ESI: $[M+H]^+$ calcd for $C_{24}H_{25}N_2O_5^+$ $[M+H]^+$ 421.1758; found 421.1757. $\nu_{max/cm^{-1}}$ 1755 (C=O), 1609 (C=N).

Dimethyl 4-(1*H*-imidazol-1-yl)-2,5-diphenyl-6-oxa-3-azabicyclo[3.1.0]hex-2-ene-1,4-dicarboxylate (5w)



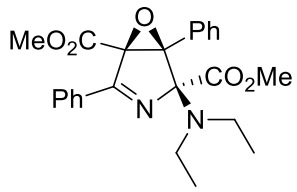
Compound **5w** (101 mg, 81%) (unseparated mixture of diastereomers, 7:1) was obtained as a colorless solid according to procedure A from oxazatriene **3a** (129 mg, 0.3 mmol) and imidazole (61 mg, 0.9 mmol) using EtOAc as eluent for chromatography. Compound **5w** (156 mg, 75%) was also obtained according to procedure B from azirine **1a** (127 mg, 0.5 mmol), diazo compound **2a** (714 mg, 3.5 mmol) and imidazole (102 mg, 1.5 mmol) using EtOAc as eluent for chromatography. M.p. 152–158 °C (dec., hexane/Et_2O/CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.53 and 3.63 (2s, 3H), 3.83 and 3.89 (2s, 3H), 6.99–7.12 (m, 2H), 7.22–7.72 (m, 9H), 7.81–7.97 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.1 (2C), 53.7, 53.9, 70.0, 70.3, 74.2, 80.2, 89.7, 90.6, 117.2, 118.4, 127.1, 127.8, 127.9, 128.3, 128.4, 128.5, 128.55, 128.6, 128.9, 129.0, 129.1, 129.5, 130.0, 130.3, 130.5, 130.8, 133.0, 133.1, 135.1, 136.5, 163.2, 163.3, 165.55, 165.6, 175.8, 176.2. HRMS–ESI: $[M+H]^+$ calcd for $C_{23}H_{20}N_3O_5^+$ $[M+H]^+$ 418.1397; found 418.1391. $\nu_{max/cm^{-1}}$ 1764 (C=O), 1735 (C=O), 1599 (C=N).

Dimethyl *rac*-(1*R*,4*R*,5*S*)-4-(dimethylamino)-2,5-diphenyl-6-oxa-3-azabicyclo[3.1.0]hex-2-ene-1,4-dicarboxylate (5x)



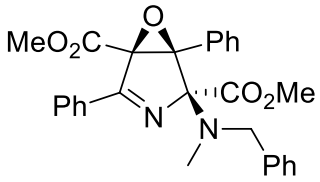
Compound **5x** (144 mg, 73%) was obtained as a colorless solid according to procedure B from azirine **1a** (127 mg, 0.5 mmol), diazo compound **2a** (714 mg, 3.5 mmol) and 2M solution of dimethylamine in CH_2Cl_2 (1 ml, 2.0 mmol) using hexane/EtOAc mixture (from 10:1 to 2:1) as eluent for chromatography. M.p. 128–130 °C (Et_2O/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.63 (s, 6H), 3.61 (s, 3H), 3.67 (s, 3H), 7.26–7.45 (m, 5H), 7.44–7.61 (m, 3H), 7.76–7.91 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 41.9, 52.7, 52.8, 67.9, 73.4, 97.6, 127.7, 128.0, 128.6, 128.7, 129.4, 130.1, 131.7, 131.9, 164.6, 168.7, 172.5. HRMS–ESI: $[M+H]^+$ calcd for $C_{22}H_{23}N_2O_5^+$ $[M+H]^+$ 395.1601; found 395.1595. $\nu_{max/cm^{-1}}$ 1745 (C=O), 1726 (C=O), 1611 (C=N).

Dimethyl *rac*-(1*R*,4*R*,5*S*)-4-(diethylamino)-2,5-diphenyl-6-oxa-3-azabicyclo[3.1.0]hex-2-ene-1,4-dicarboxylate (5y)



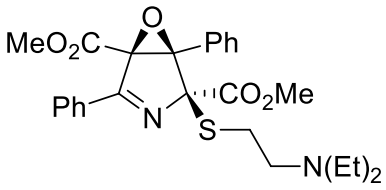
Compound **5y** (165 mg, 78%) was obtained as a colorless solid according to procedure B from azirine **1a** (127 mg, 0.5 mmol), diazo compound **2a** (714 mg, 3.5 mmol) and diethylamine (110 mg, 1.5 mmol) using hexane/EtOAc mixture (from 10:1 to 2:1) as eluent for chromatography. M.p. 101–103 °C (Et_2O/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.09 (t, 6H, *J* 7.1 Hz), 2.92–3.10 (m, 4H), 3.56 (s, 3H), 3.70 (s, 3H), 7.32–7.57 (m, 8H), 7.77–7.87 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5, 44.9, 52.4, 52.7, 68.8, 74.0, 98.8, 127.9, 128.0, 128.3, 128.6, 129.2, 131.1, 131.5, 132.2, 164.6, 169.9, 170.5. HRMS–ESI: $[M+H]^+$ calcd for $C_{24}H_{27}N_2O_5^+$ $[M+H]^+$ 423.1914; found 423.1917. $\nu_{max/cm^{-1}}$ 1755 (C=O), 1740 (C=O), 1608 (C=N).

Dimethyl *rac*-(1*R*,4*R*,5*S*)-4-[benzyl(methyl)amino]-2,5-diphenyl-6-oxa-3-azabicyclo-[3.1.0]hex-2-ene-1,4-dicarboxylate (5z)



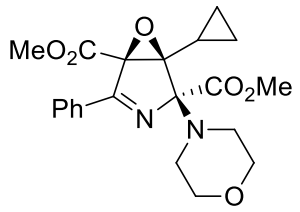
Compound **5z** (183 mg, 78%) was obtained as a colorless solid according to procedure B from azirine **1a** (127 mg, 0.5 mmol), diazo compound **2a** (714 mg, 3.5 mmol) and *N*-benzyl-*N*-methyl-amine (182 mg, 1.5 mmol) using hexane/EtOAc mixture (from 10:1 to 2:1) as eluent for chromatography. Compound **5z** (140 mg, 99%) was also obtained according to procedure C from chlorohydrin **6c** (152 mg, 0.3 mmol). M.p. 76–78 °C (Et_2O/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.49 (s, 3H), 3.63 (s, 3H), 3.72 (s, 3H), 3.98 and 4.12 (AB-q, 2H, *J* 14 Hz), 7.22–7.62 (m, 13H), 7.85–7.94 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 37.4, 52.5, 52.8, 58.0, 68.6, 73.9, 97.8, 126.7, 127.9, 128.0, 128.1, 128.4, 128.5, 128.7, 129.3, 130.7, 131.7, 131.9, 139.8, 164.6, 169.1, 172.1. HRMS–ESI: $[M+H]^+$ calcd for $C_{28}H_{27}N_2O_5^+$ $[M+H]^+$ 471.1914; found 471.1920.

Dimethyl *rac*-(1*R*,4*S*,5*R*)-4-[2-(diethylamino)ethylsulfanyl]-2,5-diphenyl-6-oxa-3-azabi-cyclo[3.1.0]hex-2-ene-1,4-dicarboxylate (5za)



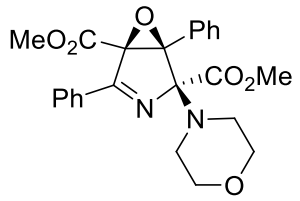
Compound **5za** (171 mg, 71%) was obtained as a colorless solid according to procedure B from azirine **1a** (127 mg, 0.5 mmol), diazo compound **2a** (714 mg, 3.5 mmol) and 2-(*N*,*N*-diethylamino)ethanethiol (200 mg, 1.5 mmol). M.p. 77–79 °C (hexane/Et_2O/CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.97 (t, 6H, *J* 7.2 Hz), 2.42–2.57 (m, 4H), 2.63–2.84 (m, 3H), 2.88–2.99 (m, 1H), 3.60 (s, 3H, CH_3), 3.65 (s, 3H), 7.34–7.61 (m, 8H), 7.80–7.90 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.8, 28.0, 46.8, 52.4, 52.9, 53.2, 69.2, 79.0, 86.9, 128.0, 128.3, 128.5, 128.7, 128.9, 129.8, 131.5, 132.0, 164.4, 166.8, 171.7. HRMS–ESI: $[M+Na]^+$ calcd for $C_{26}H_{30}N_2NaO_5S^+$ $[M+Na]^+$ 505.1768; found 505.1779. $\nu_{max/cm^{-1}}$ 1754 (C=O), 1735 (C=O), 1599 (C=N).

Dimethyl *rac*-(1*R*,4*R*,5*S*)-5-cyclopropyl-4-(morpholin-4-yl)-2-phenyl-6-oxa-3-azabicyclo-[3.1.0]hex-2-ene-1,4-dicarboxylate (5zb)



Compound **5zb** (113 mg, 94%) was obtained as a colorless solid according to procedure C from bromohydrin **6d** (144 mg, 0.3 mmol). M.p. 135–136 °C (Et_2O/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.46–0.57 (m, 1H), 0.60–0.87 (m, 3H), 1.30–1.41 (m, 1H), 2.74–3.04 (m, 4H), 3.68–3.82 (m, 7H), 3.84 (s, 3H), 7.34–7.60 (m, 3H), 7.64–7.84 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 2.0, 3.3, 7.0, 49.2, 52.8, 53.1, 67.3, 68.2, 72.3, 96.2, 127.8, 128.7, 131.77, 131.8, 165.1, 168.7, 173.1. HRMS–ESI: $[M+H]^+$ calcd for $C_{21}H_{25}N_2O_6^+$ $[M+H]^+$ 401.1707; found 401.1711. $\nu_{max/cm^{-1}}$ 1748 (C=O), 1602 (C=N).

4. Gram-scale synthesis of epoxypyrroline 5j



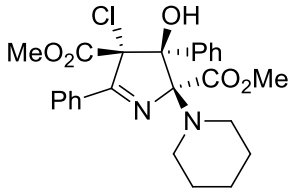
To a solution of diazo compound **2a** (5.712 g, 28.0 mmol) and azirine **1a** (1.016 g, 4.0 mmol) in anhydrous 1,2-dichloroethane (10 mL) at reflux under inert atmosphere $Rh_2(OAc)_4$ (35 mg, 2 mol %) was added. The stirred mixture was heated under reflux until nitrogen evolution stopped (1.5 min). The resulting mixture was evaporated under reduced pressure, and the residue was filtered through a pad of silica gel using toluene/EtOAc 30:1 mixture as eluent. The filtrate was concentrated under reduced pressure, and the residue was dissolved in anhydrous CH_2Cl_2 (30 mL). A solution of morpholine (1.044 g, 12 mmol) in CH_2Cl_2 (10 mL) was added dropwise to the resulting mixture under stirring. The mixture was stirred at room temperature for 24 h, the solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel (hexane/EtOAc, from 10:1 to 2:1) to afford epoxypyrroline **5j** (1.33 g, 76%).

5. Synthesis of halohydrins 6a−d

General procedure for preparation of halohydrins 6a−c

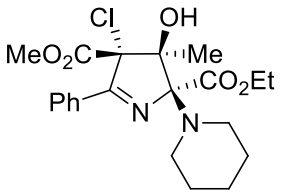
To a solution of oxazatriene **3zb**–**zd** (0.3 mmol) in anhydrous CH_2Cl_2 (2 mL) a solution of the amine (quantities are indicated below) in CH_2Cl_2 (1 mL) was added dropwise under stirring. The mixture was stirred at room temperature for 6 h, the solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel.

Dimethyl *rac*-(2*R*,3*S*,4*S*)-4-chloro-3-hydroxy-3,5-diphenyl-2-(piperidin-1-yl)-3,4-dihydro-2*H*-pyrrole-2,4-dicarboxylate (6a)



Compound **6a** (116 mg, 82%) was obtained as a colorless solid according to the general procedure from oxazatriene **3zb** (116 mg, 0.3 mmol) and piperidine (28 mg, 0.33 mmol) using hexane/EtOAc mixture (5:1) as eluent for column chromatography. M.p. 137–139 °C (Et_2O/hexane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35–1.80 (m, 6H), 2.60–2.90 (m, 2H), 2.88–3.65 (m, 2H), 3.75 (s, 6H), 6.79 (br. s, 1H), 7.30–7.70 (m, 8H), 7.96–8.19 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.7, 26.7, 49.2, 51.9, 52.9, 77.1, 86.2, 97.5, 127.1, 128.0 (2C), 128.1, 129.6, 131.1, 132.3, 137.0, 167.0, 168.7, 169.8. HRMS–ESI: $[M+H]^+$ calcd for $C_{25}H_{28}{}^{35}ClN_2O_5^+$ $[M+H]^+$: 471.1681; found 471.1689. $\nu_{max/cm^{-1}}$ 1750 (C=O), 1741 (C=O), 1626 (C=N).

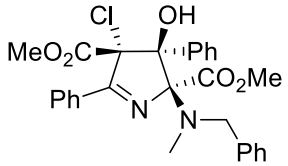
2-Ethyl 4-methyl *rac*-(2*R*,3*S*,4*S*)-4-chloro-3-hydroxy-3-methyl-5-phenyl-2-(piperidin-1-yl)-3,4-dihydro-2*H*-pyrrole-2,4-dicarboxylate (6b)



Compound **6b** (46 mg, 36%) was obtained as a colorless solid according to the general procedure from oxazatriene **3zc** (101 mg, 0.3 mmol) and piperidine (28 mg, 0.33 mmol) using hexane/EtOAc mixture (from 10:1 to 5:1) as eluent for chromatography. M.p. 124–126 °C (Et_2O/hexane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (t, 3H, *J* 7.3 Hz), 1.48–1.73 (m, 6H), 1.83 (s, 3H), 2.73–3.07 (m, 2H), 3.20–3.63 (m, 2H), 3.78 (s, 3H), 4.11–4.34 (m, 2H), 5.67 (br. s, 1H), 7.35–7.52 (m, 3H), 7.90–8.00 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 22.0, 24.7, 26.8,

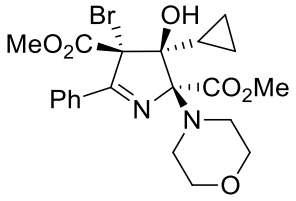
49.4, 53.0, 61.3, 78.2, 83.4, 96.3, 128.0, 129.2, 131.0, 131.9, 166.6, 167.8, 168.4. HRMS–ESI: $[M+H]^+$ calcd for $C_{21}H_{28}{}^{35}ClN_2O_5^+$ $[M+H]^+$: 423.1681; found 423.1704.

Dimethyl *rac*-(2*R*,3*S*,4*S*)-2-(benzyl(methyl)amino)-4-chloro-3-hydroxy-3,5-diphenyl-3,4-dihydro-2*H*-pyrrole-2,4-dicarboxylate (6c)



Compound **6c** (136 mg, 89%) was obtained as a colorless solid according to the general procedure from oxazatriene **3zb** (116 mg, 0.3 mmol) and *N*-benzyl-*N*-methylamine (40 mg, 0.33 mmol) using hexane/EtOAc mixture (5:1) as eluent for column chromatography. M.p. 118–120 °C (Et_2O/hexane). ^1H NMR (400 MHz, $CDCl_3$) δ 2.54 (br. s, 3H), 3.72 (s, 3H), 3.79–3.91 (m, 4H), 4.38 (br. s, 1H), 6.67 (br. s, 1H), 7.26–7.57 (m, 11H), 7.62–7.72 (m, 2H), 8.06–8.16 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 37.1, 52.2, 52.8, 56.5, 77.7, 85.6, 99.0, 127.16, 127.2, 128.0, 128.1, 128.3, 128.4, 128.7, 129.6, 131.2, 132.3, 136.4, 138.6, 166.4, 169.1, 170.0. HRMS–ESI: $[M+H]^+$ calcd for $C_{28}H_{28}{}^{35}ClN_2O_5^+$ $[M+H]^+$: 507.1681; found 507.1691. $\nu_{max/cm^{-1}}$ 1748 (C=O), 1616 (C=N).

Dimethyl *rac*-(2*R*,3*S*,4*S*)-4-bromo-3-cyclopropyl-3-hydroxy-2-(morpholin-4-yl)-5-phenyl-3,4-dihydro-2*H*-pyrrole-2,4-dicarboxylate (6d)

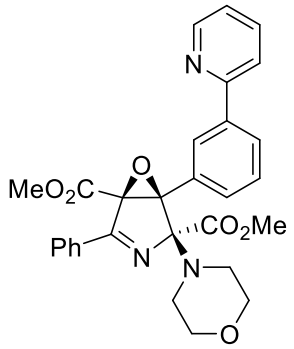


To a solution of diazo compound **2i** (101 mg, 0.6 mmol) and azirine **1a** (76 mg, 0.3 mmol) in anhydrous 1,2-dichloroethane (1 mL) at reflux under argon $Rh_2(OAc)_4$ (2 mol %) was added. The stirred mixture was heated under reflux until nitrogen evolution stopped. The resulting mixture was evaporated under reduced pressure, and the residue was filtered through a pad of silica gel using toluene/EtOAc 30:1 mixture as eluent. The filtrate was concentrated under reduced pressure, and the residue was dissolved in anhydrous CH_2Cl_2 (3 mL). A solution of morpholine (29 mg, 0.33 mmol) in CH_2Cl_2 (1 mL) was added dropwise to the resulting mixture under stirring. The mixture was stirred at room temperature for 6 h, the solvent was removed under reduced pressure and the residue was purified by column chromatography on

silica gel using hexane/EtOAc mixture (5:1). Compound **6d** (122 mg, 85%) was obtained as a colorless solid. M.p. 155–157 °C (Et_2O/hexane). ^1H NMR (400 MHz, $CDCl_3$) δ 0.39–0.50 (m, 1H), 0.51–0.61 (m, 1H), 0.62–0.81 (m, 2H), 1.87–1.99 (m, 1H), 3.06–3.20 (m, 2H), 3.20–3.41 (m, 2H), 3.63–3.88 (m, 10H), 5.35 (s, 1H), 7.36–7.53 (m, 3H), 7.92–8.00 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 3.1, 3.6, 14.7, 49.0, 52.1, 53.2, 67.6, 71.4, 84.1, 95.9, 128.1, 129.2, 131.2, 131.7, 166.5, 167.4, 170.3. HRMS–ESI: $[M+H]^+$ calcd for $C_{21}H_{26}{}^{79}BrN_2O_6^+$ $[M+H]^+$ 481.0969; found 481.0961.

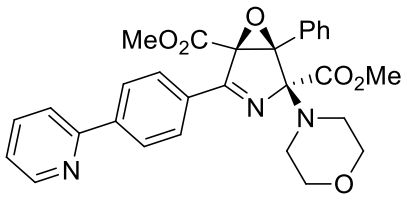
6. Synthesis of epoxypyrrolines 5zd,5ze

Dimethyl *rac*-(1*R*,4*R*,5*S*)-4-(morpholin-4-yl)-2-phenyl-5-(3-(pyridin-2-yl)phenyl)-6-oxa-3-azabicyclo[3.1.0]hex-2-ene-1,4-dicarboxylate (5zd)



The mixture of epoxypyrroline **5l** (103 mg, 0.2 mmol), 2-(tributylstannyl)pyridine (220 mg, 0.6 mmol), CuI (11 mg, 30 mol %) and $Pd(PPh_3)_4$ (23 mg, 10 mol %) in anhydrous 1,4-dioxane (2 mL) was placed in a screw-capped tube, degassed with argon and then heated at 100 °C for 2 h under stirring. The resulting mixture was cooled, the solvent was evaporated under reduced pressure and the residue was purified by column chromatography (hexane/EtOAc, from 2:1 to 1:2) to give compound **5zd** (71 mg, 69%) as a colorless solid. M.p. 114–116 °C (Et_2O/hexane). ^1H NMR (400 MHz, $CDCl_3$) δ 2.83–2.97 (m, 2H), 3.12–3.26 (m, 2H), 3.62 (s, 3H), 3.74 (s, 3H), 3.79 (t, 4H, *J* 4.7 Hz), 7.22–7.28 (m, 1H), 7.43–7.61 (m, 5H), 7.69–7.81 (m, 2H), 7.81–7.89 (m, 2H), 8.01–8.12 (m, 2H), 8.67–8.70 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 49.5, 52.9 (2C), 67.2, 68.4, 73.3, 97.0, 120.2, 122.5, 126.4, 127.7, 128.1, 128.4, 128.7, 129.0, 130.8, 131.8, 131.9, 136.8, 139.5, 149.8, 156.1, 164.5, 168.3, 172.5. HRMS–ESI: $[M+H]^+$ calcd for $C_{29}H_{28}N_3O_6^+$ $[M+H]^+$ 514.1973; found 514.1969.

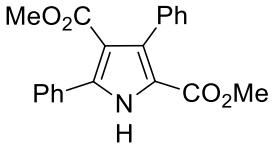
Dimethyl *rac*-(1*R*,4*R*,5*S*)-4-(morpholin-4-yl)-5-phenyl-2-(4-(pyridin-2-yl)phenyl)-6-oxa-3-azabicyclo[3.1.0]hex-2-ene-1,4-dicarboxylate (5ze)



The mixture of epoxypyrroline **5q** (103 mg, 0.2 mmol), 2-(tributylstannyl)pyridine (110 mg, 0.3 mmol), CuI (11 mg, 30 mol %) and $Pd(PPh_3)_4$ (23 mg, 10 mol %) in anhydrous 1,4-dioxane (2 mL) was placed in a screw-capped tube, degassed with argon and then heated at 100 °C for 2 h under stirring. The resulting mixture was cooled, the solvent was evaporated under reduced pressure and the residue was purified by column chromatography (hexane/EtOAc, from 2:1 to 1:2) to give compound **5ze** (90 mg, 88%) as a colorless solid. M.p. 175–177 °C (Et_2O/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.81–2.95 (m, 2H), 3.11–3.24 (m, 2H), 3.62 (s, 3H), 3.70 (s, 3H), 3.78 (t, 4H, *J* 4.7 Hz), 7.25–7.34 (m, 1H), 7.37–7.45 (m, 5H), 7.76–7.85 (m, 2H), 7.90–7.94 (m, 2H), 8.12–8.15 (m, 2H), 8.73–8.76 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 49.5, 52.7, 52.9, 67.2, 68.1, 73.3, 97.1, 120.8, 122.8, 127.1, 127.9, 128.5, 129.5, 130.2, 132.0, 136.9, 142.5, 149.9, 156.1, 164.5, 168.2, 172.1. HRMS–ESI: $[M+H]^+$ calcd for $C_{29}H_{28}N_3O_6^+$ $[M+H]^+$ 514.1973; found 514.1965.

7. Synthesis of pyrrole 11

Dimethyl 3,5-diphenyl-1*H*-pyrrole-2,4-dicarboxylate (11)



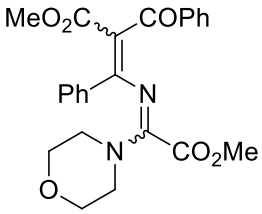
To a solution of epoxypyrroline **5j** (218 mg, 0.5 mmol) in CH_2Cl_2/MeOH mixture (3/3 mL) Pd/C (80 mg, 10 wt %) was added, and the resulting suspension was stirred overnight under an atmosphere of hydrogen. After the completion of the reaction (control by TLC) the reaction mixture was filtered and evaporated to give after recrystallization from hexane/EtOAc mixture (1:1) compound **11** (152 mg, 91%) as a colorless solid. M.p: 123–124 °C (EtOAc–hexane) (lit.,[11] 124–125 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.51 (s, 3H), 3.64 (s, 3H), 7.32–7.52 (m, 8H), 7.56–7.67 (m, 2H), 9.55 (br. s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 51.0, 51.5, 114.6, 119.3, 127.16, 127.19, 128.4, 128.8, 129.0, 129.9, 131.1, 133.5, 134.0, 139.0, 161.4, 165.0. HRMS–ESI: $[M+H]^+$ calcd for $C_{20}H_{18}NO_4^+$ $[M+H]^+$: 336.1230; found 336.1231.

8. Synthesis of oxazatrienes 12a–c

General procedure

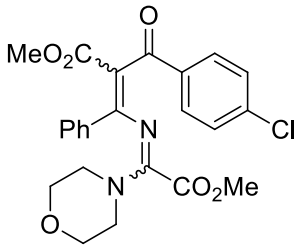
The solution of epoxypyrroline **5j**,**k**,**n** (0.4 mmol) in anhydrous toluene (10 mL) was stirred and irradiated by UV lamp for 4 h. The resulting mixture was evaporated under reduced pressure and the residue was purified by column chromatography (hexane/EtOAc, 1:1) to give oxazatriene **12a**–**c**.

Methyl 2-benzoyl-3-[(2-methoxy-1-morpholino-2-oxoethylidene)amino]-3-phenylacrylate (12a)



Compound **12a** (unseparated mixture of C=C isomers 1:1) (164 mg, 94%) was obtained as a yellow oil according to the general procedure from epoxypyrroline **5j** (174 mg, 0.4 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.00–3.12 (m, 2H), 3.31–3.40 (m, 2H), 3.48–3.65 and 3.77–3.85 (2m, 10H), 7.09–7.21 and 7.26–7.54 (2m, 8H), 7.78–7.86 (m, 1H), 7.91–7.99 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.6, 46.2, 51.3, 51.6, 52.5, 52.7, 65.8, 66.4, 115.0, 117.6, 127.75, 127.8, 128.0, 128.1, 128.5, 128.8, 128.9, 129.0, 129.3, 129.6, 131.9, 132.4, 137.2, 137.8, 138.2, 138.6, 149.3, 150.3, 161.2, 161.27, 161.28, 162.3, 165.7, 167.3, 194.3, 194.5. HRMS–ESI: $[M+H]^+$ calcd for $C_{24}H_{25}N_2O_6^+$ $[M+H]^+$ 437.1707; found 437.1719.

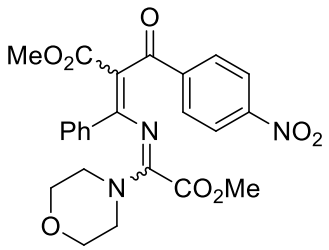
Methyl 2-(4-chlorobenzoyl)-3-[(2-methoxy-1-morpholino-2-oxoethylidene)amino]-3-phenyl-acrylate (12b)



Compound **12b** (unseparated mixture of C=C isomers 1:0.9) (181 mg, 96%) was obtained as a yellow oil according to the general procedure from epoxypyrroline **5k** (188 mg, 0.4 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.07–3.19 (m, 2H), 3.38–3.49 (m, 2H), 3.50–3.69 and 3.76–3.87 (2m, 10H), 7.11–7.49 (m, 7H), 7.74–7.78 (m, 1H), 7.88–7.92 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.7, 46.3, 51.5, 51.7, 52.7, 52.8, 66.0, 66.5, 114.6, 117.3, 127.9, 128.0, 128.4, 128.5,

128.53, 128.9, 129.6, 129.8, 130.4, 130.6, 136.7, 137.1, 137.14, 137.7, 138.3, 138.8, 149.3, 150.6, 161.25, 161.29, 161.7, 162.8, 165.6, 167.1, 193.2, 193.4. HRMS–ESI: $[M+H]^+$ calcd for $C_{24}H_{24}{}^{35}ClN_2O_6{}^+$ $[M+H]^+$ 471.1317; found 471.1321.

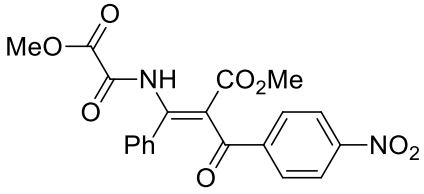
Methyl 3-[(2-methoxy-1-morpholino-2-oxoethylidene)amino]-2-(4-nitrobenzoyl)-3-phenyl-acrylate (12c)



Compound **12c** (unseparated mixture of isomers 1:1) (179 mg, 93%) was obtained as a yellow oil according to the general procedure from epoxypyrroline **5n** (192 mg, 0.4 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.80–4.10 (m, 14H), 6.90–7.63 (m, 5H), 7.74–8.50 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.8, 46.4, 51.6, 52.8, 66.1, 66.4, 114.1, 117.0, 123.3, 128.1, 128.8, 129.7, 130.0, 137.0, 137.5, 143.3, 149.5, 150.9, 161.1, 163.3, 164.2, 165.5, 167.0, 193.1 (other signals are overlapped). HRMS–ESI: $[M+H]^+$ calcd for $C_{24}H_{24}N_3O_8{}^+$ $[M+H]^+$ 482.1558; found 482.1563.

9. Synthesis of compound 13

Methyl (*Z*)-3-(2-methoxy-2-oxoacetamido)-2-(4-nitrobenzoyl)-3-phenylacrylate (13)

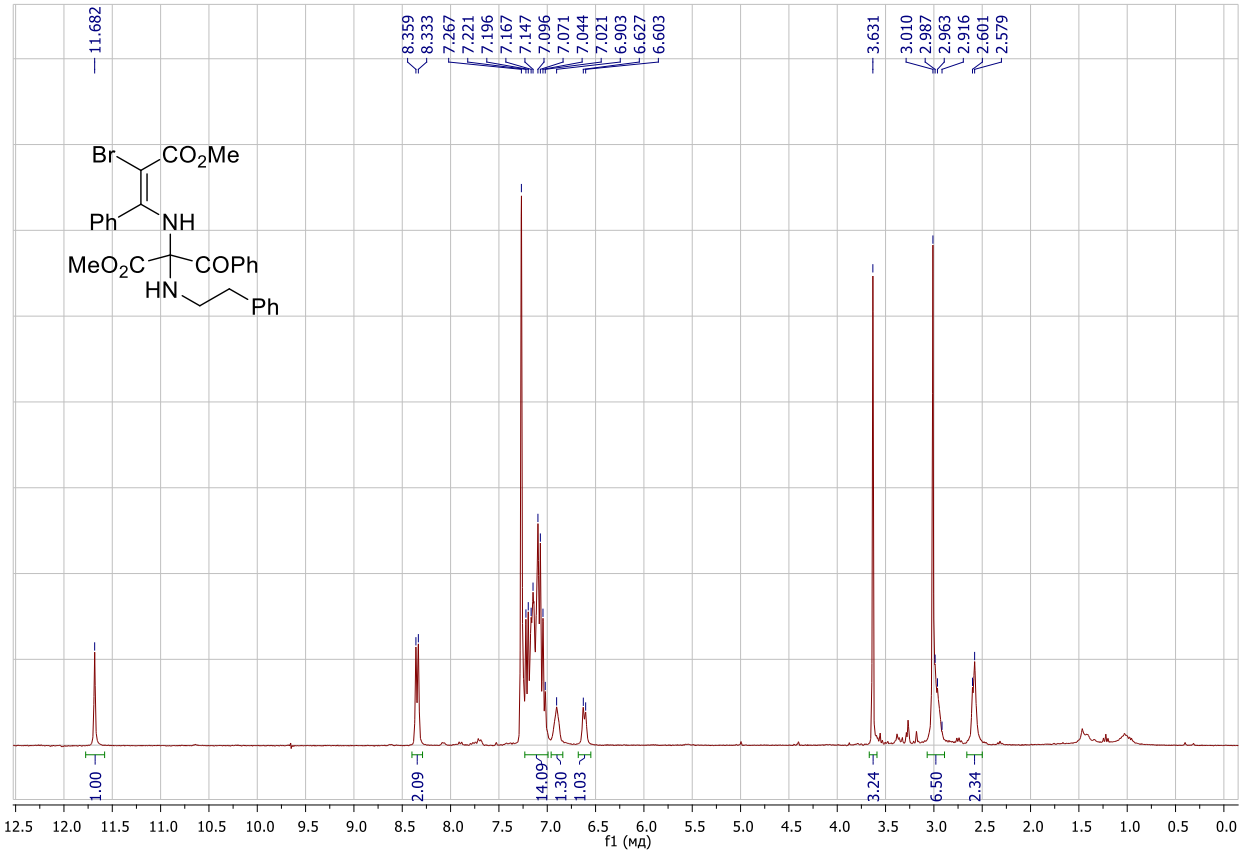


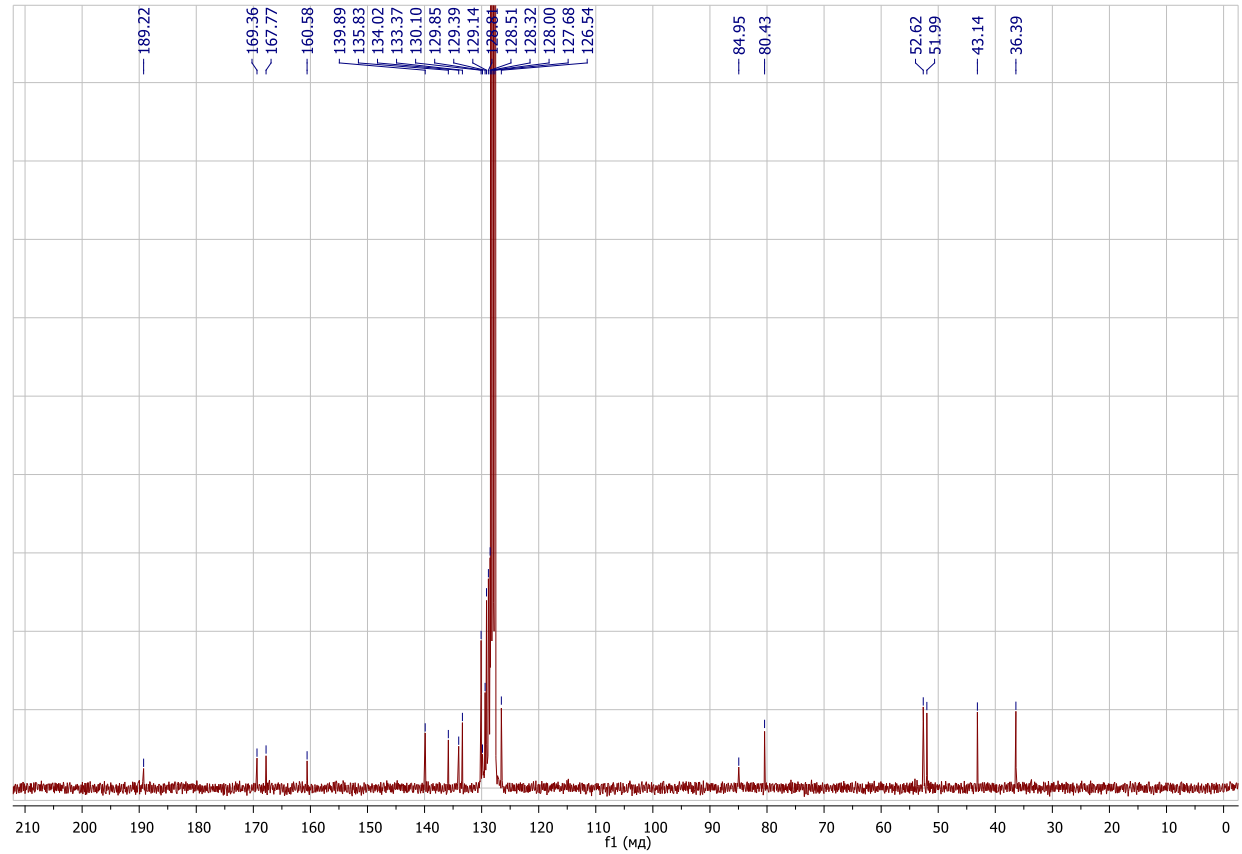
To a solution of oxazatriene **12c** (192 mg, 0.4 mmol) in CH_2Cl_2 (3 mL) a saturated solution of HCl in Et_2O (1 mL) was added, and the resulting emulsion was stirred overnight. The reaction mixture was washed with 10% solution of Na_2CO_3 (10 mL) and the aqueous layer was extracted with CH_2Cl_2 (2×5 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (hexane/EtOAc, from 8:1 to 2:1) to give **13** (67 mg, 41%) as a colorless solid. M.p. 177–178 °C (EtOAc–hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.80 (s, 3H), 3.98 (s, 3H), 7.11–7.28 (m, 5H), 7.80–7.87 (m, 2H), 8.12–8.20 (m, 2H), 12.55 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.8, 54.2, 113.9, 123.6, 128.2,

128.3, 129.7, 130.2, 131.6, 141.8, 150.1, 152.3, 153.8, 160.2, 166.3, 190.7. HRMS–ESI: $[M+H]^+$ calcd for $C_{20}H_{17}N_2O_8^+$ $[M+H]^+$: 413.0979; found 413.0971.

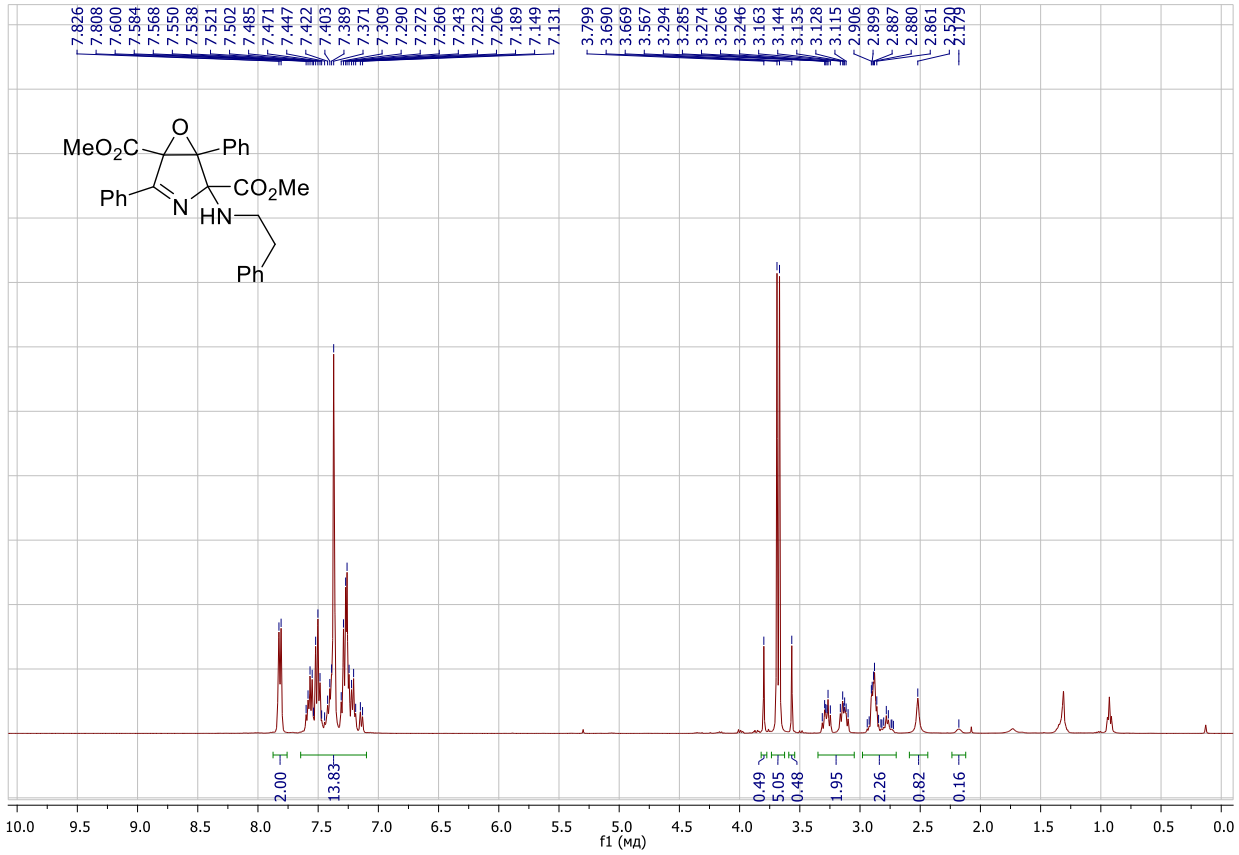
10. ^{1}H and ^{13}C NMR spectra

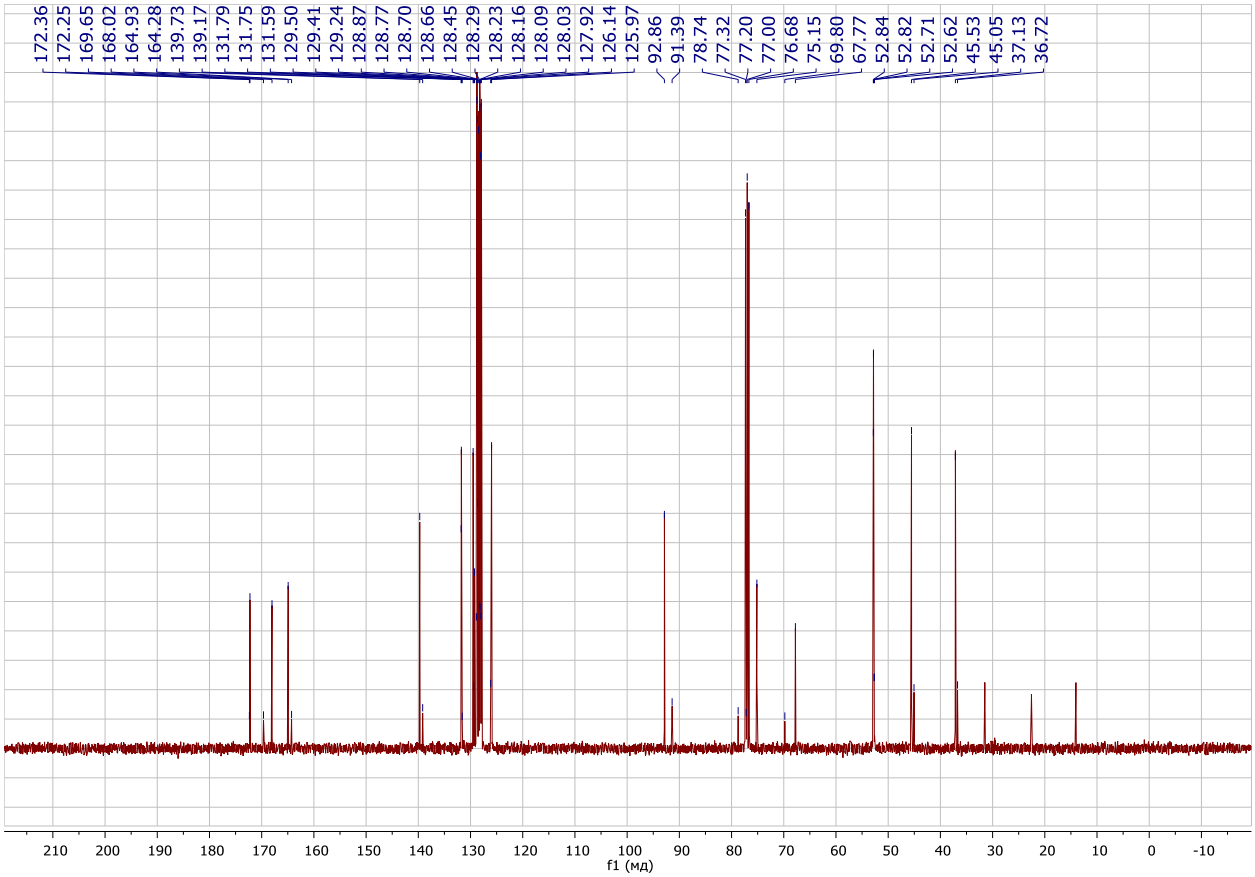
^{1}H and ^{13}C NMR spectra of compound **4a**



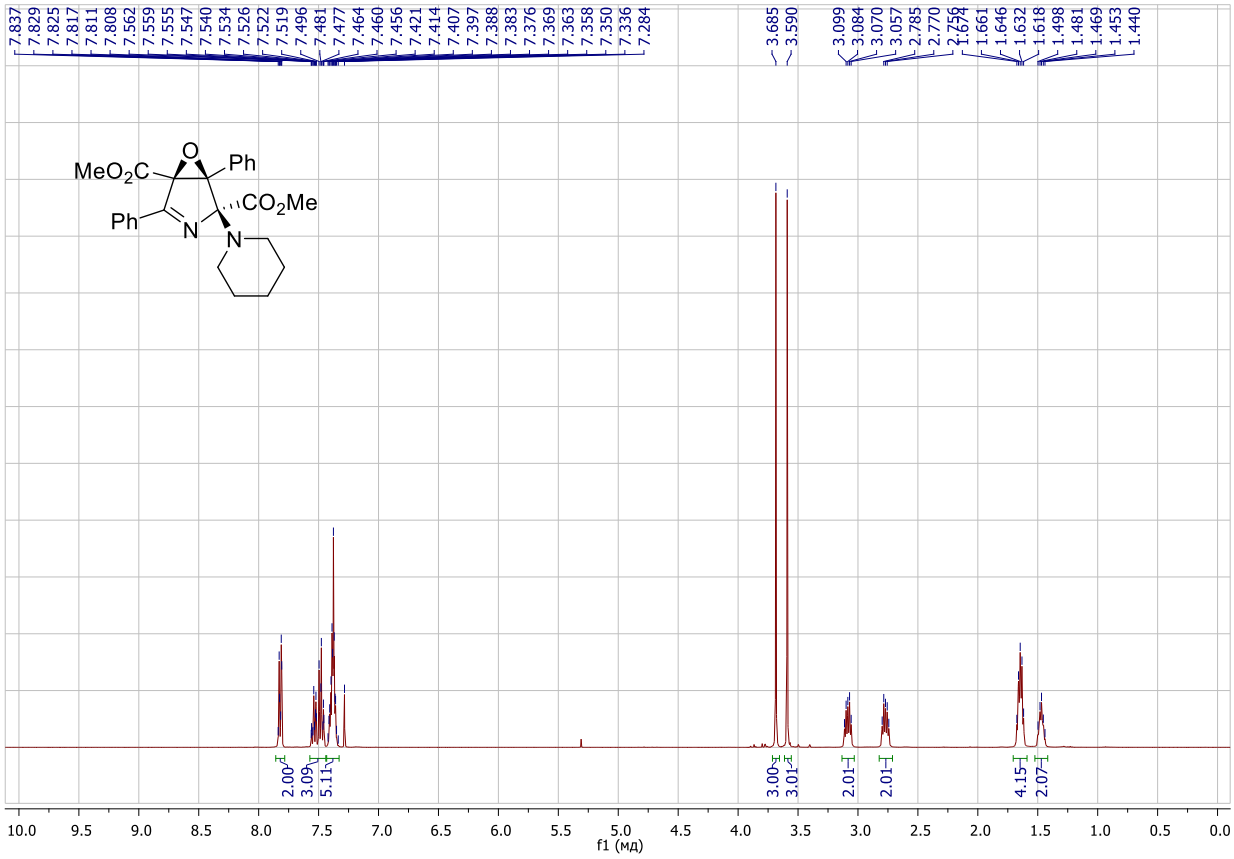


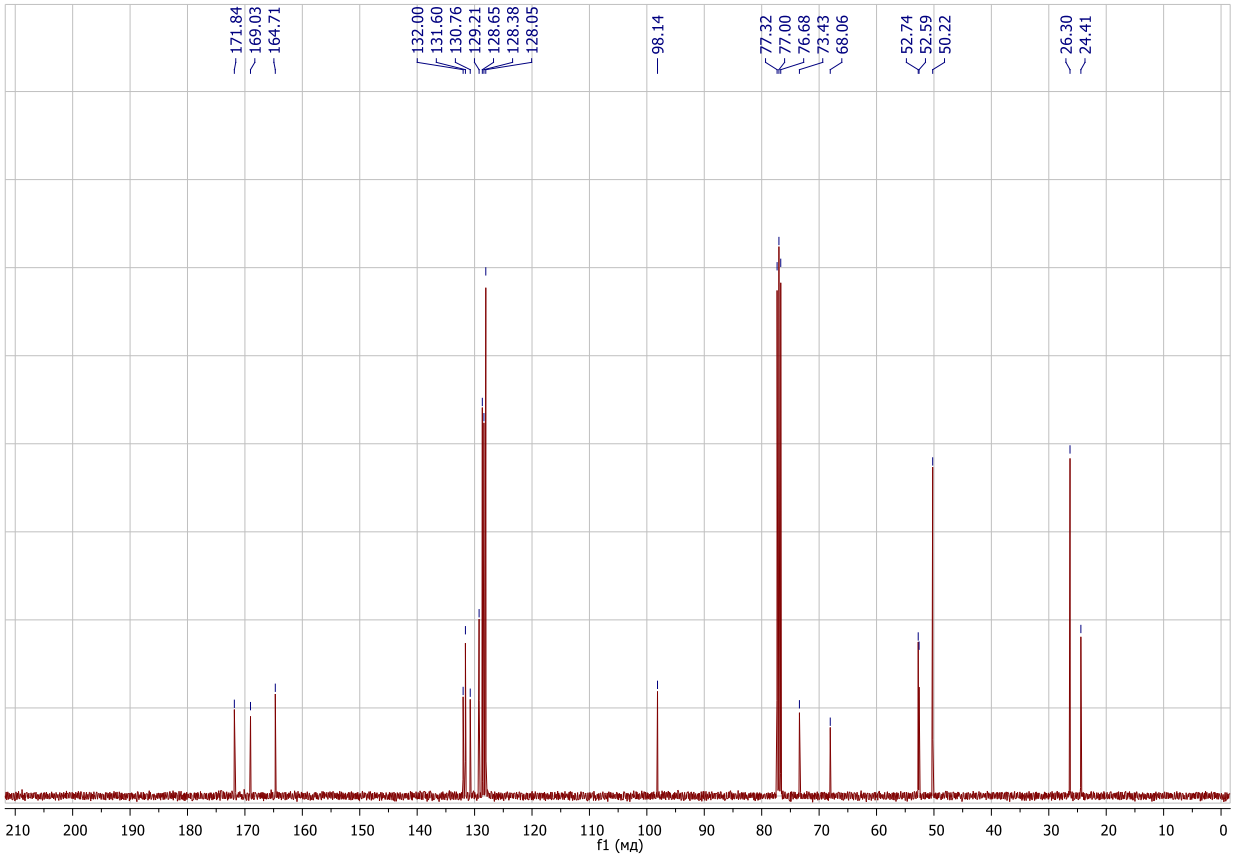
^{1}H and ^{13}C NMR spectra of compound **5a**



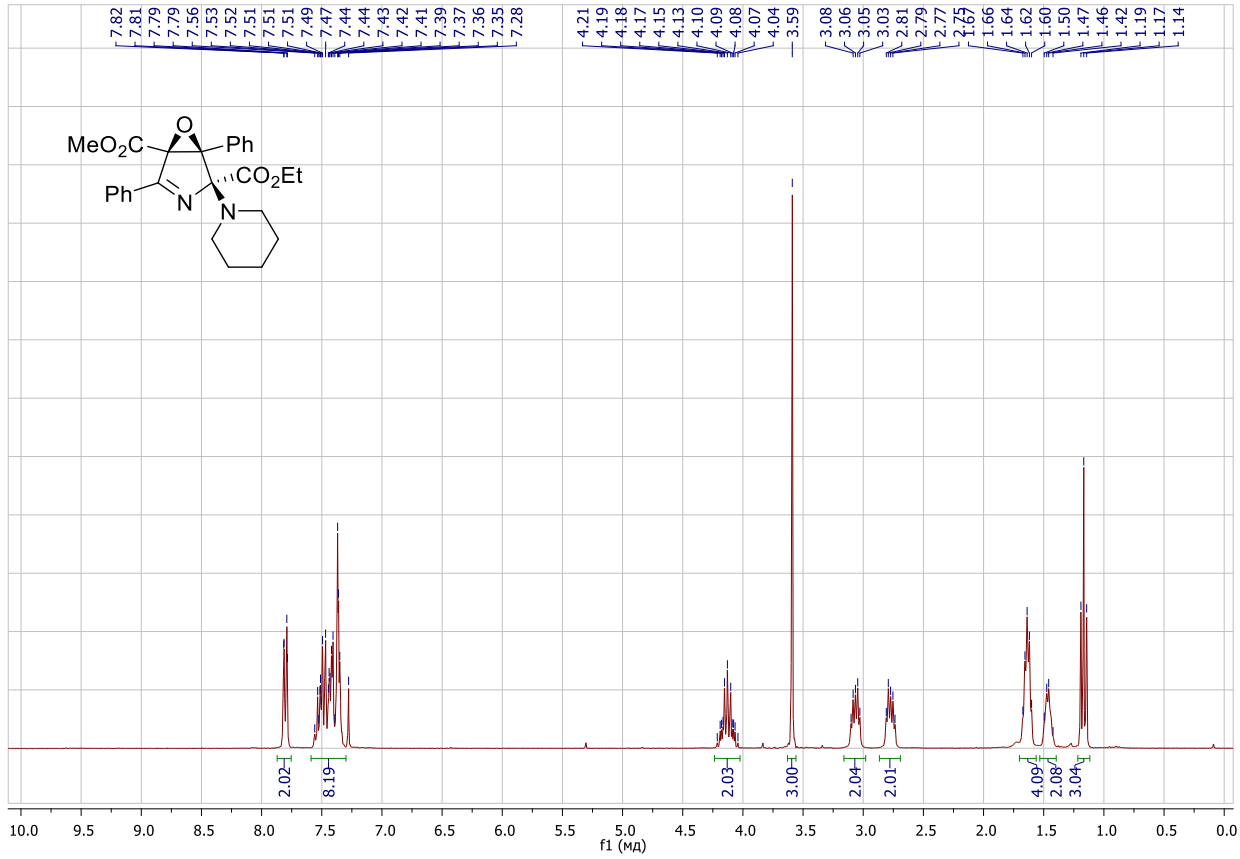


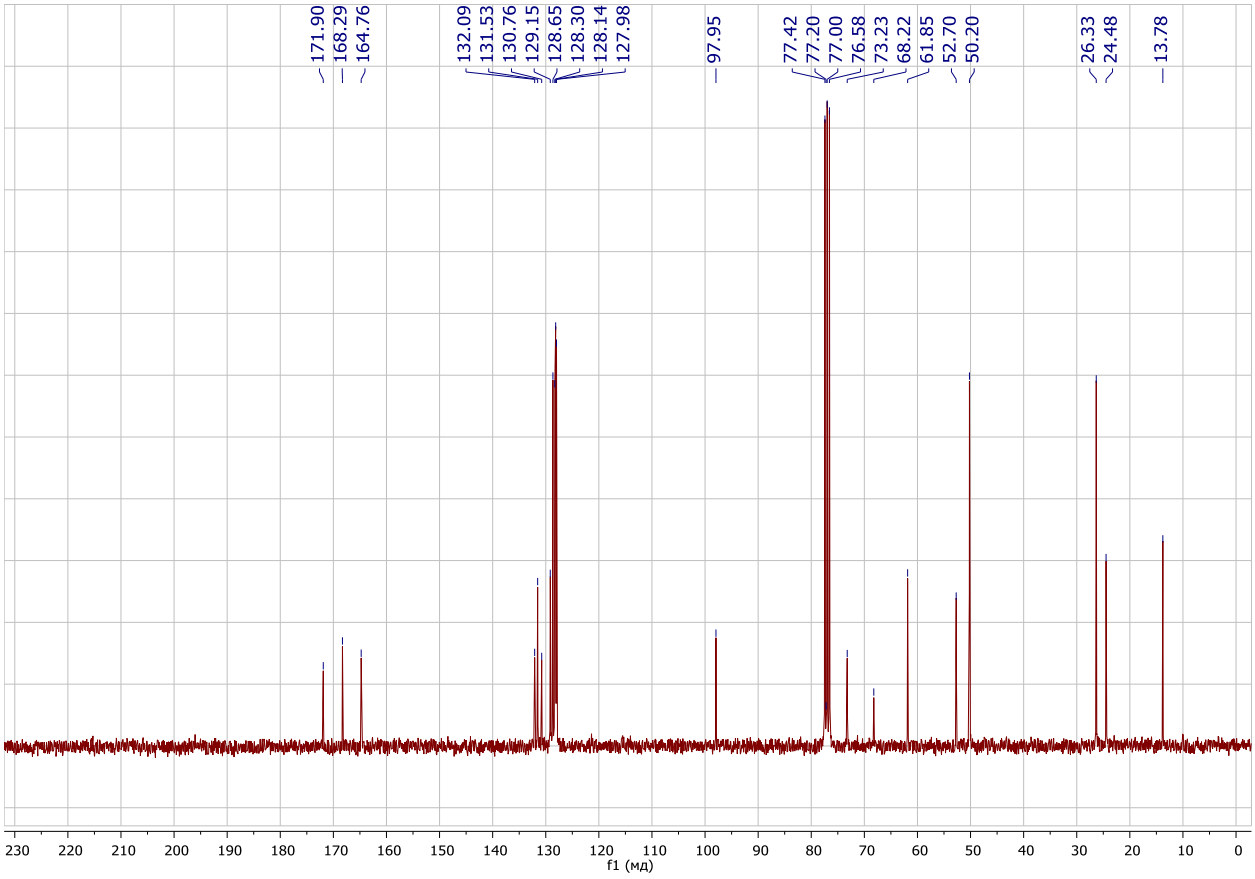
^{1}H and ^{13}C NMR spectra of compound **5b**



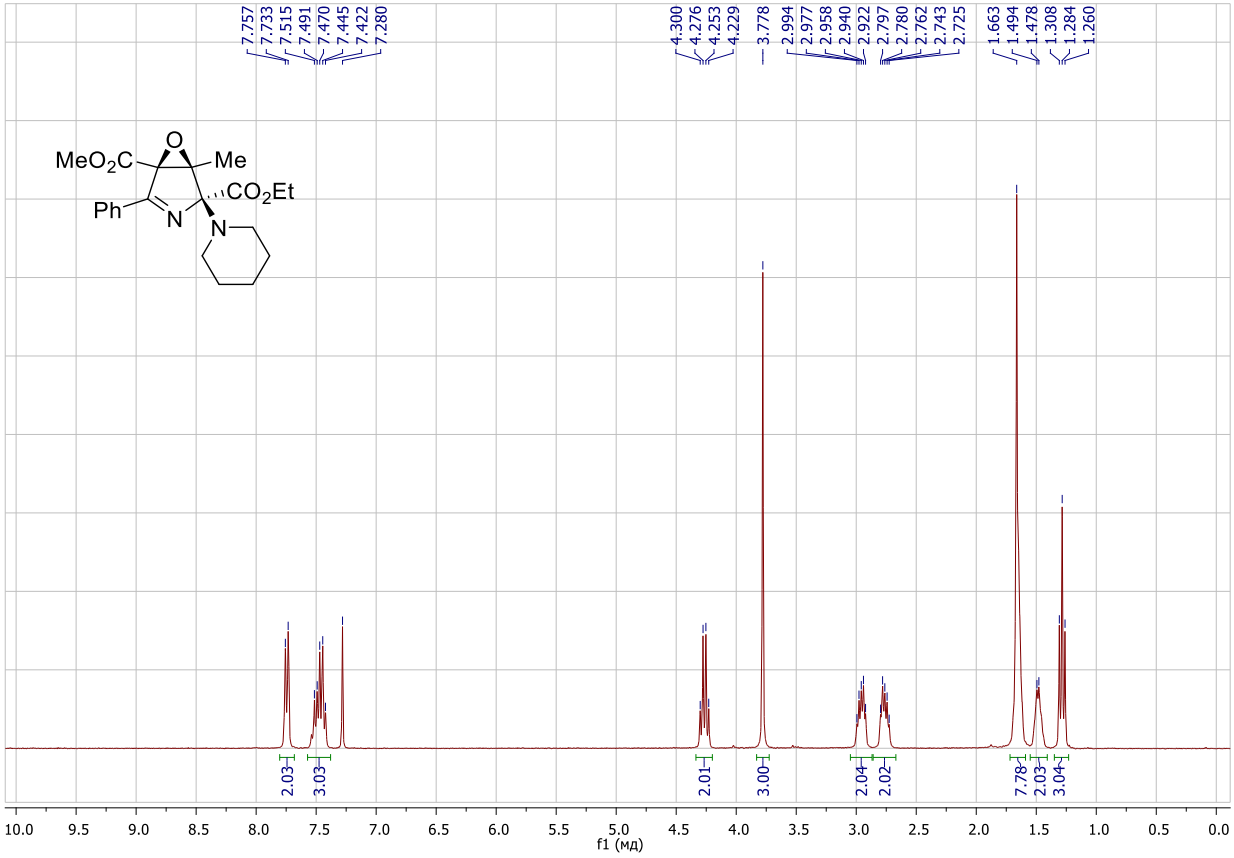


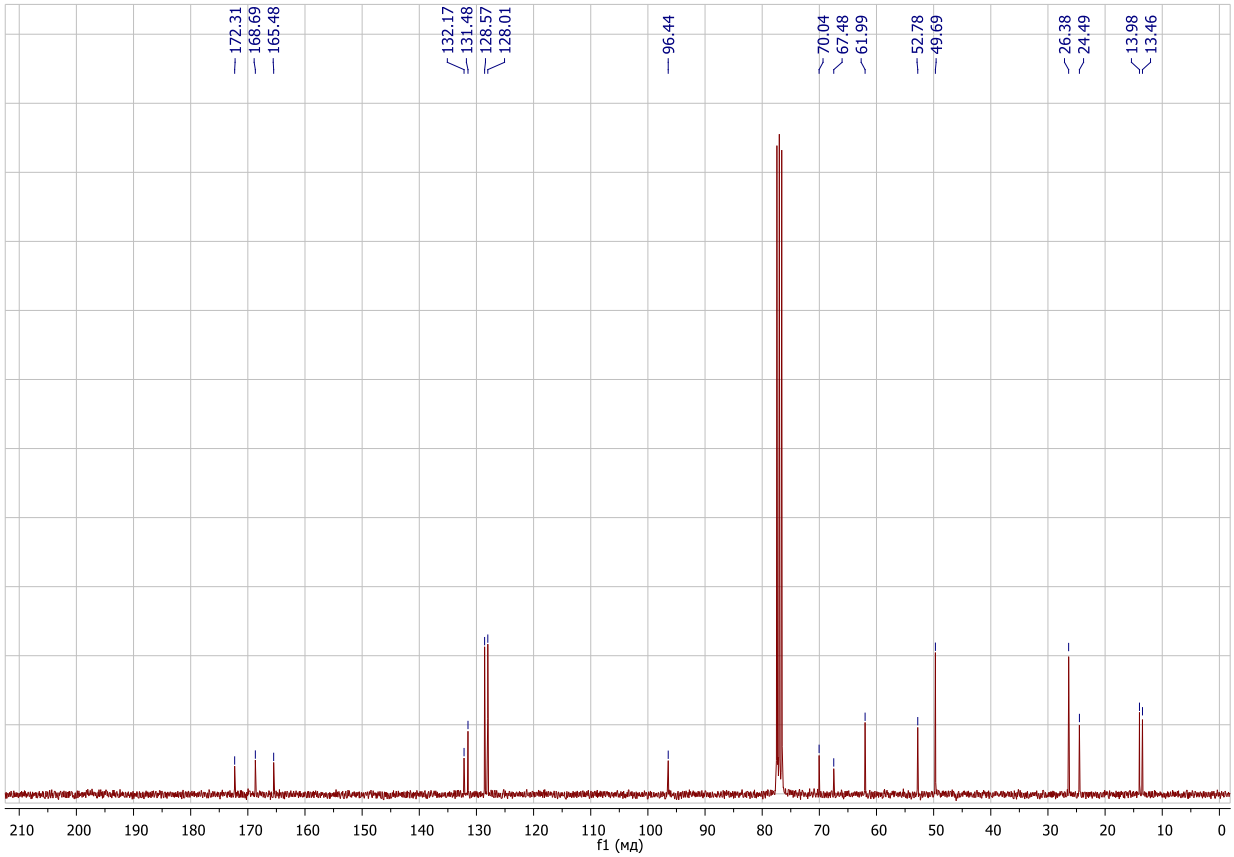
^{1}H and ^{13}C NMR spectra of compound **5c**



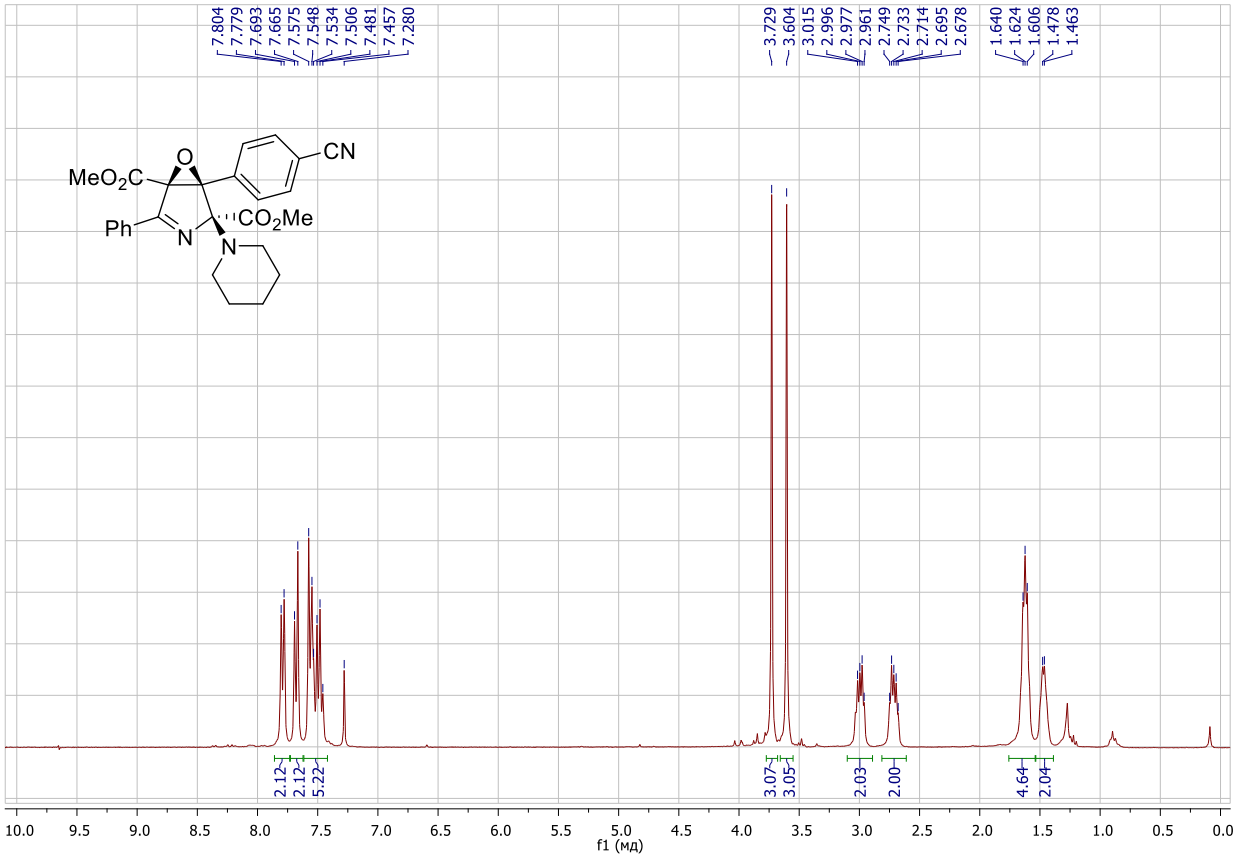


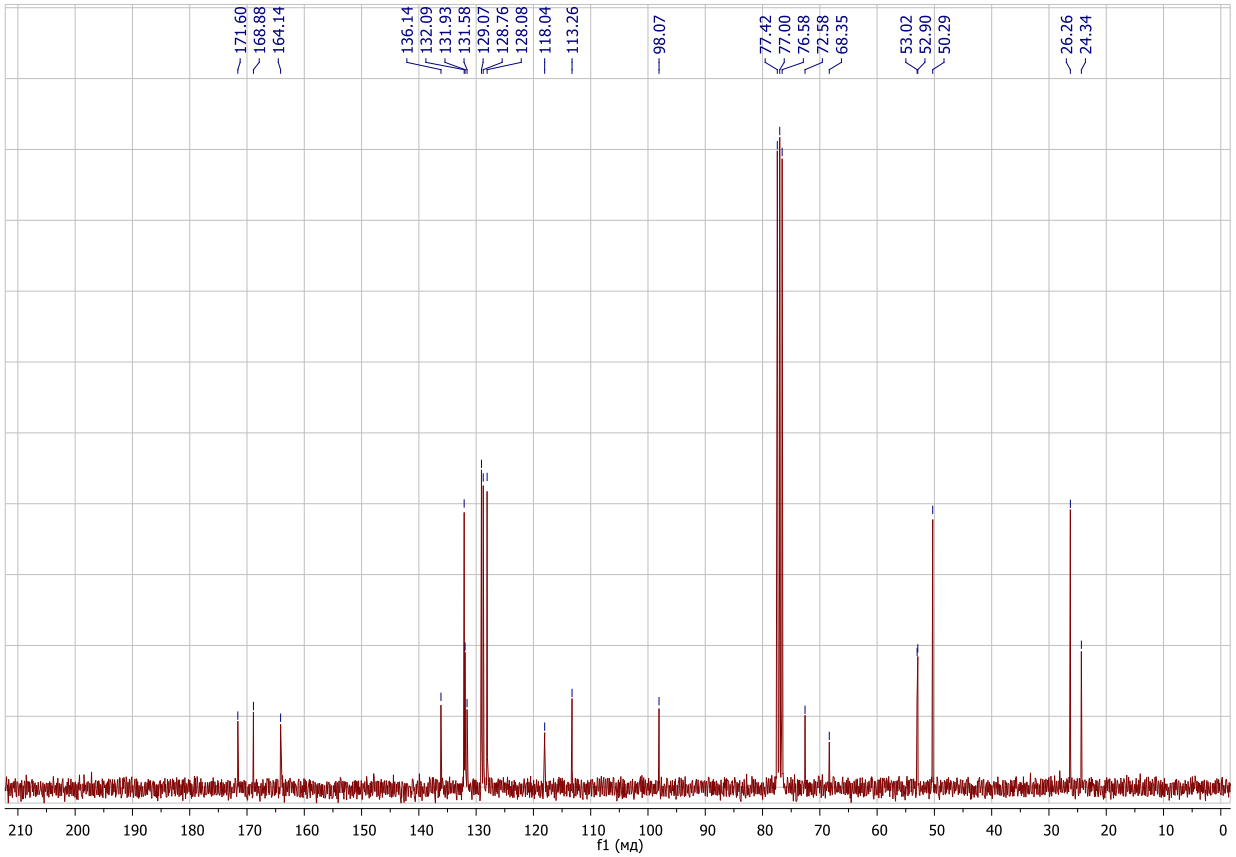
^{1}H and ^{13}C NMR spectra of compound **5d**



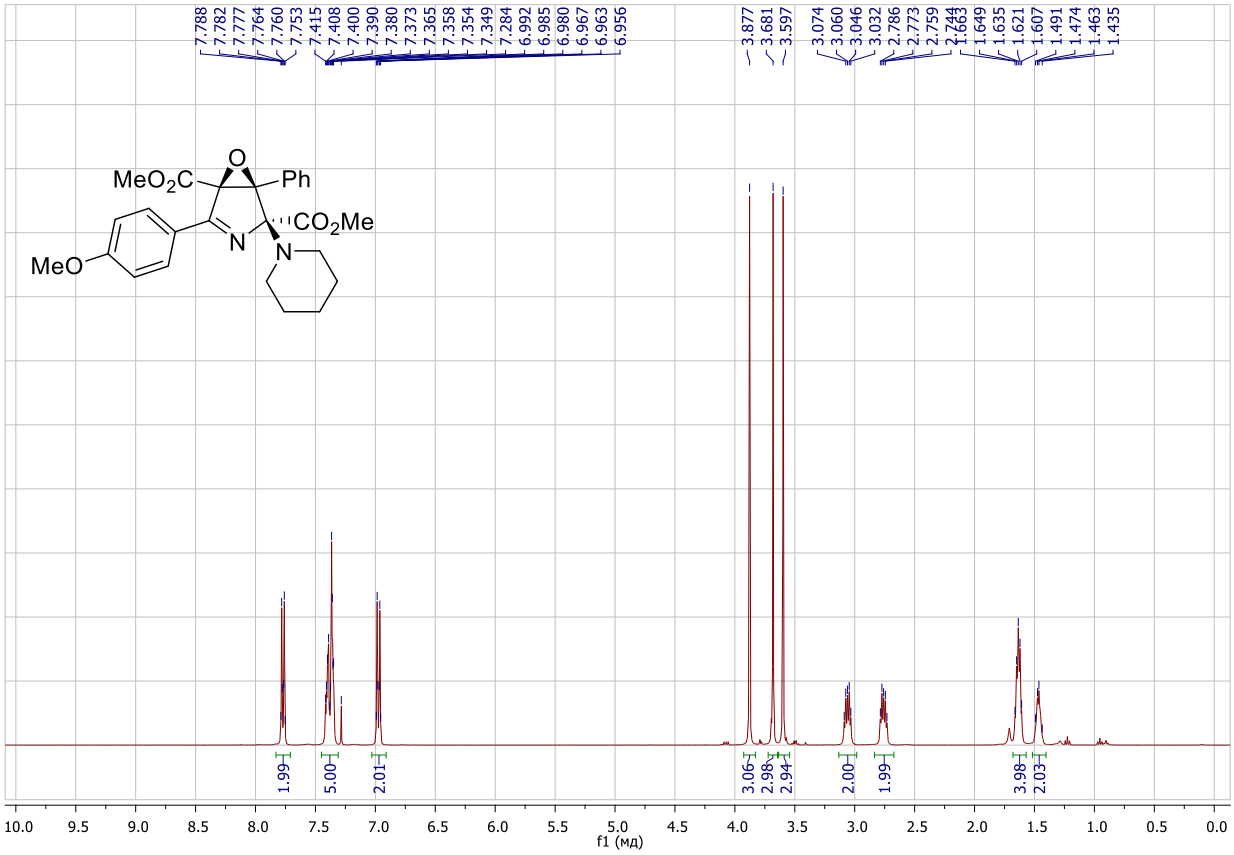


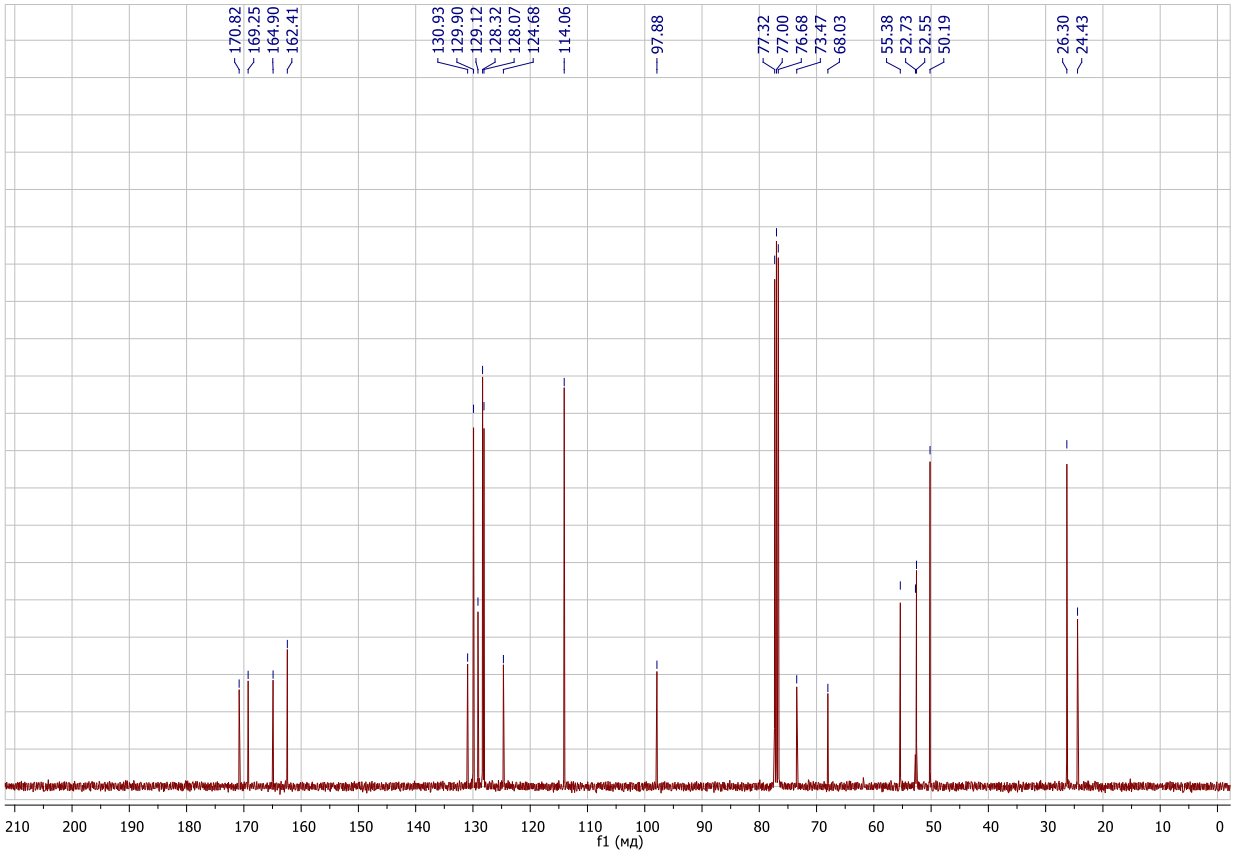
^{1}H and ^{13}C NMR spectra of compound **5e**



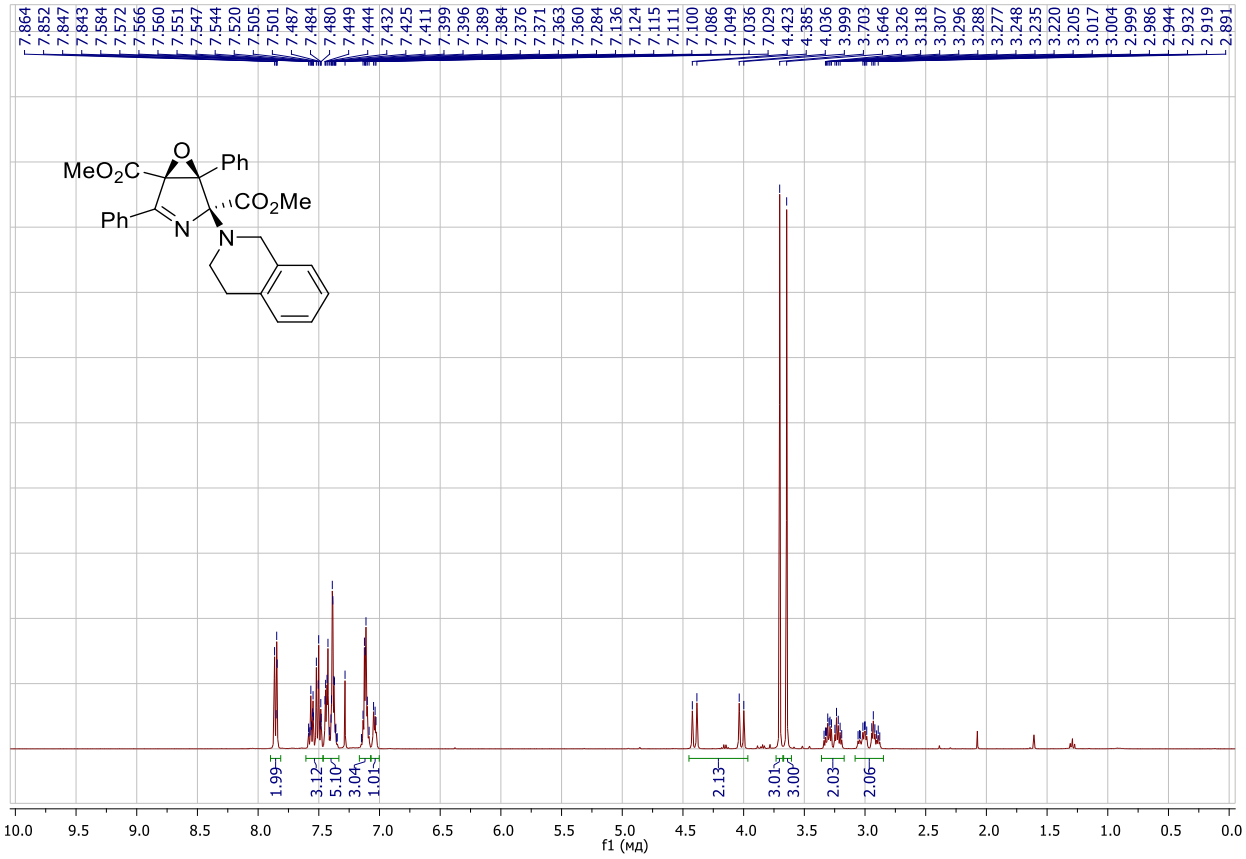


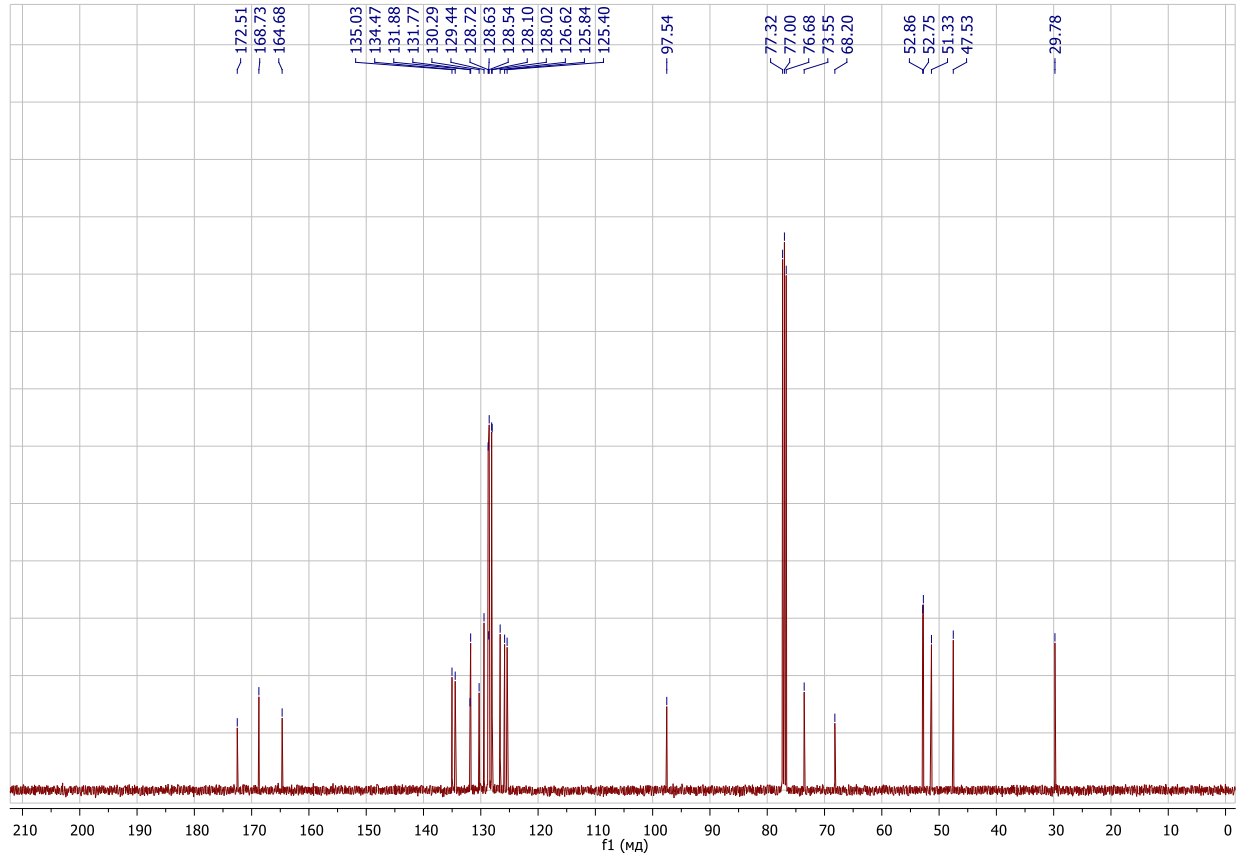
^{1}H and ^{13}C NMR spectra of compound **5f**



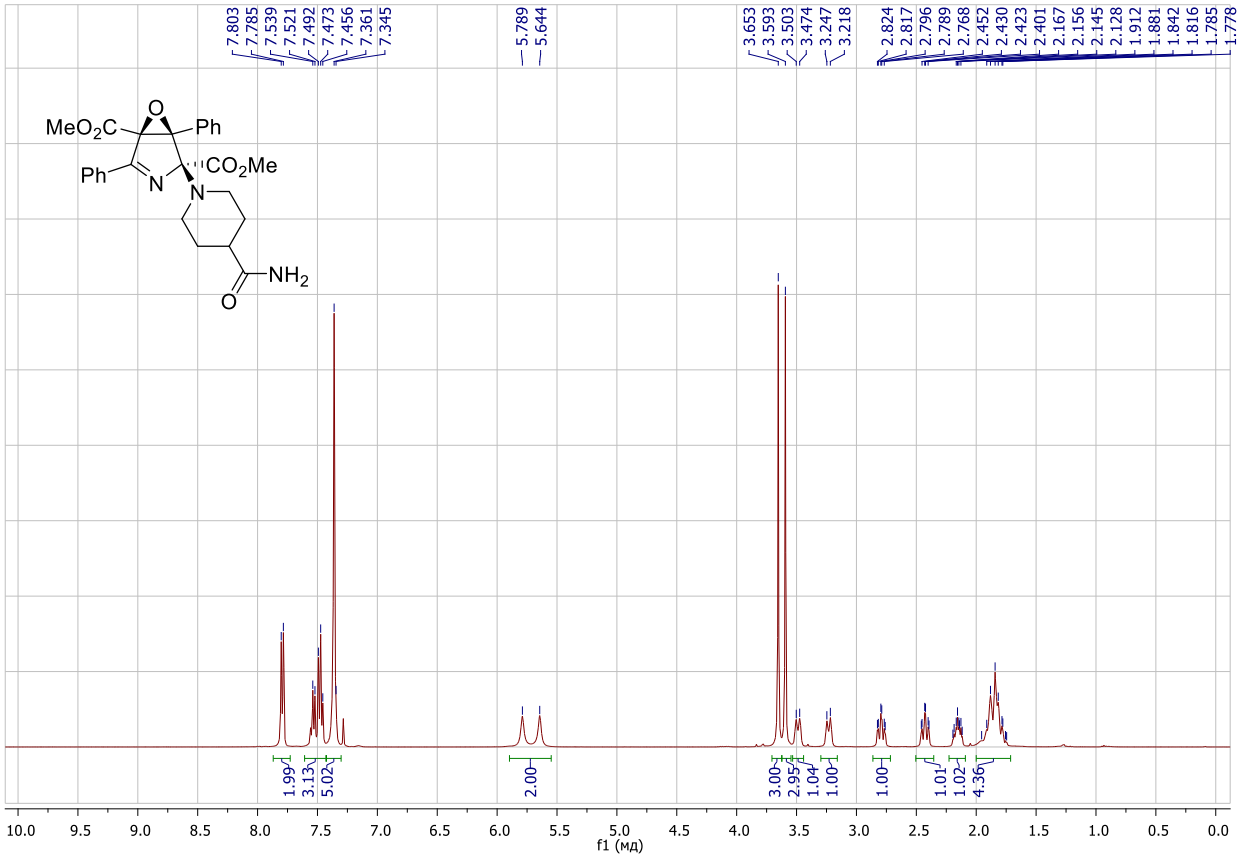


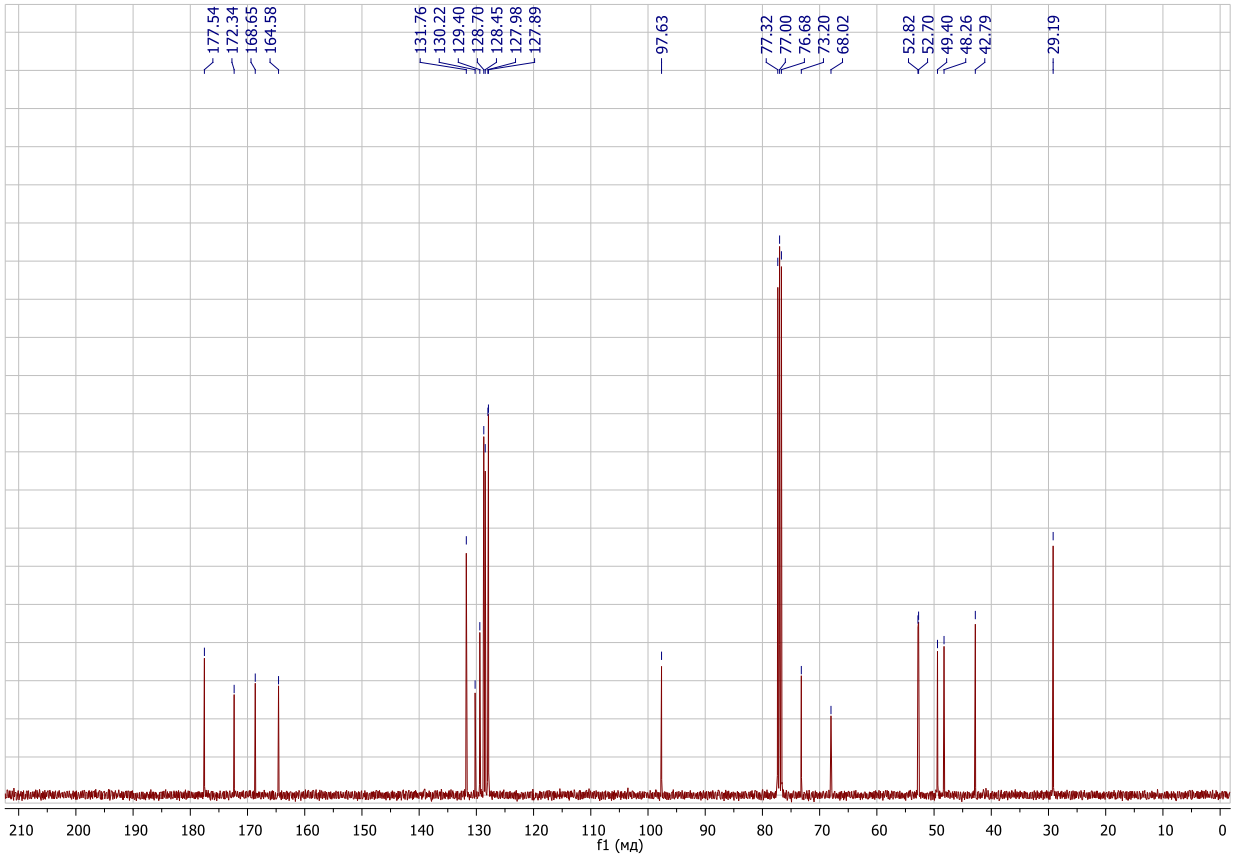
^{1}H and ^{13}C NMR spectra of compound **5g**



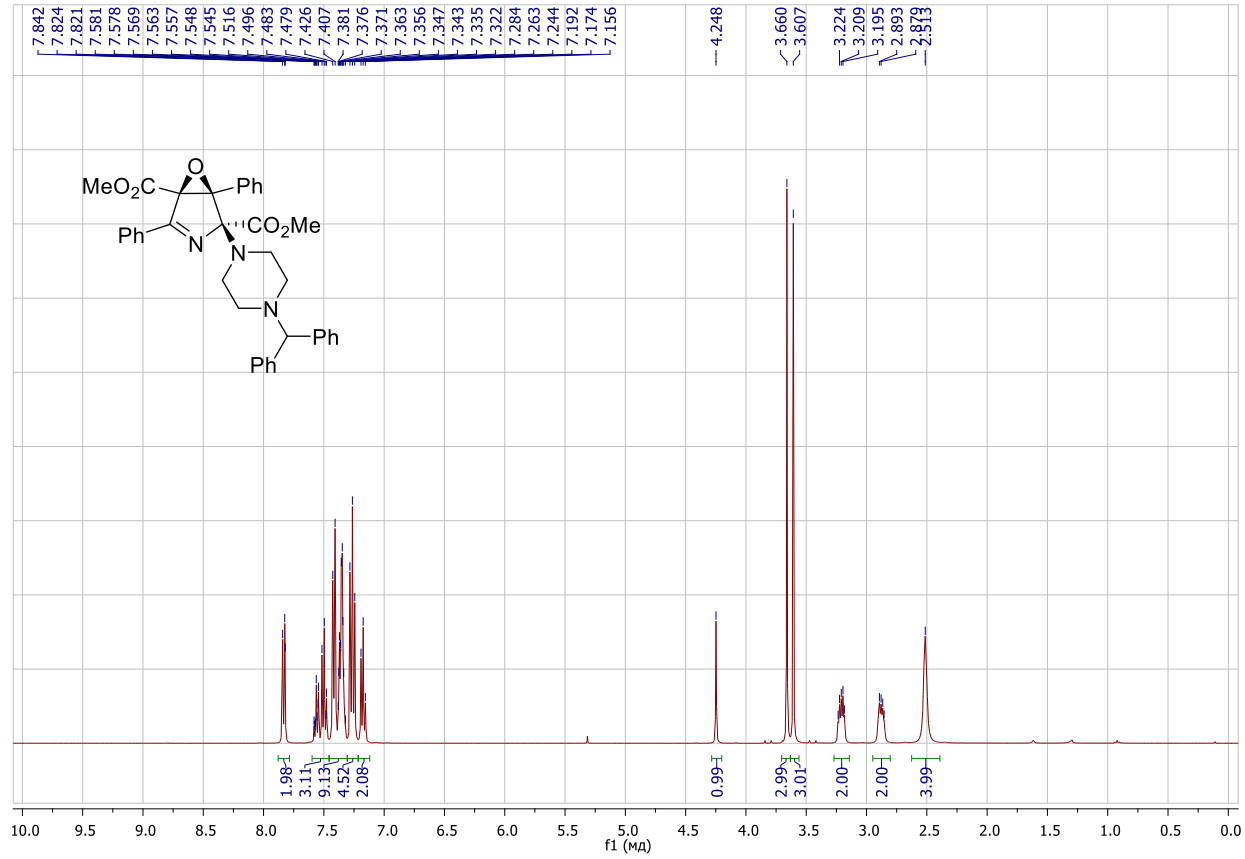


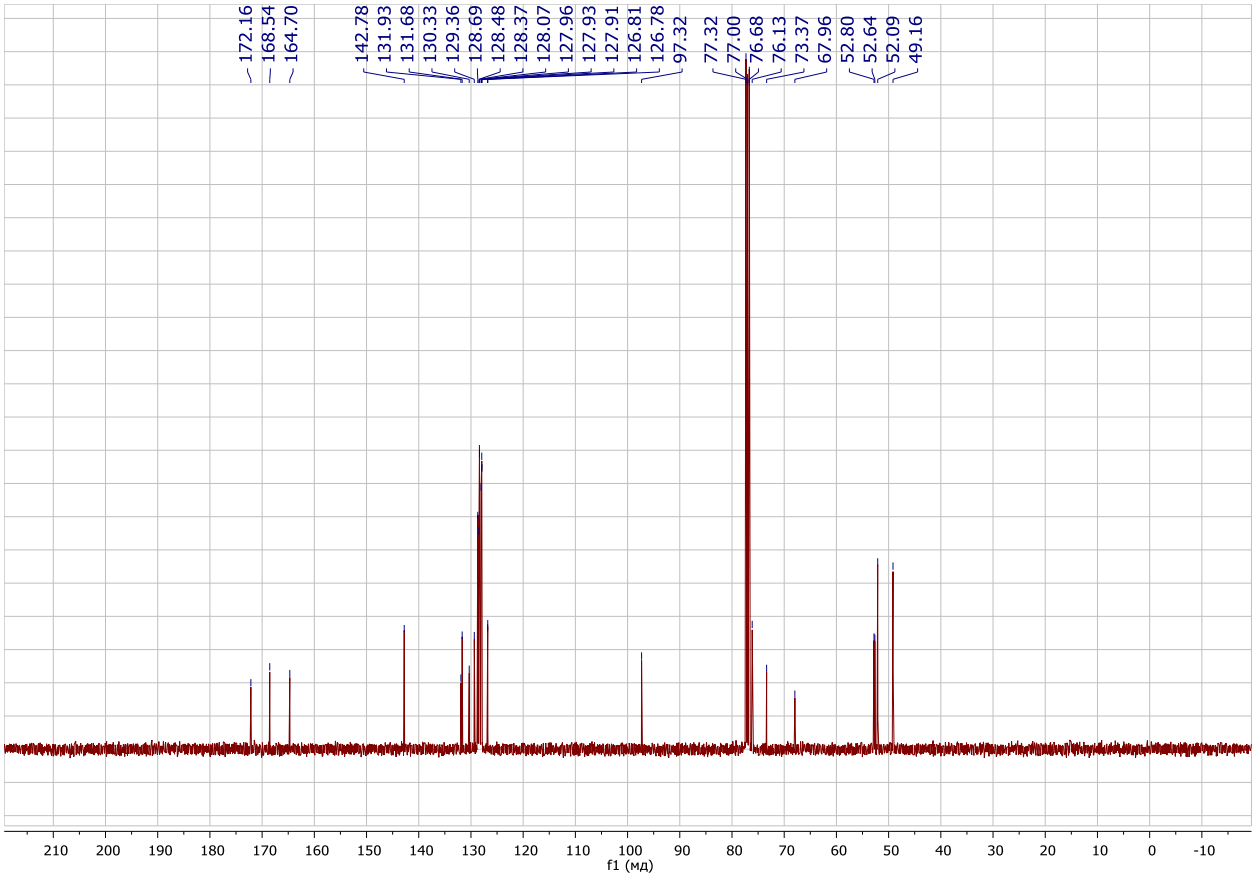
^{1}H and ^{13}C NMR spectra of compound **5h**



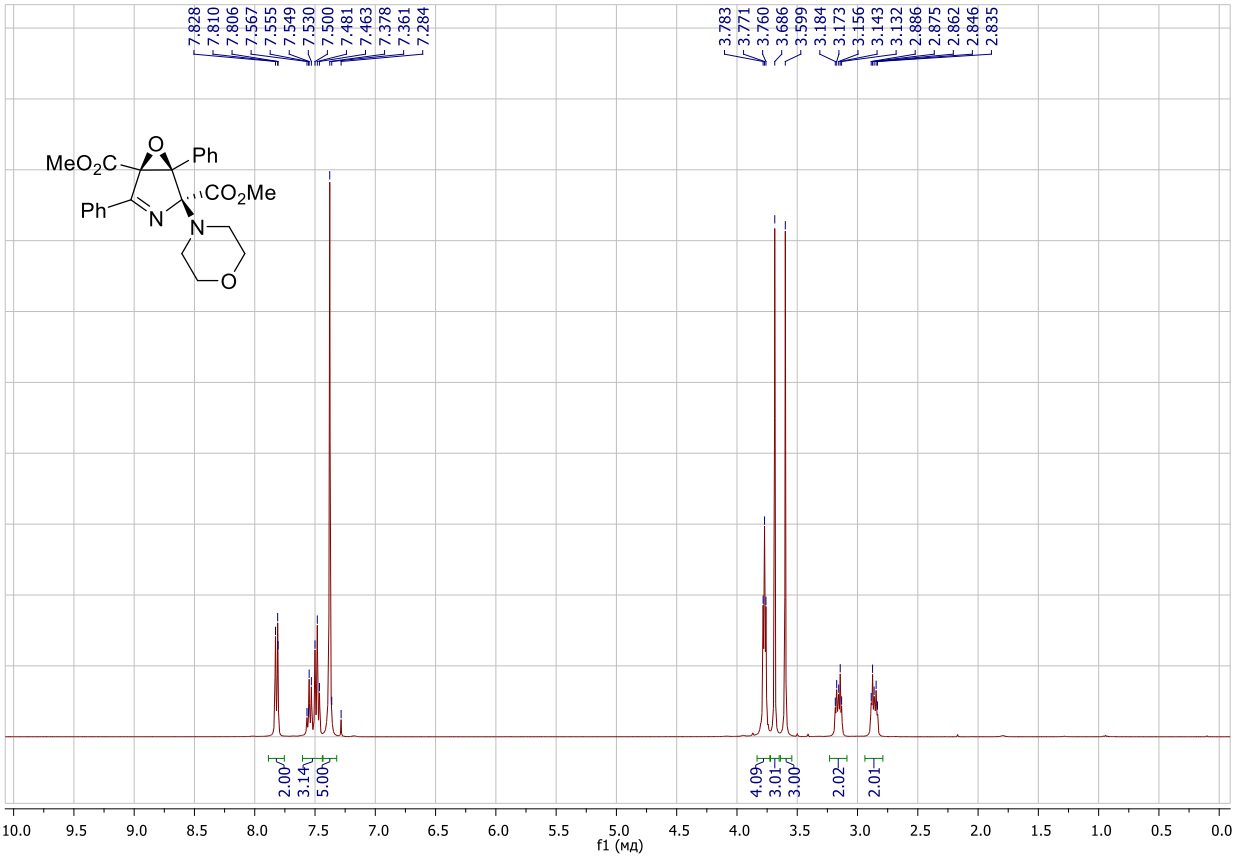


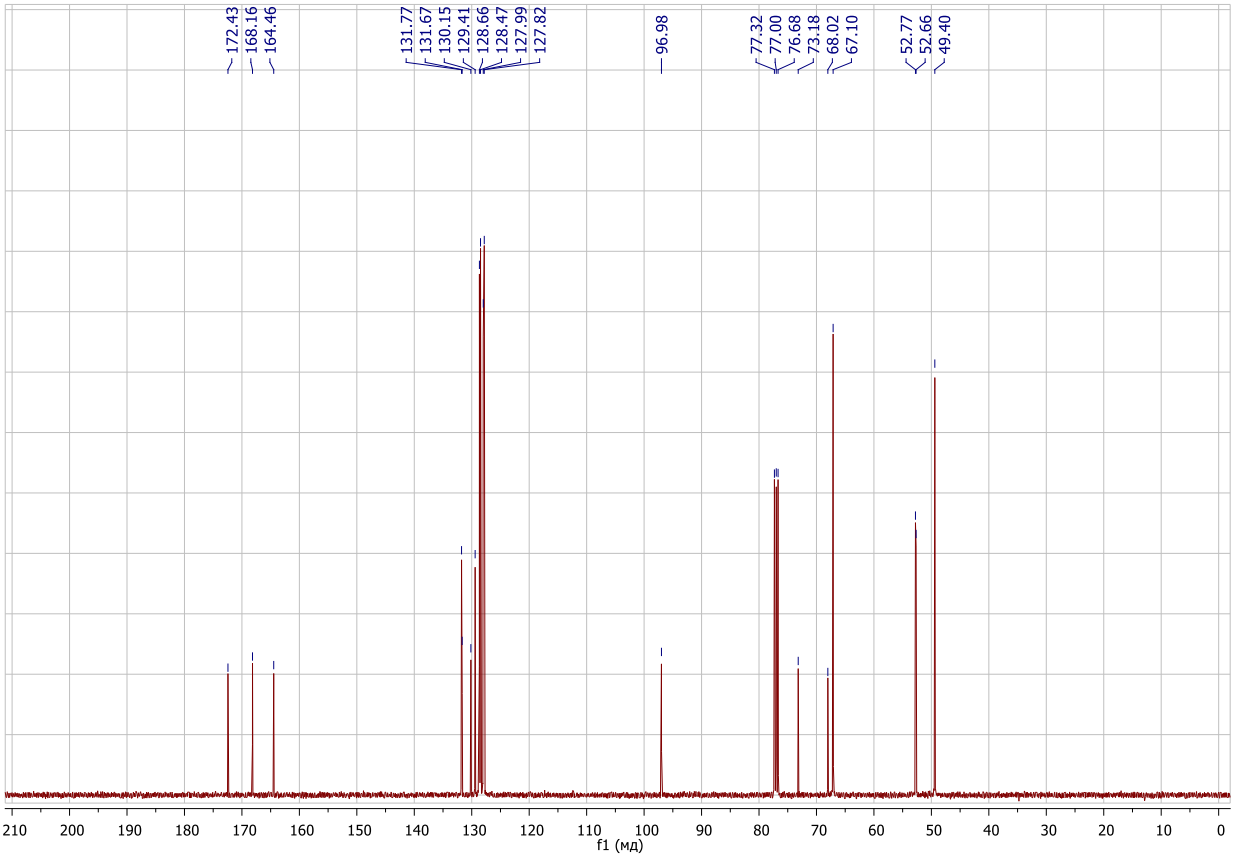
^{1}H and ^{13}C NMR spectra of compound **5i**



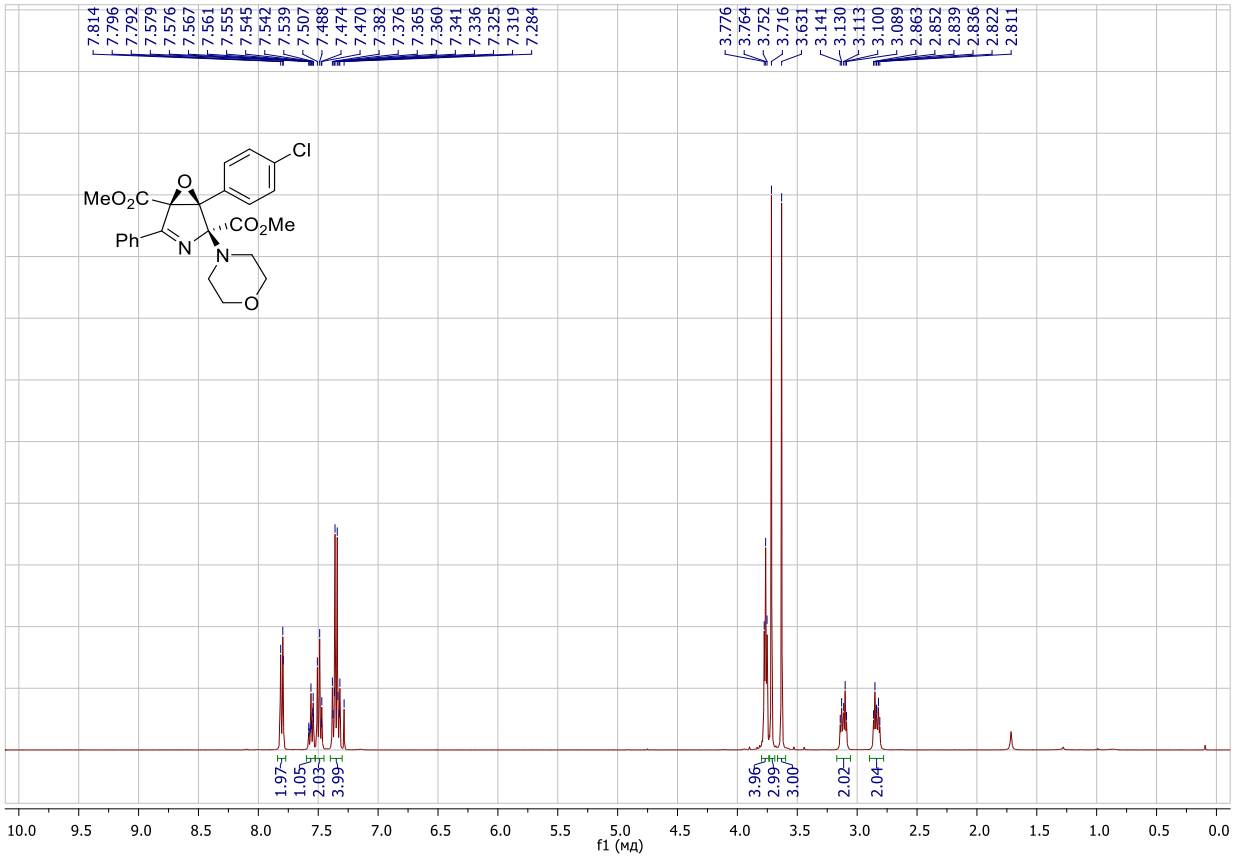


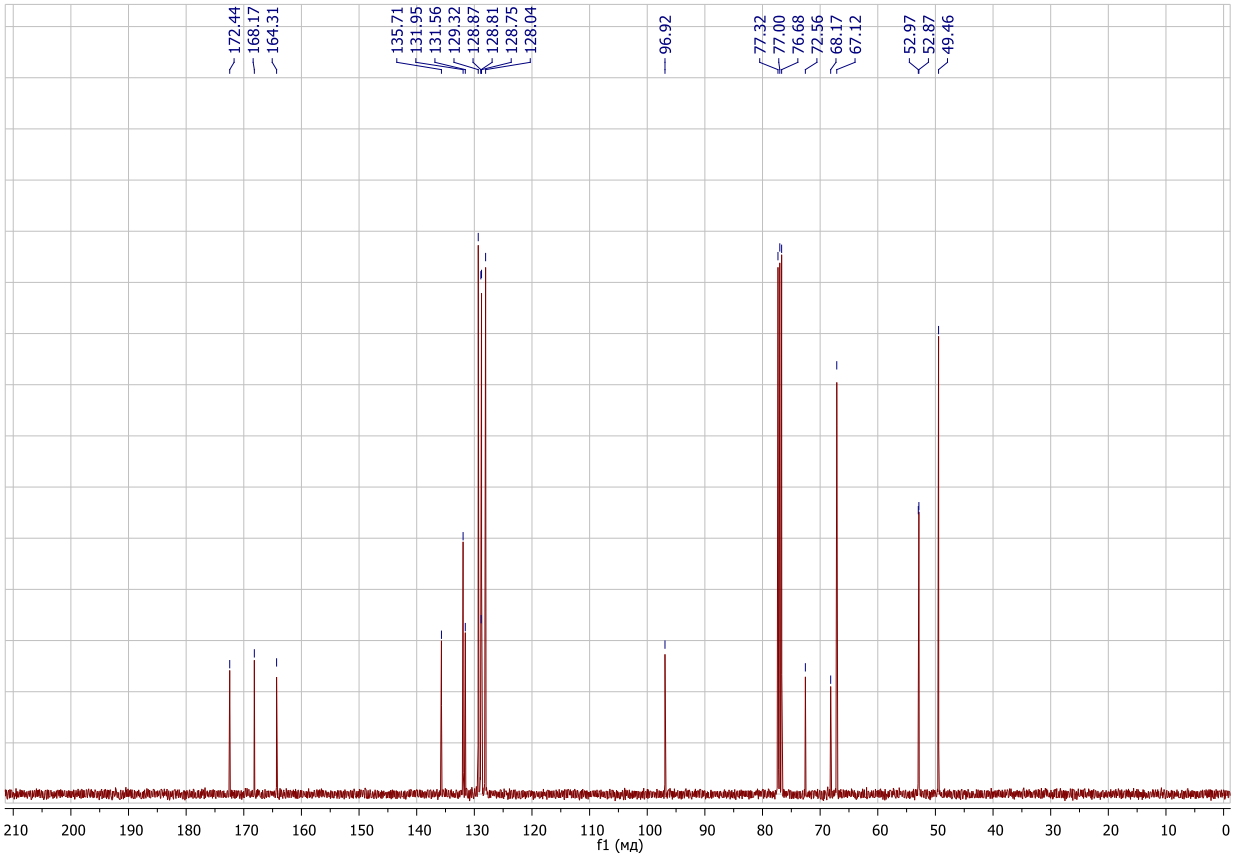
^{1}H and ^{13}C NMR spectra of compound **5j**



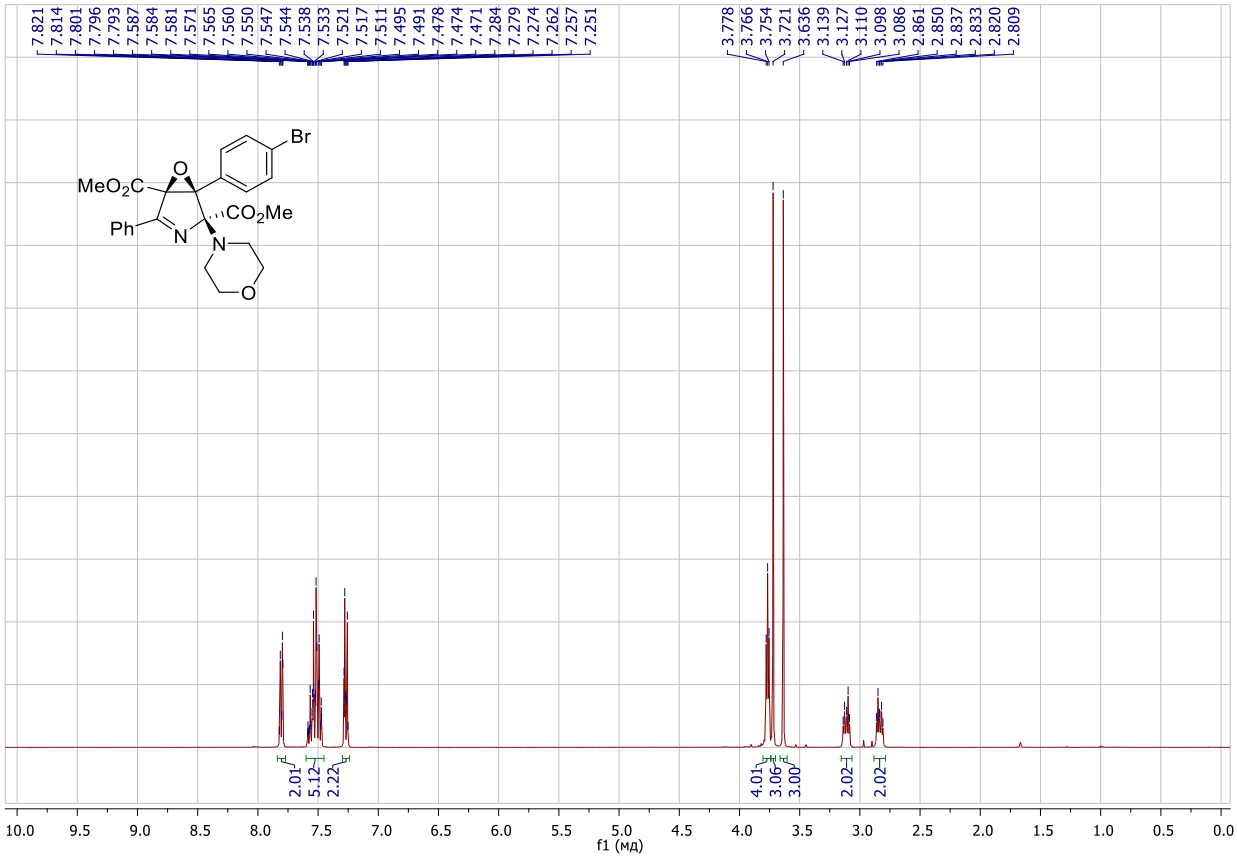


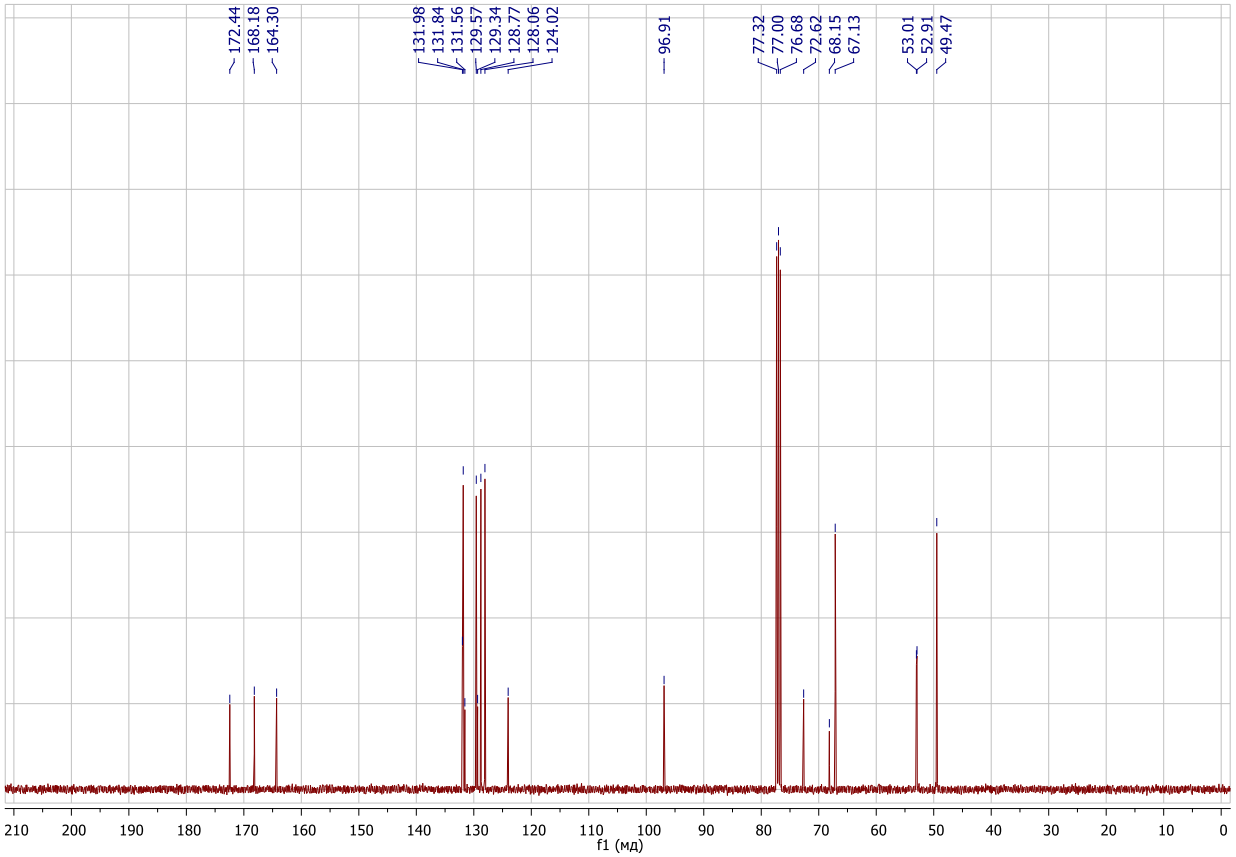
^{1}H and ^{13}C NMR spectra of compound **5k**



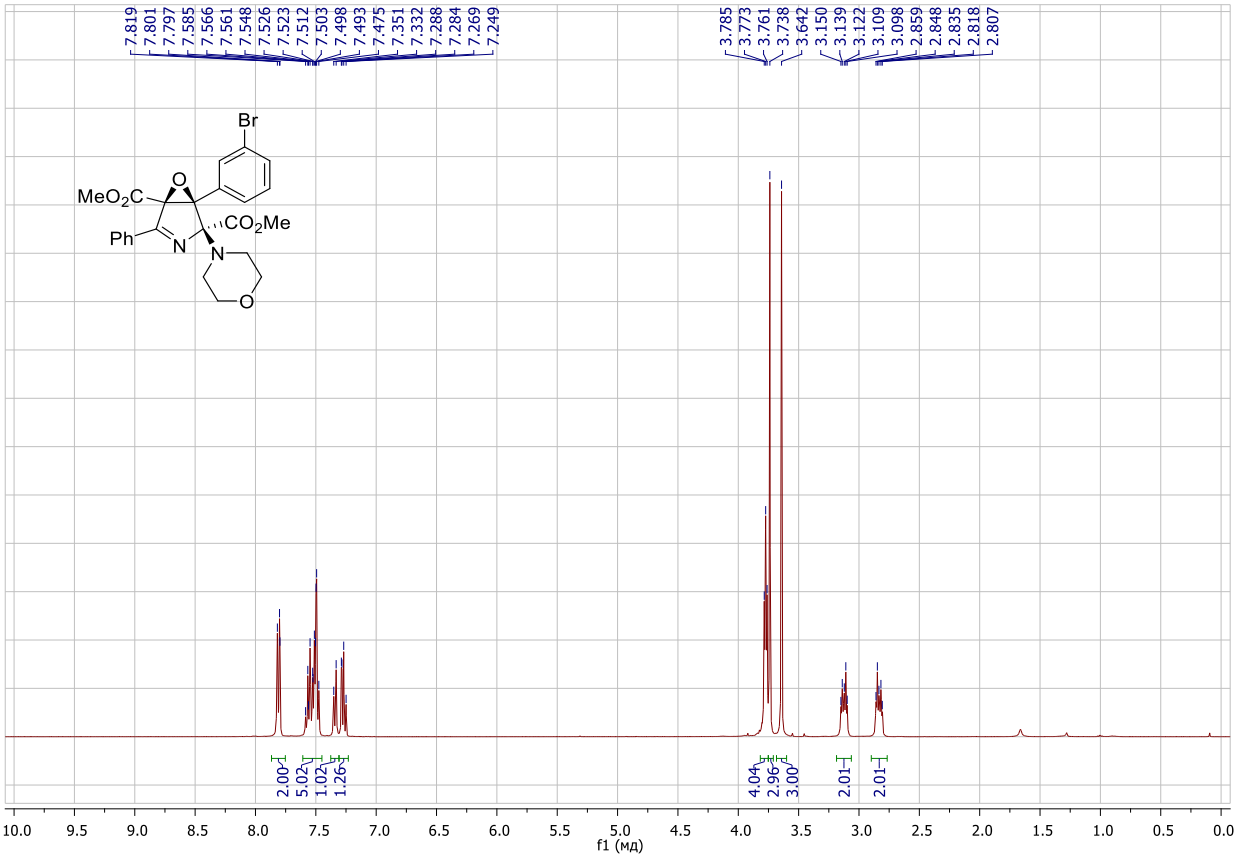


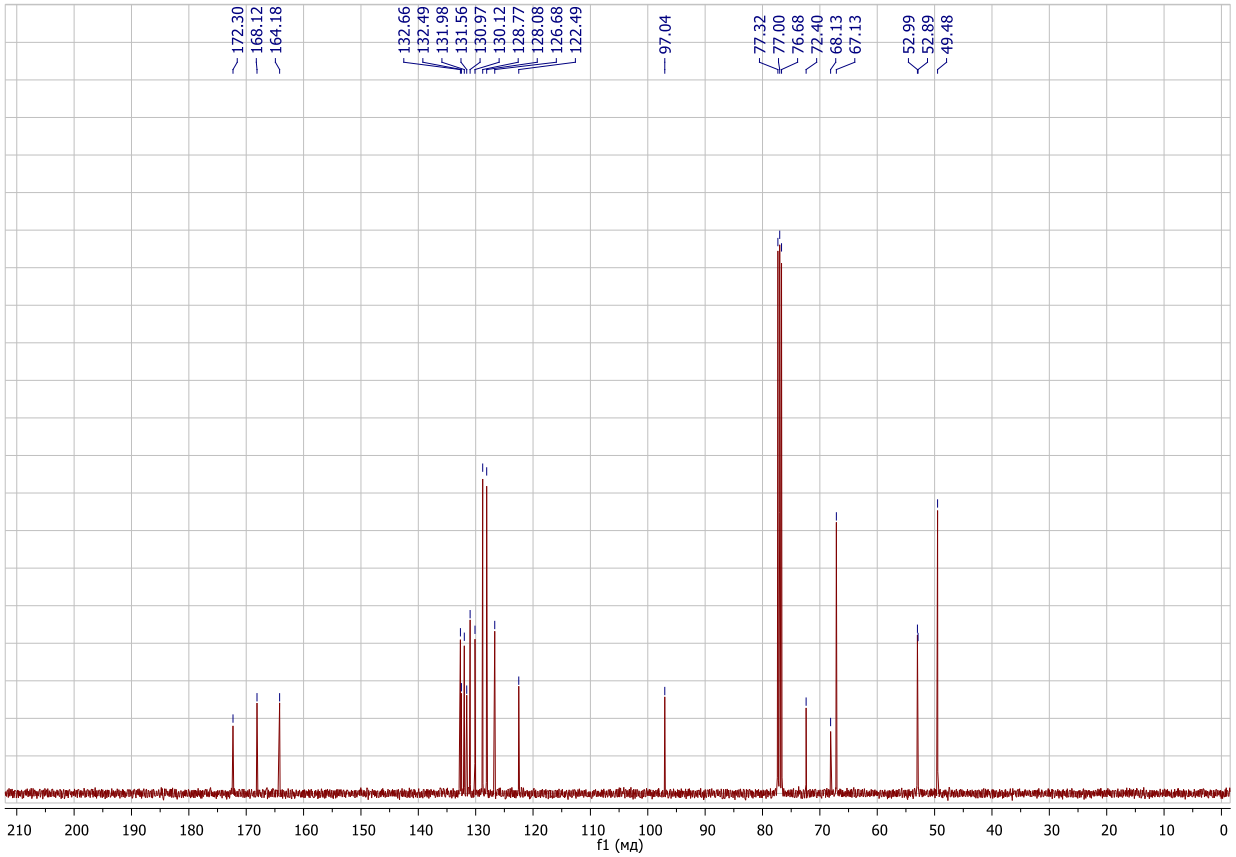
^{1}H and ^{13}C NMR spectra of compound **5l**



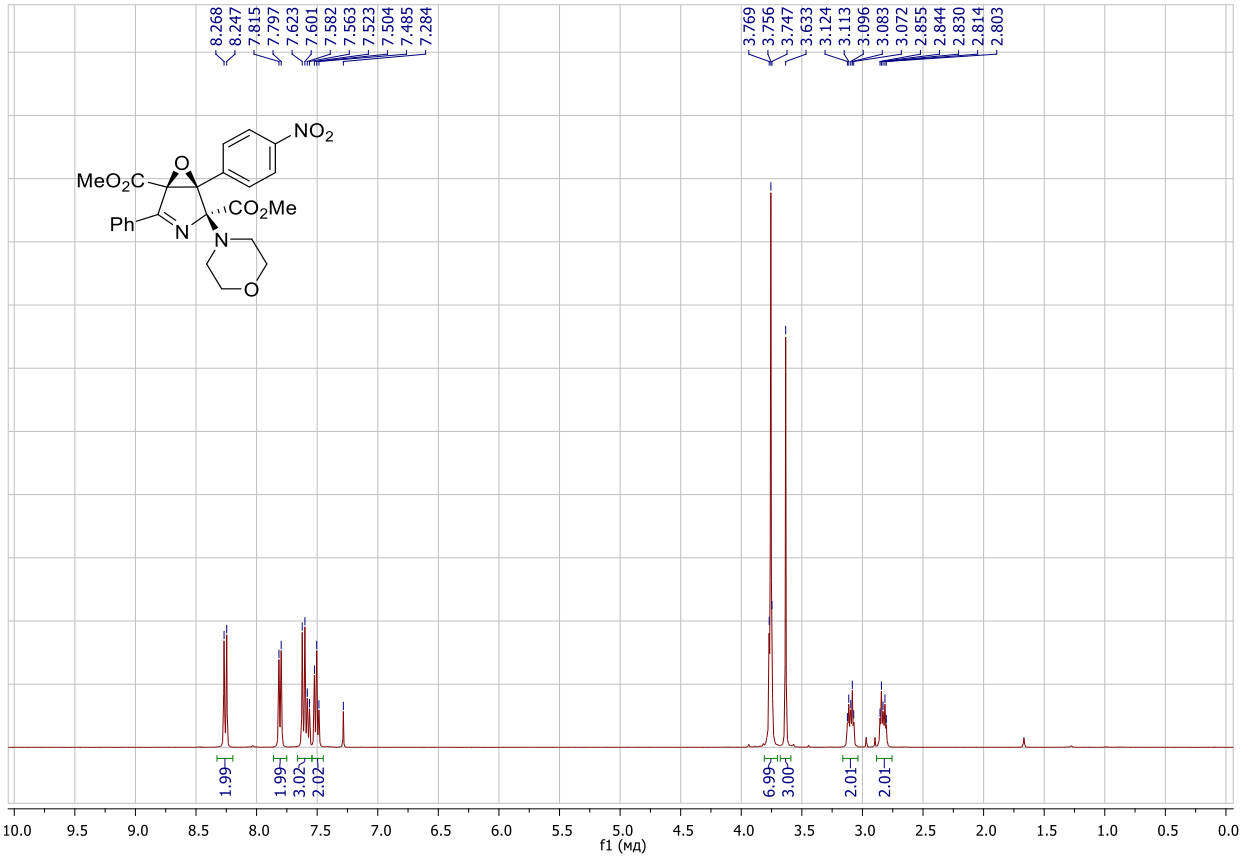


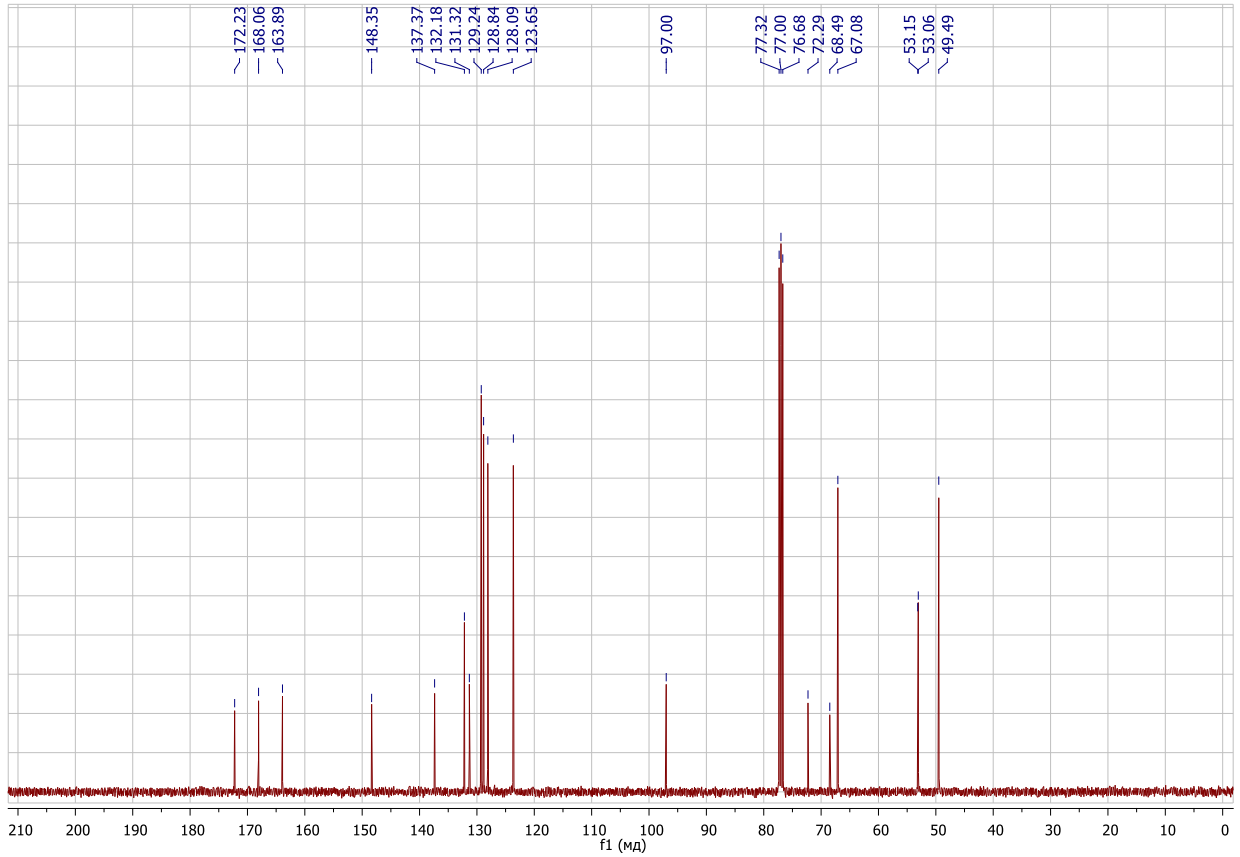
^{1}H and ^{13}C NMR spectra of compound **5m**



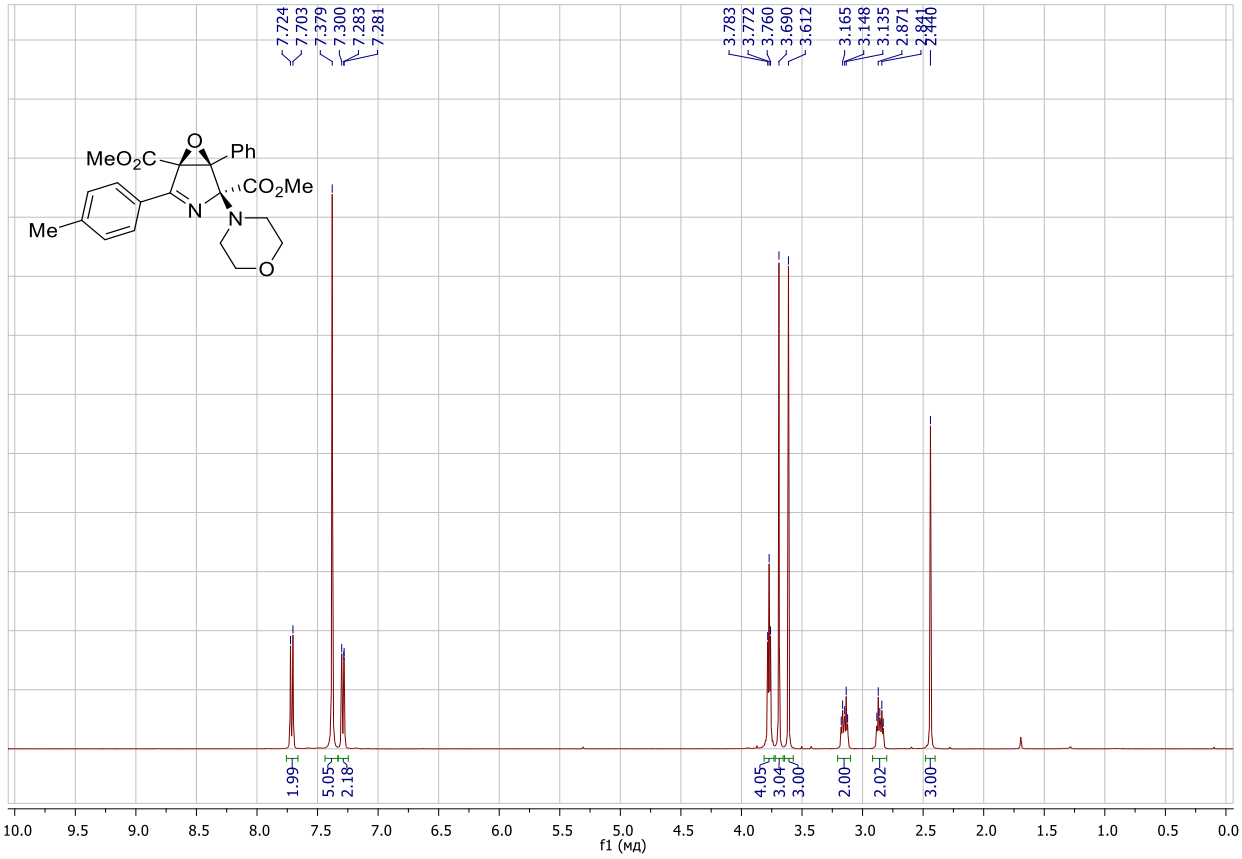


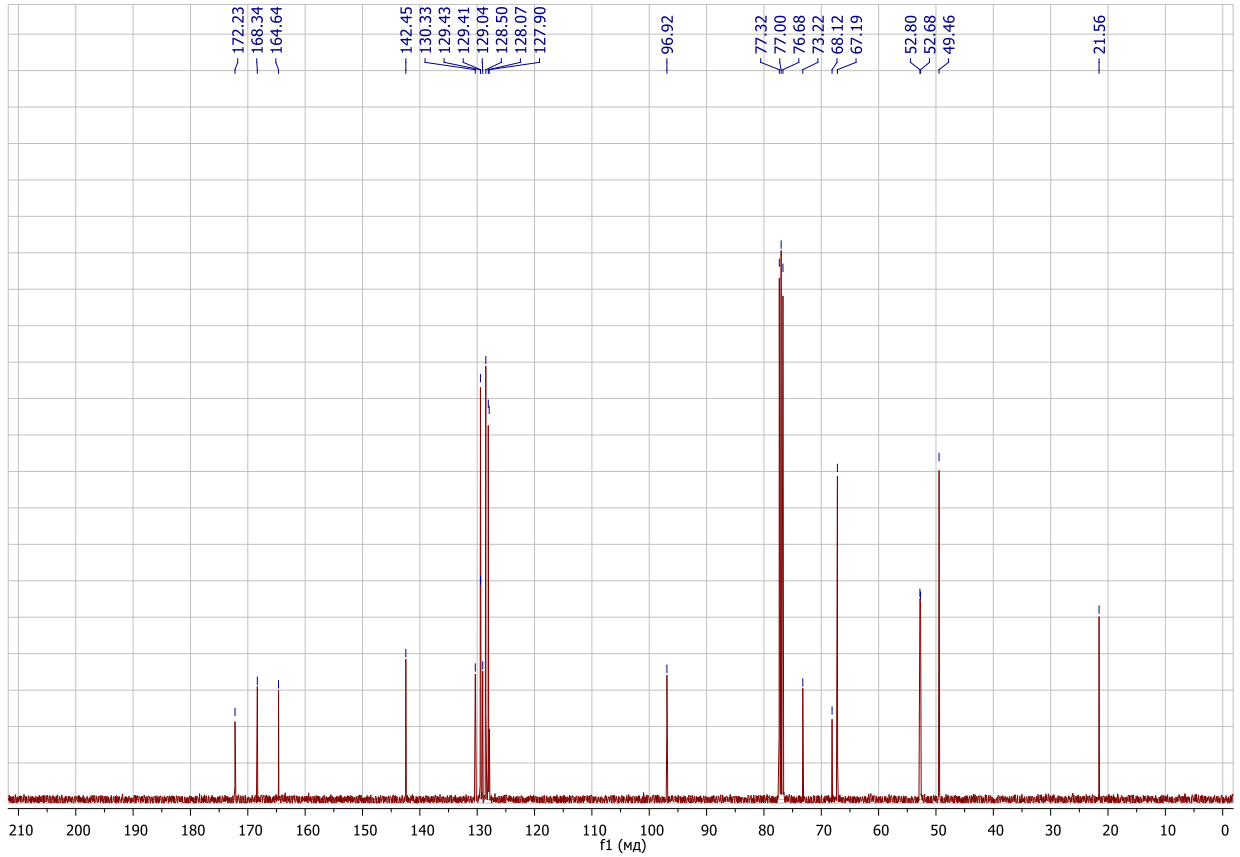
^{1}H and ^{13}C NMR spectra of compound **5n**



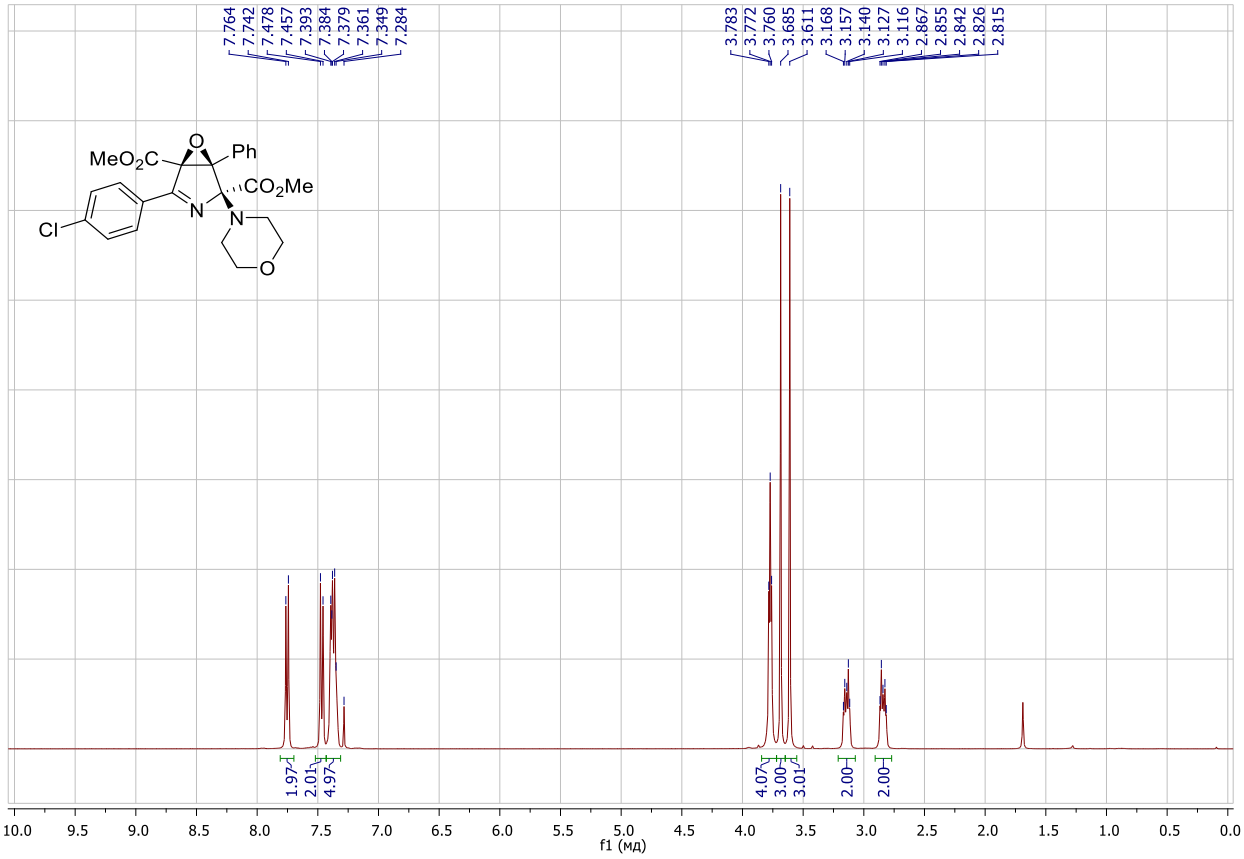


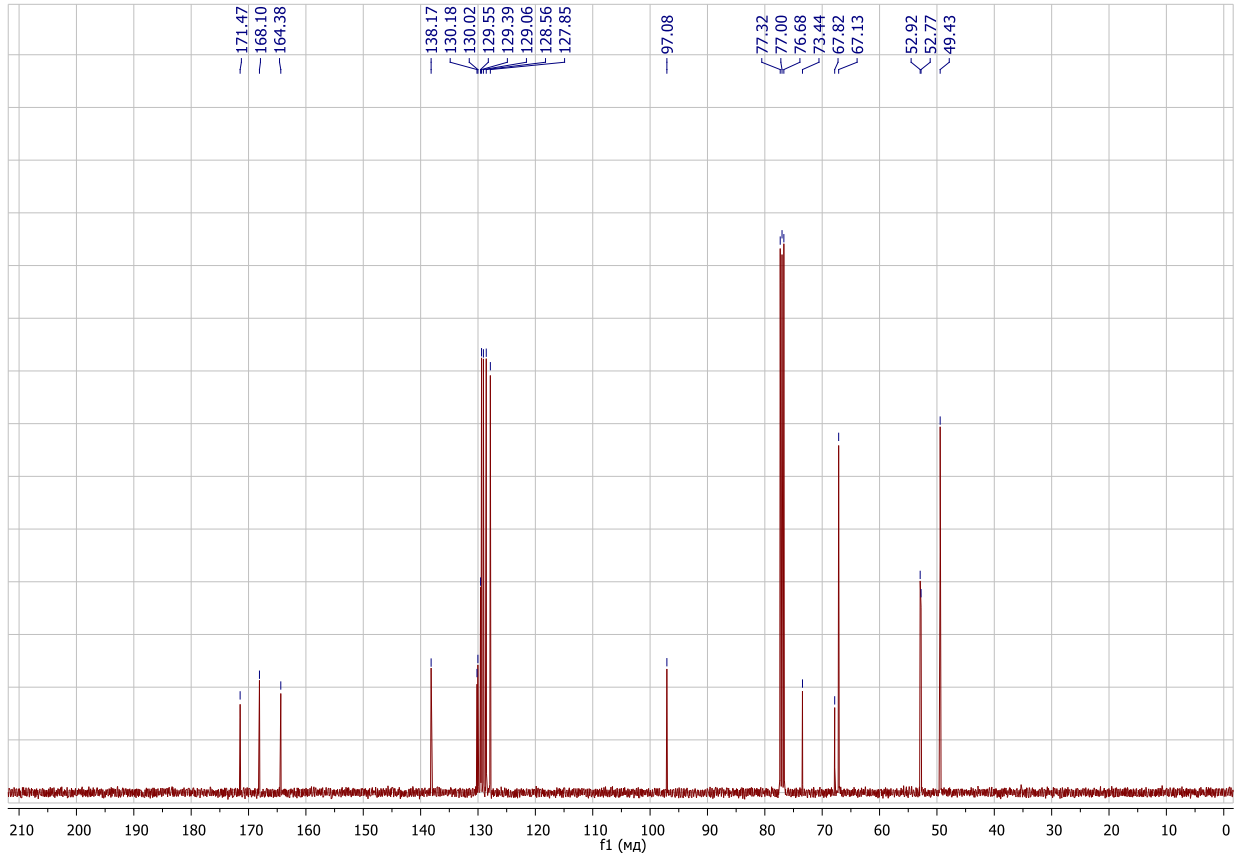
^{1}H and ^{13}C NMR spectra of compound **5o**



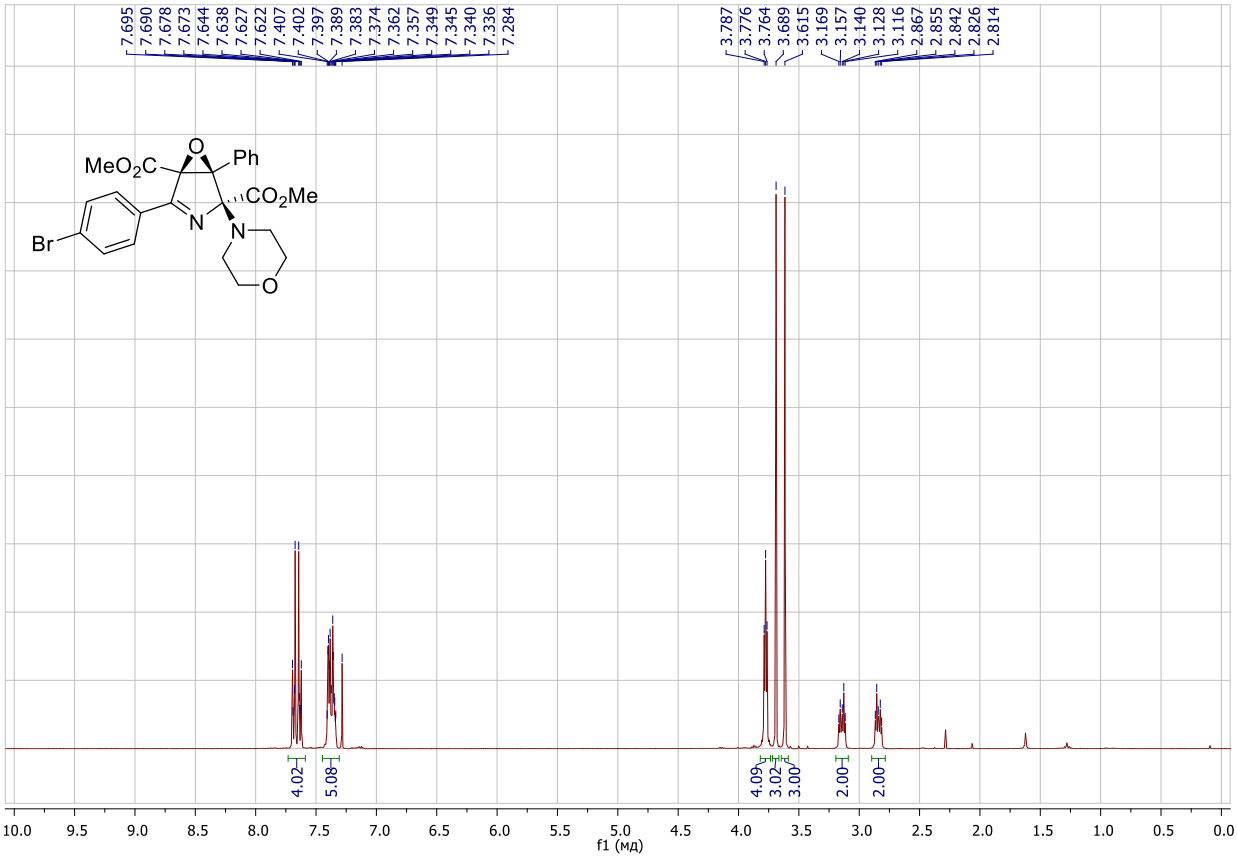


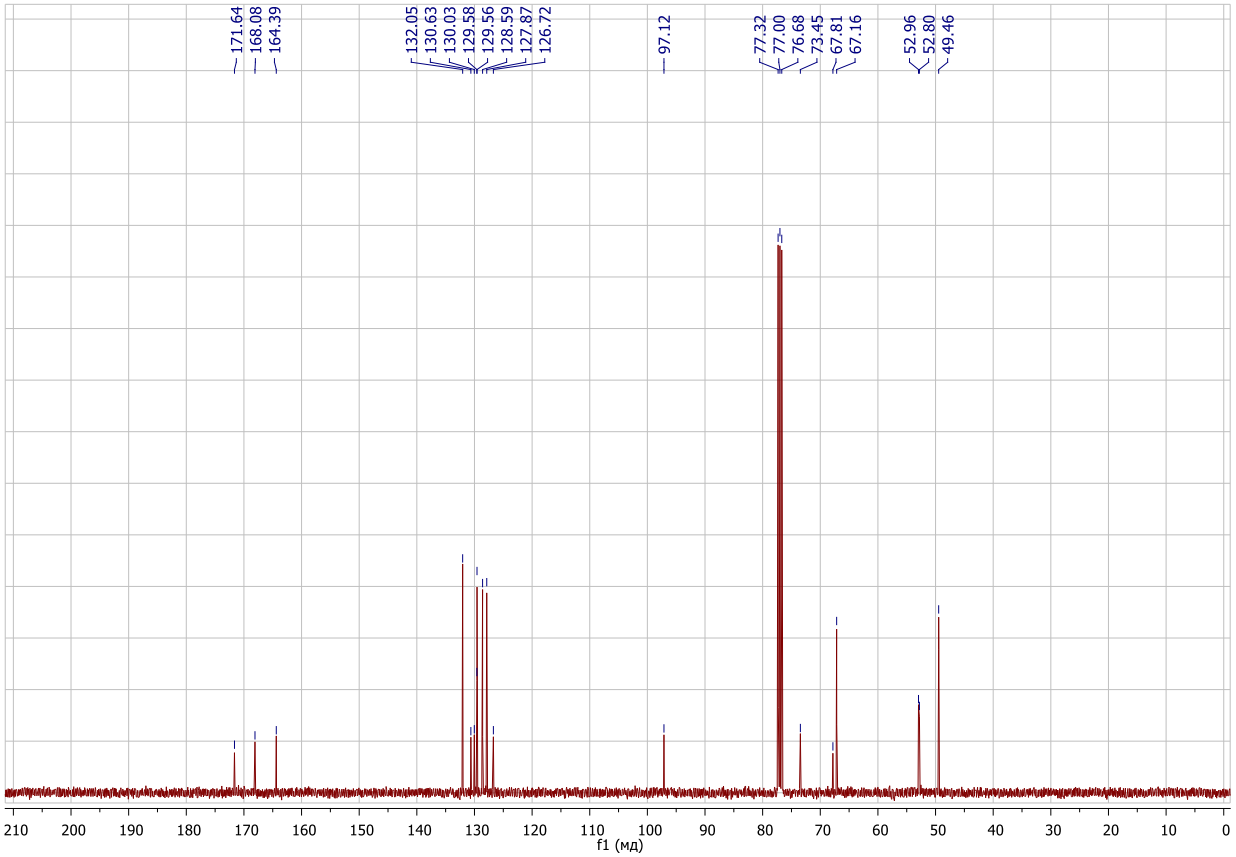
^{1}H and ^{13}C NMR spectra of compound **5p**



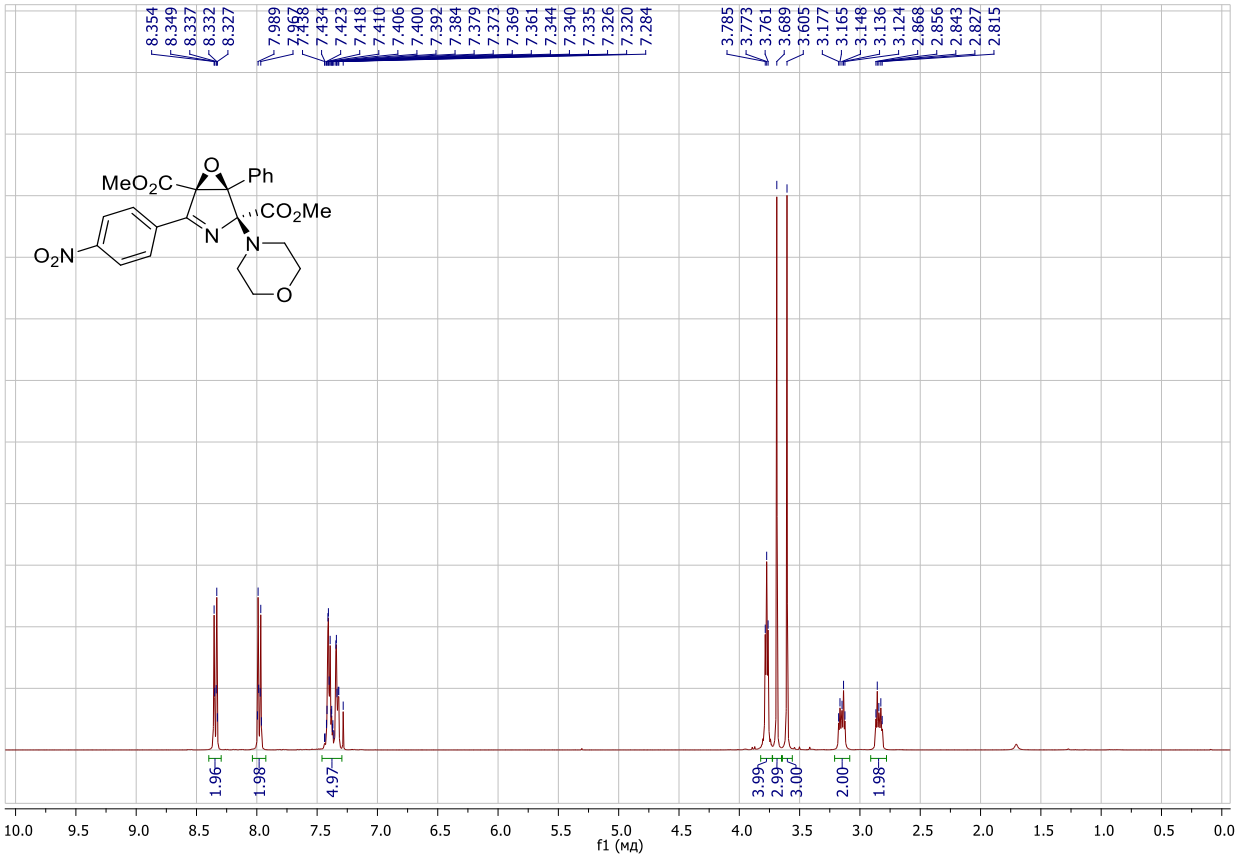


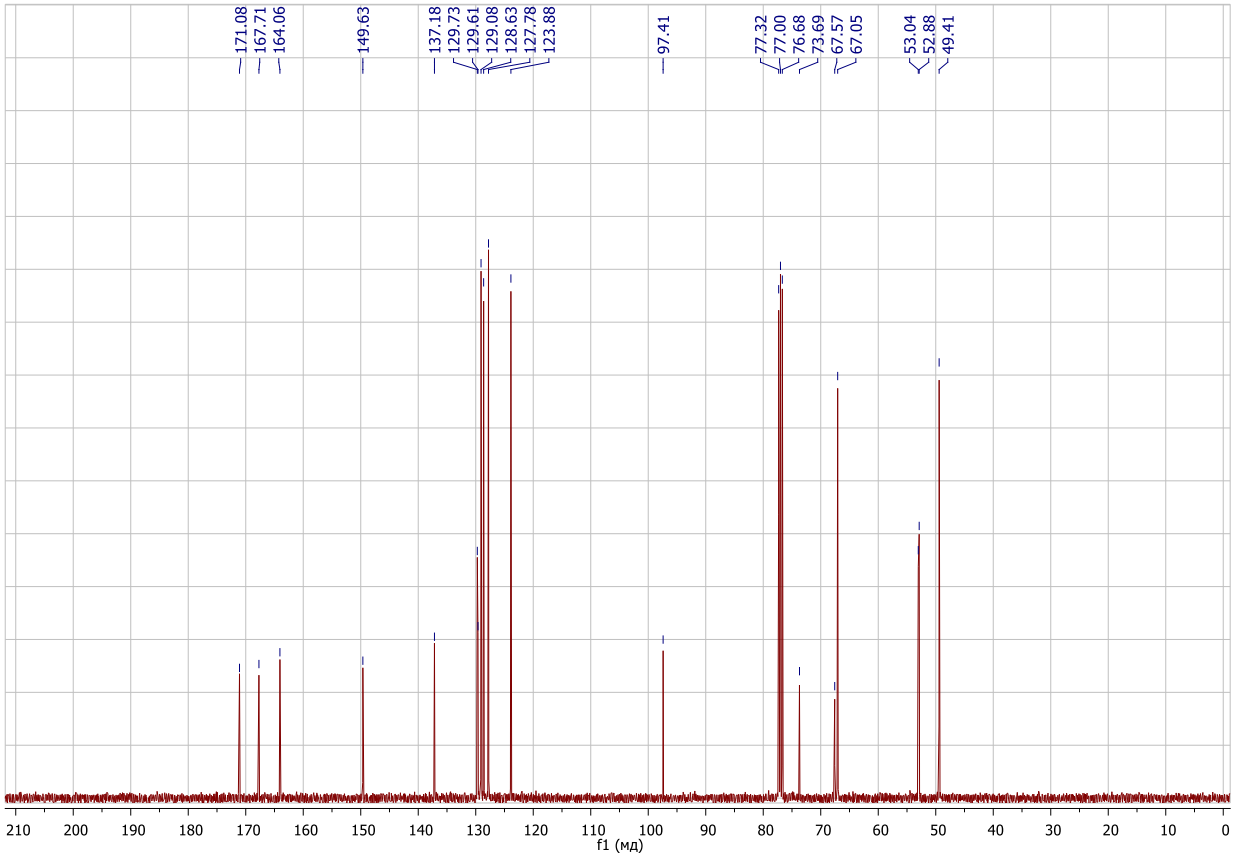
^{1}H and ^{13}C NMR spectra of compound **5q**



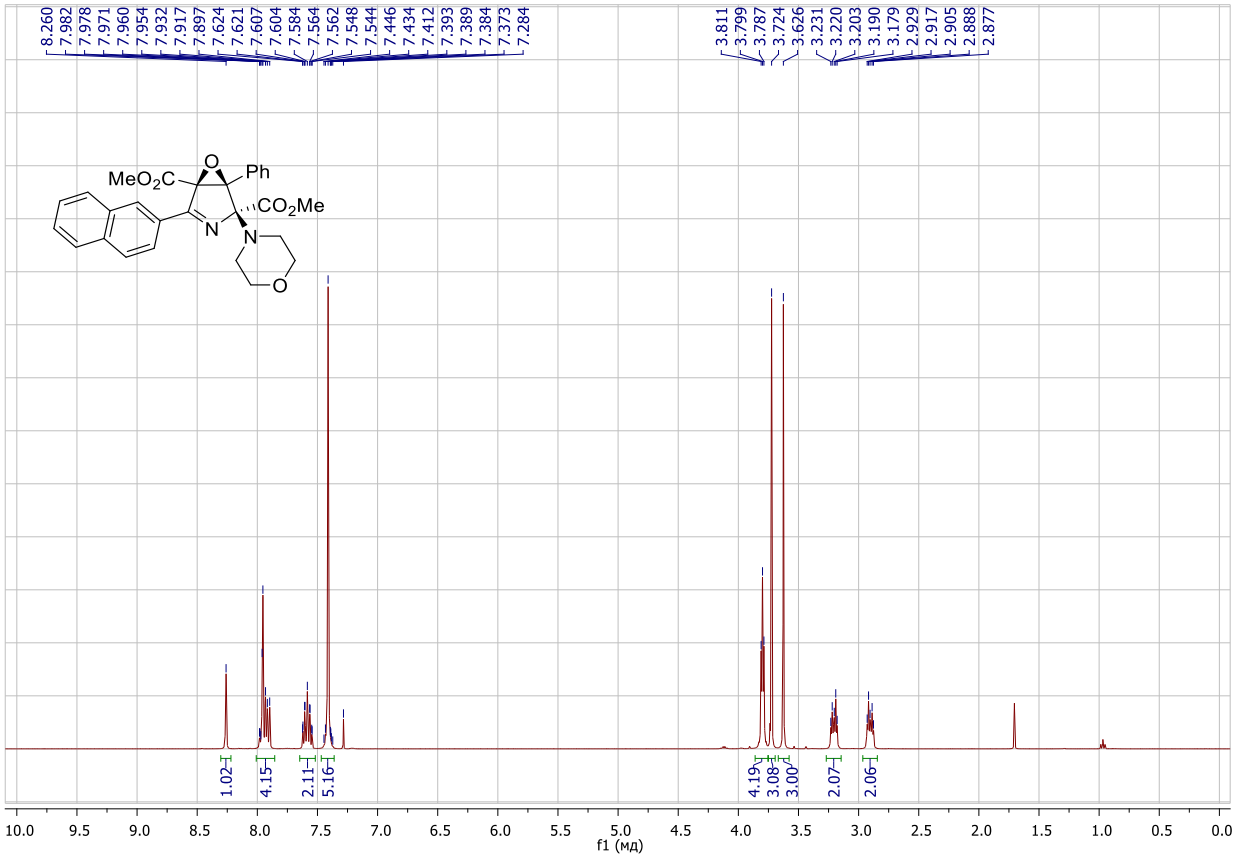


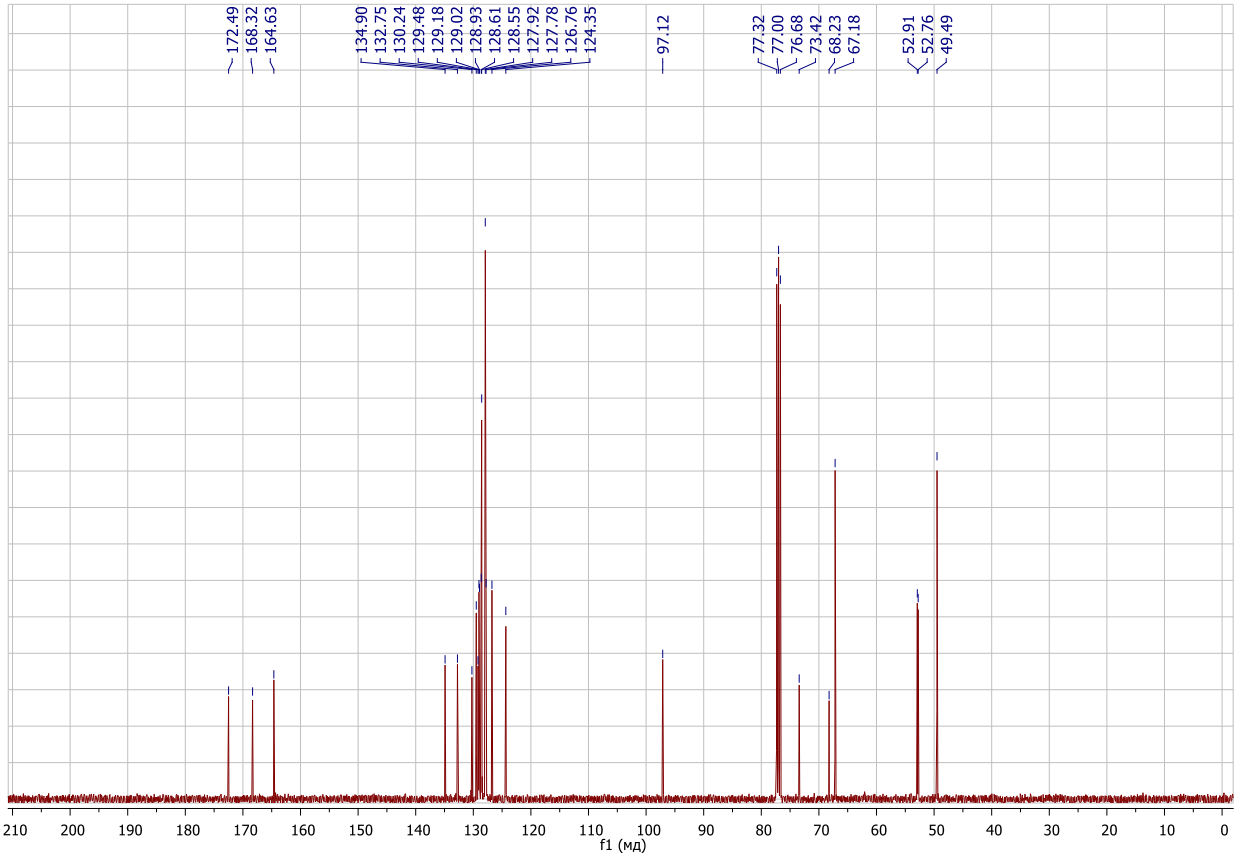
^{1}H and ^{13}C NMR spectra of compound **5r**



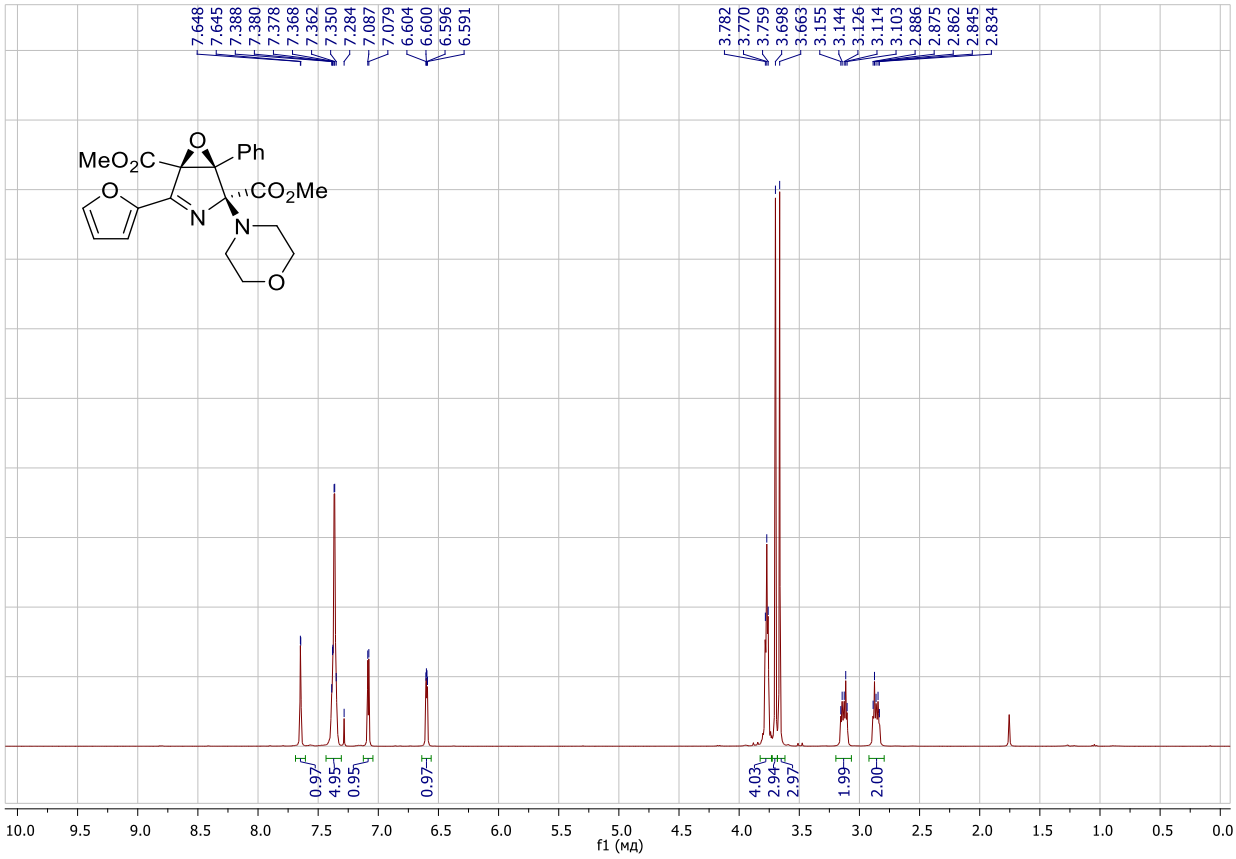


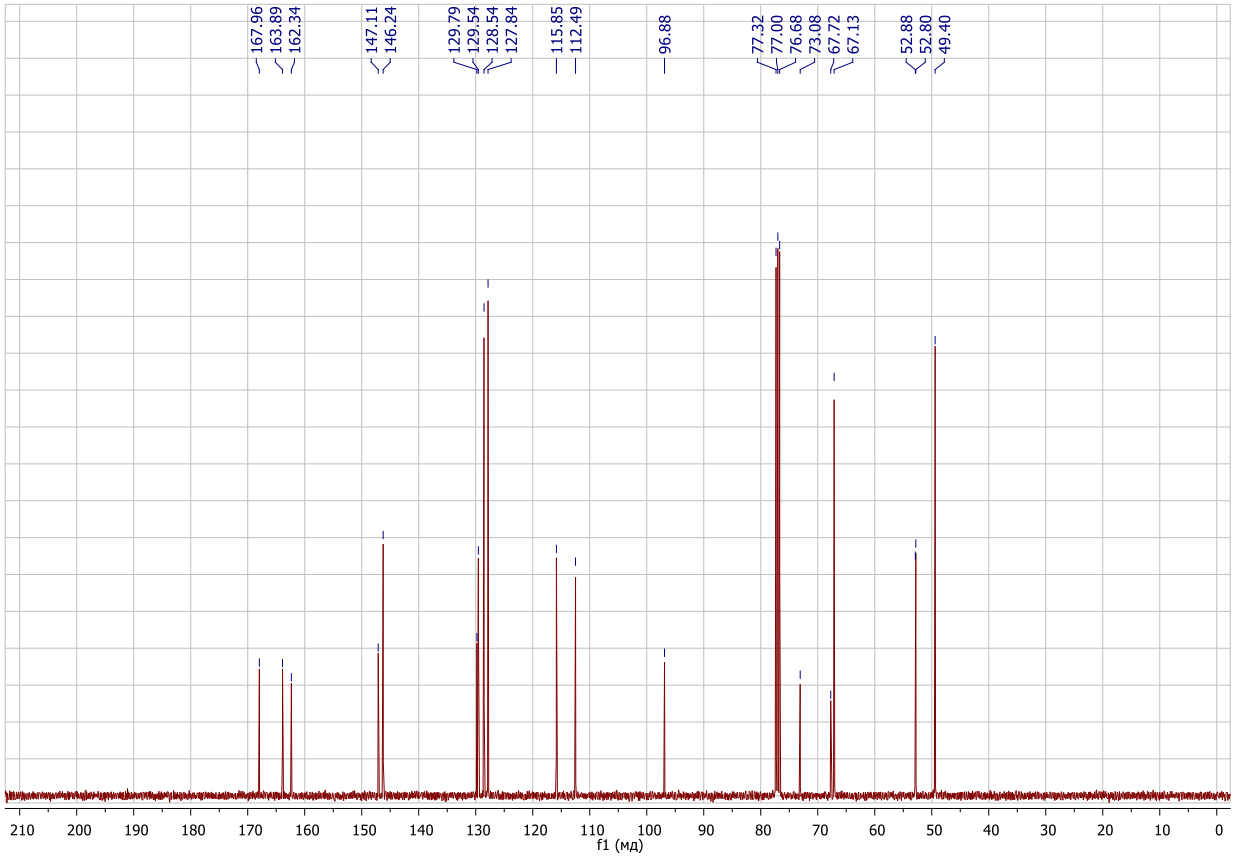
^{1}H and ^{13}C NMR spectra of compound **5s**



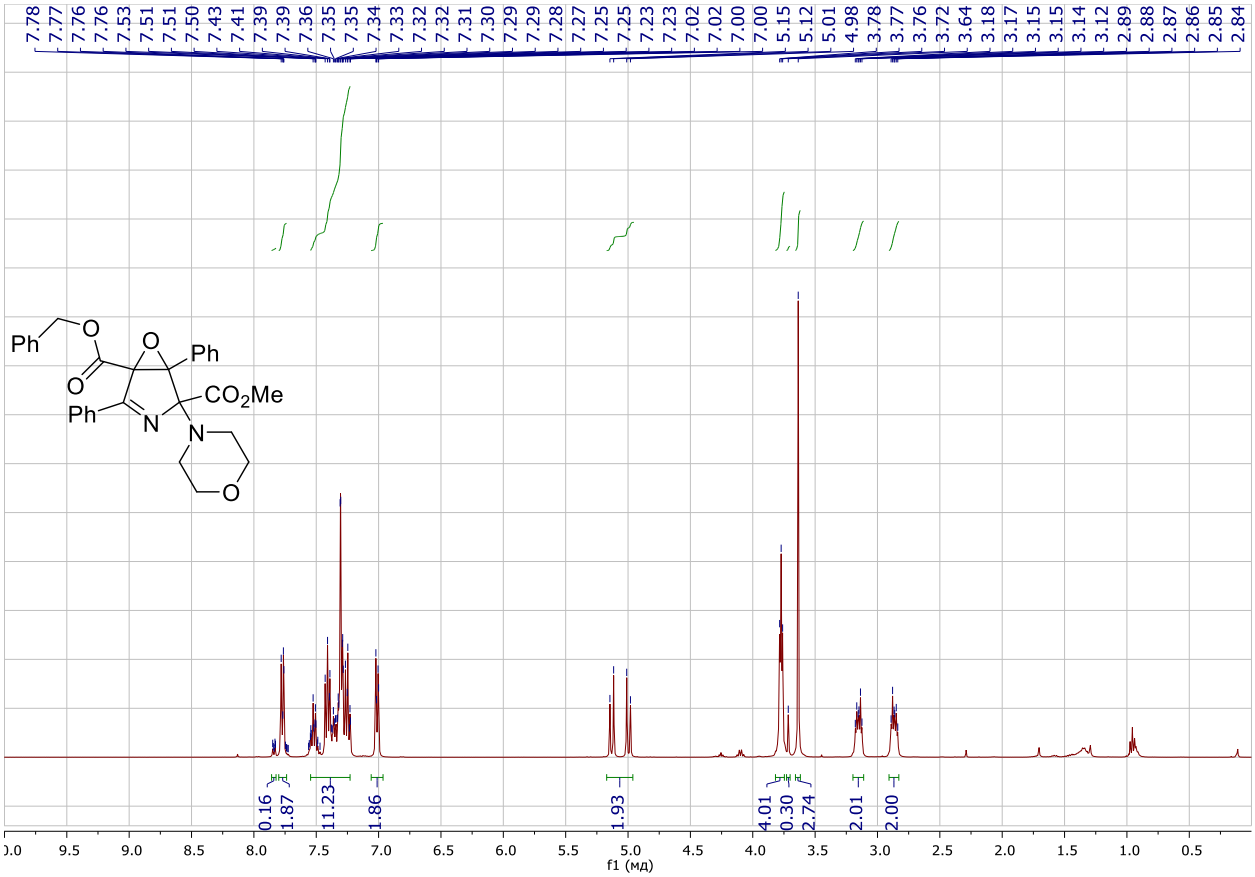


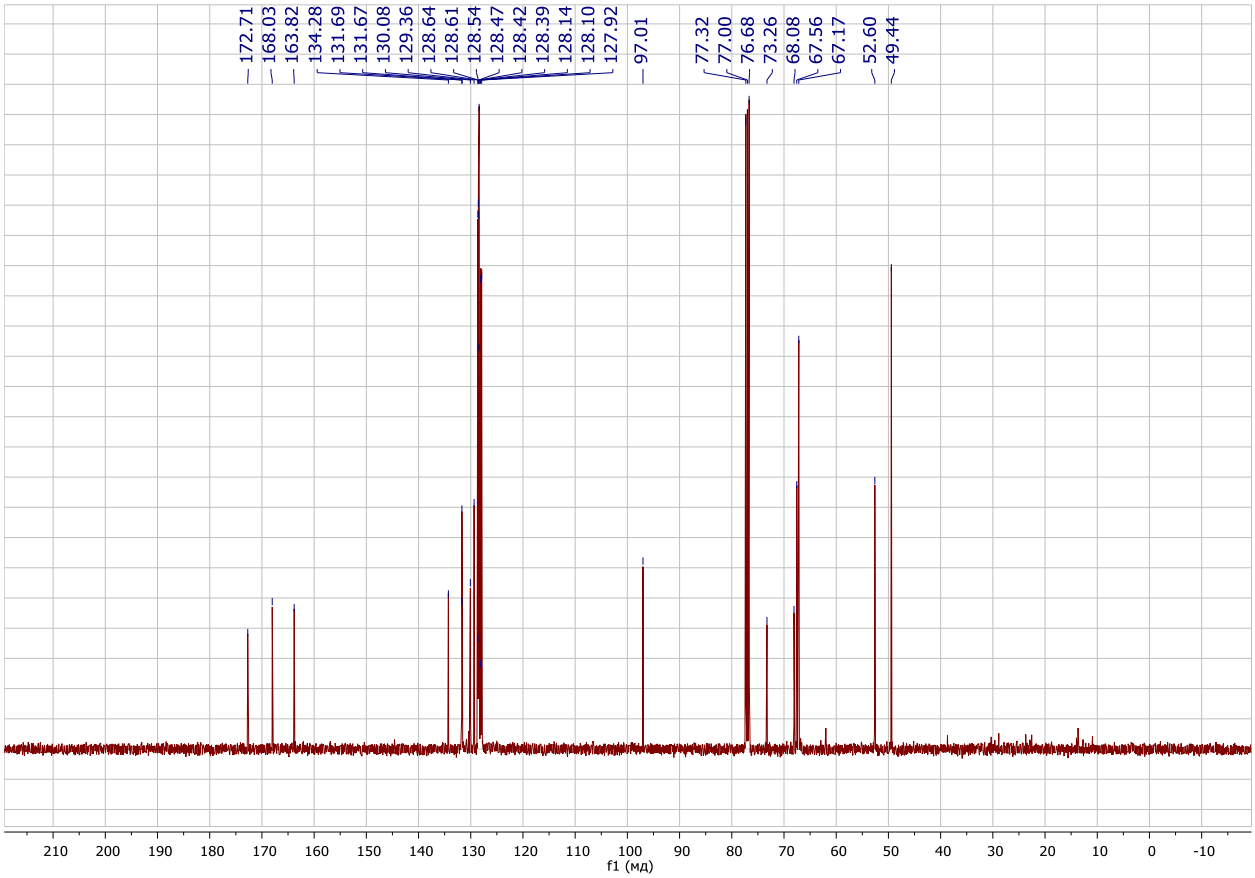
^{1}H and ^{13}C NMR spectra of compound **5t**



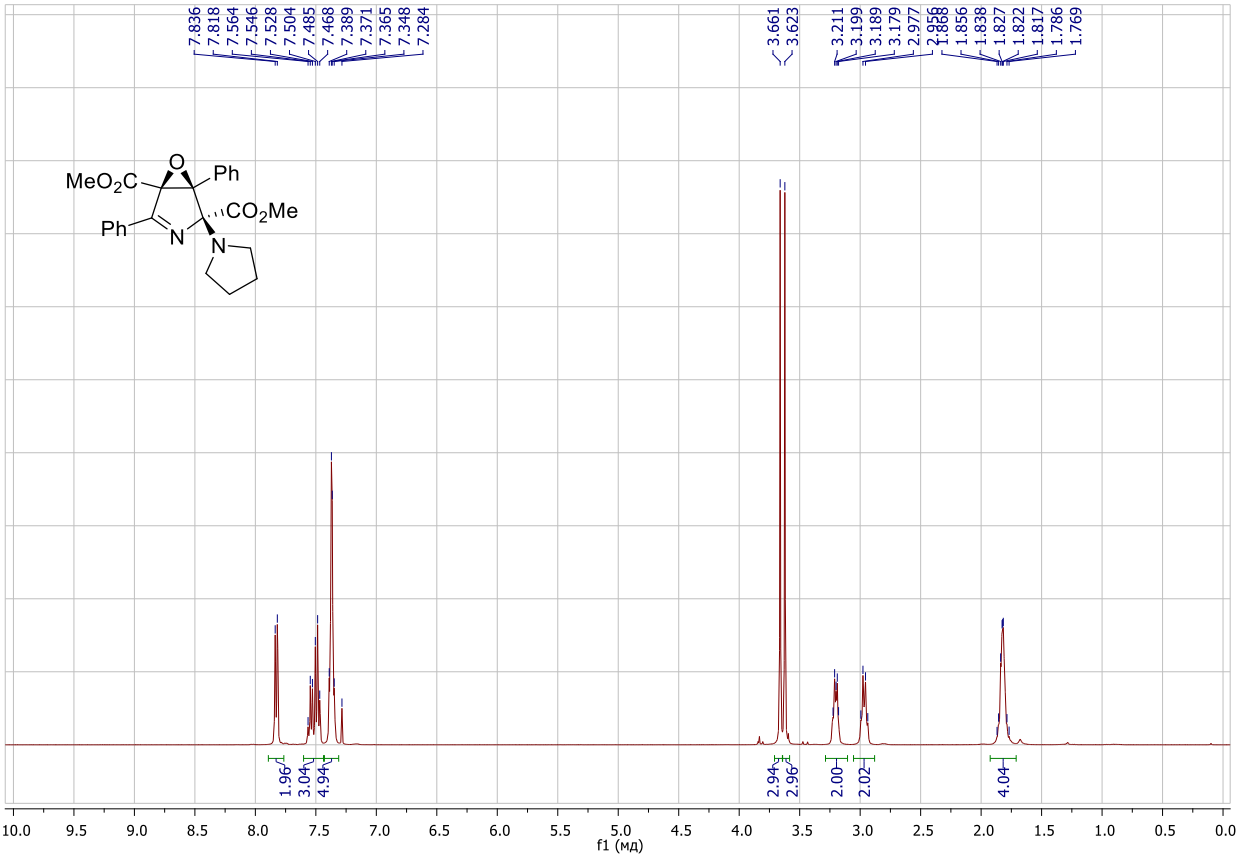


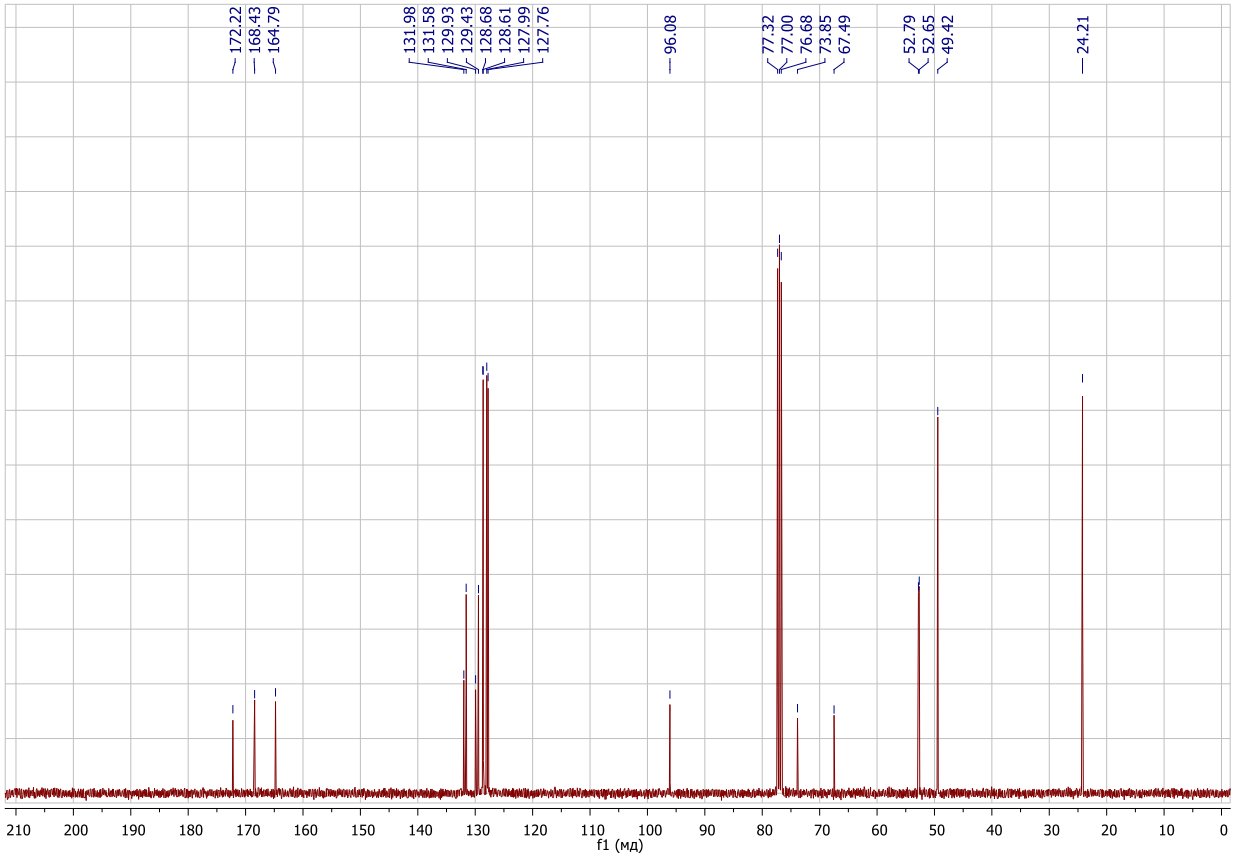
^{1}H and ^{13}C NMR spectra of compound **5u**



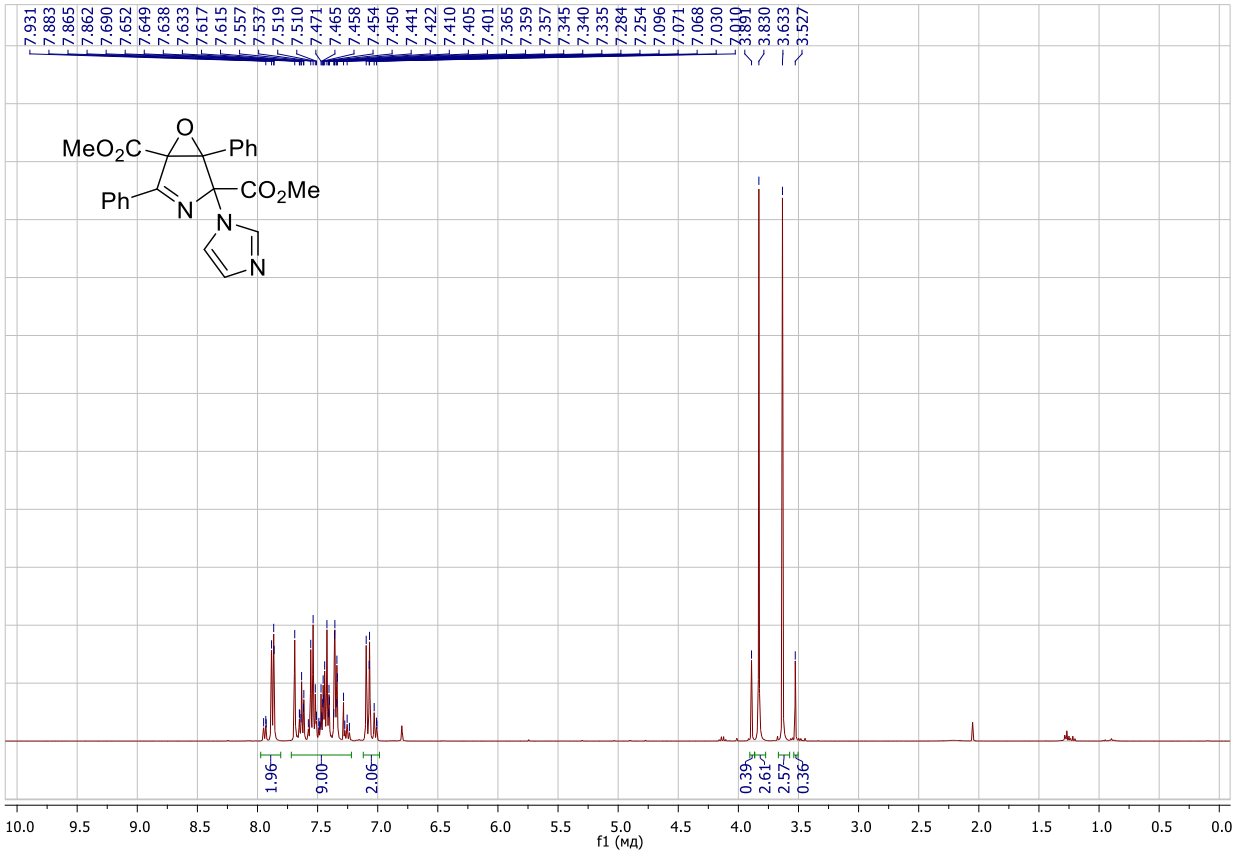


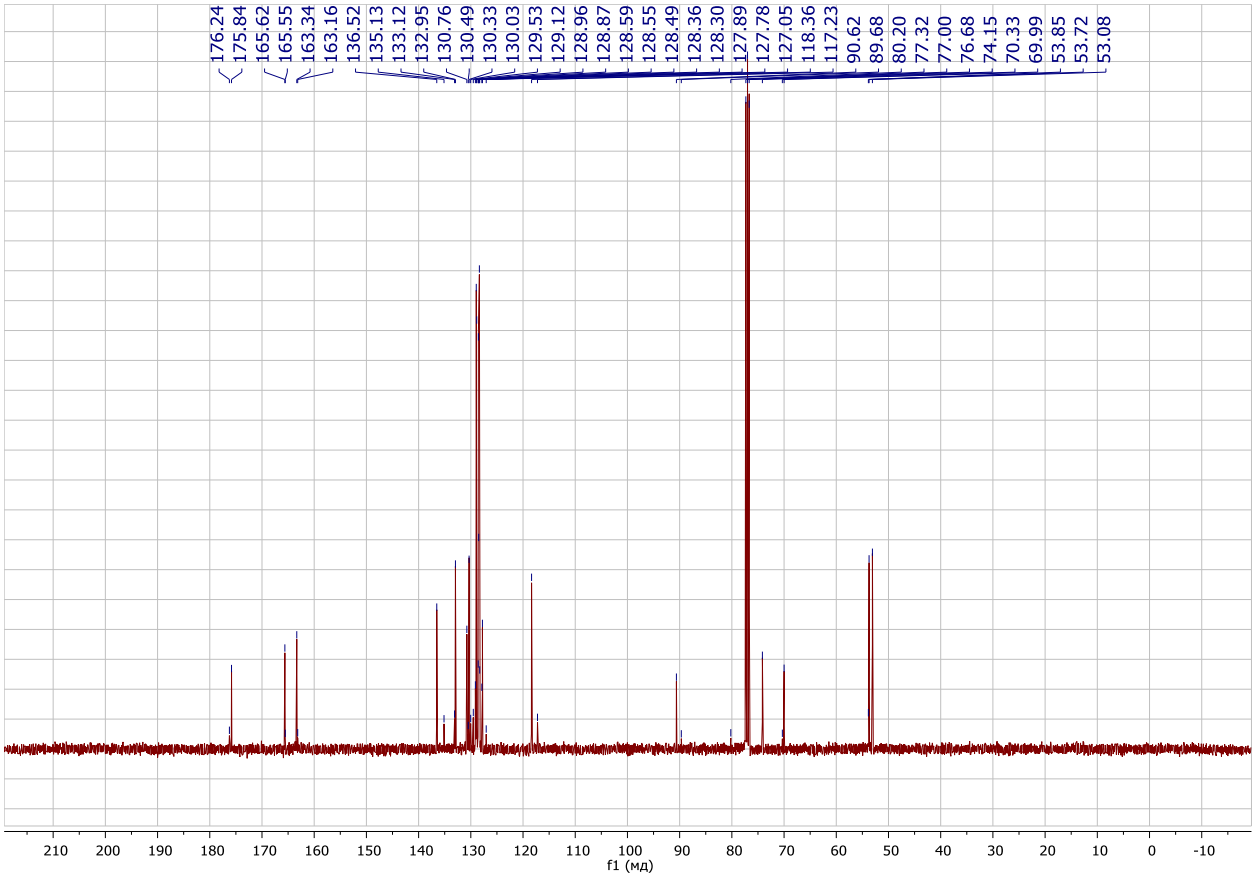
^{1}H and ^{13}C NMR spectra of compound **5v**



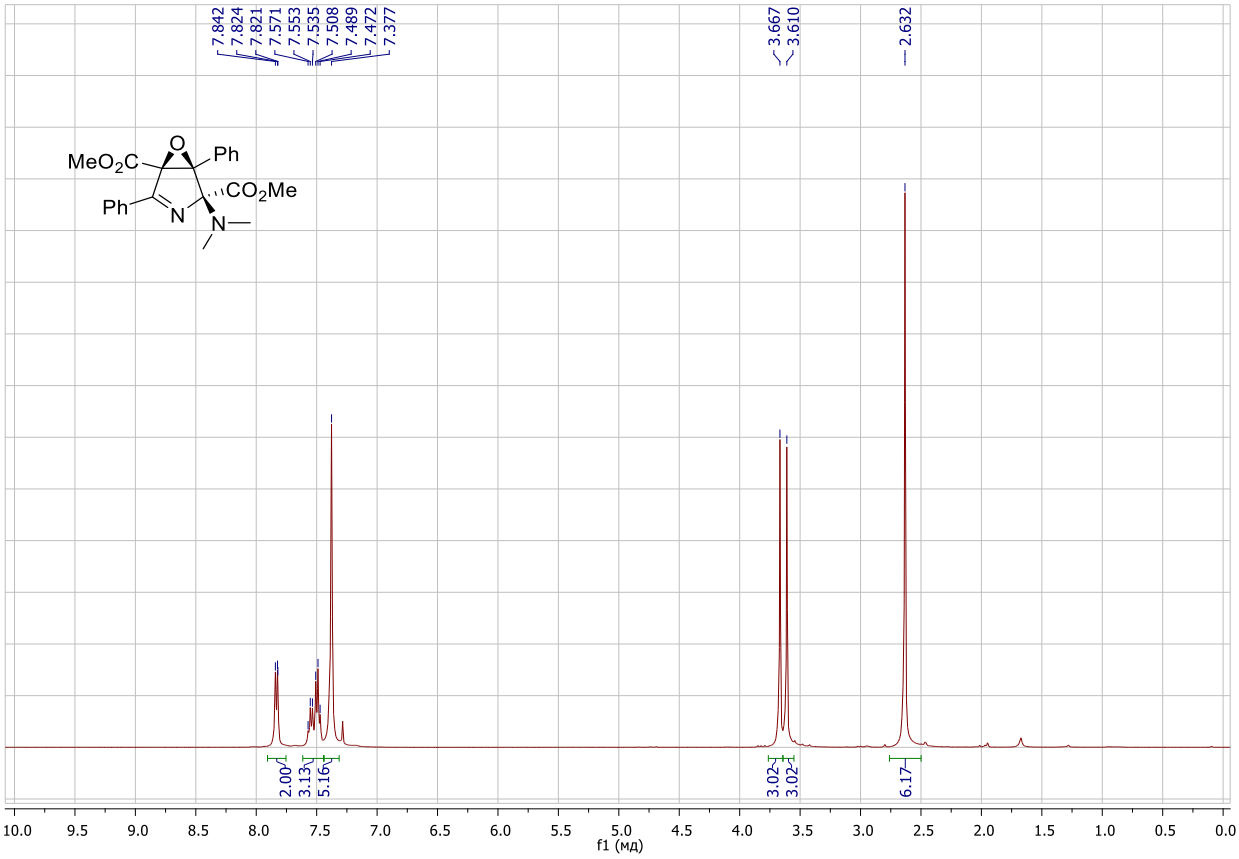


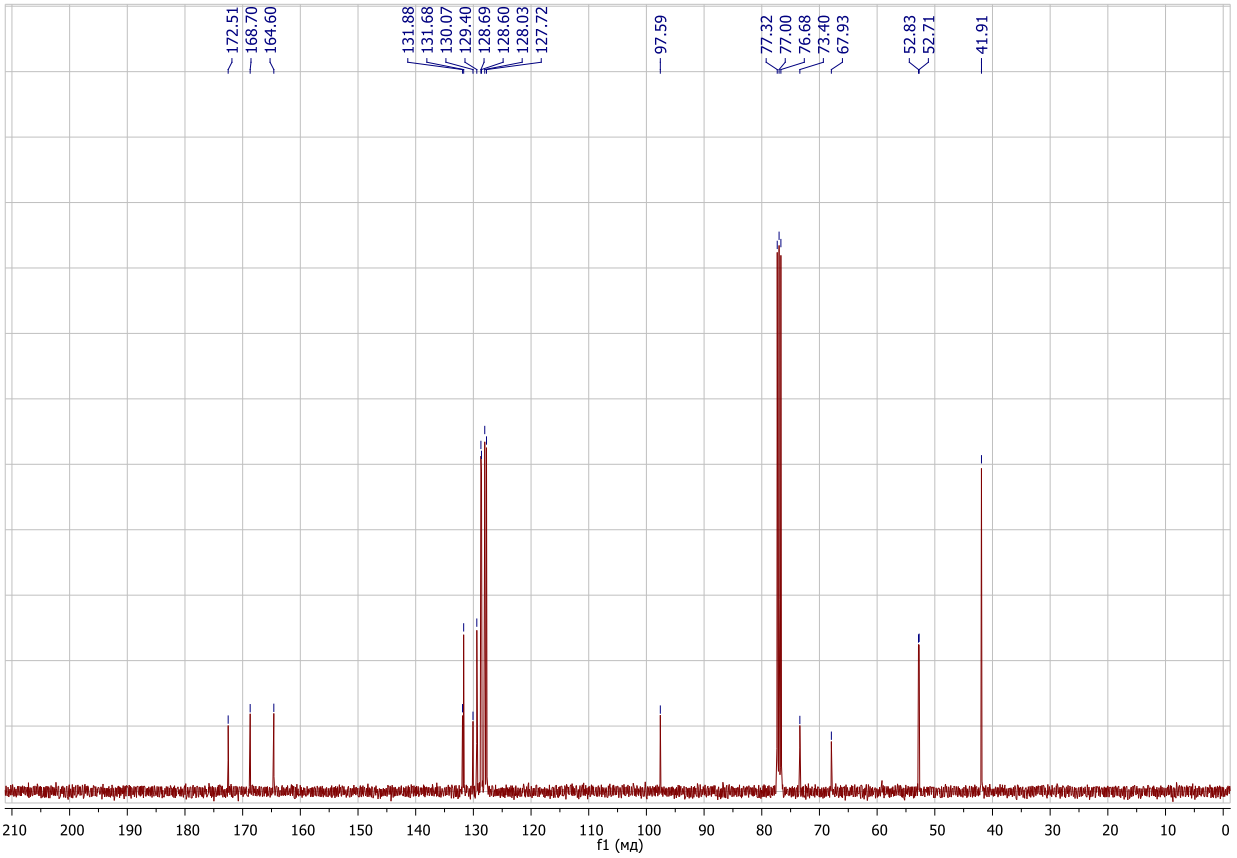
^{1}H and ^{13}C NMR spectra of compound **5w**



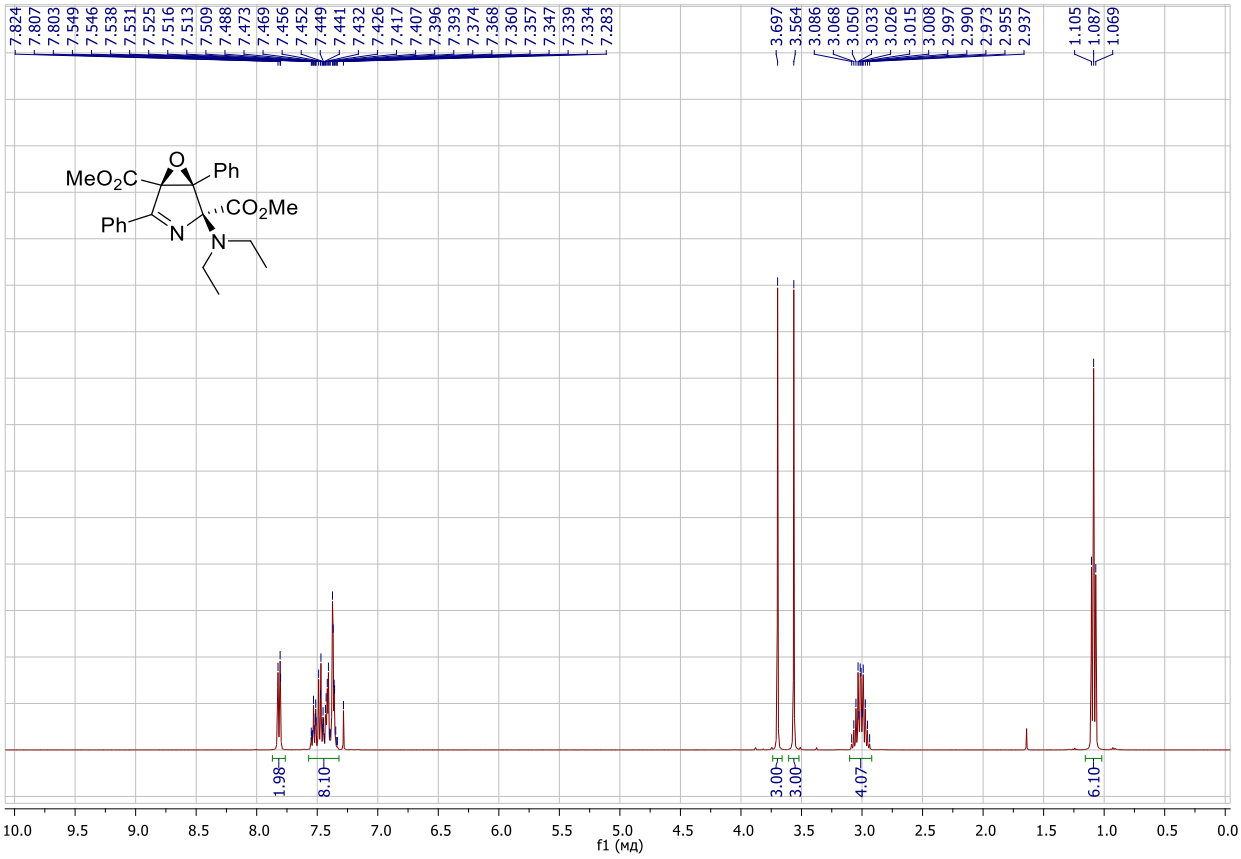


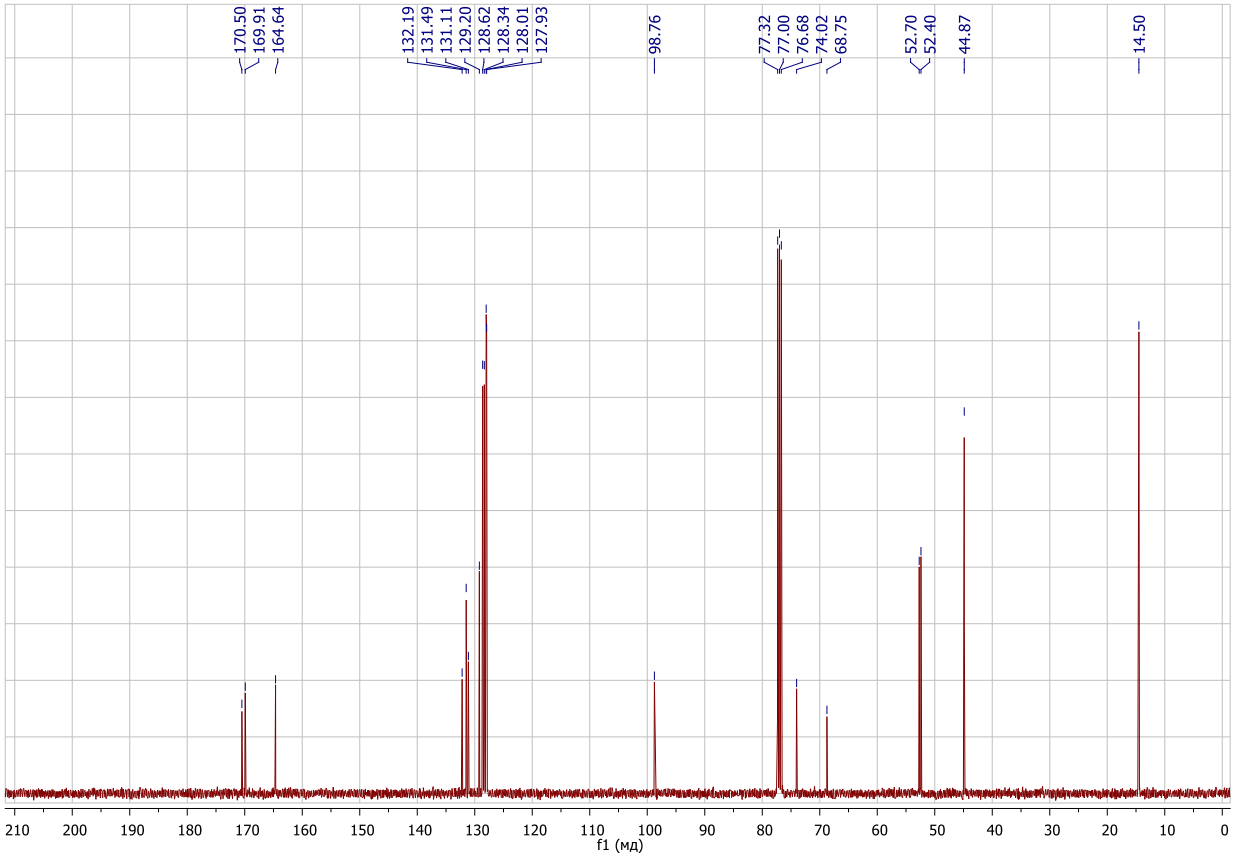
^{1}H and ^{13}C NMR spectra of compound **5x**



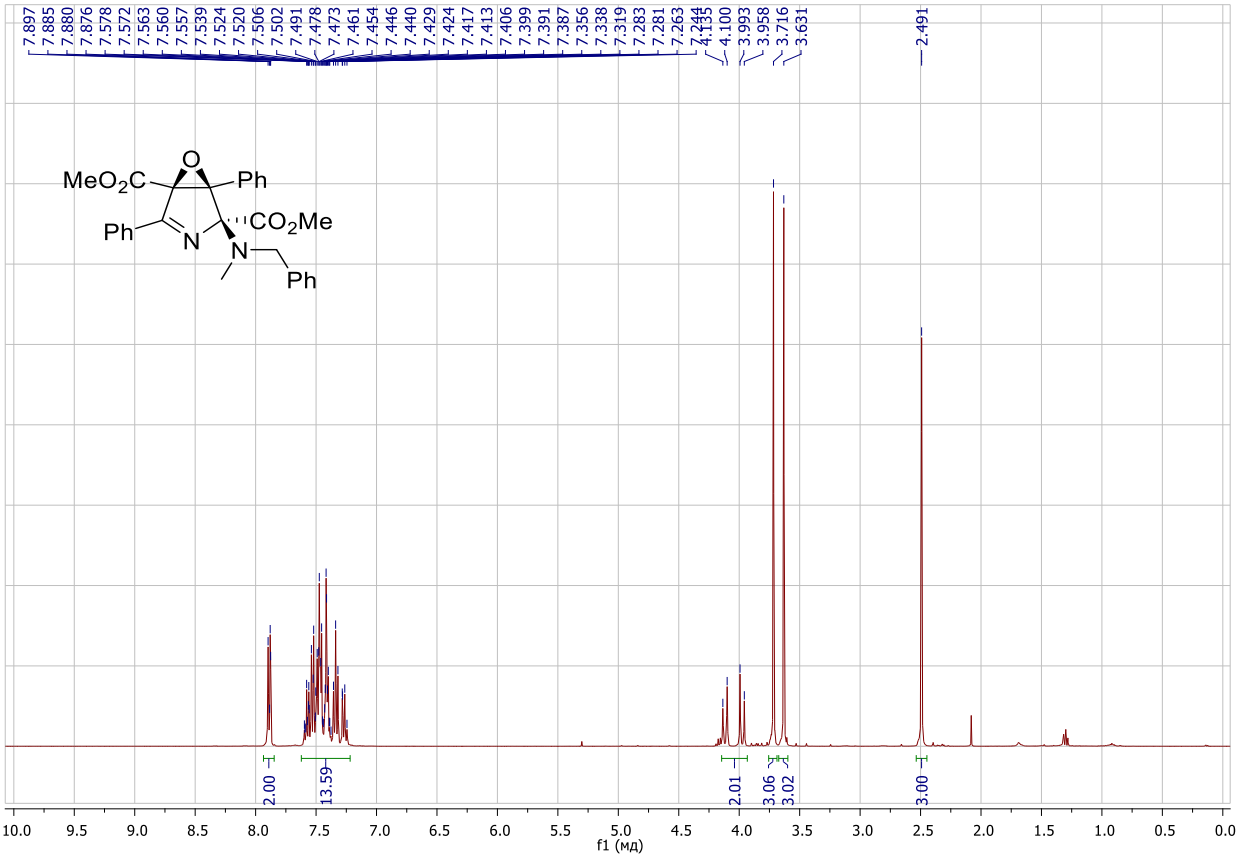


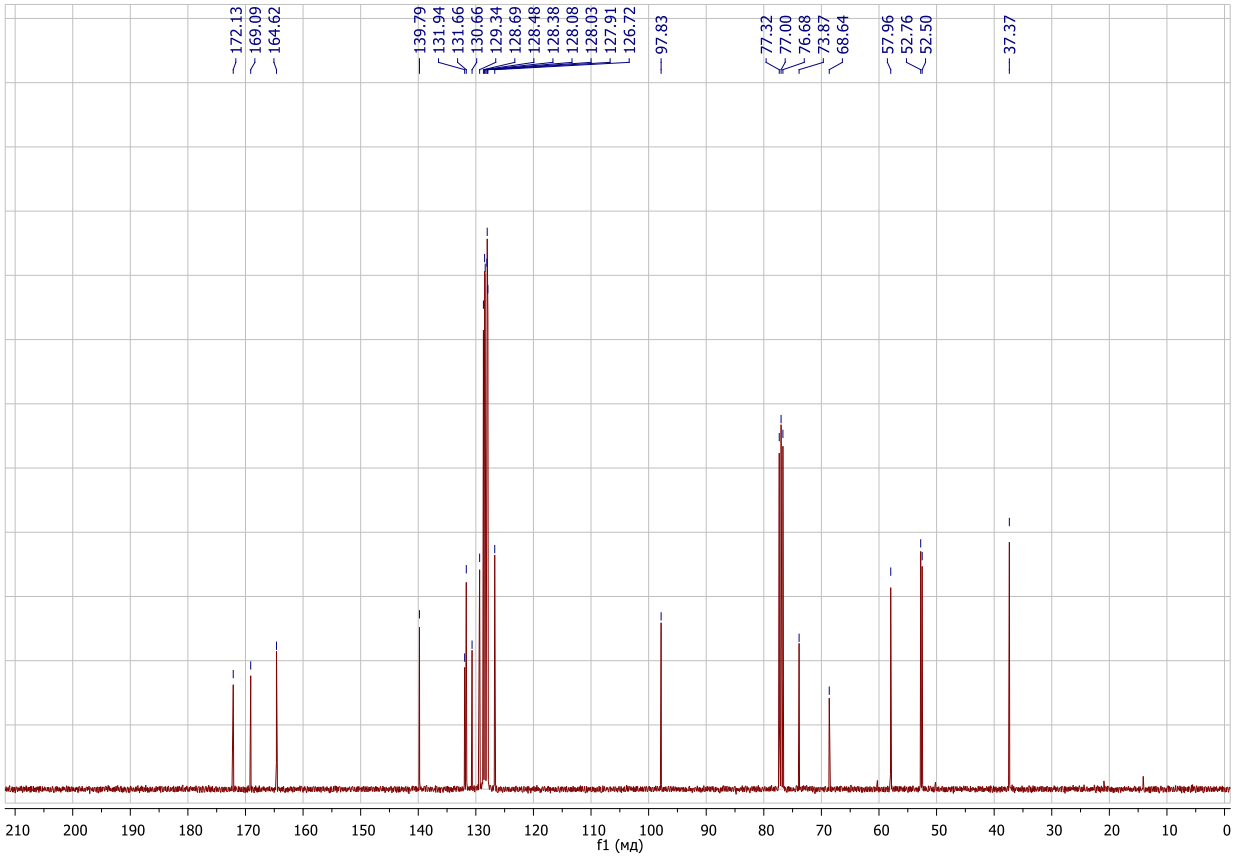
^{1}H and ^{13}C NMR spectra of compound **5y**



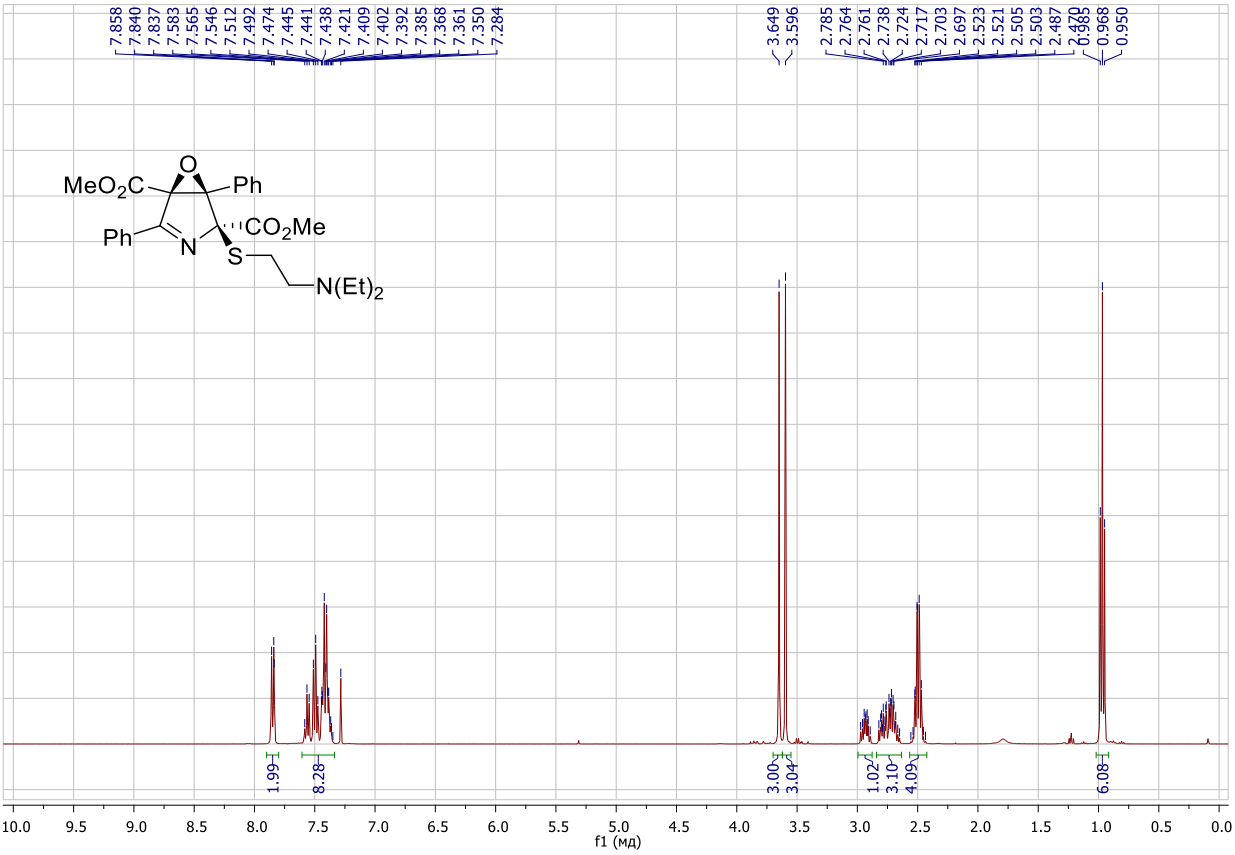


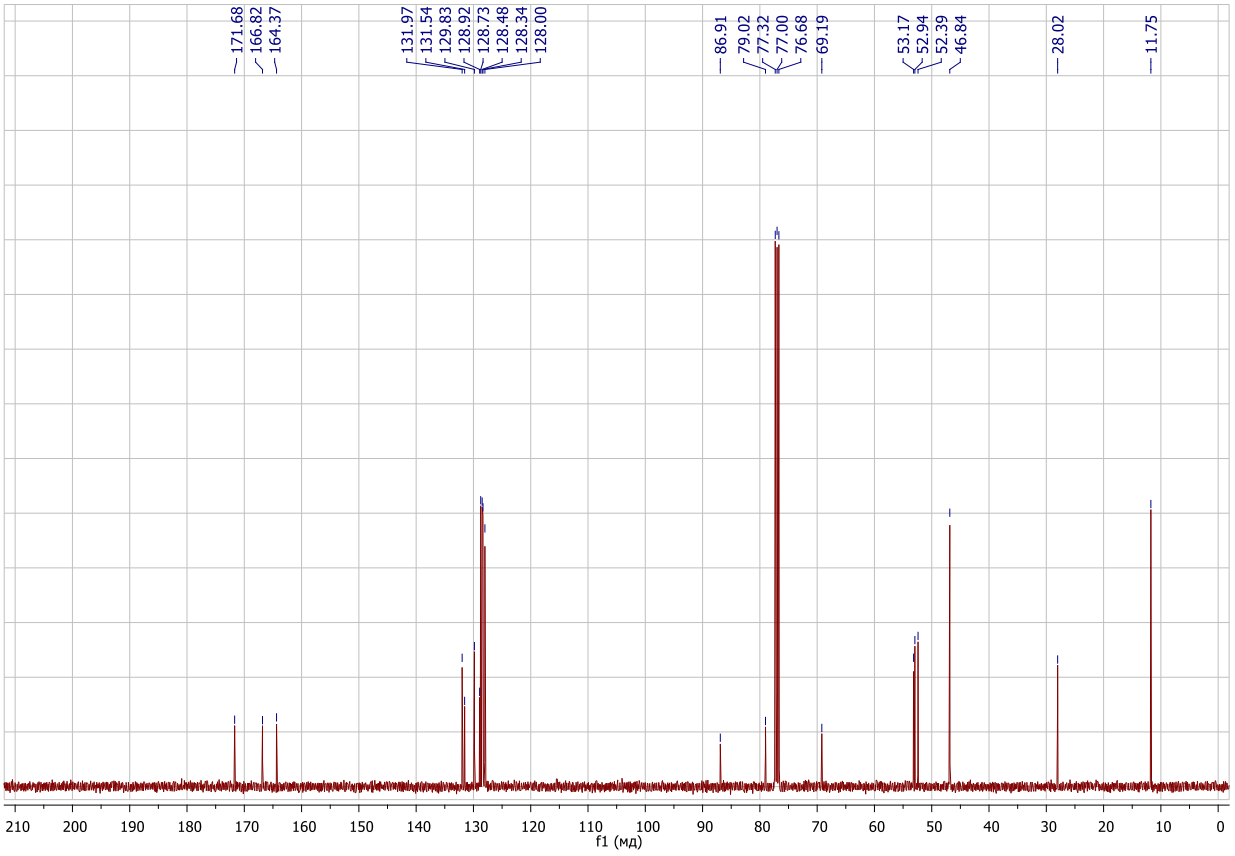
^{1}H and ^{13}C NMR spectra of compound **5z**



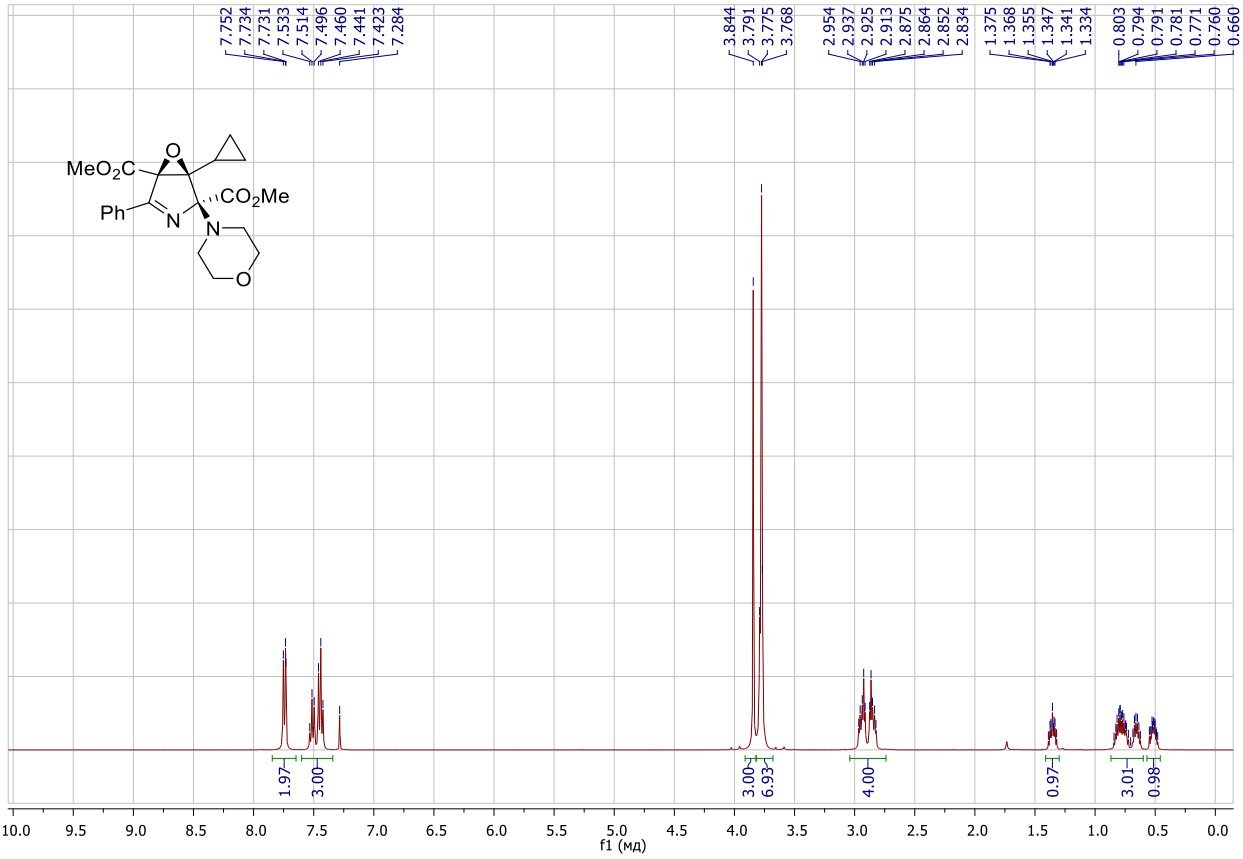


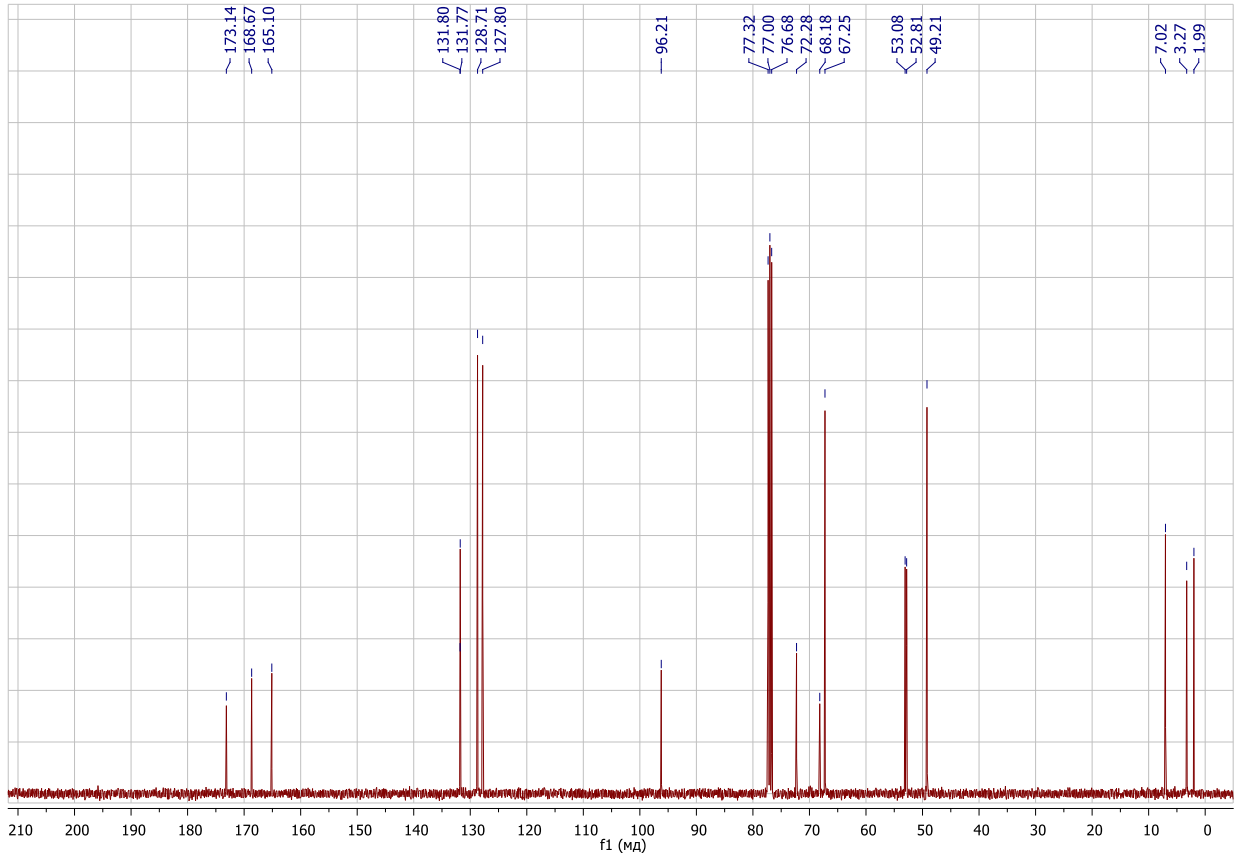
^{1}H and ^{13}C NMR spectra of compound **5za**



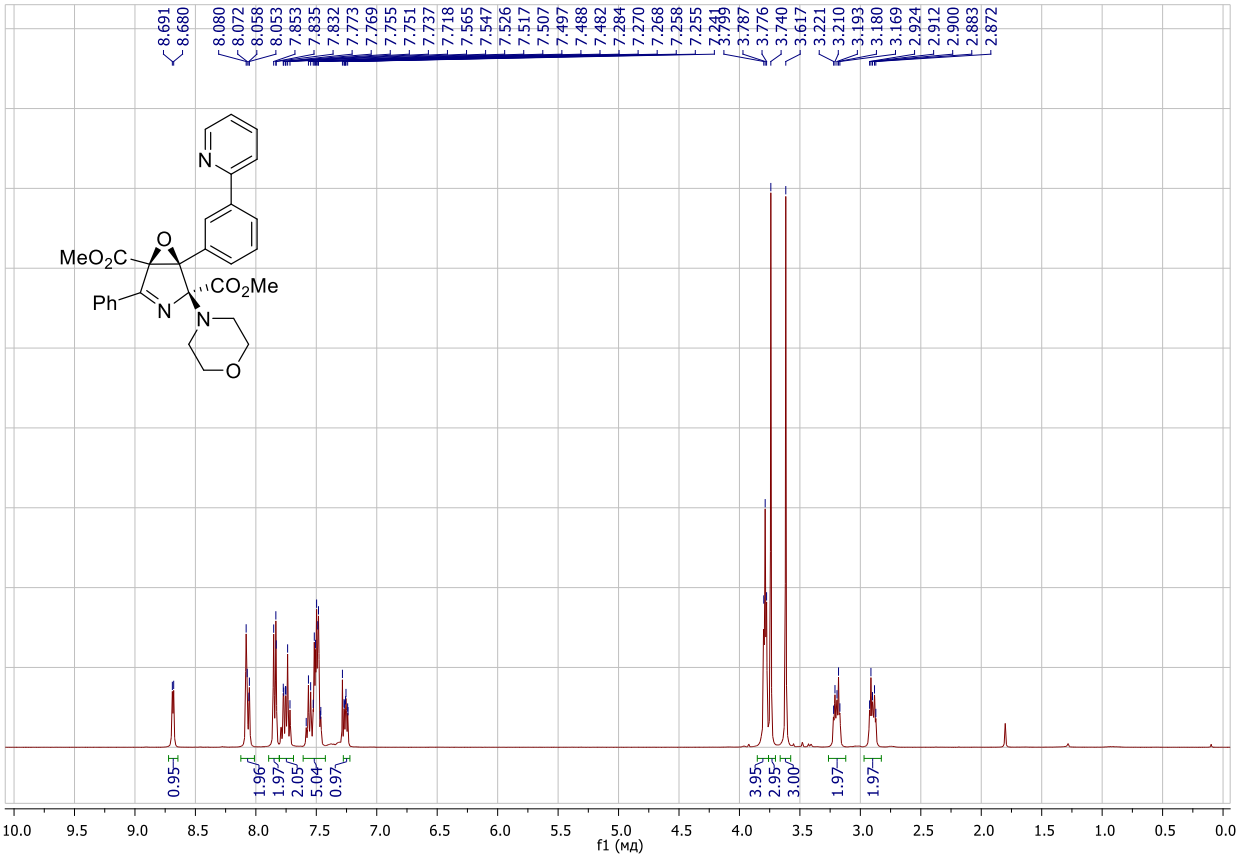


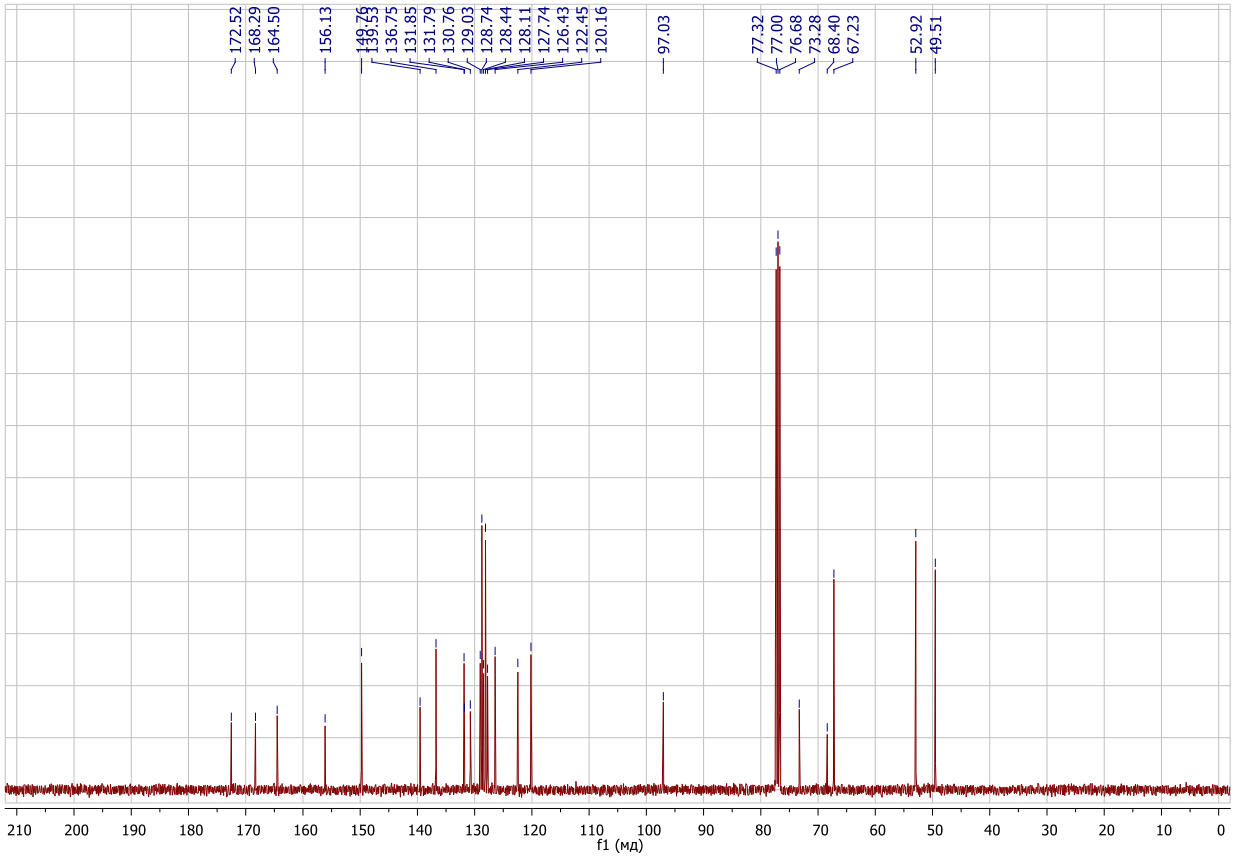
^{1}H and ^{13}C NMR spectra of compound **5zb**



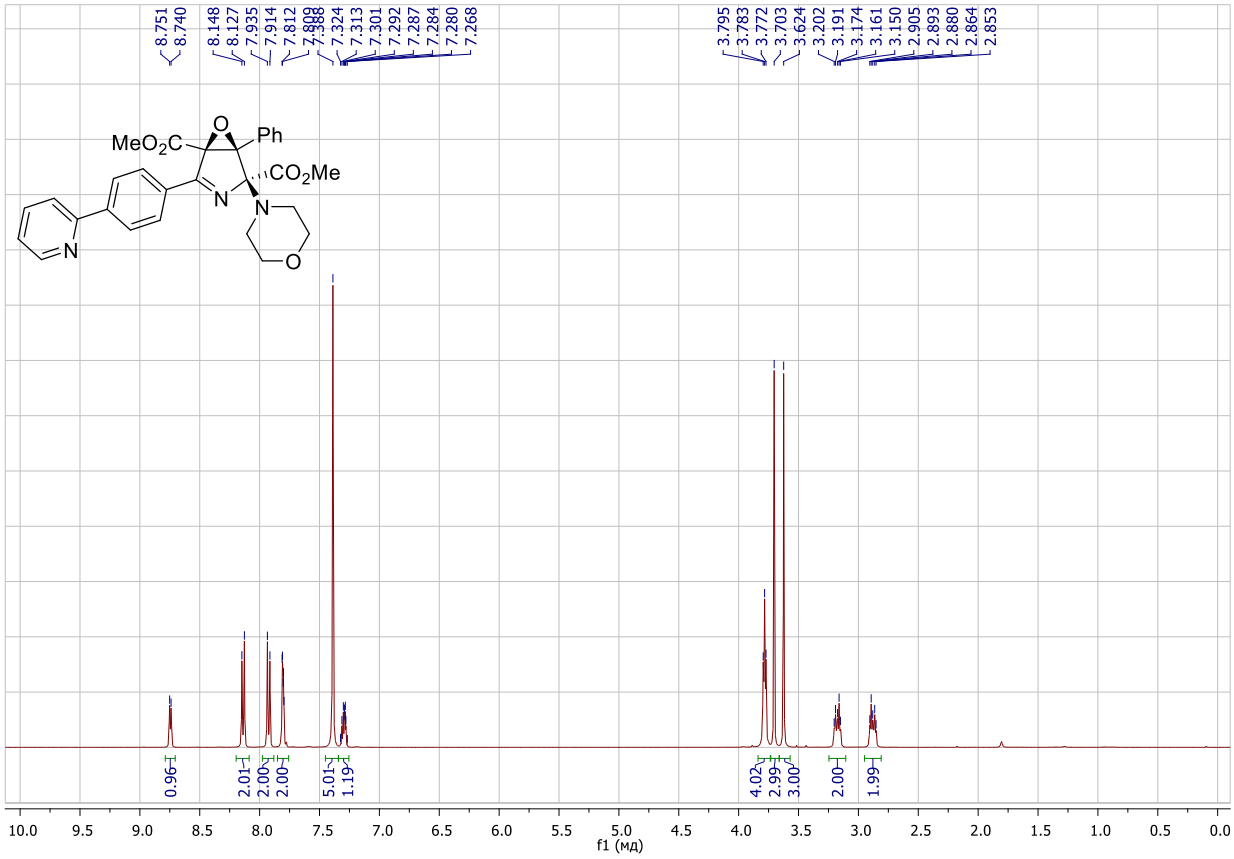


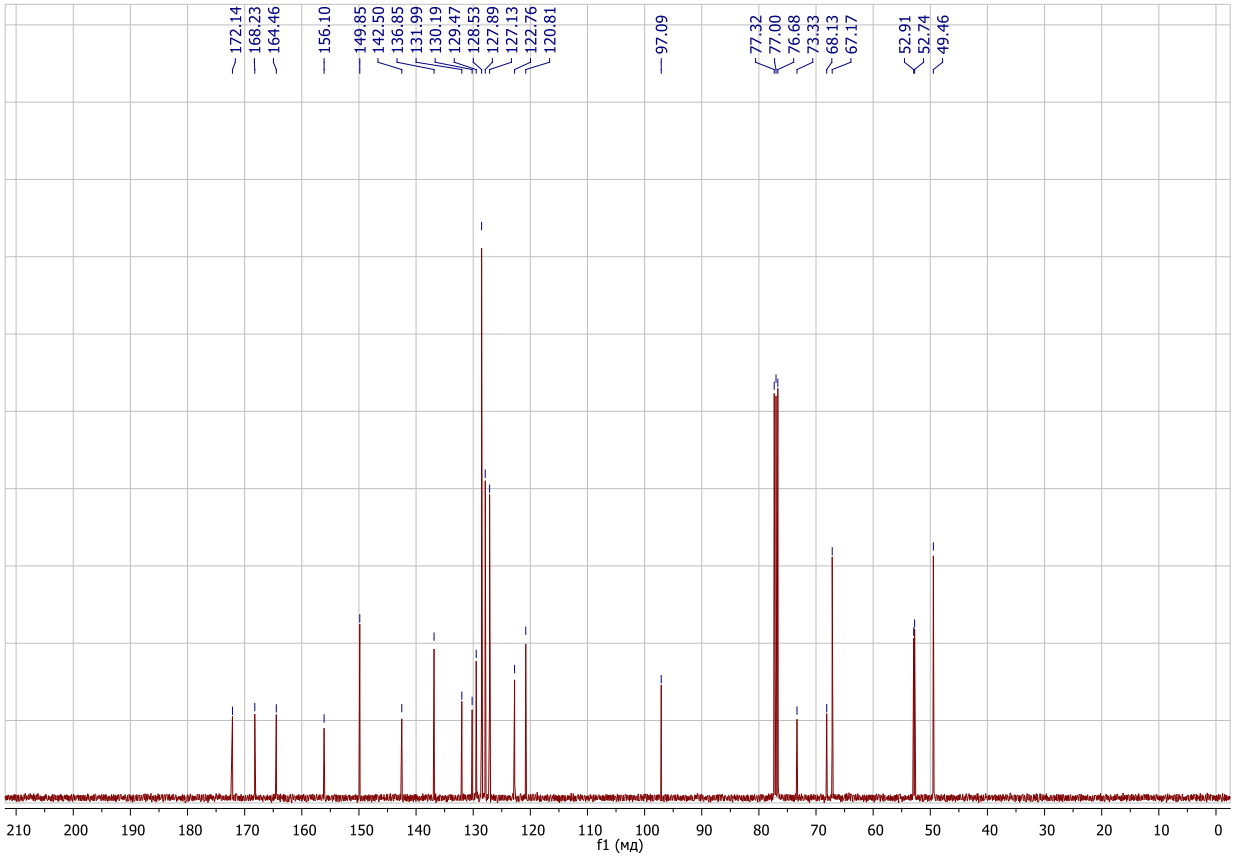
^{1}H and ^{13}C NMR spectra of compound **5zd**



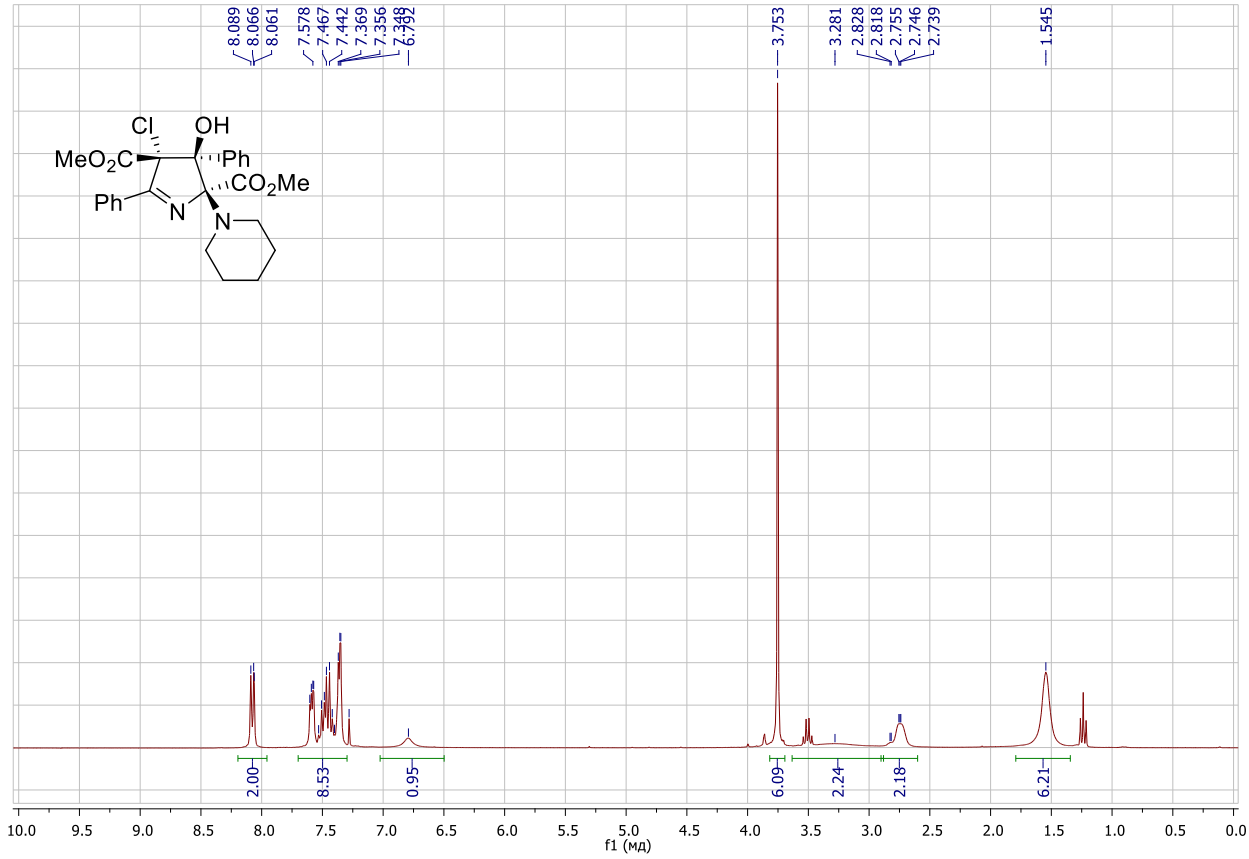


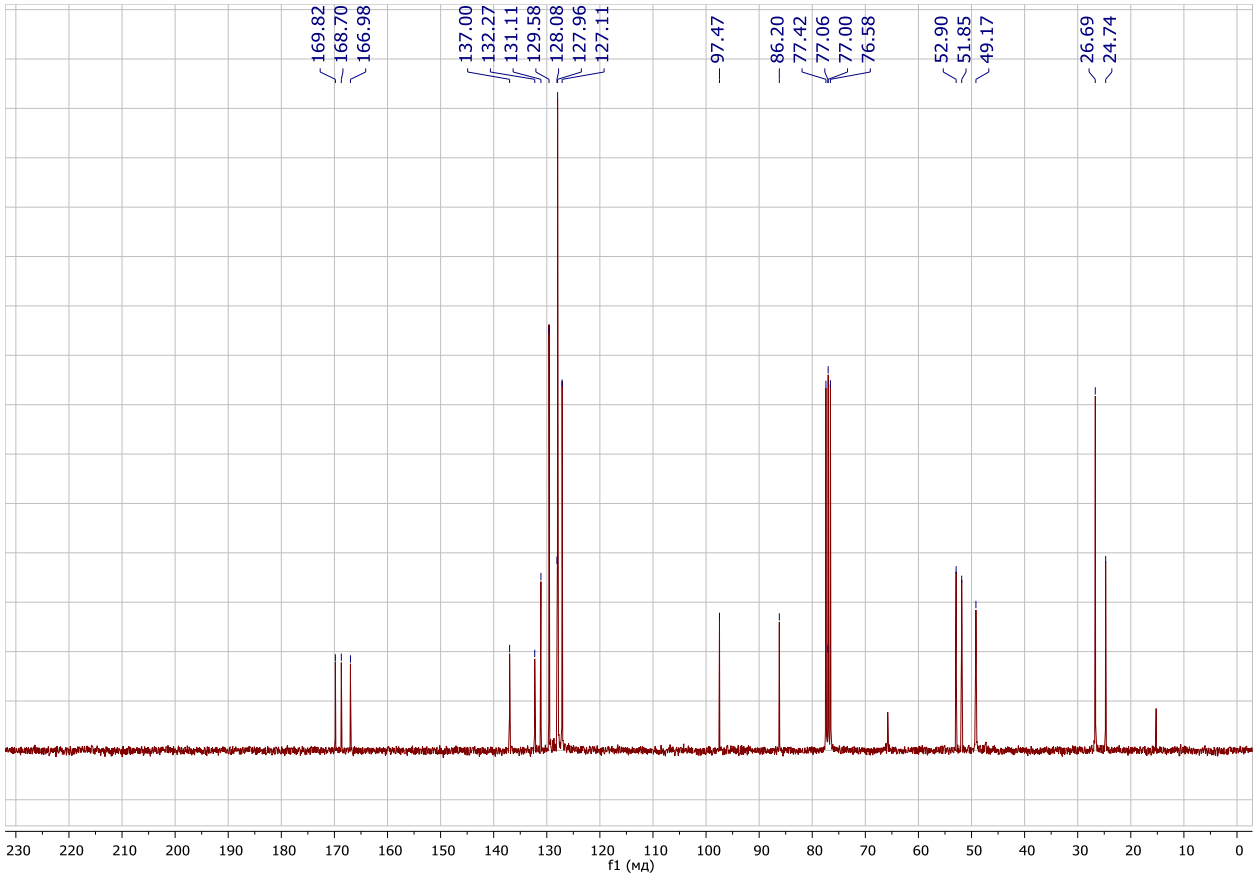
^{1}H and ^{13}C NMR spectra of compound **5ze**



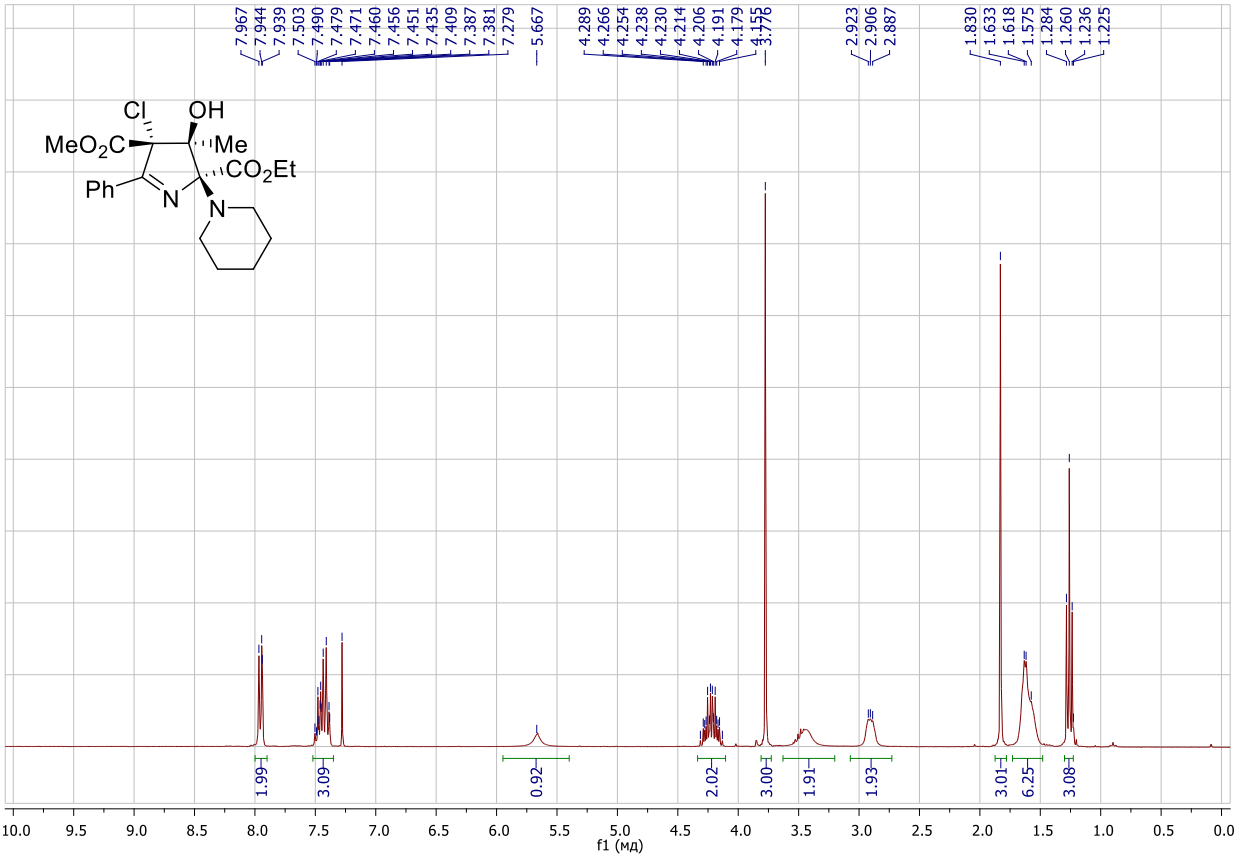


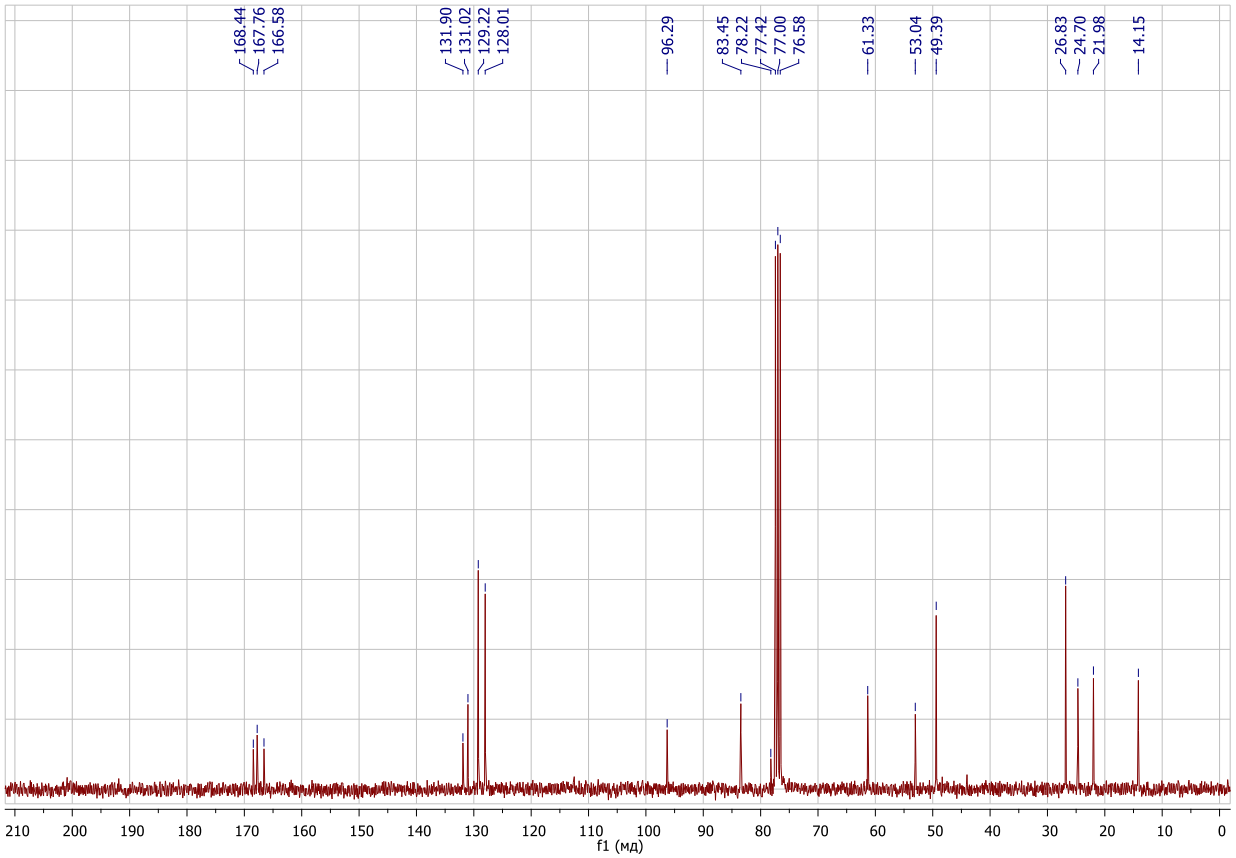
^{1}H and ^{13}C NMR spectra of compound **6a**



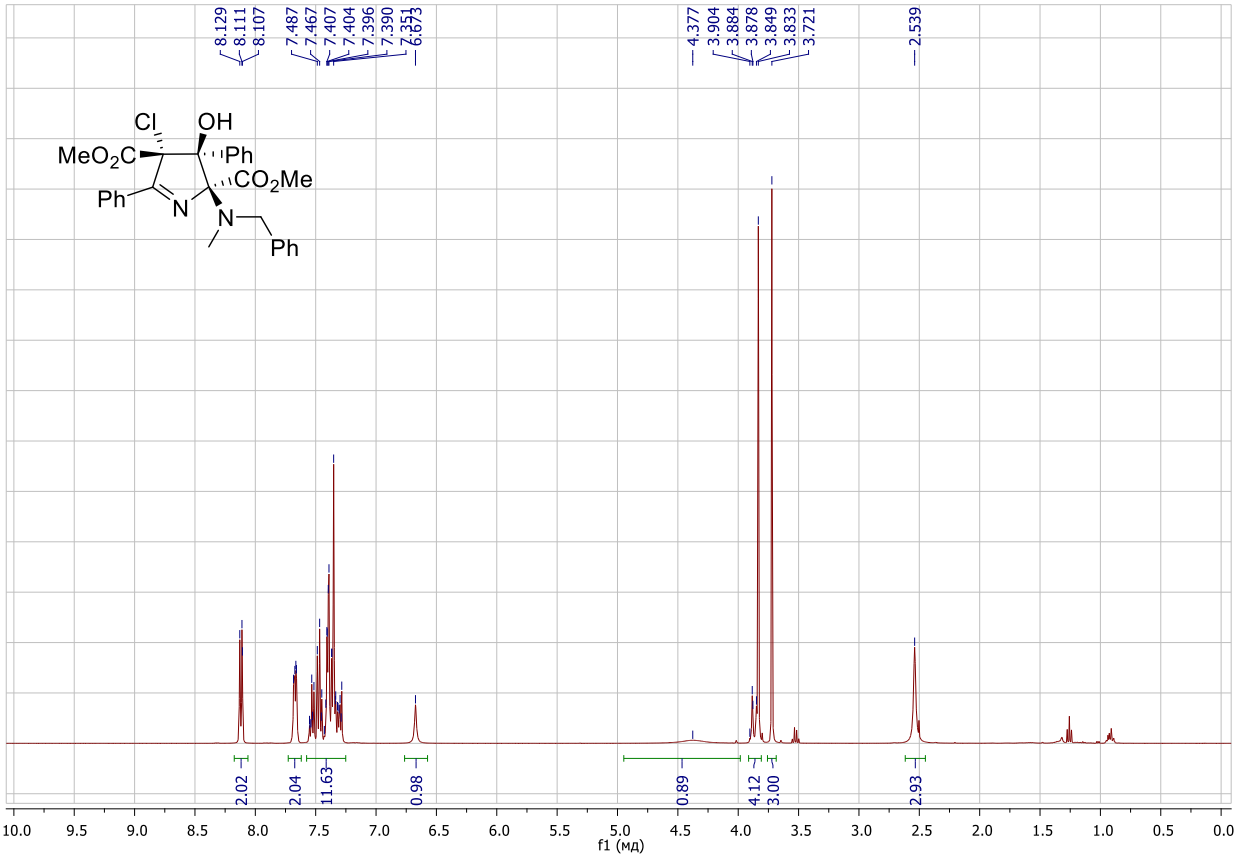


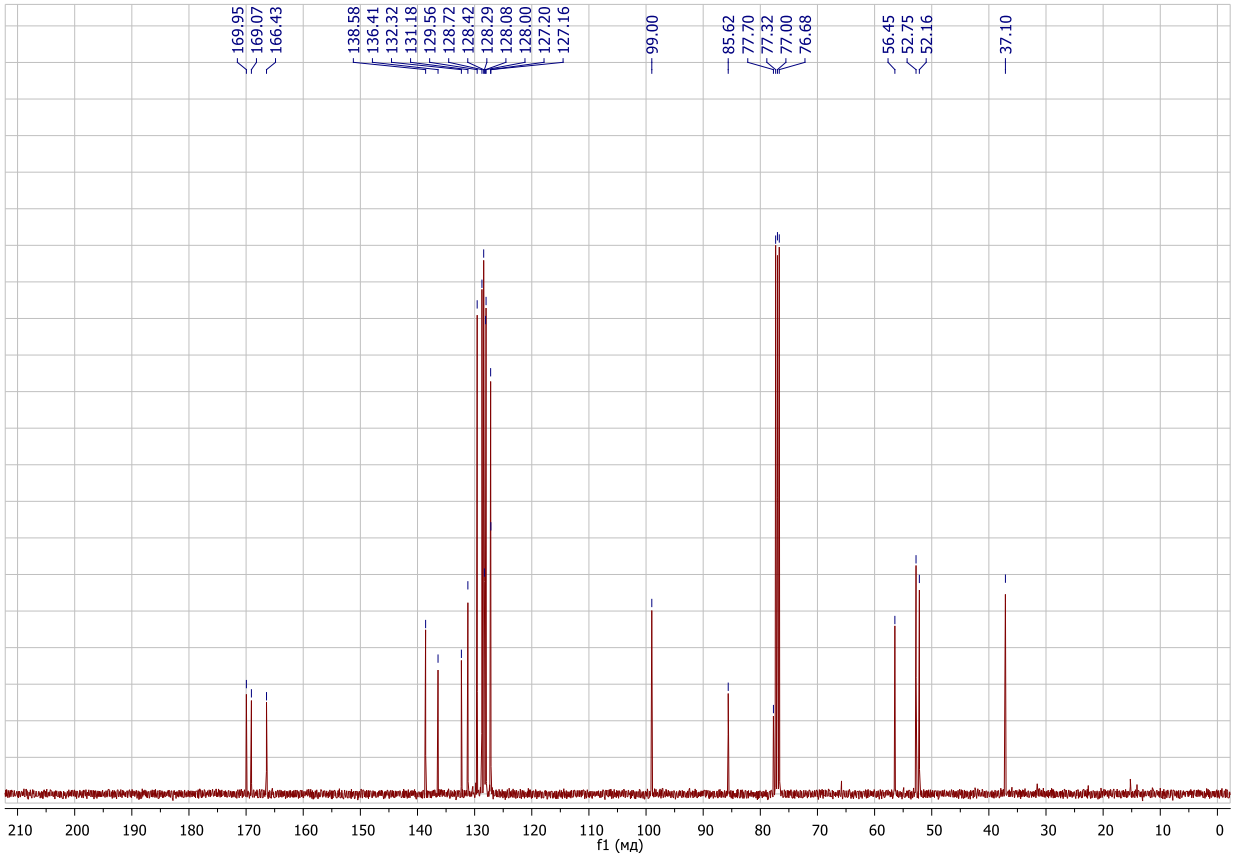
^{1}H and ^{13}C NMR spectra of compound **6b**



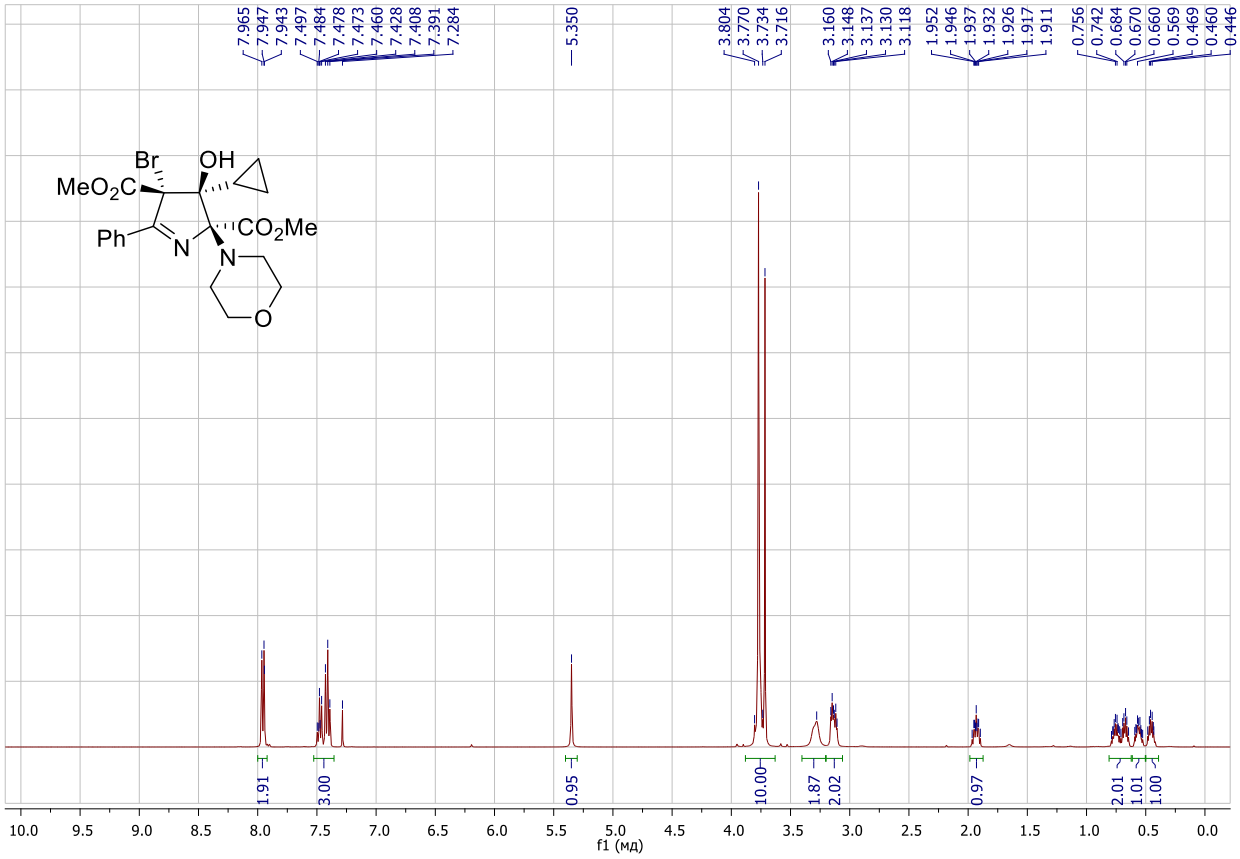


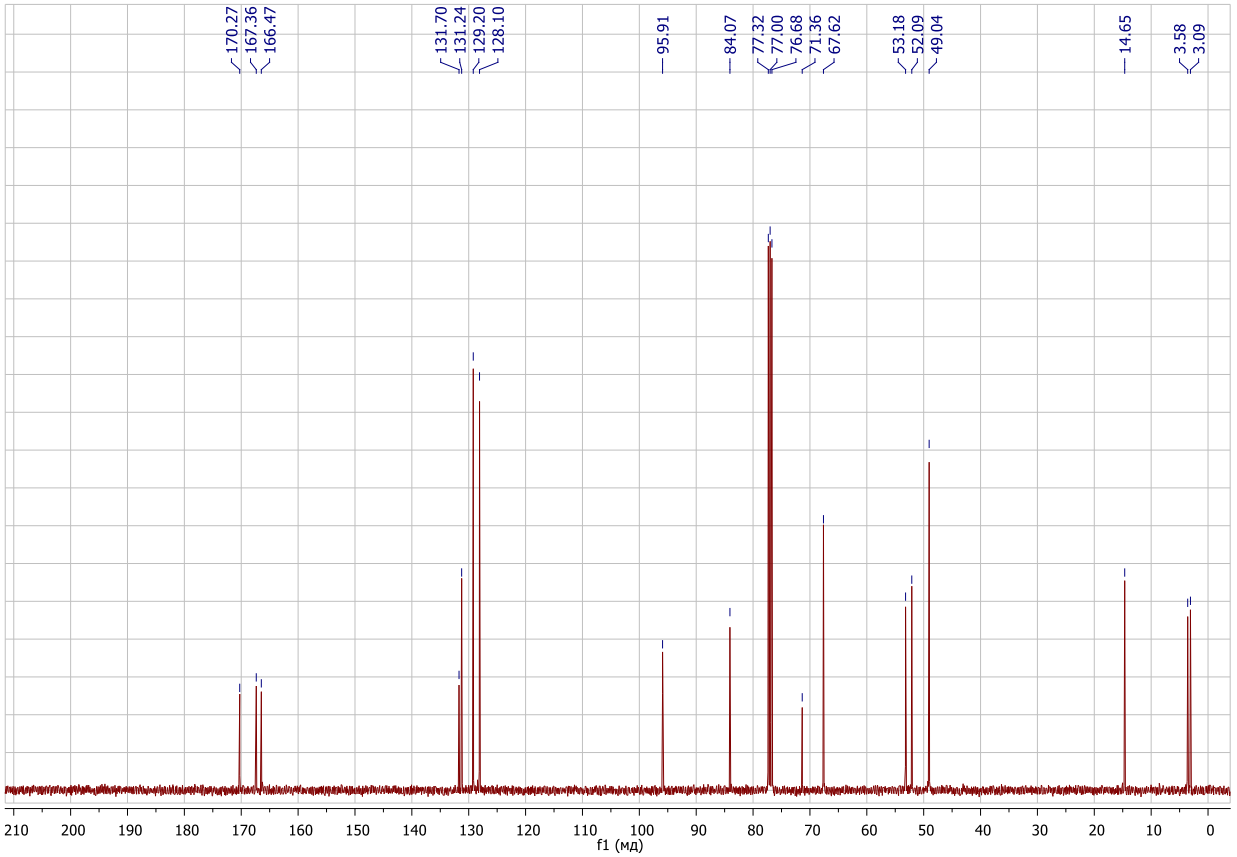
^{1}H and ^{13}C NMR spectra of compound **6c**



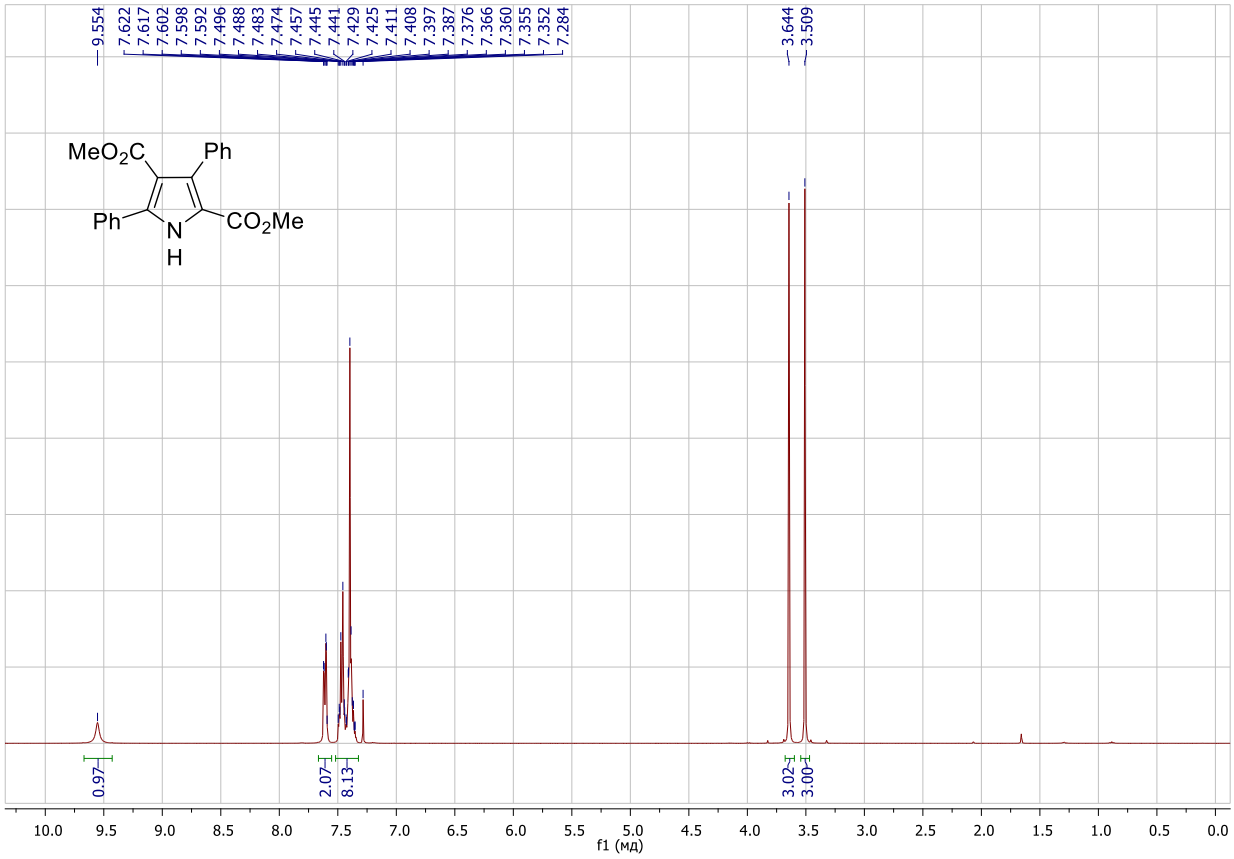


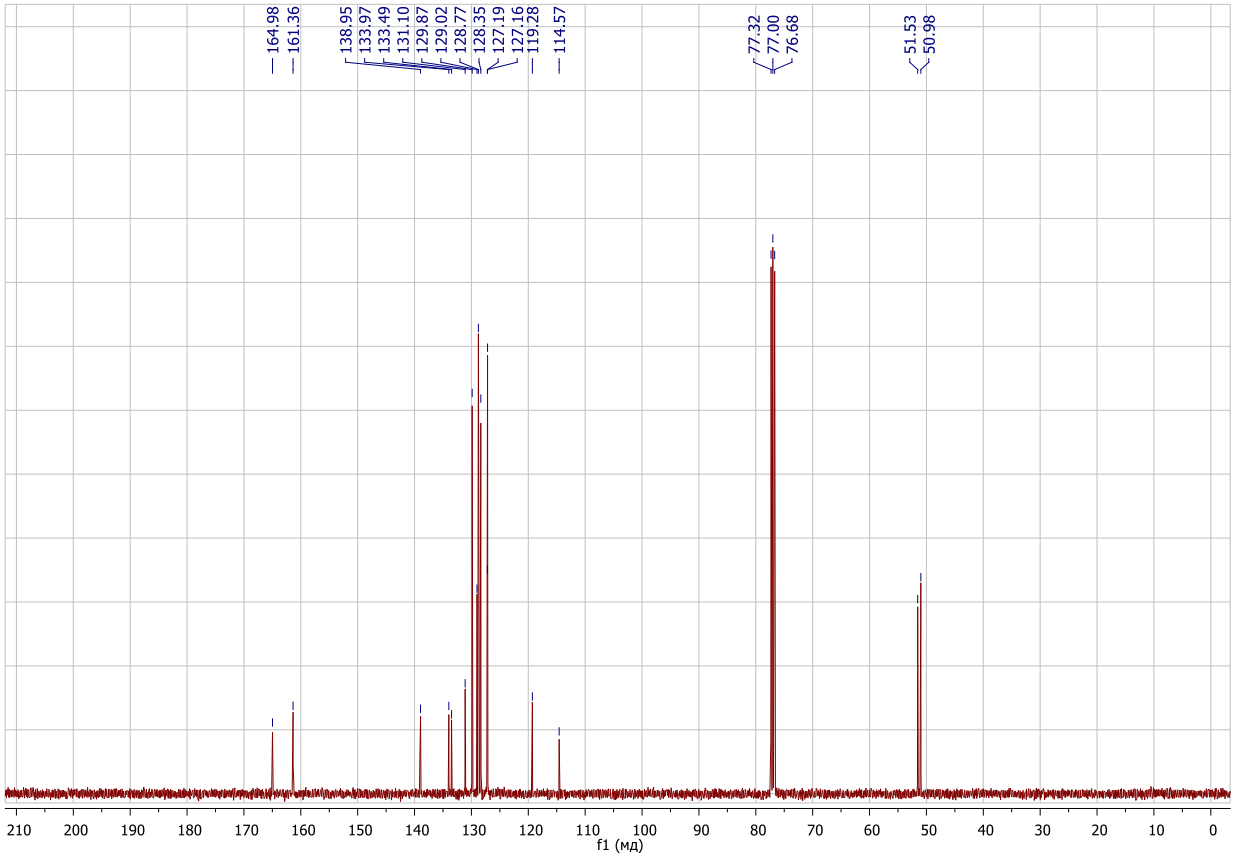
^{1}H and ^{13}C NMR spectra of compound **6d**



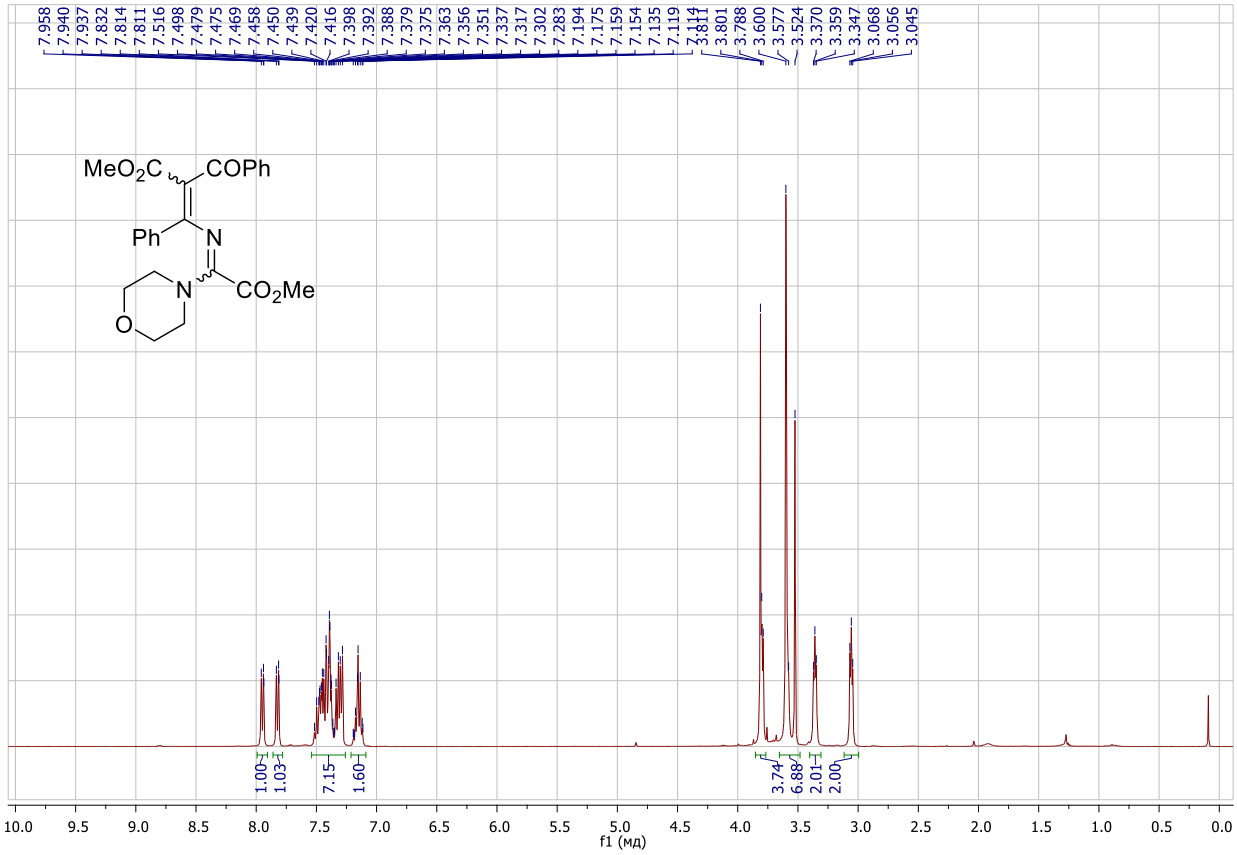


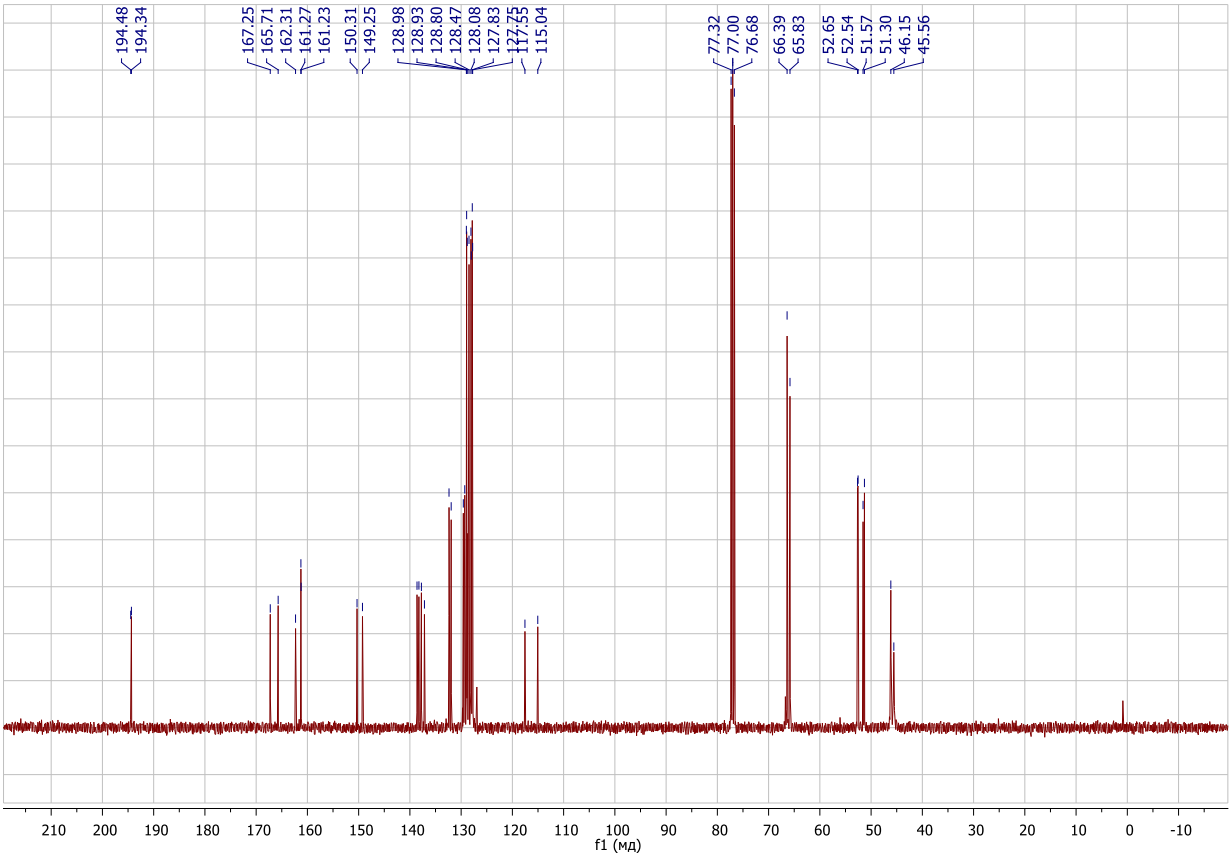
^{1}H and ^{13}C NMR spectra of compound **11**



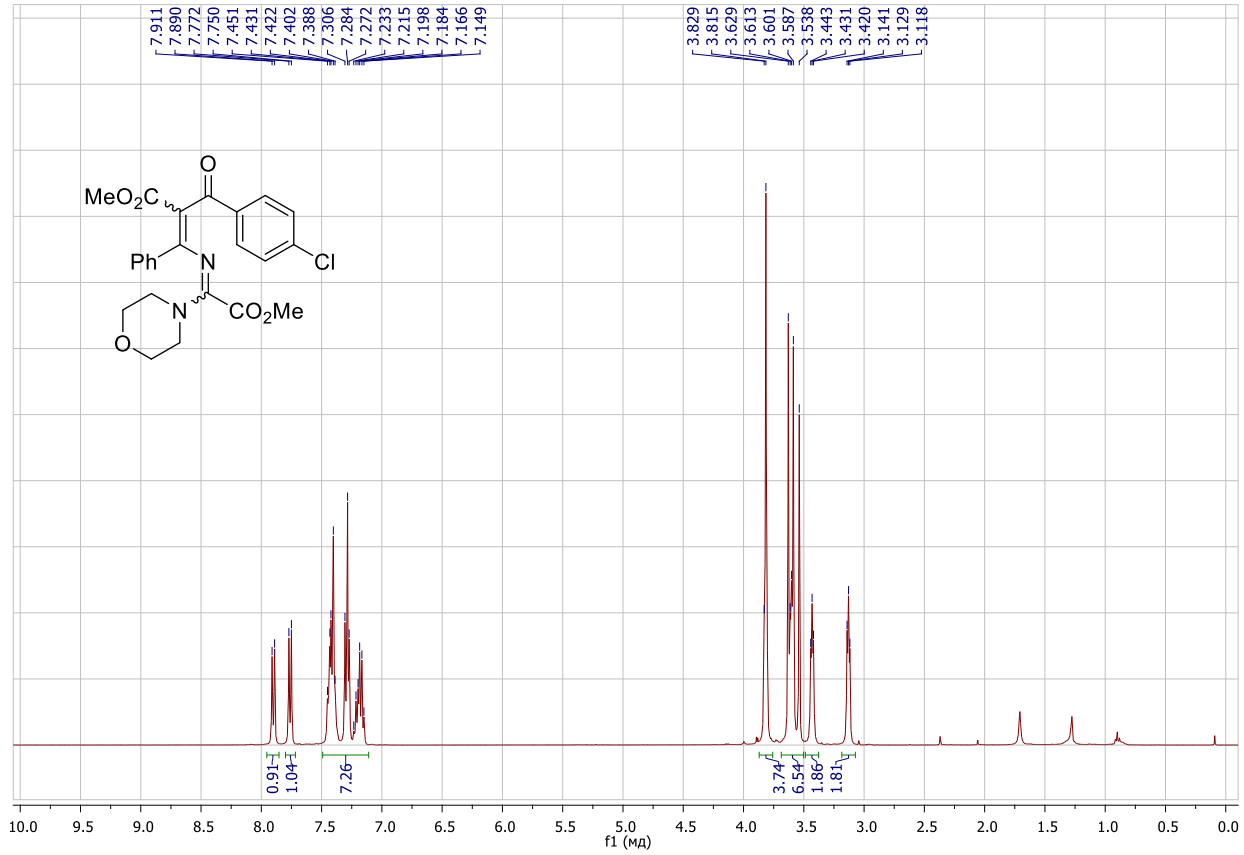


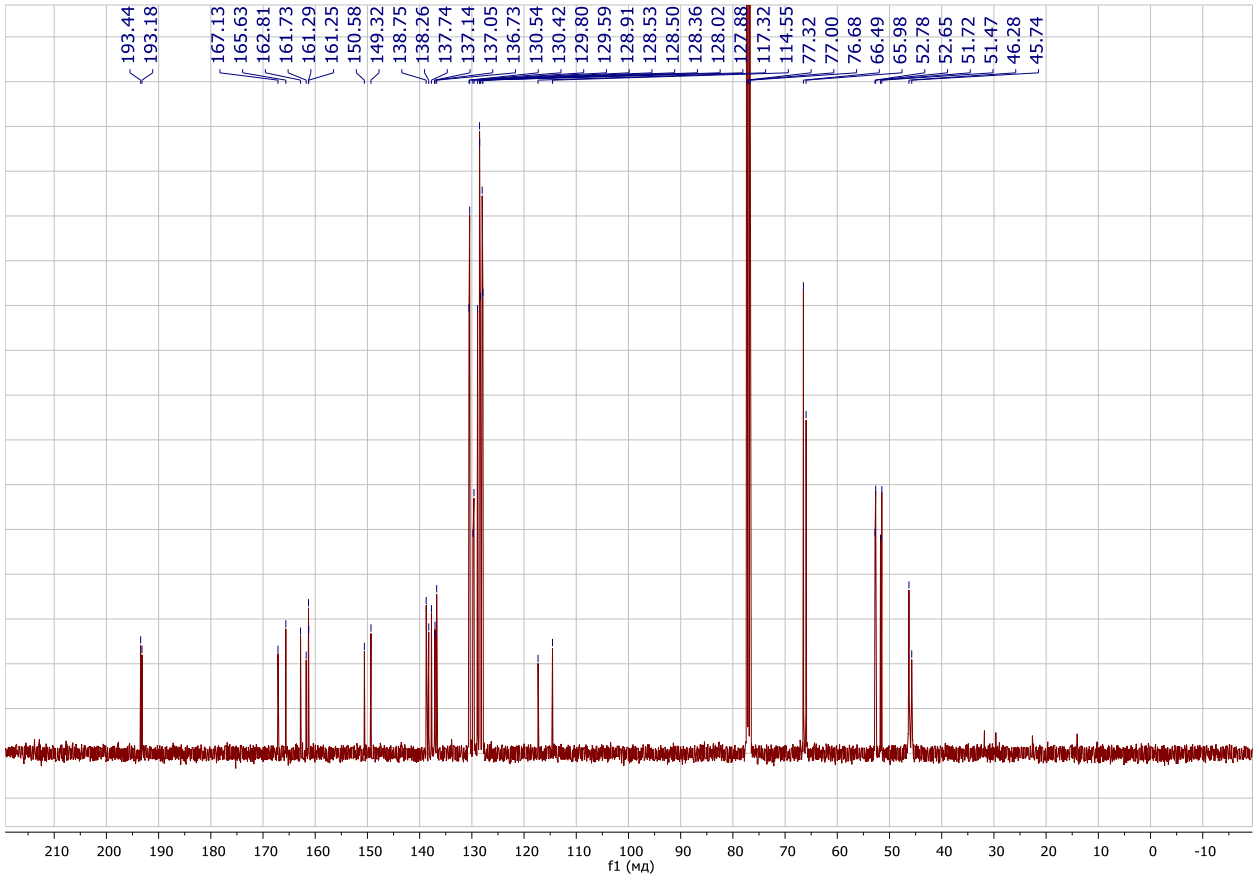
^{1}H and ^{13}C NMR spectra of compound **12a**



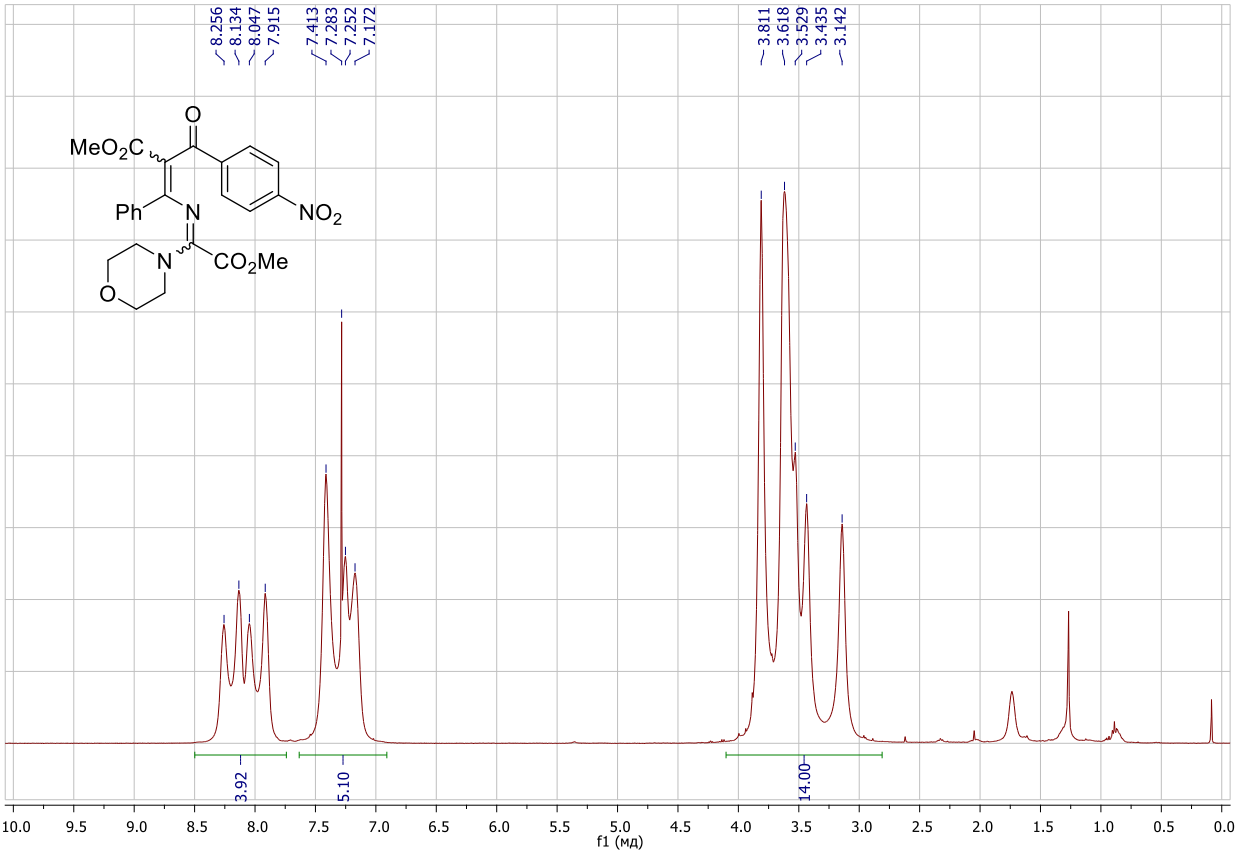


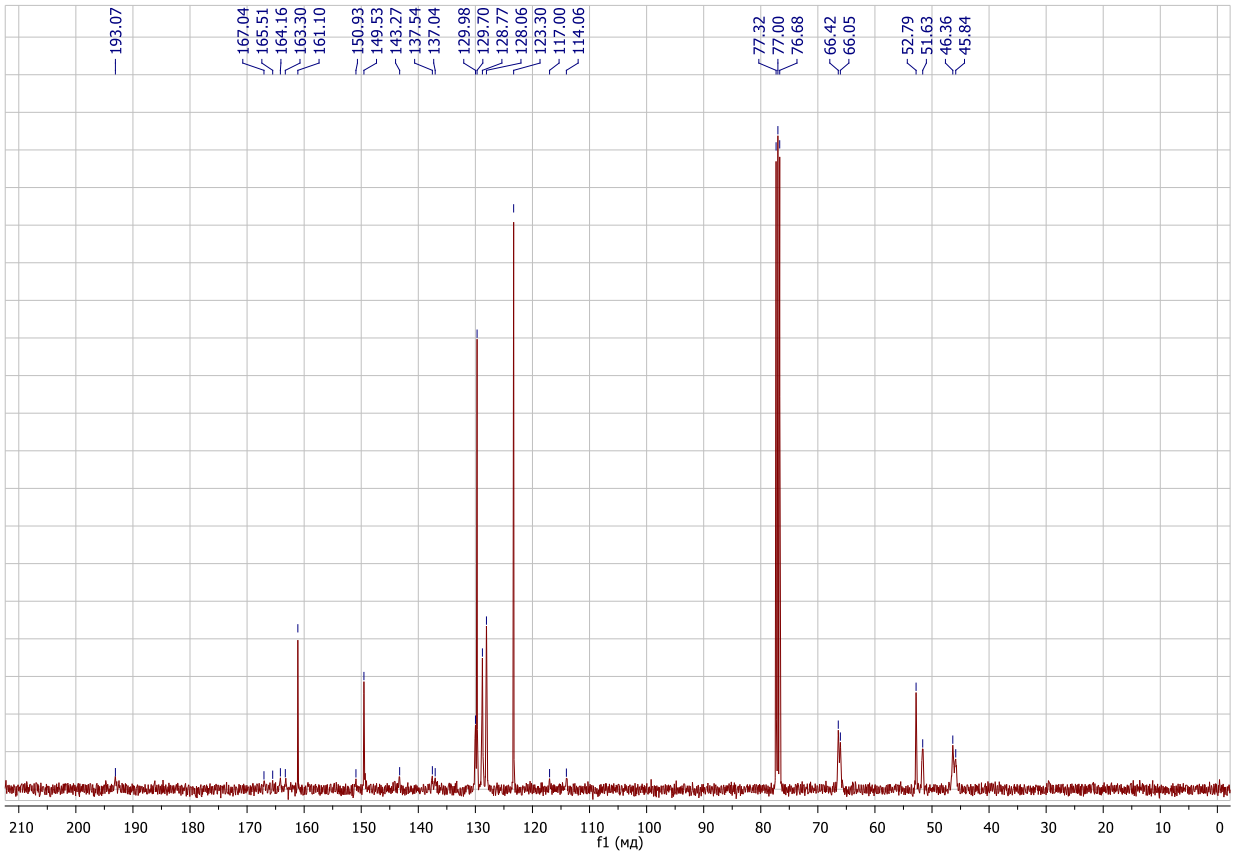
^{1}H and ^{13}C NMR spectra of compound **12b**



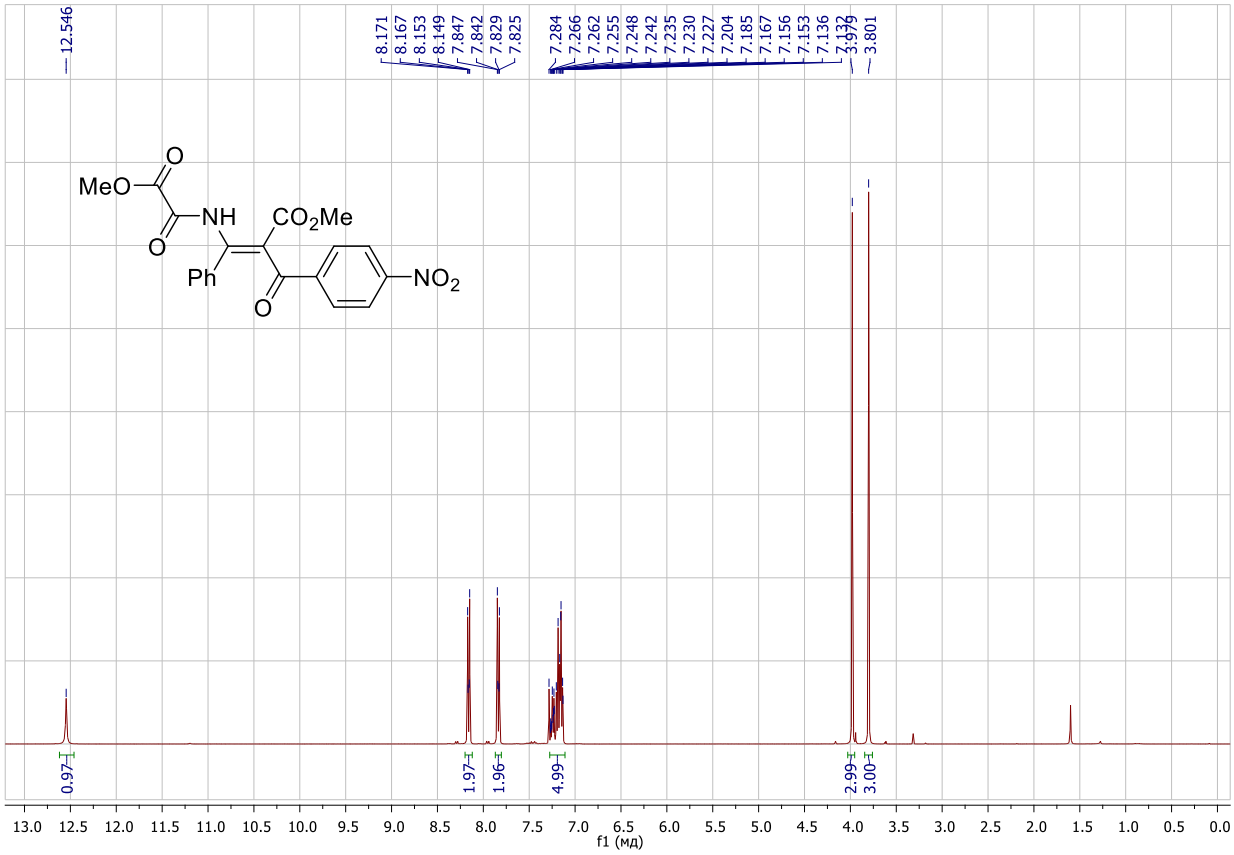


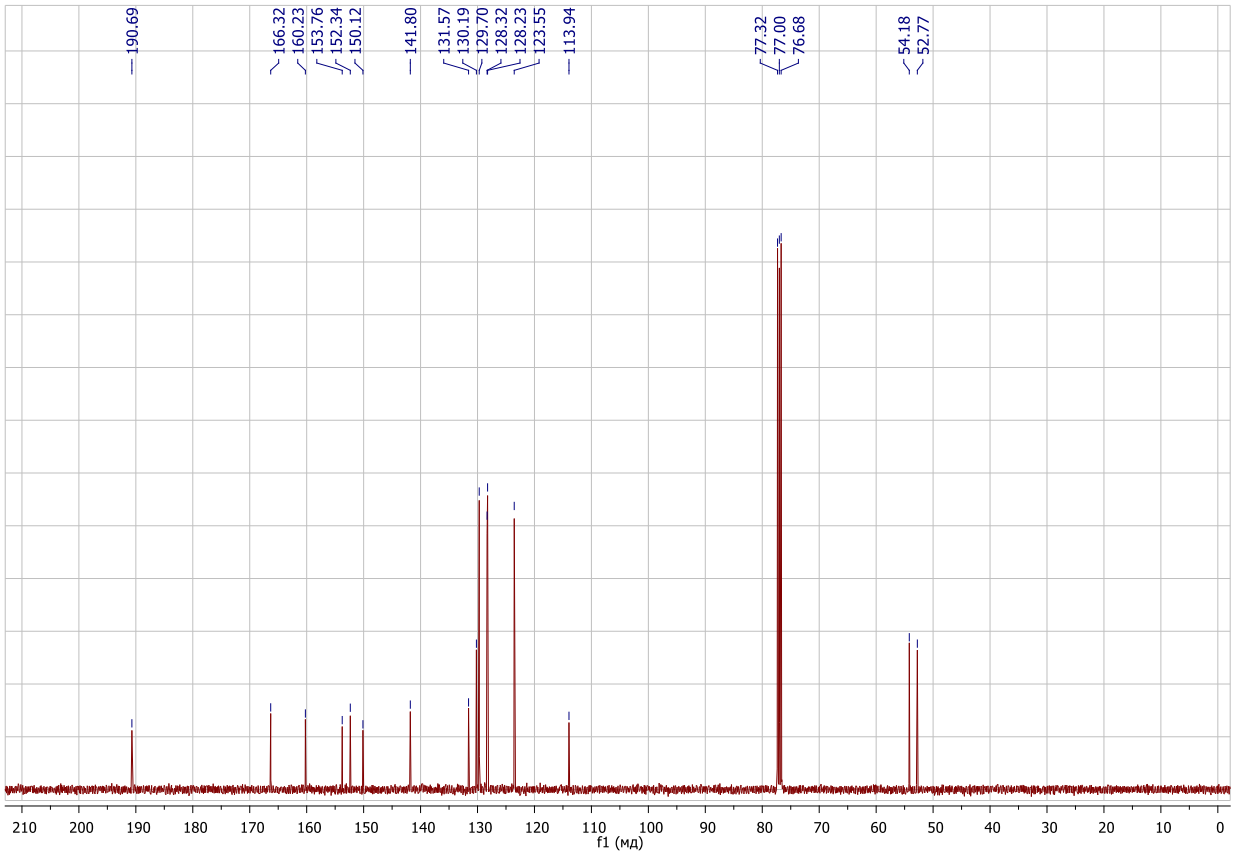
^{1}H and ^{13}C NMR spectra of compound **12c**





^{1}H and ^{13}C NMR spectra of compound **13**





11. X-ray data of compounds 5c,6b,13

Single crystals of compounds **5c**, **6b** and **13** were grown by slow evaporation of their solutions in CH_2Cl_2–hexane mixture at room temperature. For single crystal X-ray diffraction experiment suitable crystals were fixed on a micro mount and placed on a diffractometer and measured at a temperature of 100K using monochromated MoKα radiation. The structures have been solved by the direct methods by means of the SHELX program[12] incorporated in the OLEX2 program package.[13] Empirical absorption correction was applied in CrysAlisPro program complex[14] using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm. The crystallographic data and some parameters of refinement are placed in Tables S1–S3.

Figure S1. X-ray crystal ctructure of compound **5c** with 50% ellipsoid probability (CCDC 1936159)

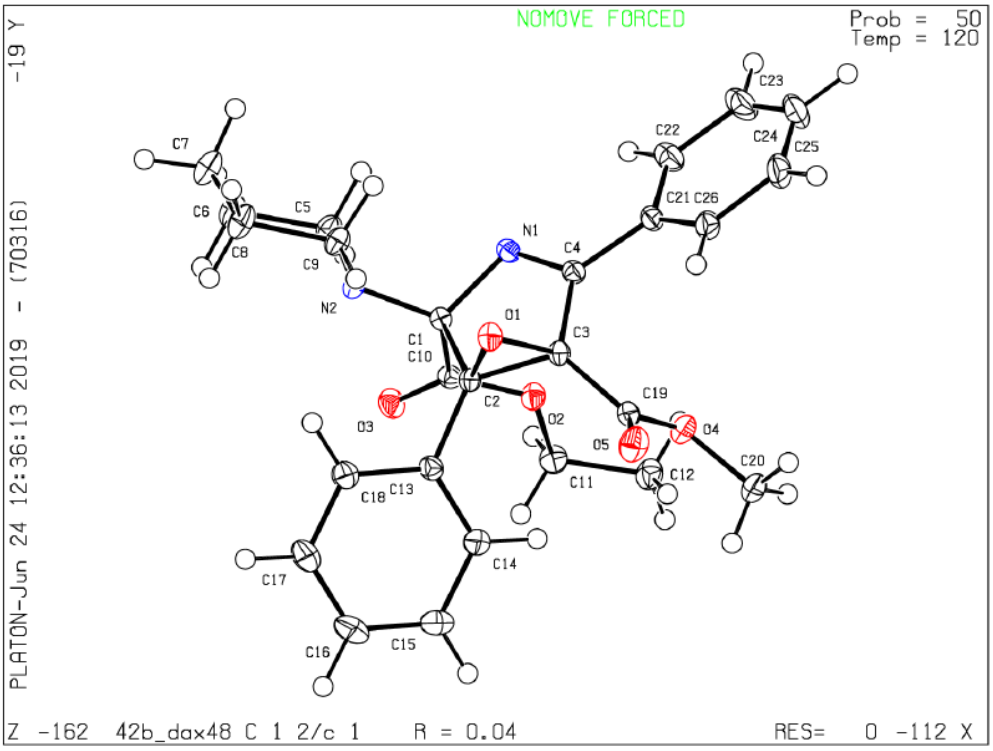


Table S1. Crystal data and structure refinement for compound **5c**

Identification code	dax48
Empirical formula	$C_{26}H_{28}N_2O_5$
Formula weight	448.50
Temperature/K	120
Crystal system	monoclinic
Space group	C2/c
a/Å	32.8032(8)
b/Å	8.35859(13)
c/Å	19.6012(5)

α/°	90.00
β/°	121.849(3)
γ/°	90.00
Volume/Å^3	4565.24(17)
Z	8
ρ_{calc}g/cm^3	1.305
μ/mm^{-1}	0.091
F(000)	1904.0
Crystal size/mm^3	0.59 × 0.39 × 0.23
Radiation	Mo Kα (λ = 0.7107)
2Θ range for data collection/°	5.28 to 61
Index ranges	-46 ≤ h ≤ 46, -11 ≤ k ≤ 11, -27 ≤ l ≤ 27
Reflections collected	60028
Independent reflections	6943 [R_{int} = 0.0497, R_{sigma} = 0.0251]
Data/restraints/parameters	6943/0/410
Goodness-of-fit on F^2	1.043
Final R indexes [I>=2σ (I)]	R_1 = 0.0409, wR_2 = 0.1000
Final R indexes [all data]	R_1 = 0.0520, wR_2 = 0.1080
Largest diff. peak/hole / e Å^{-3}	0.48/-0.21

Figure S2. X-ray crystal ctructure of compound **6b** with 50% ellipsoid probability (CCDC 1936158)

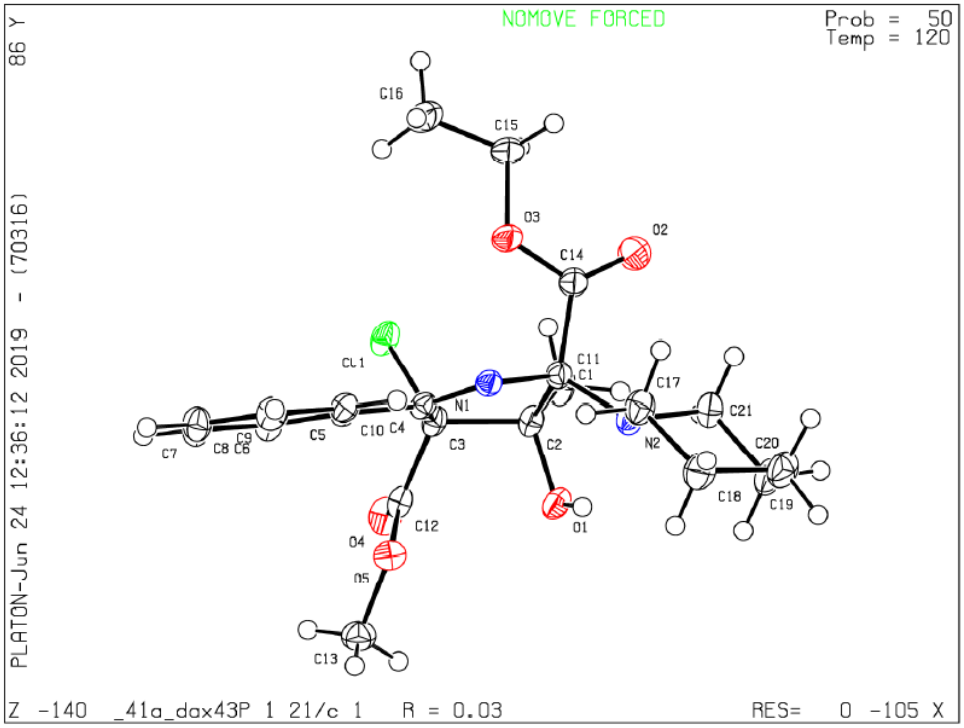


Table S2. Crystal data and structure refinement for compound **6b**

Identification code	dax43
Empirical formula	$C_{21}H_{27}ClN_2O_5$
Formula weight	422.90
Temperature/K	120

Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	8.9966(3)
b/Å	10.4109(3)
c/Å	22.3370(7)
α/°	90.00
β/°	92.301(10)
γ/°	90.00
Volume/$Å^3$	2090.46(11)
Z	4
$\rho_{calc}g/cm^3$	1.344
μ/mm^{-1}	0.218
F(000)	896.0
Crystal size/mm^3	0.44 × 0.4 × 0.08
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	3.64 to 60
Index ranges	$-12 \leq h \leq 12$, $-14 \leq k \leq 14$, $-31 \leq l \leq 31$
Reflections collected	36120
Independent reflections	6112 [R_{int} = 0.0314, R_{sigma} = 0.0210]
Data/restraints/parameters	6112/0/370
Goodness-of-fit on F^2	0.997
Final R indexes [I>=2σ (I)]	R_1 = 0.0340, wR_2 = 0.0878
Final R indexes [all data]	R_1 = 0.0465, wR_2 = 0.0960
Largest diff. peak/hole / e $Å^{-3}$	0.40/-0.21

Figure S3. X-ray crystal ctructure of compound **13** with 50% ellipsoid probability (CCDC 1936916)

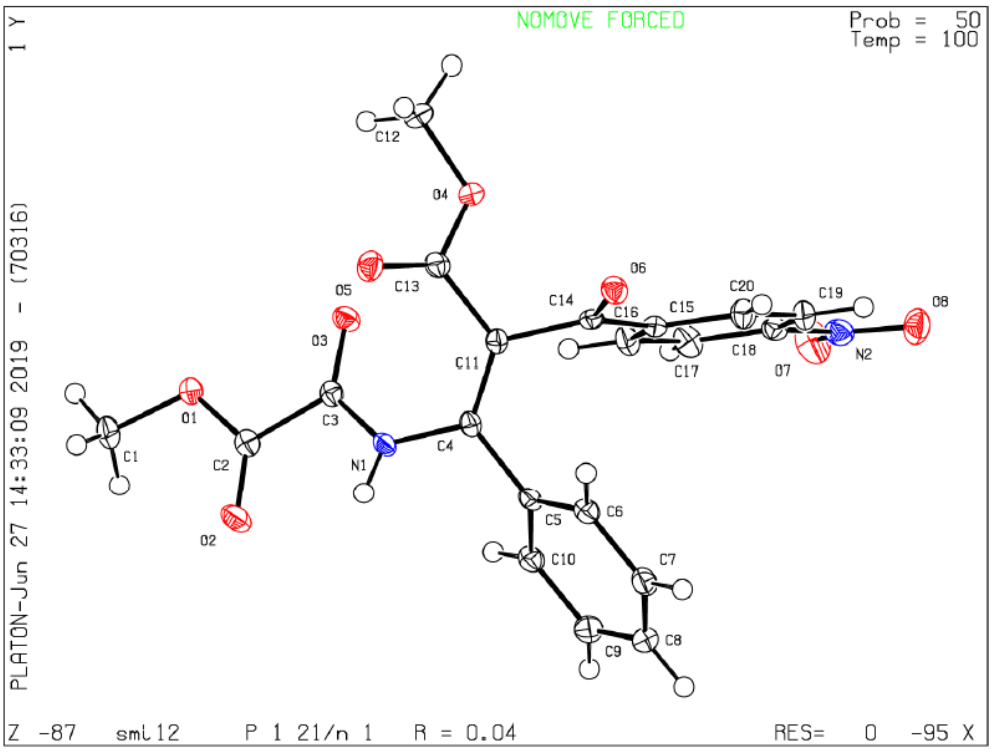


Table S3. Crystal data and structure refinement for compound **13**

Identification code	smi12
Empirical formula	$C_{20}H_{16}N_2O_8$
Formula weight	412.35
Temperature/K	100(2)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	11.9680(4)
b/Å	11.1729(4)
c/Å	13.8802(4)
α/°	90
β/°	92.759(3)
γ/°	90
Volume/Å^3	1853.86(10)
Z	4
ρ_{calc}g/cm^3	1.477
μ/mm^{-1}	0.116
F(000)	856.0
Crystal size/mm^3	0.30 × 0.22 × 0.12
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.818 to 54.988
Index ranges	$-15 \leq h \leq 14$, $-12 \leq k \leq 14$, $-18 \leq l \leq 18$
Reflections collected	12802
Independent reflections	4254 [R_{int} = 0.0379, R_{sigma} = 0.0396]
Data/restraints/parameters	4254/0/273
Goodness-of-fit on F^2	1.041
Final R indexes [I>=2σ (I)]	R_1 = 0.0393, wR_2 = 0.0844
Final R indexes [all data]	R_1 = 0.0550, wR_2 = 0.0952
Largest diff. peak/hole / e Å^{-3}	0.31/-0.25

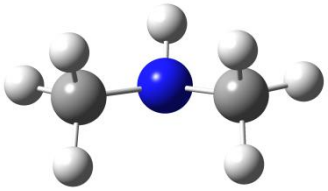
12. Calculation details

All calculations were performed by using the Gaussian 09 suite of quantum chemical programs.[15] Geometry optimizations of dimethylamine, compounds **3zb**,**6e**,**7a**,**8a** and transition states TS1–TS3 were performed at the DFT B3LYP/6-31+G(d,p) level using PCM model for CH_2Cl_2. Stationary points on the respective potential-energy surfaces were characterized at the same level of theory by evaluating the corresponding Hessian indices. Careful verification of the unique imaginary frequencies for transition states was carried out to check whether the frequency indeed pertains to the desired reaction coordinate. Single point calculations of energies for stationary points were carried out at the DFT wB97XD/cc-pVTZ level using PCM solvation model for toluene. Thermal corrections to Gibbs free energies obtained in the optimization calculations were used.

Table S4. Energies (au) and cartesian coordinates of stationary points for dimethylamine, compounds **3zb,6e,7a,8a** and transition states TS1–TS3 calculated at wB97XD/cc-pVTZ level (PCM, CH_2Cl_2).

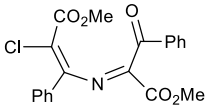
Me_2NH

Zero-point correction = 0.092285
Thermal correction to Energy = 0.096680
Thermal correction to Enthalpy = 0.097624
Thermal correction to Gibbs Free Energy = 0.066822
E_0 = -135.0810186, E = -135.0766236,
H = -135.0756796, G = -135.1064816.
Imaginary frequency = 0.

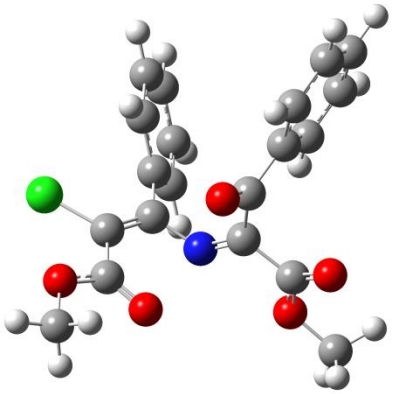


N	-0.00008700	0.56771200	-0.15253900
C	1.21785300	-0.22417600	0.02025700
C	-1.21781600	-0.22418700	0.02026800
H	-0.00000700	1.32945100	0.52109400
H	1.26304000	-0.76106100	0.98495600
H	1.28342100	-0.97097600	-0.77921200
H	2.09500200	0.42564600	-0.05389700
H	-1.26301400	-0.76126600	0.98489900
H	-2.09507200	0.42542600	-0.05401000
H	-1.28298800	-0.97103000	-0.77920500

Oxazatriene **3zb**



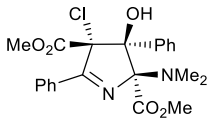
Zero-point correction = 0.320660
Thermal correction to Energy = 0.346556
Thermal correction to Enthalpy = 0.347500
Thermal correction to Gibbs Free Energy = 0.259104
E_0 = -1662.8389561, E = -1662.5182961,
H = -1662.5182961, G = -1662.5798521.
Imaginary frequency = 0.



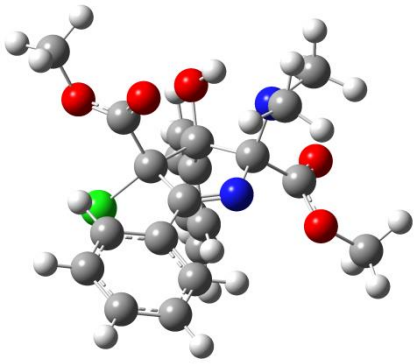
C	-1.62065859	-1.51927360	-1.17317372
C	1.56017641	0.09979440	-0.27976772
C	0.35331941	0.10810340	0.35256728
N	-0.23167159	-1.06381260	0.84497628
C	-1.11942759	-1.75773260	0.25925028

C	2.29730041	-1.14937760	-0.58349772
Cl	2.36558841	1.61671040	-0.66510072
O	-0.85103959	-1.76578560	-2.09262372
C	-2.98955259	-0.98847960	-1.36744072
C	-0.40632159	1.33388640	0.73457328
C	-1.66640259	-2.99926560	0.92773228
C	-0.79662359	2.27338240	-0.23307372
C	-1.54942159	3.38843440	0.13863128
C	-1.91418859	3.57958540	1.47514628
C	-1.53109159	2.64429640	2.44121328
C	-0.78988259	1.51965040	2.07382528
C	-3.50906859	-0.91523260	-2.67289272
C	-4.79304159	-0.42211260	-2.88569672
C	-5.56785259	0.00706940	-1.79964772
C	-5.05617559	-0.05740060	-0.50001672
C	-3.77150059	-0.55574460	-0.28254772
O	-2.32529759	-3.80887560	0.29724528
O	-1.34680159	-3.09911260	2.21315028
C	-1.80864859	-4.29023860	2.89922428
O	1.93179741	-2.25445060	-0.21065772
O	3.41646241	-0.94242760	-1.29650072
C	4.19168541	-2.11908060	-1.61550772
H	-0.52004759	2.12876040	-1.27177972
H	-1.85136159	4.10650440	-0.61768672
H	-2.49520159	4.45119940	1.76120928
H	-1.80975059	2.78710340	3.48087428
H	-0.49448759	0.79310340	2.82370928
H	-2.89745159	-1.25298660	-3.50267472
H	-5.19421059	-0.37209860	-3.89312972
H	-6.56955859	0.39099240	-1.96798572
H	-5.65463359	0.27949040	0.34031928
H	-3.38035259	-0.59173260	0.72997928
H	-1.45700459	-4.18188260	3.92317528
H	-1.37770459	-5.17749860	2.43221728
H	-2.89838459	-4.34154760	2.86488528
H	5.03740441	-1.75413260	-2.19596072
H	4.53417941	-2.60559360	-0.69987872
H	3.59283141	-2.81796160	-2.20284972

Chlorohydrin **6e**

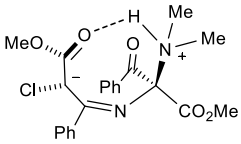


Zero-point correction = 0.418346
Thermal correction to Energy = 0.447078
Thermal correction to Enthalpy = 0.448022
Thermal correction to Gibbs Free Energy = 0.358145
E_0 = -1797.6268591, E = -1797.5981271,
H = -1797.5971831, G = -1797.6870601.
Imaginary frequency = 0.

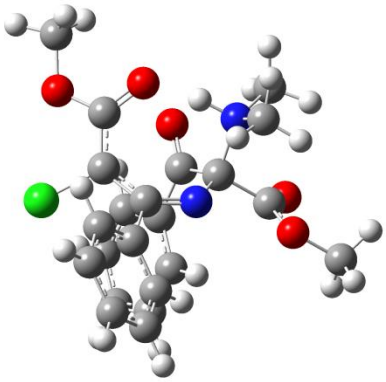


C	1.29559625	1.10545968	0.70210801
C	-0.24033975	1.36734068	0.26198001
C	-0.83390475	-0.04228832	0.24474701
N	-0.08300475	-0.94882432	0.75175801
C	1.18743625	-0.43940932	1.22892101
C	-0.91640475	2.22759068	1.35009701
Cl	-0.44146975	2.16816168	-1.36254999
O	1.61147225	1.93415768	1.78712401
C	2.28597725	1.32634068	-0.43262699
C	-2.17229175	-0.38872332	-0.28780599
C	2.34171025	-1.34957232	0.72174701
N	1.19156325	-0.40506332	2.72512201
C	2.48514425	-0.58720332	3.41419001
C	0.14108225	-1.19194732	3.39557901
C	-2.43664275	-1.72845632	-0.63076699
C	-3.69176475	-2.10587432	-1.10372999
C	-4.70833975	-1.15285632	-1.23572999
C	-4.45751775	0.17936668	-0.89617499
C	-3.19775975	0.56162768	-0.43147199
C	3.25974425	2.32607968	-0.32719099
C	4.17971325	2.53602768	-1.35997199
C	4.13859025	1.74877768	-2.51275599
C	3.16577425	0.74987668	-2.62739799
C	2.24644825	0.54498368	-1.59846999
O	3.51885325	-1.06756632	0.83524901
O	1.90437925	-2.50235032	0.20348901
C	2.92526225	-3.42850432	-0.24307299
O	-1.40653475	1.71715368	2.34088001
O	-0.87832875	3.53162868	1.10871501
C	-1.42864275	4.39250368	2.13758701
H	1.34230125	1.38990668	2.57170501

Betaine **7a**



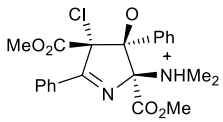
Zero-point correction = 0.417567
Thermal correction to Energy = 0.447190
Thermal correction to Enthalpy = 0.448134
Thermal correction to Gibbs Free Energy = 0.356143
E_0 = -1797.6046046, E = -1797.5749816,
H = -1797.5740376, G = -1797.6660286.
Imaginary frequency = 0.



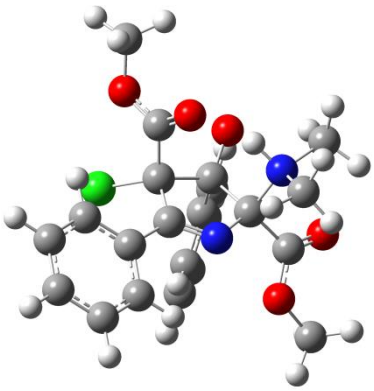
C	-1.48801404	0.91555469	0.52815023
C	1.39914196	1.40083369	0.20792323
C	1.23374496	0.04183169	-0.24906777
N	0.16413096	-0.55433331	-0.73286077
C	-1.15764404	-0.01656631	-0.70603177
C	1.01702696	2.57664569	-0.47884377
Cl	2.43705396	1.61031069	1.65329923
O	-1.88846904	2.05503369	0.33879523
C	-1.34874004	0.35588469	1.90501923
C	2.43170196	-0.86744831	-0.20560577
C	-2.22495404	-1.15518731	-0.70129677
N	-1.41104104	0.79234269	-2.01684277
C	-2.81628804	1.24261769	-2.29110277
C	-0.86612204	0.10212369	-3.23360477
C	2.29627096	-2.21345731	0.16752223
C	3.39748296	-3.07223131	0.14930223
C	4.64757296	-2.60047231	-0.26446977
C	4.79029796	-1.26344331	-0.65201177
C	3.69272396	-0.40182531	-0.61363577
C	-1.63211704	1.21788269	2.98089723
C	-1.54896804	0.76278569	4.29447223
C	-1.18471104	-0.56367431	4.55441223
C	-0.90348604	-1.42926031	3.49339723
C	-0.98379804	-0.97442231	2.17674923
O	-3.35077104	-0.95979331	-0.27866377
O	-1.79820504	-2.30197531	-1.21503777
C	-2.75918104	-3.39059931	-1.24763077
O	0.38836996	2.62475069	-1.57136777
O	1.42046796	3.73872769	0.09787523
C	1.09301896	4.95313669	-0.60128977
H	-0.77941804	1.63974069	-1.86096177

H	2.34354025	-0.28157432	4.45418301	H	-2.75977004	2.00819569	-3.06592877
H	2.83280425	-1.63039632	3.40474201	H	-3.40471904	0.40001269	-2.65393377
H	3.25443625	0.03954068	2.96690001	H	-3.25695204	1.66028769	-1.39318377
H	0.18388825	-0.94830132	4.46012701	H	-0.99453404	0.78401169	-4.07451577
H	-0.84383075	-0.92151632	3.02216901	H	0.18667496	-0.11696631	-3.08449577
H	0.28640325	-2.27561632	3.28013001	H	-1.41791204	-0.82034531	-3.41478077
H	-1.64622775	-2.46310232	-0.52464799	H	1.32339096	-2.58179431	0.47326323
H	-3.87720475	-3.14181132	-1.37103699	H	3.27936596	-4.10808531	0.45412223
H	-5.68715375	-1.44638732	-1.60315599	H	5.50352796	-3.26883131	-0.28608577
H	-5.24090975	0.92461768	-0.99354299	H	5.75566196	-0.89222231	-0.98367877
H	-3.03013375	1.60177868	-0.17891499	H	3.80667896	0.63558269	-0.91266077
H	3.30109825	2.93366568	0.56855101	H	-1.91533104	2.24314869	2.76998323
H	4.92906825	3.31584868	-1.25828299	H	-1.76773804	1.43896069	5.11518723
H	4.85407525	1.91012968	-3.31374999	H	-1.12088704	-0.92018531	5.57814123
H	3.11937525	0.13118168	-3.51879699	H	-0.62015504	-2.45873931	3.68890723
H	1.49378825	-0.22901932	-1.71945299	H	-0.74811804	-1.66100131	1.37215823
H	2.37982625	-4.28709932	-0.63057899	H	-2.22140704	-4.22834231	-1.68663277
H	3.56105325	-3.72025132	0.59480801	H	-3.61671904	-3.11310831	-1.86268877
H	3.53146025	-2.96894532	-1.02588599	H	-3.08649404	-3.62619331	-0.23367377
H	-1.30524875	5.40404068	1.75606501	H	1.49532696	5.75429869	0.01854423
H	-2.48397075	4.16200268	2.29231501	H	1.55807096	4.97086269	-1.58984877
H	-0.87495975	4.25753168	3.06829401	H	0.01116696	5.06153369	-0.70554977

Zwitterion **8a**

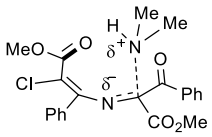


Zero-point correction = 0.419218
Thermal correction to Energy = 0.448002
Thermal correction to Enthalpy = 0.448946
Thermal correction to Gibbs Free Energy = 0.360024
E_0 = -1797.6039113, E = -1797.5751273,
H = -1797.5741833, G = -1797.6631053.
Imaginary frequency = 0.

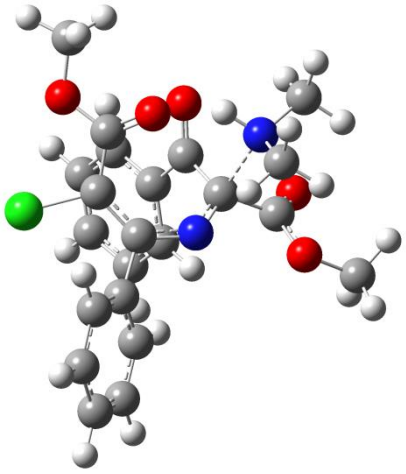


C	1.18993494	0.60307697	0.15225807
C	-0.43388706	0.50059297	-0.25275593
C	-0.87936806	-0.82102103	0.35582507
N	-0.06084506	-1.33608503	1.20669807
C	1.13136794	-0.53571403	1.38664507
C	-1.09371806	1.67781597	0.46807307
Cl	-0.74078306	0.57096397	-2.04022193
O	1.50798994	1.80735397	0.54893707
C	2.07286594	0.04018697	-0.99445193

TS1



Zero-point correction = 0.415736
Thermal correction to Energy = 0.445695
Thermal correction to Enthalpy = 0.446639
Thermal correction to Gibbs Free Energy = 0.352807
E_0 = -1797.5902829, E = -1797.5603239,
H = -1797.5593799, G = -1797.6532119.
Imaginary frequency = 1.

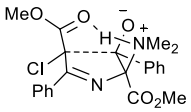


C	-1.70755412	0.97493476	0.63161231
C	1.03698488	1.79750476	-0.62192869
C	0.93798888	0.40774676	-0.69690569
N	-0.16285312	-0.38851624	-0.83466169

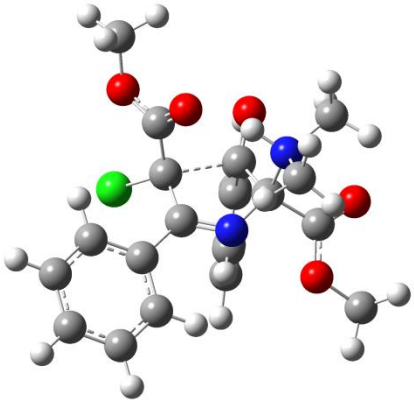
C	-2.15321806	-1.50852603	0.04767207
C	2.39089894	-1.40335203	1.49245907
N	0.95232094	0.23803697	2.71818207
C	2.13116194	1.03474497	3.22189907
C	0.41065994	-0.61803803	3.82827607
C	-2.25637706	-2.89405003	0.27389207
C	-3.45426006	-3.56316203	0.03128807
C	-4.57165506	-2.85747303	-0.43010393
C	-4.48082506	-1.48058403	-0.65318593
C	-3.27808406	-0.81031603	-0.42450493
C	3.09396994	0.86864097	-1.47437693
C	3.94778994	0.44331597	-2.49650793
C	3.79305294	-0.82718803	-3.05806693
C	2.77532994	-1.66383503	-2.58870693
C	1.92292494	-1.23231803	-1.56875293
O	3.49234394	-0.95430703	1.75423907
O	2.15610394	-2.69318203	1.23077007
C	3.31497194	-3.55951403	1.20448807
O	-1.27071306	1.65513897	1.68302307
O	-1.43242906	2.69407397	-0.30230693
C	-1.97477006	3.86360297	0.36312707
H	0.21515894	0.92402797	2.47123907
H	1.73076394	1.75315997	3.93911707
H	2.83347494	0.36451097	3.71073607
H	2.57537794	1.54812597	2.37558807
H	0.26212894	0.02464097	4.69622507
H	-0.52965206	-1.06569603	3.51897307
H	1.13696994	-1.39620103	4.06482607
H	-1.38753106	-3.43366803	0.63440707
H	-3.51750406	-4.63390203	0.20016007
H	-5.50575506	-3.37859103	-0.61770893
H	-5.34413006	-0.92703303	-1.00932893
H	-3.22620506	0.25614197	-0.61212093
H	3.20144494	1.84911697	-1.02407193
H	4.73369494	1.10425397	-2.85240393
H	4.45423394	-1.16201403	-3.85249293
H	2.63818394	-2.65167903	-3.02022893
H	1.13733394	-1.90191203	-1.23497293
H	2.92548694	-4.54865503	0.97004807
H	3.80834894	-3.55929703	2.17819107
H	4.01264994	-3.22472503	0.43446807
H	-2.16809806	4.57671797	-0.43559093
H	-2.89753506	3.60197197	0.88340907
H	-1.24287206	4.25794997	1.06936407

C	-1.41097212	-0.13221424	-0.42750469
C	0.13854488	2.78053976	-1.22225769
Cl	2.48593088	2.49562176	0.14943531
O	-2.36279112	1.96477476	0.33595931
C	-1.15056312	0.80215176	2.00692831
C	2.19577388	-0.41618024	-0.64928069
C	-2.28334812	-1.36011124	-0.18130769
N	-2.51584912	0.48827876	-1.96370269
C	-3.98210712	0.48404076	-1.82451969
C	-2.03955412	-0.17288024	-3.18762469
C	2.29635188	-1.53408924	0.19142031
C	3.44028188	-2.33527824	0.17908631
C	4.48877088	-2.04737224	-0.69988669
C	4.38808088	-0.94921624	-1.56082769
C	3.25485888	-0.13519124	-1.52853269
C	-1.22034812	1.90319076	2.88065431
C	-0.73882112	1.80333076	4.18330431
C	-0.18927212	0.59779076	4.63612831
C	-0.12101012	-0.50378424	3.77837931
C	-0.59536112	-0.40240624	2.47020731
O	-3.22654512	-1.33198524	0.59329431
O	-1.92544112	-2.42795924	-0.89138769
C	-2.71562912	-3.62639024	-0.69422369
O	-0.67609412	2.52555876	-2.11260369
O	0.31928888	4.03674576	-0.77296869
C	-0.48618712	5.06028276	-1.39260269
H	-2.15610212	1.44567476	-1.94888469
H	-4.43474012	1.01854476	-2.66849369
H	-4.35545512	-0.54211624	-1.82314369
H	-4.26230212	0.97647076	-0.89502969
H	-2.36373412	0.39241676	-4.06821569
H	-0.95045912	-0.21544224	-3.16812569
H	-2.44078612	-1.18677624	-3.24059269
H	1.47760988	-1.77396424	0.85951731
H	3.50803588	-3.18805924	0.84838231
H	5.37411388	-2.67631824	-0.71875469
H	5.19116488	-0.72643924	-2.25732069
H	3.18278388	0.71670376	-2.19746569
H	-1.64906912	2.83158076	2.51963131
H	-0.78990112	2.66191476	4.84580431
H	0.18371288	0.51806176	5.65288131
H	0.30004188	-1.44166324	4.12697331
H	-0.53625112	-1.26848824	1.82214131
H	-2.27055012	-4.37077824	-1.35181869
H	-3.75685812	-3.44287024	-0.96561069
H	-2.65604012	-3.94602924	0.34776631
H	-0.17554212	5.99129376	-0.92039569
H	-0.29919212	5.09473076	-2.46806069
H	-1.54619712	4.87253776	-1.20943469

TS2

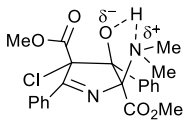


Zero-point correction = 0.418406
Thermal correction to Energy = 0.446918
Thermal correction to Enthalpy = 0.447862
Thermal correction to Gibbs Free Energy = 0.359460
E_0 = -1797.5967545, E = -1797.5682425,
H = -1797.5672985, G = -1797.6557005.
Imaginary frequency = 1.

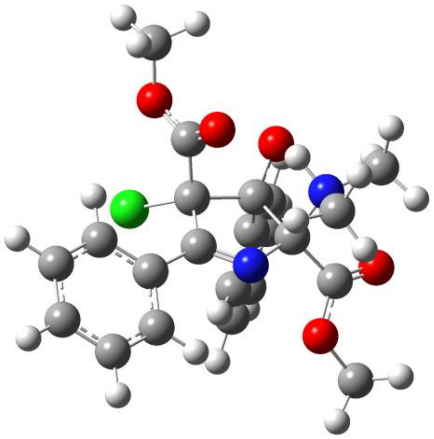


C	1.18342686	-0.72645067	0.00002480
C	-0.83102814	-0.78065267	0.41928880
C	-1.15824314	0.55551633	-0.15857920
N	-0.29981614	1.12886633	-0.93781220
C	0.93014386	0.40729033	-1.13673220
C	-1.23261014	-1.95155367	-0.36782620
Cl	-1.19039314	-0.90768667	2.17528380
O	1.57647586	-1.85486667	-0.40281120
C	1.77738986	-0.18495667	1.29783080
C	-2.42500414	1.27648233	0.13242480
C	2.14129686	1.36497833	-1.22952720
N	0.80164086	-0.32311767	-2.50731020
C	2.02913486	-0.98902067	-3.07647220
C	0.18009286	0.54167733	-3.56782320
C	-2.46158914	2.68112633	0.07021480
C	-3.65322314	3.36857833	0.29684980
C	-4.82851314	2.66212633	0.57741480
C	-4.80315614	1.26532733	0.63627880
C	-3.60800314	0.57655233	0.42382080
C	2.64293286	-1.03585667	2.00124280
C	3.24903186	-0.62240067	3.18914980
C	3.00151386	0.65723233	3.69561280
C	2.13912286	1.51344433	3.00475980
C	1.52908286	1.09519133	1.81942080
O	3.27566886	0.96613333	-1.41794220
O	1.81894786	2.64664933	-1.05015420
C	2.92208786	3.58601133	-1.03857920
O	-1.23386014	-1.95482867	-1.60850020
O	-1.50620614	-3.04978167	0.33933380

TS3



Zero-point correction = 0.419212
Thermal correction to Energy = 0.447174
Thermal correction to Enthalpy = 0.448118
Thermal correction to Gibbs Free Energy = 0.361469
E_0 = -1797.6037276, E = -1797.5757656,
H = -1797.5748216, G = -1797.6614706.
Imaginary frequency = 1.



C	1.20201565	0.82726179	0.39590971
C	-0.40399735	0.82115779	-0.07558629
C	-0.90636735	-0.55795621	0.32635671
N	-0.12669235	-1.22169821	1.10648371
C	1.10175565	-0.51863621	1.39784871
C	-1.06693035	1.89477879	0.79263871
Cl	-0.66417235	1.14989079	-1.84271529
O	1.49590065	1.92137479	1.05858871
C	2.12992765	0.51330979	-0.79990029
C	-2.20162835	-1.14079221	-0.09070729
C	2.31223065	-1.45960521	1.32790871
N	0.98359965	0.06478179	2.82865871
C	2.25140365	0.55212379	3.48454771
C	0.22344265	-0.81199421	3.78058971
C	-2.35934935	-2.53942021	-0.07454029
C	-3.57757735	-3.11831221	-0.42478329
C	-4.66122335	-2.30936521	-0.78589129
C	-4.51615935	-0.91919921	-0.80065629
C	-3.29294935	-0.33748521	-0.46390729
C	3.14790965	1.43055079	-1.08302129
C	4.03949665	1.21348179	-2.13800729
C	3.92578065	0.06712479	-2.92941229
C	2.90996265	-0.85545221	-2.65774629
C	2.01900265	-0.63133821	-1.60502429
O	3.44491965	-1.12697421	1.62540671
O	1.99439165	-2.67160621	0.85964071
C	3.09802465	-3.58682521	0.66294371
O	-1.31878235	1.67692879	1.97156671
O	-1.31532735	3.03928579	0.17885771

C	-1.78338114	-4.25447667	-0.41123320	C	-1.85302335	4.10960379	0.99556871
H	0.11003186	-1.07219767	-2.28319920	H	0.43417465	0.92362879	2.65170471
H	1.67234486	-1.70166167	-3.82181420	H	1.93831965	1.19147879	4.31141571
H	2.65744086	-0.23675367	-3.54840120	H	2.81695765	-0.29779821	3.85796571
H	2.55411886	-1.50399467	-2.28089620	H	2.81524265	1.12527979	2.75702371
H	0.07480486	-0.06852467	-4.46493720	H	0.16455365	-0.28679121	4.73393771
H	-0.78999814	0.89540933	-3.23152720	H	-0.77202235	-0.99984921	3.38964871
H	0.83692886	1.38788133	-3.77222020	H	0.76084265	-1.75227621	3.90621071
H	-1.54755814	3.22113833	-0.15141820	H	-1.51645335	-3.16011821	0.20894171
H	-3.66639614	4.45371433	0.25668680	H	-3.68265535	-4.19902721	-0.41783029
H	-5.75716814	3.19740433	0.75230580	H	-5.61117335	-2.76025121	-1.05722829
H	-5.71224014	0.71162833	0.85044680	H	-5.35316035	-0.28575921	-1.07769629
H	-3.59991614	-0.50681667	0.47627680	H	-3.20000735	0.74227579	-0.48876229
H	2.83449086	-2.02258267	1.59447780	H	3.22319865	2.31204079	-0.45594329
H	3.91727486	-1.29764267	3.71636780	H	4.82284265	1.93920579	-2.33989729
H	3.47370986	0.98344333	4.61787580	H	4.61702865	-0.10598821	-3.74948829
H	1.93355586	2.50812533	3.39016580	H	2.80479565	-1.74726821	-3.26961429
H	0.85457886	1.77831933	1.31610980	H	1.23203465	-1.35739021	-1.42736329
H	2.46523786	4.55786533	-0.86146120	H	2.64674565	-4.49668421	0.27108271
H	3.43890786	3.57027233	-1.99984020	H	3.59928865	-3.78217321	1.61277371
H	3.61928986	3.33190433	-0.23808420	H	3.80852465	-3.16681821	-0.05167729
H	-1.95539014	-5.02215167	0.34141180	H	-1.97755935	4.94884579	0.31415471
H	-2.67182314	-4.11780967	-1.03085920	H	-2.81165035	3.80948579	1.42199871
H	-0.92878114	-4.51322267	-1.03835420	H	-1.14853435	4.35602779	1.79140771

13. References

1. N. V. Rostovskii, A. V. Agafonova, I. A. Smetanin, M. S. Novikov, A. F. Khlebnikov and G. L. Starova, Metal-catalyzed isomerization of 5-heteroatom-substituted isoxazoles as a new route to 2-halo-2*H*-azirines, *Synthesis*, 2017, **49**, 4478–4488.

2. A. V. Agafonova, I. A. Smetanin, N. V. Rostovskii, A. F. Khlebnikov and M. S. Novikov, Synthesis of 2-halo-2*H*-azirine-2-carboxylic acid amides and esters by isomerization of 5-(dialkylamino/alkoxy)-substituted isoxazoles, catalyzed by iron(II) sulfate, *Chem. Hetetocycl. Com.*, 2017, **53**, 1068–1071.

3. I. A. Smetanin, M. S. Novikov, A. V. Agafonova, N. V. Rostovskii, A. F. Khlebnikov, I. V. Kudryavtsev, M. A. Terpilowski, M. K. Serebriakova, A. S. Trulioff and N. V. Goncharov, A novel strategy for the synthesis of thermally stable and apoptosis-inducing 2,3-dihydroazetes, *Org. Biomol. Chem.*, 2016, **14**, 4479–4487.

4. I. A. Smetanin, M. S. Novikov, N. V. Rostovskii, A. F. Khlebnikov, G. L. Starova and D. S. Yufit, 4-Halo-2-azabuta-1,3-dienes as intermediates in the rhodium carbenoid-initiated transformation of 2-halo-2*H*-azirines into 2,3-dihydroazetes and 2,5-dihydrooxazoles, *Tetrahedron*, 2015, **71**, 4616–4628.

5. A. V. Agafonova, I. A. Smetanin, N. V. Rostovskii, A. F. Khlebnikov and M. S. Novikov, Easy access to 2-fluoro- and 2-iodo-2*H*-azirines via the Halex reaction, *Synthesis*, 2019, **51**, 4582–4589.

6. K. E. Coffey, G. K. Murphy, Dichlorination of α-diazo-β-dicarbonyls using (dichloroiodo)benzene, *Synlett*, 2015, **26**, 1003–1007.

7. Z. Long, Z. Wang, D. Zhou, D. Wan and J. You, Rh(III)-catalyzed regio- and chemoselective [4 + 1]-annulation of azoxy compounds with diazoesters for the synthesis of 2*H*-indazoles: roles of the azoxy oxygen atom, *Org. Lett.*, 2017, **19**, 2777–2780.

8. N. V. Rostovskii, M. S. Novikov, A. F. Khlebnikov, V. A. Khlebnikov, S. M. Korneev, Rh(II)-carbenoid mediated 2*H*-azirine ring-expansion as a convenient route to non-fused photo- and thermochromic 2*H*-1,4-oxazines, *Tetrahedron*, 2013, **69**, 4292–4301.

9. J. Wang, M. Wang, K. Chen, S. Zha, C. Song and J. Zhu, C–H activation-based traceless synthesis via electrophilic removal of a directing group. Rhodium(III)-catalyzed entry into indoles from *N*-nitroso and α-diazo-β-keto compounds, *Org. Lett.*, 2016, **18**, 1178–1181.

10. Y. Jiang, V. Z. Y. Khong, E. Lourdusamya and C. Park, Synthesis of 2-aminofurans and 2-unsubstituted furans*via*carbenoid-mediated [3 + 2] cycloaddition, *Chem. Commun.*, 2012, **48**, 3133–3135.

11. Z. Chen, L. Zheng, J. Liu, Divergent Synthesis of Multisubstituted Unsymmetric Pyrroles and Pyrrolin-4-ones from Enamino Esters via Copper-Catalyzed Aerobic Dimerization, *Eur. J. Org. Chem.*, 2019, **2019**, 3051–3060.

12. G. M. Sheldrick, A short history of *SHELX*, *Acta Crystallogr*., 2008, **A64**, 112–122.

13. O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard, H. Puschmann, *OLEX2*: a complete structure solution, refinement and analysis program, *J. Appl. Crystallogr*., 2009, **42**, 339–341.

14. CrysAlisPro, Agilent Technologies, Version 1.171.36.32.

15. Gaussian 09, Revision D.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2013.